Published in final edited form as:

Transfusion. 2012 April ; 52(4): 870–879. doi:10.1111/j.1537-2995.2011.03344.x.

HIV prevalence, incidence and residual risk of transmission by transfusions at REDS-II blood centers in Brazil

Ester C Sabino^{1,5}, Thelma T Gonzalez², Anna Bárbara Carneiro-Proietti³, Moussa Sarr⁴, João Eduardo Ferreira⁵, Divaldo A Sampaio⁶, Nanci A Salles¹, David J. Wright⁴, Brian Custer², and Michael Busch² for the NHLBI Retrovirus Epidemiology Donor Study-II (REDS-II), International Component.

¹Pró-Sangue Foundation

²Blood Systems Research Institute

³Hemominas Foundation

⁴Westat, USA

⁵University of São Paulo

⁶Hemope Foundation

Abstract

Background—In Brazil nationally representative donor data are limited on HIV prevalence, incidence and residual transfusion risk. The objective of this study was to analyze HIV data obtained over 24 months by the REDS-II program in Brazil.

Methods—Donations reactive to 3rd and 4th generation immunoassays (IAs) were further confirmed by a less-sensitive (LS) IA algorithm and Western blot (WB). Incidence was calculated for first-time (FT) donors using the LS-EIA results and for repeat donors with a model developed to include all donors with a previous negative donation. Residual risk was projected by multiplying composite FT/repeat donor incidence rates by HIV marker-negative infectious window periods.

Results—HIV prevalence among FT donors was 92.2/10⁵ donations. FT, repeat donor and composite incidence were 38.5 (95%CI: 25.6–51.4), 22.5 (95%CI: 17.6–28.0) and 27.5 (95%CI: 22.0–33.0) per 100,000 person-years, respectively. Male and community donors had higher prevalence and incidence rates than female and replacement donors. Estimated residual risk of HIV transfusion-transmission was 11.3 per 10⁶ donations (95%CI: 8.4–14.2), which could be reduced to 4.2 per 10⁶ donations (95%CI: 3.2–5.2) by use of individual donation nucleic acid testing (NAT).

Conclusion—Incidence and residual transfusion risk of HIV infection are relatively high in Brazil. Implementation of NAT testing will not be sufficient to decrease transmission rates to levels seen in the US or Europe, therefore other measures focused on decreasing donations by at-risk individuals are also necessary.

Keywords

Blood donors; HIV; Residual risk

Corresponding author: Ester C. Sabino, Department Infectious Disease, University of Sao Paulo, Av Dr Eneas de Carvalho Aguiar 470. São Paulo. SP 05403-000, Brazil, sabinoec@usp.br.

Conflict of Interest: no conflict of interest.

Introduction

The HIV/AIDS epidemic began in Brazil in the early 1980s, and Brazil now has the largest HIV-1 infected population in South America, with 544,846 reported cases of AIDS and 630,000 individuals known to be living with HIV in 2009.¹ The epidemic in Brazil is considered a “concentrated epidemic”, with an overall prevalence below 1% in the general population², but levels as high as 50% among vulnerable population such as males who have sex with males (MSM), injection drug users (IDUs) or sex workers³. Incidence of AIDS cases vary across Brazilian regions, with the highest incidence rates concentrated in the South and the Southeast (29.3 and 19.2/100,000), followed by the Midwest, North and Northwest (16.4; 15.4; and 11/100,000)¹.

