HIV prevalence and incidence estimates among blood donors in five regions in China

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BACKGROUND: Previous data, although scant, indicated that the incidence of HIV in China has increased over the past decade. There is a growing concern about the impact of the HIV epidemic on blood safety.

METHODS AND MATERIALS: We used donation data from five geographically-disperse blood centers in 2013-2016 participating in the Recipient Epidemiology and Donor Evaluation Study-III (REDS–III) China program to estimate HIV prevalence and incidence among blood donors. Multivariable logistic regression model was used to examine factors associated with HIV infection in Chinese blood donors.

RESULTS: The overall HIV prevalence among first-time donors from 2013 through 2016 was 68.04 per 100,000 donors (95% CI 61.68–74.40). The HIV incidence rate was estimated to be 37.93 per 100,000 person-years (95% CI 30.62–46.97) among first-time donors and 20.55 per 100,000 person-years (95% CI 16.95–24.91) among repeat donors. There was substantial variation in HIV prevalence and incidence rates across blood centers. Multivariable logistic regression results showed that among first-time donors, being male, older than 25 years, minority ethnicity, less than college education, and certain occupations (commercial services, factory workers, retired, unemployed, or self-employed) were associated with positive HIV confirmatory testing results.

CONCLUSION: HIV prevalence and incidence among blood donors remain low in the selected five regions in China; however, an increasing trend is observed at some blood centers. It is important to monitor HIV epidemiology in Chinese blood donors on a continuous basis, especially among populations and regions of higher risk.

Despite a relatively low national prevalence of Human Immunodeficiency Virus (HIV) in China (0.06%), the world's most populous country has a large number of HIV infections with 850,000 people living with HIV out of a 1.4 billion population.[1] A recent report by the Chinese Centre for Disease Control and Prevention showed more than 96,000 new HIV infections in the first 9 months of 2016.[2] In addition, there is an increasing concern about the impact of the HIV epidemic on young people. The number of reported HIV infections among people aged 15 to 24 years doubled between 2008 and 2015, rising from 8,300 to 17,000.[3] The increasing HIV risk among young people is posing potential new

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threats to blood safety because young people represent a large proportion of blood donors in China, with nearly half of donors 25 years or younger.[4]

The HIV epidemic in China was profoundly influenced by illegal blood collection practices in the early 1990s, which combined with other routes of transmission led to the spread of HIV across the country. Although the risk of transfusion-transmitted infections (TTI) has been substantially reduced through enhanced screening techniques, screening capacity, and the nationwide adoption of nucleic acid testing (NAT), HIV infection through sexual contact, especially men who have sex with men (MSM) transmission has increased over time. According to the national surveillance data, the proportion of sexually transmitted HIV infections increased from 33.1% in 2006 to 92.2% in 2014, with MSM transmission increasing from 2.5% in 2006 to 25.8% in 2014.[5] Among young people aged 15-24, more than 90% of HIV/AIDS cases acquired HIV through sexual contact, 42% through MSM transmission.[6] With sexual transmission as the dominant route for HIV infection, it may play a bridging role in spreading HIV from high-risk groups to the general population.[7] The upward trend of HIV infections and sexual transmission as the primary transmission mode underscores the importance of monitoring HIV prevalence and incidence in Chinese blood donors. Several studies reported HIV prevalence among Chinese blood donors had increased significantly over the past years.[8–10] However, they are limited in terms of the width and recency of the data sources (using data from one blood center, and up to the year of 2014). Furthermore, there is a lack of data on HIV incidence among blood donors.

The National Heart, Lung, and Blood Institute (NHLBI) of the US National Institutes of Health (NIH) launched the Recipient Epidemiology and Donor Evaluation - III (REDS-III) China program in 2011. It includes the collection of donation and donor data at five geographically-disperse blood centers in China between 2012 and 2016. This allowed us to estimate HIV prevalence and incidence temporally in different donor groups and to identify donor and donation characteristics associated with HIV infection.

