Prevalence of HIV-1 infection among foreign applicant to residency in Shanghai, China, 2005-2016

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ABSTRACT
Shanghai is one of the largest cities in China and has the highest proportion of inbound travelers in the world. The HIV (human immunodeficiency virus) infection status of this population can reflect the global HIV epidemic trend to a certain extent. Therefore, we conducted a retrospective epidemic survey to clarify the prevalence and characteristics of HIV-1 infection among inbound travelers applying for Shanghai residency. The retrospective cohort analysis included a total of 50,830 inbound tourists/travelers who applied for Shanghai residency from 2005 to 2016. HIV-1 infection rates were determined based on HIV-1 antibody testing. Among all the recruited inbound travelers, 245 were HIV-1 positive, with an infection rate of 0.48%. The detection rate of HIV in males was significantly higher than in females ($\chi^2 = 62.584, P < 0.0001$). Those aged 18–30 years, 31–40 years, and >40 years accounted for 34.3%, 39.6%, and 26.1% of the infected population, respectively. Although the annual detection rates were different, the trend analysis results showed no increase in HIV-1 prevalence rates among the sampling years ($Z = 2.543, P = 0.111$). Proportions of individuals infected through homosexual transmission increased over the study period ($Z = 5.41, P < 0.001$), while the proportion infected through heterosexual declined over time ($Z = 3.38, P = 0.001$). The rate and characteristics of HIV-1 infection among foreign applicants for residency in Shanghai were identified in the study. The results provide the necessary epidemiological data for monitoring the HIV-1 epidemic among international entry travelers and contribute to establishing relevant policies and regulations for HIV control and prevention.

Background
Since the peak of the AIDS epidemic in 1993, it has become the leading cause of death for men and women aged 25 to 44 and the eighth most common cause of mortality worldwide (Hariri & McKenna, 2007). Although human immunodeficiency virus (HIV)-1 infection and mortality rates have been declining due to highly active antiretroviral therapy and effective preventive measures globally, there are still an estimated

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35.3 million people living with HIV worldwide, and every year about 2.3 million people are newly infected with HIV (Malik et al; B Wang et al., 2015). The International Health Regulations (2005) were implemented on 15 June 2007, and the new regulations fully reflect the respect for the sovereignty of the State party and the human rights of travelers, emphasizing that travelers are subject to involuntary medical examinations, and there is no certain medical examination to allow travelers to enter. On 24 April 2010, the executive meeting of the State Council of China passed the ‘Decision of the State Council on Amending the Implementation Rules of the Frontier Health Quarantine and Inspection Law of the People’s Republic of China’, which stipulates that overseas AIDS patients are no longer restricted. These regulations are consistent with most developed countries.

Shanghai is a major destination for international business and trade and, as such, has many cross-border travelers. Inbound travelers and their activities often lead to the spreading infectious diseases in China and around the world, so they are considered a bridge population for spreading infectious diseases (Rui-sheng et al., 2017). Although HIV-1 infection in cross-border travelers has been reported in other major cities (Li et al; B Wang et al., 2015), the HIV-1 prevalence and related epidemiological characteristics of this bridge population in Shanghai remain unclear. Therefore, to clarify the HIV epidemic characteristics of inbound travelers, a large-scale retrospective study of HIV-1 screening was conducted on cross-border travelers entering Shanghai port from 2005 to 2016.

### Methods study population and data collection

Foreigners who applied to stay in China for one year or more completed a physical examination at the Shanghai International Travel Health Center. The routine physical examination included blood routine, serum chemistry tests, and detection of major infectious diseases. All applicants who had completed a health check at the Shanghai International Travel Health Center underwent HIV testing, and patients who already had a health checkup report had the option to recheck or not. Applicants who voluntarily declared HIV-positive were re-examined to confirm the diagnosis before entry. The preliminary screening was performed using enzyme-linked immunoassay (ELISA) or enzyme immunoassay (EIA). The samples screened for reactivity were repeated in duplicate with the same assay. If two of the three test results were positive, the sample was transferred to an FDA-approved supplemental/confirmation assay, HIV-1 Western Blot (Genetic Systems HIV-1 Western Blot, Bio-Rad Laboratories, Redmond, Washington, US)) and/or an immunofluorescence antibody (IFA) test (Fluorognost HIV-1 IFA, Waldheim Pharmazeutika, GmbH, Vienna, Austria) would be performed. The diagnosis of HIV was based on HIV assays approved by the China Food and Drug Administration (FDA). Testing methods and quality control strictly referred to the ‘National AIDS Testing Technical Specifications’ and ‘National AIDS Testing Work Management Measures’(Haghdooest et al). The face-to-face interviews were conducted to collect information on the socio-demographic characteristics of those with a confirmed diagnosis of HIV. The nationalities of all HIV patients were classified as developed, developing, and less developed countries (Country Income Groups (World Bank Classification), 2011).
Data analysis

The statistical analysis was performed using the SPSS 12.0 software. A comparison of characteristics between groups was performed using the \( \chi^2 \) test. Cochran-Mantel-Haenszel was used to compare differences in the total population while controlling for the time factor. Time trends were calculated using the Cochran-Armitage trend test. A P-value of <0.05 was considered statistically significant.