To address the growing HIV/AIDS epidemic⁴, the Brazilian government implemented early measures such as creating free Volunteer Counseling and Testing Centers (VCTs), offering free health services for the diagnosis, treatment and prevention of HIV and other sexually transmitted diseases, and providing technical and financial support towards maximizing the safety of the blood supply. However, despite offering these programs that benefit individuals and society, many at risk and HIV-infected persons in Brazil do not utilize these services to get tested.⁵ Furthermore, there are significant regional variations in the rates and demographics of people seeking HIV testing in Brazil, including disparities by gender and socioeconomic characteristics.⁵ For instance, in the general population, 27.2% of HIV testing is performed during prenatal care and 23.2% during the process of blood donation⁵. Among men, blood donation has been the most common site for HIV testing (36 – 39%)⁵, which poses a threat to blood supply, since previous studies have indicated that 9% of donors were motivated to give blood for the purpose of obtaining test results and these “test-seekers” have higher rates of blood-borne infectious markers and Herpes 2 antibodies.⁶

Monitoring HIV prevalence and incidence among donors is important for evaluating the safety of the blood supply and also for tracking the epidemic and efficacy of public health intervention measures and policies^{7–11}. There are few published studies on HIV prevalence and incidence among Brazilian donors, or estimates for residual risk of transfusion-transmitted HIV infection in Brazil. This is in part due to the lack of mandatory confirmatory testing at the time of donation; most blood centers only confirm screening immunoassay (IA)-reactive results for those donors who return for counseling and retesting, and approximately 40% of the HIV-IA repeat reactive individuals in Brazil never return for counseling either at the blood banks or at local VCT centers¹². Moreover, until recently there has not been the capacity to merge and analyze data across multiple blood centers. Representative national data on HIV infection rates and residual risk among Brazilian donors/transfusions are needed, particularly because due to economic constraints HIV (and HCV) NAT implementation has been delayed over the past decade with launch of NAT testing now planned for 2011–2012. The objective of this study was to analyze HIV data obtained in the three large Brazilian blood centers who are part of the NHLBI International REDS-II program¹³.

Methods

Participating blood centers in Brazil

The present study is part of the NHLBI Retrovirus Epidemiology Donor Study-II (REDS-II), International program that conducts research studies involving safety and adequacy of the blood supply in participating countries. The REDS II study in Brazil includes three blood centers, Pró-Sangue Foundation in São Paulo (FPS), Hemominas Foundation in Minas Gerais (FH-MG), both in the Southeastern part of Brazil, and Hemope Foundation in the State of Pernambuco (FH-PE), which is located in the Northeastern part of the country.

Details regarding the organization of the REDS-II Brazil program including donor demographics relative to population characteristics at the three core centers have recently been published¹³.

Data collection and storage

Demographic data from all donors from January 1st, 2007 to December 31st, 2008 were extracted from the computer systems of each center and sent to a data warehouse at the University of São Paulo. These data included coded donor ID, age, gender, self-reported skin color (captured as 5 options but recoded into white, black, mixed or other), and educational attainment. Standardized testing data on all blood donations are also collected, prepared and electronically sent a single data warehouse in São Paulo. Following integration and quality control the data are transferred on a monthly basis to the REDS-II Coordinating Center in the USA (Westat, Rockville, MD) for compilation and analysis.

HIV testing procedures

All samples were screened at each center with two tests (4th and 3rd generation IAs) performed in parallel. When a donor tested repeat reactive by either of the two screening IAs, the unit was discarded and the sample was sent to the central study laboratory in São Paulo, for further testing. Samples reactive on both IA's were sent to Blood Systems Research Institute to classify the infection as recent (i.e., incident) or remote using the Standardized Testing Algorithm for Recent HIV Seroconversion (STARHS), which is based on a sensitive/less-sensitive enzyme immunoassay (LS- or "detuned" EIA).¹⁸ Samples were considered confirmed seropositive if they were highly reactive by the LS-EIA; if they were weakly or non-reactive by the LS-EIA Western blot (WB) was performed as well as selective PCR testing. The sensitivity, specificity and positive predictive value of this supplemental testing algorithm has recently been reported¹⁴.