MATERIALS AND METHODS

Participants and study procedure

Details about the REDS-III study design and implementation were published elsewhere.[11] Briefly, the REDS-III China was a collaboration between NHLBI, Johns Hopkins School of Medicine, Stanford University School of Medicine, University of Massachusetts Boston, and the Institute of Blood Transfusion (IBT) of the Chinese Academy of Medical Sciences (CAMS). Five Chinese regional blood centers participated in the study: Chongqing Blood Center (Chongqing), Liuzhou Blood Center (Liuzhou, Guangxi), Luoyang Blood Center (Luoyang, Henan), Mianyang Blood Center (Mianyang, Sichuan), and Urumqi Blood Center (Urumqi, Xinjiang). These five blood centers collected approximately 350,000 donations per year, representing 3% of national blood donations. The study protocol was reviewed and approved by the institutional review boards (IRBs) at all participating institutions and by the IRB at the data coordinating center, Research Triangle Institute, Inc. (RTI).

The study collected routine donor and donation data for all blood donations made at the five participating blood centers from April 1, 2012 through December 31, 2016. Donation data from June 1, 2013 through December 31, 2016 were used for analysis because the missing rate of the confirmatory test results was high (over 54% missing) prior to June 2013. The participating blood centers built the standardized data collection procedures into their daily routine operations. After obtaining the informed consent for this research study, prospective donors provided basic demographic information and completed a health history questionnaire. They received a physical exam, including weight, height, blood pressure, pulse, and body temperature. After that, they provided a blood sample for pre-donation rapid testing on ABO typing, hemoglobin level, hepatitis B surface antigen (HBsAg), and alanine aminotransferase (ALT). Only donors with qualifying hemoglobin levels as well as negative HBsAg and ALT rapid testing results proceeded to donate blood. The donated blood underwent two rounds of enzyme-linked immunosorbent assay (ELISA) testing for HBsAg, anti-HIV, anti-HCV, and syphilis antibodies using kits produced by two different manufacturers (Manufacturer names provided in Table S1, available as supporting information in the online version of this paper). NAT test for HBV, HCV, and HIV was performed on all donations at Chongqing and Liuzhou blood centers using assays by Grifols (Procleix Tigris System) on every individual donor sample (ID). For the remaining blood centers at Luoyang, Mianyang, and Urumqi, NAT was not initiated until 2017, therefore they do not have NAT results for this study. If found to be reactive in any round of ELISA or NAT test, the donated blood was discarded and not used for transfusion.

HIV confirmatory testing and recency infection testing

Samples of blood donations screened reactive for HIV-1/2 on one or both rounds of routine ELISA tests or positive by NAT were sent to the IBT laboratory for confirmatory testing by Western Blot (WB) (MP Diagnostics HIV BLOT 2·2, MP Biomedicals AsiaPacific Pte Ltd, Singapore). Samples were stored at -20°C at the blood centers before being shipped in batches to the IBT laboratory on a monthly basis. Once an HIV positive case was identified, he/she would be referred to the local Center for Disease Control (CDC) for further confirmatory testing, case registration, counseling, and free treatment.

HIV infection stage was determined using the single-well LAg-Avidity EIA (LAg-Avidity EIA, Sedia Biosciences CO.). HIV recent infection was identified as being infected within approximately 129 days based on avidity of HIV antibodies; while long-term infection was identified as being infected more than 129 days ago.[12]

Statistical analysis

Donors were categorized into first-time donors and repeat donors. First-time donors were defined as donors who made no blood donations prior to the study period. Repeat donors include two types of donors: 1) donors who had made at least 1 donation prior to the study period and one or more during the study period; and 2) first-time donors (i.e., a donor without previous donation history) who made two or more donations during the study period. Therefore, the categories of first-time donors and repeat donors are not fully mutually exclusive, depending on the number of donations made during the study period. If a first-time donor made two or more donations in the study period, then that donor contributed the first donation to the analysis of first-time donors and all donations to the analysis of repeat donors.

HIV prevalence was calculated among first-time donors as total HIV cases among first-time donors' first donations divided by the total number of first-time donors, where HIV cases were based on being confirmed positive by WB.

HIV incidence rate was calculated as the number of HIV cases divided by total person-time at risk. The methods for calculating number of cases (numerator) and person-time at risk (denominator) were different for first-time donors and repeat donors with single and multiple donations in the study period. For first-time donors (first donation if they made multiple donations), HIV incidence was estimated based on the LAg test results among first-time donors who were confirmed as recently infected (within 129 days).[12] For repeat donors with multiple donations in the estimation interval, their donation data were treated using the "classical method."[13] For repeat donors who had made only one donation in the study period, each infected donor contributed a partial case to the numerator (details of calculation for first-time and repeat donors are presented in Supplemental Materials).