Results

Characteristics of HIV-1 positive travelers

From 2005–2016, 50 830 travelers entered China through the Shanghai port and completed HIV-1 infection screening tests. The annual recruited population (range 2640–5764) did not differ significantly among sampling years. Based on ELISA and WB results, there were 245 people infected with HIV-1, and the infection rate was 0.48%. Among them, there were 215 males (87.8%) and 30 females (12.2%), with a male-to-female ratio of 7.17:1. The HIV detection rate in males was significantly higher than in females (\( \chi^2 = 62.584, P < 0.0001 \)). The age range of this population was 18–69 years old (median, 34.2 years). Most patients were aged 31–40 (39.6%). Most positive cases were employed (53.88%) and had a second or higher degree (81.22%). In addition, 54.70% of the positive cases were unmarried, of which 40.82% were from low-income countries (Table 1).

Infection rates over the years

Despite differences in annual detection rates, the trend analysis showed no increase in HIV-1 prevalence in the sampling years (Cochran-Armitage \( Z = 2.543, P = 0.111; \) Table 2). The gender-based trend analysis showed that HIV-1 positivity rates were high for both men (\( Z = 1.944, P = 0.163 \)) and women (\( Z = 0.198, P = 0.656 \)) (Figure 1).

The change of transmission route

During the study period, the proportion of individuals infected through homosexual transmission increased (Cochran-Armitage \( Z = 5.41, P < 0.001 \)), while the proportion of infected through heterosexual transmission declined over time (Cochran-Armitage \( Z = 3.38, P = 0.001 \)). The proportion of injecting drug use infections declined over time (\( Z = 3.52, P < 0.001 \)). With the change in major HIV-1 risk factors, the heterosexual spreading of HIV-1 was gradually elevated to be the main transmission route.

Discussion

The epidemiology of infectious diseases has changed dramatically, requiring health care workers to understand the status of these diseases, especially for HIV and other epidemic diseases (DA, 2009; Gk et al; Haghdoost et al). Efforts and investments are being made globally to strengthen national HIV monitoring and evaluation (M&E) capacity (Alfven et al., 2014). Global priorities to end the HIV epidemic, such as achieving UNAIDS 90–90-90 targets, now focus on treatment as prevention and rapidly closing gaps in HIV
### Table 1. Demographic characteristics of positive cases.

|                        | Subjects | Proportion(%) |
|------------------------|----------|---------------|
| Total                  | 245      |               |
| Gender                 |          |               |
| male                   | 215      | 87.76%        |
| female                 | 30       | 12.24%        |
| Age                    |          |               |
| 18-30                  | 84       | 34.3%         |
| 31-40                  | 97       | 39.6%         |
| >40                    | 64       | 26.1%         |
| Current employment status |        |               |
| Employed               | 132      | 53.88%        |
| Unemployed             | 38       | 15.51%        |
| Student                | 54       | 22.04%        |
| Housewife/ husband     | 21       | 8.57%         |
| Education              |          |               |
| Less than secondary    | 46       | 18.78%        |
| Secondary or higher    | 199      | 81.22%        |
| Marital status         |          |               |
| Never married          | 134      | 54.70%        |
| Married or cohabitating | 45      | 18.37%        |
| Previously married     | 66       | 26.94%        |
| Host country           |          |               |
| high-income countries  | 56       | 22.86%        |
| middle-income countries| 89       | 36.33%        |
| low-income countries   | 100      | 40.82%        |
| Risk behaviors of transmission |    |               |
| Heterosexual           | 61       | 24.90%        |
| Homosexual             | 142      | 57.96%        |
| Blood/Plasma           | 8        | 3.27%         |
| Injecting drugs        | 2        | 0.82%         |
| Unknown/others         | 24       | 9.80%         |
| Condom use             |          |               |
| never                  | 45       | 18.37%        |
| sometimes              | 92       | 37.55%        |
| Almost always          | 90       | 36.73%        |
| always                 | 10       | 4.08%         |