Calculation of prevalence, incidence and residual risk

a. Prevalence—Analysis of HIV prevalence was restricted to FT donors, and was calculated based on rates of confirmed positive FT donors divided by number of FT donors, overall, by center, by donation type, and by donor demographic subcategories.

b. Incidence among FT blood donors—For all HIV positive donations in 2007 we used the LS-Vironostika® HIV-1 Microelisa assay (BioMérieux Industry, Raleigh, NC, USA) for anti-HIV, which was modified for "detuned" EIA application by increasing the sample dilution from 1:76 to 1:20,000 and reducing the sample incubation time from 100 minutes to 30 minutes while retaining the kit-specified conjugate incubation time of 30 minutes¹⁶. Donors with remote HIV infection will remain positive in this detuned procedure whereas recently infected or false positive donors will give negative assay results^{15,16}. For HIV positive donations in 2008 we used the LS-HIV Vitros assay (Ortho Diagnostics, Raritan NJ, USA); this test was similarly "detuned" relative to the licensed screening assay to yield a recent infection window period identical to that of the LS- Vironostika assay¹⁷. Both these incidence assays have been developed to discriminate donors as recently infected for approximately 170 days following seroconversion by sensitive IAs at the cutoffs employed. For LS-IA non-reactive samples, if the donor had returned for confirmation we used the final WB results obtained on the follow-up samples by the blood banks to classify the donor as HIV infected or not infected. If the donor had not returned for follow-up testing, the sample from the index donation was tested by WB. The following formulas were used to estimate incidence among FT donors: FT Incidence = (number of recently infected FT donors × 365 days/170 days)/number of FT donations. Confidence intervals for FT incidence rates are derived from poisson regressions, and ignore the minimal additional

variability attributable to variance on the estimated 170 detuned WP. HIV incidence rates among FT donors was calculated overall, by center, by donation type, and by donor demographic subcategories.

c. Incidence among repeat donors—An outline for the calculation of the study period incidence rate among repeat donors is shown in Figure 1. For each repeat donor donation during the study period there is an associated inter-donation interval (donation date – previous donation date). If the previous donation date is in the study period (i.e. 2007–2008), then the person-time is equal to the inter-donation interval. And if the donation is confirmed positive then an incident infection within the study period is known to occur (right hand column of Figure 1).

If the previous donation date precedes 2007, the person time is truncated to time within the study period (donation date – December 31, 2006). If the donation is confirmed positive, then an incident infection is known to have occurred within the inter-donation interval, however the incident is not necessarily within the study period. Assuming that the incident infection event was equally likely to occur on any date within the inter-donation interval, the probability it occurred within the study period can be estimated as a fraction of time (i.e. person-time/inter-donation interval). This probability is used to define a fractional incident infection (left hand column of Figure 1).

The study period incident rate is estimated as the sum of incident infections and fractional incident infections divided by the sum of person time, and was calculated overall, by center, by donation type, and by donor demographic subcategories.

d. Residual risk calculation—Residual risk was calculated using a 15.0 day infectious WP for current 4th generation EIA screening (which detects HIV-1 p24 Ag as well as antibodies to HIV-1 and 2), a 5.6 day WP for individual donation (ID) NAT, and a 9.0 day WP for mini-pool (MP) NAT¹⁸. We used the following formula to compute residual risk: Residual risk = Composite Incidence Rate $\times$ Infectious WP/365.25 days. We calculated the Composite Incidence Rate as being equal to (FT% vs. FT donor incidence) + (Rpt% vs. repeat donor incidence), where FT% and Rpt% are the proportions of first-time and repeat donations in our study sample, respectively. Confidence intervals were computed using a normal approximation and estimating standard errors by Taylor series expansion.