Chi-square test was used to assess the difference in WB positive rate by demographic and donation characteristics among first-time donors. Multivariable logistic regression model was then fit to examine factors associated with HIV WB positive testing results. Multiple imputation was used to deal with missing data. According to the current practice in China, donations with reactive or inconclusive results in ELISA screening testing should have confirmatory testing. In the donation data, 171 (6.29%) out of 2,718 cases with reactive or inconclusive screening results had their confirmatory test results missing. These missing confirmatory test results were imputed via a multiple imputation procedure (m = 10) using the PROC MI Fully Conditional Specification (FCS) logistic regression method with subsequent analysis using PROC MIANALYZE. After imputation, around 42 cases on average, with the range from 40 to 44 in the 10 imputations, had their missing confirmatory test results imputed as positive and the others were imputed as negative. The average imputed positive cases was 28.3 (range 25-30) for first-time donors and 13.9 (range 11-16) for repeat donors. Around 10% of the confirmed positive cases had missing LAg test results. After imputing the missing confirmatory test results for the first-time donors, all the confirmed positive cases, including those with imputed positive confirmatory test results, if having missing LAg test results, had their LAg test results imputed using a multiple imputation procedure. All analyses were conducted with SAS version 9.4 (SAS Institute).

RESULTS

From June 1, 2013 through December 31, 2016, a total of 1,276,544 whole blood and apheresis platelet donations with post-donation screening results were collected at five Chinese blood centers, including 648,607 donations from

TABLE 1. HIV prevalence estimates among first-time donors at five Chinese blood centers, June 2013-Dec 2016

Blood Center	Total N of donations	# of HIV WB Testing positive donations*	Prevalence (per 100,000 donations)*	95% Confidence interval* Lower level	Upper level
Chongqing	267,131	205	76.63	66.09	87.17
Liuzhou	92,056	92	99.94	79.39	120.49
Luoyang	113,815	31	27.59	17.82	37.36
Mianyang	71,532	31	43.90	28.47	59.32
Urumqi	104,073	82	78.60	61.55	95.65
Total	648,607	441	68.04	61.68	74.40

* Average number of HIV positive, prevalence, and 95% CI after multiple imputation. (Missing values in the dataset were imputed 10 times, which yielded 10 imputed datasets. Each imputed dataset was used to calculate the prevalence estimate along with its estimated variance. The final estimate is the average of the estimates derived from the 10 imputed datasets and the variance of the final estimate is the sum of the within-imputation variance and the between-imputation variance.)

first-time donors and 627,937 donations from 332,780 repeat donors.

HIV prevalence in first-time donors

Among the 648,607 donations from first-time donors, there were 413 known positive cases confirmed by WB and an "average" of 28.3 imputed positive cases. The HIV prevalence estimate among first-time donors was 68.04 (95% CI 61.68-74.40) per 100,000 donations, varying between 27.59 and 99.94 per 100,000 donations across the five blood centers (Table 1).

Among first-time donors, HIV positive confirmatory testing results were associated with donor's age, sex, race/ethnicity, education, and occupation (Table 2). Overall, younger (18-25 years), female, and non-minority ethnicity donors as well as donors with at least a college education, students, and donors working in the public sector (military, government and healthcare) were less likely to have an HIV WB positive test result. Multivariable logistic regression among first-time donors showed that donors older than 25 years had higher odds of having an HIV WB positive test than 18-25 year old donors, with the highest risk among donors older than 45 years (OR = 1.66, 95% CI 1.17-2.34). Compared to Han ethnicity, donors reporting Zhuang or Uygur ethnicity had a higher likelihood of testing HIV WB positive (OR = 2.03, 95% CI 1.46-2.83; and OR = 3.88, 95% CI 2.77-5.42, respectively). Donors with lower education were more likely to test HIV positive than donors who had a college or higher level education. Certain occupations, such as working at home, factory workers, commercial service staff, and being retired/unemployed were associated with higher odds of being HIV positive. Among them, commercial service as a donor self-reported occupation has the strongest association with HIV positive status (OR = 2.34, 95% CI 1.53-3.60). Female donors were less likely to test positive than their male counterparts (OR = 0.28, 95% CI 0.21-0.36, Table 3).