### Table 2. HIV antibody positive rates among entry travelers 2005–2016 (/10,000).

| Year  | Male       | Female    | Total    |
|-------|------------|-----------|----------|
| 2005  | 65(10/1532)| 18(2/1108)| 45(12/2640)|
| 2006  | 54(10/1854)| 8(1/1202) | 36(11/3056)|
| 2007  | 59(13/2198)| 15(2/1374)| 15(15/3572)|
| 2008  | 58(15/2588)| 39(6/1532)| 51(21/4120)|
| 2009  | 45(12/2665)| 14(2/1445)| 34(14/4120)|
| 2010  | 80(15/1878)| 12(2/1676)| 48(17/3554)|
| 2011  | 84(19/2254)| 9(2/2136) | 48(21/4390)|
| 2012  | 85(20/2353)| 10(2/2023)| 50(22/4376)|
| 2013  | 65(17/2604)| 20(4/1969)| 46(21/4573)|
| 2014  | 99(29/2934)| 5(1/2062) | 60(30/4996)|
| 2015  | 59(27/4541)| 18(2/1128)| 51(29/5669)|
| 2016  | 77(28/3633)| 19(4/2131)| 56(32/5764)|
| Total | 69(215/31 034)| 15(30/19 796)| 48(245/50 830)|

* Detection rate = positive number/number of samples
prevention and care continuums (Wirtz et al., 2017). Due to the wide use of highly active retroviral therapy and effective prevention measures, the AIDS epidemic has been effectively curbed, and the number of new HIV-1 infections had been declined (Y Wang et al., 2015). According to official statistics, as of 2011, the number of people living with HIV-1 in China was 780,000 (REF, 2012). Cross-border travelers with HIV-1 infection may contribute to local HIV-1 transmission and are defined as a bridge population (Xiao et al). Shanghai has the largest cross-border population entering China from all countries worldwide. This is the first study showing the prevalence and characteristics of HIV-1 infection in inbound travelers over such a long period in such a large population in Shanghai, China.

The HIV prevalence among active-duty inbound travelers in Shanghai peaked in 2014 and declined to a stable but lower rate than observed in the USA and other under-developed countries (Castel et al; Haghgoo et al., 2015; Paudel et al., 2016). Overall, we found that the HIV-1 infection rate among inbound travelers in Shanghai has not shown an upward trend in recent years.

In the last decade, we have seen a dramatic change in the demographic structure of the population of people living with HIV (PLWH; Sabin & Reiss). This study found that HIV-1 infection of entry travelers in Shanghai also had certain demographic characteristics. The major age population of HIV-1 infected travelers was 18–40 years. Our findings are consistent with those of Wang et al., who found that travelers aged 21–30 and 31–40 were the most commonly infected individuals among entry travelers in Yunnan Province (B Wang et al., 2015).

Demographic characteristics were also reflected in marital status, working conditions, and education level. The detection rate was higher for employed travelers than those without employment in the last two years. In addition, HIV-1 infection was more frequently detected among individuals with certain occupations, such as businessmen and entertainers. Furthermore, unmarried applicants had a higher proportion of infection than the married group. People with better education and cognitive
ability generally have healthier behaviors and better health outcomes (Jia et al). Nevertheless, our study found that most of the infected people were highly educated, related to the characteristics of the applicants and that most of the international travelers have higher education levels. Our data further show that most positive cases were from middle-income and low-income countries, which is consistent with expectations. Furthermore, our data imply that sexual contact was the major high-risk behavior identified, especially in homosexual men. A study in the US reports that the most common HIV transmission route is now homosexual contact in men (Hariri & McKenna, 2007), which is consistent with our results. This study found that those not using condoms accounted for many positive cases. Inconsistent condom use and several risk-taking behaviors were also reported among young people in the United States and Uganda (Kogan et al., 2010). Insufficient AIDS-related knowledge and low self-risk awareness may be associated with an increasing number of AIDS patients.

**Strengths and limitations**

There are some limitations to this study. This was a records-based study, and some applicants had incomplete records. Face-to-face interviews were conducted only in HIV populations. Additionally, the sample may not represent the total population of inbound travelers in China. Despite limitations and incomplete information, this study is one of the few population-based studies in China. We believe this study can contribute to our understanding of the dynamics of HIV transmission among international travelers.

**Conclusion**

This study proposes the target areas of HIV/AIDS prevention and control for international travelers. Identifying high-risk groups and carrying out targeted prevention is crucial.

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