Statistical Analyses

HIV prevalence among first time donors per 100,000 donations was computed, with related 95% confidence intervals. HIV incidence among first time donors (per 100,000 person-years) was computed as the number of new infections divided by the total number of first-time donations times the estimated 170 day detuned WP. For repeat donors, we computed the incidence rate of HIV infection per 100,000 person-years as the number of new events divided by the number of person-years of follow-up (see section c above). Differences in prevalence rates among the first time donors by socio-demographic characteristics, type of donation and location were assessed by logistic regression models. Reliable multivariable analyses could not be performed for HIV incidence among first time or repeat donors due to small numbers. Hence, only unadjusted poisson regression models were used to assess differences in incidence rates among first time and repeat donors by socio-demographic characteristics, location and donor type. All statistical tests were performed using SAS^{TM} 9.1 software (SAS Institute, 2004), with a two-sided p-value < 0.05 considered to be statistically significant.

Results

From January 1, 2007 to December 31, 2008, a total of 615,317 blood donations were made in the three blood centers participating in this study; 189,802 of these donations (31%) were by FT donors and 425,515 donations (69%) by repeat donors.

HIV Prevalence and Incidence in First Time Donors

Of the 189,802 FT blood donations, 175 individuals were HIV antibody confirmed positive, resulting in a prevalence of 92.2/100,000 donors. As shown in Table 1, unadjusted analyses demonstrated that HIV prevalence rates were highest in Recife (119.1/100,000), in community blood donors (110.3/100,000), in the 25 to 45 years age group (115.0/100,000), in male (126.4/100,000), and non-white (111.0/100,000) individuals. After logistic regression, only gender (males higher than females), type of donation (community donors higher than replacement donors), and educational level (donors who completed 11 years educational levels had lower prevalence), remained associated with HIV infection status (see adjusted odds ratios in Table 1).

Among FT blood donors HIV incidence was 38.5/100,000 person-years (Table 2). HIV incidence among community FT donors was over two-fold higher than among replacement donors (55.0 vs. 19.5/100,000 person-years, $p=0.006$). HIV incidence was highest among individuals who had less than 8 years of education (50.1/100,000 person-years) though not statistically significantly higher than other education categories ($p=0.42$), and there was a trend toward higher incidence among males (48.7 vs 22.9/100,000 person-years in males vs. females, $p=0.06$).

HIV Incidence in Repeat Blood Donors

A calculation based on repeat donors who had multiple donations in the two year study period yields an incidence rate estimate of 26.7 (95% CI 17.7–31.8) per 100,000 person-years, with 30 seroconvertors observed. However, this estimate excludes over half of repeat donors during the study period. By including all repeat donors who had previously donated in the centers, there were an additional 115 confirmed incident HIV cases, and the calculated incidence rate decreased to 19.3 (95% CI 13.9 – 24.7) per 100,000 person-years. However, this second incidence rate estimate accumulates person time from the pre-study period (some person-time from the 1990's is accumulated). We have developed a model (see methods) to estimate the incidence rate during the study period that includes the 30 seroconverters known to be incident in the study period and estimated that 34.6 of the 115 additional observed seroconverters were incident infections acquired in the study period. By using this method the study period incidence rate estimate was 22.5 (95% CI 17.05–28.04) per 100,000 person-years.

The demographic characteristics associated with HIV incidence among repeat donors are also presented in Table 2. In the unadjusted analysis, males ($p=0.04$) and younger donors ($p=0.03$) had higher incidence rates than females and older donor groups. Community donors (25.5 per 100,000 person-years) also had a trend toward a higher incidence than replacement donors (15.8 per 100,000 person-years), but this was not statistically significant ($p=0.10$).