HIV incidence in first-time donors

Among the 441 confirmed positive cases (after imputation) in first-time donors, there were 86.9 "recent" infections and 354.4 "not recent." The average 86.9 'recent' infections included 80 confirmed incident cases from LAg test and an average of 6.9 imputed cases (range = 4-9). HIV incidence

TABLE 2. Univariate analysis of donor and donation characteristics associated with HIV confirmatory testing positive results among first-time donors (N, %)

Factors	Number of Donors	WB positive	p-value
Donation type			0.065
Whole blood	629,196	421 (0.07%)	
Apheresis platelet	19,411	20 (0.1%)	
Age			<0.001
18-25	314,669	133 (0.04%)	
26-35	144,484	154 (0.11%)	
36-45	126,754	99 (0.08%)	
46+	62,700	56 (0.09%)	
Sex			<0.001
Males	375,962	374 (0.1%)	
Females	272,645	67 (0.02%)	
Race/ethnicity			<0.001
Han	560,872	335 (0.06%)	
Zhuang	28,641	42 (0.15%)	
Uygur	17,438	40 (0.23%)	
Zang	9,126	5 (0.05%)	
Tujia	8,501	4 (0.05%)	
Other	24,029	15 (0.06%)	
Education			<0.001
College and above	156,758	56 (0.04%)	
Some College or Associate	189,645	114 (0.06%)	
High School	113,048	100 (0.09%)	
Middle School and 6th Grade	169,478	151 (0.09%)	
Other and missing	19,678	20 (0.1%)	
Occupation			<0.001
Student	178,515	46 (0.03%)	
Farming, fishing, and forestry	81,681	48 (0.06%)	
Working at home	125,919	126 (0.1%)	
Factory worker	50,540	50 (0.1%)	
Commercial Services staff	61,297	67 (0.11%)	
Military, government, healthcare	56,467	21 (0.04%)	
Retired, unemployed, other and missing	94,188	84 (0.09%)	

TABLE 3. Multiple logistic regression results: factors associated with HIV confirmatory testing positive results among first-time donors at five Chinese blood centers

Factors	Categories	Odds Ratio (95% CI)
Donation type	Whole blood	
	Apheresis platelet	1.05 (0.66, 1.67)
Age	18-25	
	26-35	1.61 (1.24, 2.10)
	36-45	1.34 (1.00, 1.80)
	46+	1.66 (1.17, 2.34)
Sex	Males	
	Females	0.28 (0.21, 0.36)
Race/ethnicity	Han	
	Zhuang	2.03 (1.46, 2.83)
	Uygur	3.88 (2.77, 5.42)
	Zang	0.79 (0.33, 1.91)
	Tujia	1.06 (0.39, 2.84)
	Other	1.08 (0.64, 1.81)
Education	College and above	
	Some College or Associate	1.34 (0.96, 1.86)
	High School	1.60 (1.12, 2.30)
	Middle School and 6th Grade	1.65 (1.15, 2.37)
	Other and missing	1.71 (0.99, 2.94)
Occupation	Student	
	Farming, fishing, and forestry	1.02 (0.62, 1.71)
	Working at home	2.03 (1.34, 3.08)
	Factory worker	1.86 (1.17, 2.98)
	Commercial Services staff	2.34 (1.53, 3.60)
	Military, government employee, and healthcare personnel	0.95 (0.55, 1.64)
	Retired, unemployed, other, and missing	1.86 (1.21, 2.86)

TABLE 4. HIV incidence estimate among first-time donors at five Chinese blood centers, June 2013-Dec 2016

Blood Center	Total N of Donors†	Total * of Person-years†	* Incident infections†	Incidence (per 100,000 person-years)†	95% Confidence Interval† Lower Level	Upper Level
Luoyang	113,790	40,219	8.1	20.13	10.06	40.26
Urumqi	104,016	36,756	24.3	66.10	44.32	98.58
Chongqing	266,964	94,348	37.6	39.83	28.65	55.36
Mianyang	71,508	25,273	6.4	25.06	10.74	58.48
Liuzhou	91,975	32,504	10.5	32.10	16.65	61.89
Total	648,253*	229,100	86.9	37.93	30.62	46.97

* The number of first-time donors in incidence estimate (N = 648,253) is different from the number of first-time donors in prevalence estimate (N = 648,607) because the first-time donors with confirmed HIV infection who are classified as not recent (i.e., LAg-test results = Long-term) were excluded from incidence calculation (average N = 354.4).
† Number of donors, total person-years, number of incident infections, and average incidence and 95% CI after multiple imputation.