Table 3 presents the composite incidence rates per site, taking into account the proportion of first time and repeat donors per center, and also presents the residual transfusion-transmission risk projections based on current infectious window period estimates^{18,19}. Incidence was relatively high in all three centers, as was the residual transfusion HIV risk in the context of current donor serological screening. Even considering the use of single-donation NAT, residual risk would remain high in Brazil, at approximately one WP donation

derived unit transfused per 250,000 donations/components, or four WP units transfused per 1,000,000 donations

Discussion

This study investigates HIV prevalence and incidence at three major blood centers in Brazil. The results show that overall prevalence of HIV among blood donors ($92.20/10^5$) is much higher compared to the rates among blood donors in the United States ($2.92/10^5$)⁷, Canada ($1/10^5$)²⁰, Australia⁸ ($1.1/10^5$), and regions of Europe (1.8, 3.8, and $37.6/10^5$ donations in Western, Central and Eastern Europe⁹, respectively). However, the prevalence in Brazilian donors is lower than the rates reported in the Ukraine ($128.4/100,000$)¹⁰ and many countries in sub-Saharan Africa^{21,22}.

In a previous study from our group focused within the city of São Paulo, we have shown that the prevalence of HIV in first-time donors decreased over time from $204/10^5$ (95% CI 183–228/ 10^5) in 1996 to $131/10^5$ (95% CI 109–156/ 10^5) in 2001.¹¹ The current data demonstrate a further decrease in prevalence among first-time donors in the city of São Paulo to $85/10^5$ (95% CI 65–104/ 10^5) in 2007–2008. Since the prevalence in the general population in São Paulo is estimated at $400\text{--}600/10^5$,²³ our data shows that blood donor candidates are effectively selected based on donor qualification criteria to represent a lower risk subset of the population, although the ratio of infection prevalence among first-time donors to the general population prevalence is not as low in Brazil (~ 0.2) as in the US (~ 0.05)²⁴. Hence additional education and deferral effort is warranted to further reduce the rates of HIV infection among individuals presenting to and accepted for donation in Brazil. In this direction Brazil does request all individuals to disclose number of sexual partner in the previous year and unprotected sex with casual partners.

In the general population in Brazil, males still have a higher prevalence of HIV compared to females; however the male/female ratio has decreased over time in the broader epidemic, from 3.1 before 1987 to 1.5 in 2009.¹ The ratio of male/female prevalence among first-time donors in our study was 3.2. One possible explanation for this higher gender prevalence ratio among donors relative to the general population ratio is that infected females are better diagnosed in Brazil due to pre-natal care and they have more access to testing in other settings. Another explanation is that males are more inclined to be test seekers at blood centers, as documented by several previous surveys conducted by our group^{6,25}.

HIV prevalence rates varied across the blood centers, and was approximately 30% higher in Recife ($119.15/10^5$) compared to Belo Horizonte ($70.98/100,000$). However in the multivariable model only male, community donors and lower levels of education remained associated with elevated HIV prevalence. The higher prevalence seen in Recife is therefore probably due to the fact that FH-PE has more male first-time donors as compared to the other two sites¹³.

Defining incidence among FT donors is challenging, since there is no perfect assay that can discriminate recent from long-standing infections.²⁶ The available assays have a number of potential limitations: they tend to misclassify as ‘recently infected’ persons with late-stage AIDS as well as persons with viral suppression by antiretroviral therapy (ART) in whom antibodies titers and avidity wane, although these limitations are probably less important for allogeneic blood donors who are newly diagnosed and generally healthy. HIV subtype may also interfere, but in the three centers subtype B HIV-1 is present in more than 80% of the HIV infected donations (data not shown). We had an additional challenge since we had to change incidence assays during the course of the study because one of the commercial kits was discontinued and this may have resulted in the imputed incidence being higher in FT

donors in 2007 as compared to 2008. Contrary to what we observed with prevalence rates in FT donors declining relative to our earlier studies, the estimated incidence among FT donors in São Paulo increased slightly (albeit non-significantly) from 25/100,000 person-years (95% CI 10–40/100,000 person-years) in 2001¹¹ to 37/100,000 person-years (95% CI 19–56/100,000 person-years) in the current study. This could be due to a limitation of the incidence assays and STAHRS methods, which are not precise for imputing very low-level incidence rates such as those observed in donor populations²⁶. Another possible explanation is that the progressively enhanced procedures used by the centers to defer at risk donors are less effective for recently infected individuals as compared to those with long-standing infections.