TABLE 5. HIV incidence estimate among repeat donors at five Chinese blood centers, June 2013-Dec 2016

Blood center	Total N of donors	Total * of person-years	Incident infections*†	Incidence (per 100,000 person-years)†	95% Confidence interval† Lower level	Upper level
Luoyang	78,660	125,615	9.84	7.81	4.08	14.95
Urumqi	40,482	58,631	14.51	24.75	14.79	41.40
Chongqing	113,632	165,713	58.00	35.00	27.03	45.31
Mianyang	48,358	76,654	8.40	10.94	5.51	21.72
Liuzhou	51,648	83,454	14.07	16.85	9.94	28.58
Total	332,780	510,067	104.82	20.55	16.95	24.91

* For repeat donors who made donation before the study period and then only one donation during the study period, if they are HIV positive, their cases were only accounted partially in the incidence estimation (see details in methods section).
† Number of incident infections, average incidence, and 95% CI after multiple imputation.

estimate among first-time donors ranged between 20.13 and 66.10 per 100,000 person-years across blood centers, with an overall incidence rate of 37.93 (95% CI 30.62–46.97) per 100,000 person-years (Table 4).

HIV incidence in repeat donors

The overall HIV incidence estimate among repeat donors was 20.55 (95% CI 16.95–24.91) per 100,000 person-years, varying from 7.81 to 35.00 per 100,000 person-years across blood centers (Table 5).

DISCUSSION

In this study, HIV prevalence was determined based on the WB confirmatory testing results, while incidence was estimated based on the LAg test results among first-time donors. To our knowledge, this is the first study using rigorous testing and estimation methods to calculate HIV prevalence and incidence rates among Chinese blood donors.

Previously, we calculated HIV prevalence in first-time donors from 2008 to 2010.[14] Although the overall HIV prevalence among first-time donors reported in the current study was very close to the prevalence reported in this previous study (66 per 100,000 donations; 95% CI 59-74), the blood centers included in the two studies are different, and direct comparisons are not appropriate. A closer look by blood centers shows that among the four blood centers included in both studies, three had increases in HIV prevalence (increase from 2 to 28 per 100,000 donations in Luoyang, 27 to 44 per 100,000 donations in Mianyang, and 38 to 79 per 100,000 donations in Urumqi)[14]; and one center, Liuzhou, had a decrease in HIV prevalence from 151 to 100 per 100,000 donations. This finding is consistent with another study in the capital city of Guangxi province (Nanning) which reported a slightly decreasing number of people living with HIV/AIDS since 2010 in people 49 years and younger.[15] The decreasing HIV prevalence in Liuzhou's blood donors may therefore be attributable to the combination of two factors: 1) the stable (i.e., non-increasing) HIV new cases (incidence) in the past years and 2) the attrition of HIV cases presenting to donate over time. For the first factor, the HIV incidence rate in Liuzhou remained largely unchanged during the two periods (17 per 100,000 person-years in 2013-2016 vs. 15 per 100,000 person-years in 2008-2010). Previously, the major cause of HIV infections in Liuzhou was shared use of injecting equipment among IDUs. In recent years, free needles and syringes are supplied to IDUs by pharmacies through the national program for HIV and AIDS prevention. This has greatly reduced the risk of HIV transmission among IDUs. However, HIV incidence was not found to be decreased probably because of the concomitant rise in sexual risk behaviors. For the second factor, those who were infected previously have been permanently deferred from blood donation if they came to donate in the past. Even if they have never made a blood donation before, some of them have become older and moved out of the donor age range (18-60 years), or become too sick or died of HIV complications. Although HIV prevalence accounts for both new (incident) and older cases, this statistic is still valuable in demonstrating the scale of the epidemic in the population.[16]

The rising HIV prevalence at the other three blood centers probably reflects the national uptrend. Nationwide, the number of people living with HIV/AIDS rose from 501,000 in 2014 to 850,000 in 2018, and newly reported HIV infections have been rising at a rate of 8 percent every year.[17] A study in Tianjin, a coastal municipality in northern China, revealed that the prevalence of AIDS increased from 0.13 per 100,000 population in 2005 to 5.68 in 2016, by 39.6% annually over a 12-year period. The greatest increase was in the MSM population (44.7%).[18] Other studies also reported marked growth in HIV epidemic over the past decade in Chongqing, a large municipality in southwest China; Shenzhen, a major city in the south; and Fujian, a southeastern province.[19–21] While most of the studies were conducted among general populations, there is a paucity of data on HIV prevalence among Chinese blood donors at either national or regional level. A meta-analysis reported that the pooled prevalence of HIV among voluntary Chinese blood donors was 13.22 per 100,000 donors between 2000 and 2009; the prevalence increased from 5.6 per 100,000 donors to 28.90 per 100,000 in that decade.[22] Our estimated prevalence is higher than that reported by the meta-analysis, which could be explained by the fact that the five participating blood centers are mostly selected from HIV high epidemic regions. The average prevalence rate from this study likely does not represent the Chinese national average blood donor HIV prevalence due to the significant variations between Chinese regions in the severity of their HIV epidemic. Therefore a potential limitation of our results is related to the selection of blood centers from high HIV epidemic regions.

The incidence rate among repeat blood donors found in the current study is higher than that reported in our previous study (20.55 per 100,000 person-years in 2013-2016 vs. 9 per 100,000 person-years in 2008-2010).[14] Among the four blood centers that participated in the 2008-2010 and the current study, three of them (except for Liuzhou as noted above) had substantial increases in HIV incidence (increase from 1 to 8 per 100,000 person-years in Luoyang, 7 to 11 per 100,000 person-years in Mianyang, and 11 to 25 per 100,000 person-years in Urumqi). The two studies used different estimation methods. In the previous study, the average inter-donation interval was estimated from a survival regression model and used as the interval before the first donation for all repeat donors.[14] According to a simulation study that compared 8 methods for estimating the incidence of infection in repeat blood donors, this approach (Method 7 in the simulation study) overestimates incidence and the upward bias increases as the average donation rate drops.[23] Given the low average donation frequency by repeat donors in China, it is likely that the previous study overestimated the actual incidence rate. Simulations also indicated that the estimation approach used in the current study produces unbiased estimates when time to infection follows the exponential distribution that underlies incidence calculations. Estimates are biased when incidence is rising but, unless the increase is very large or sudden and abrupt, the bias is fairly small. Comparing to the HIV incidence estimates in the previous years which used a method that is likely to overestimate, the incidence calculated in this study with a less biased method is higher than the previous estimates, therefore it is reasonable to conclude that we detected an actual rising HIV rate in the donor population in China. One thing worthy to note is that NAT can shorten the window period, but in our study only two blood centers had NAT results. Using WB confirmatory testing may miss some cases in the window period and therefore underestimating the prevalence and incidence.

There is a lack of published data on overall HIV incidence in China. The incidence rate reported in the previous period was just among repeat donors.[22] In the current study, however, the calculation of incidence rates accounts for incidence in first time donors as well as for repeat donors who donate very infrequently and is based on a much more complete assessment of HIV because of the lower percentage of missing information. There are several computation assumptions in our HIV incidence estimates. For example, for repeat donors who made only one donation in the study period but had made donations prior to the start of the study period, each infected donor was only counted as a partial case in the incidence estimate. This is based on the assumption that time to infection follows an exponential distribution and it works well when the probability of an event is near zero. As incidence is estimated as cases over person-time, we assume that time to infection follows an exponential distribution, noting that cases over person-time is the maximum likelihood estimate of the parameter of an exponential distribution. If time to event follows an exponential distribution and the exponential parameter is close to zero, the probability that an event has happened by time T is approximately a linear function of T. For a repeat donor who was negative at the last donation prior to the study period and positive at the first donation in the estimation interval, it is known that the infection occurred between the two donations. Assuming the probability that the event occurred by time T is approximately a linear function of T, the probability that the event happened in the estimation interval is approximately the proportion of time between donations that fell in the estimation interval. The HIV incidence rates are low enough that we can assume approximate linearity for time to event; therefore we expect that the bias is little or small when using this partial case approach. Another computation assumption is the mean duration of recent infection (MDRI) of 129 days. However, a normally distributed random component (mean = 0 and SD = 10) was added to the estimate to allow the uncertainty in the estimated MDRI. Lastly, there were indeterminate and missing results of confirmatory testing and recency of infections. It is very likely that there are positive cases among the missing observations and the missing cases from the numerator will cause bias (i.e., underestimating incidence). In this study, multiple imputations were used to eliminate the potential bias caused by missing data. The incident cases in our study were determined using LAg results for first time donors and represent actual recent cases; therefore the incidence rate reported in the current study provides for the first time a more accurate and robust estimate of the HIV incidence rate. In countries where repeat donations are much less frequent than in other countries like the US, the classic incidence model is a necessary but insufficient tool that needs to be supplemented with incidence methodology that accounts for infrequent repeat donors, and first-time donor incidence based on recency assays. The methods used in this study are readily applicable in these countries. Furthermore, monitoring the residual risk of TTIs is a crucial step in the assessment of the safety of the blood supply. Several models have been developed to estimate residual risk and they are all derived from incidence rates.[24,25] Therefore, higher incidence rates will negatively impact the blood supply safety; that is why it is so important to accurately measure incidence.[26]

Our study revealed a substantial regional variation in HIV prevalence and incidence. For example, HIV prevalence ranged between 28 to 100 per 100,000 donors, and incidence rate among first-time donors varied from 20 and 66 per 100,000 person-years. Among all provinces (autonomous regions and municipalities) in China, 12 provinces with high HIV prevalence account for 84% of all HIV cases.[5] The participating blood centers in the REDS-III China study were selected from these HIV epidemic regions, and represent a wide range of geographic and cultural and economic backgrounds. They are all located at strategic positions. For example, Liuzhou is a critical portal city for commercial transportation and population migration between China and its many southeastern neighboring countries; Luoyang represents the most interior Chinese region and is in the region of the highly publicized HIV cluster in paid plasma donors; Urumqi is China's gate to central Asia and Middle-East nations including Pakistan and several former Soviet Union countries. Among the five blood centers, Urumqi and Chongqing have high prevalence and incidence rate, Luoyang and Mianyang have relatively low prevalence and incidence, while Liuzhou has the highest prevalence but medium incidence rate. Potential explanations for such regional variation include different population structure, distribution of risk behaviors, and geographic and historic factors. For example, the regions with high HIV prevalence and incidence may have higher numbers of injection drug users (IDU) and recently growing MSM population.[27]

This study identified donor and donation characteristics associated with HIV confirmatory results among first-time donors. Donors younger than 25 years had a lower chance of having HIV confirmatory positive results. This is consistent with our previous study which showed that first-time donors aged 25-45 years, compared to donors younger than 25, had a higher risk of HIV infection (OR = 1.6-1.8).[14] Although studies from general population reported a rising trend of HIV infections among young people under 25 years of age, other age groups also experienced a marked increase. A study showed that while the number of HIV/AIDS infections among youth nearly doubled from 2005 to 2012, with the increasing number of overall HIV cases, the proportion of young people among all HIV/AIDS cases actually decreased, with a statistically significant trend ($p < 0.001$).[6] Our study suggest that younger donors maybe a safer source for the blood supply.

Similar to our previous findings, we found that minority ethnicity and having a middle school or lower level of education were associated with HIV positivity. Commercial service was the occupation associated with the highest risk of HIV infection. This suggests that it is critically important to implement education and prevention strategies in this population. An HIV risk factor case–control study in REDS-III has recently been completed and will provide detailed HIV risk factor information. It is anticipated that these results will further inform how best to reduce HIV infection among blood donors and enhance blood safety.

CONCLUSION

Using data from five blood centers in China, we provided robust estimations of HIV prevalence and incidence among blood donors in these high HIV-prevalence selected regions. Although HIV prevalence and incidence rate remain relatively low among Chinese blood donors, we observed increasing rates of HIV infections in blood donors in some regions. Being male, older than 25 years, minority, less than college education, working in commercial services or factory, or being retired, unemployed, or self-employed were associated with higher HIV risks. Continued close monitoring of HIV risk in Chinese blood donors will be critical to safeguard blood safety.

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CONFLICT OF INTEREST

The authors have disclosed no conflicts of interest.

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SUPPORTING INFORMATION

Additional Supporting Information may be found in the online version of this article.

Appendix S1: Supplemental materials.
Table S1: Manufactures of ELISA Testing Assays by Blood Centers.