Defining incidence among repeat donors also poses challenges. If a short period of time is used to monitor a donor population, only very frequent donors are counted and few incident cases are documented. On the other hand, if a very large period is used, we may underestimate incidence due to the fact that the return rate is probably lower for HIV seroconvertors as compared to negative donors. Due to these considerations, we developed a new model in which all repeat donors were taken into consideration, but only the time from the beginning of the study period to their first observed donation was counted. This resulted in more than doubling the number of confirmed incident cases but avoided dilution of the denominator by long-interval donations.

The incidence among repeat donors (22.6/100,000 person-years; 95% CI 17.1–28.0/100,000 person-years) was 40% lower than among FT donors (38.5/100,000 person-years; 95% CI 25.6 – 51.4/100,000 person-years), consistent with findings from the US and other countries. In a previous study in São Paulo, the calculated incidence among repeat donors was 25.9/100,000 person-years (95% CI, 18.2–36.1/100,000 person-years) during the 1996–98 periods. Accordingly, it seems that although prevalence among FT donors has decreased, incidence has remained the same in the past 15 years for FT and repeat donors. This incidence among Brazilian repeat donors is approximately 20-fold higher when compared to similar studies in France²⁷, the US^{7,18,24}, Canada²⁰, Australia⁸, Germany and Greece¹⁰, and two times higher compared to incidence rates in Serbia & Montenegro¹⁰.

Studies worldwide have demonstrated that the blood donor selection is an important component for the blood safety, and that replacement blood donors generally present an increased risk of HIV infection^{28,29}. The present study goes in the other direction, and confirms our previous study focused in São Paulo, that community donors have a higher HIV prevalence.¹¹ Similar results with respect to risk of transfusion-transmitted HCV among family-replacement relative to community donors have recently been described in several African countries^{30–32} and Spain³³. Our current and previous¹¹ studies show that “community” donors, i.e., donors that come spontaneously to the blood center, were more likely to be HIV positive when compared to replacement blood donors who donate in the name of a specific recipient to “replace” the blood supply. This finding has several explanations, some of them related to cultural/social aspects of blood donation in Brazil. Our results suggest that replacement blood donors, i.e., those who donate blood to help a friend, family or relative, do not want to harm their loved ones by their donations. In this sense, replacement blood donors who are at risk might avoid blood donation, either because they do not want to disclose any risk factor that they might have or had or because they are unwilling to be responsible for any blood contamination exposure towards their relatives or friends. Community volunteer donors come to donate to help the general (unspecified) recipient population, and although they might in principle have a stronger social commitment, there is not a strong relationship between the donor and the recipient to prevent the harm of failure to fully disclose risk.

Indeed, studies from several countries that have interviewed HIV positive blood donors have demonstrated a substantial proportion of infected donors were aware of risk exposures but did not disclose their risks in the pre-donation questionnaire^{34–36}. One previous study from our group showed that 9% of the individuals who came to donate at FPS/HSP^{6,25} were test-seekers. These test-seekers tend to be male, community and lapsed donors, and were more likely to have positive serological markers for HSV-2⁶²⁵. Since blood donation is a valued activity in the community, they may get social approval for donating blood. The donation setting may be ideal for some at risk individuals, since they get tested in a highly respected “laboratory”, without arousing suspicion in partners, family and friends, and get positive recognition for the donation. This situation could be addressed by blood banks by various modification to current practices, such as by postponing the delivery of test results to the donors so that they would know that they cannot get the results immediately, and by education of the population and prospective donors on the risks to patients that this behavior elicits.

Furthermore, our study shows that although NAT testing for HIV and HCV is being implemented in Brazil to reduce the relatively high current residual risk, it will not be sufficient to decrease the risk of transfusion-transmitted HIV in Brazil to US and European levels. Other strategies are necessary to reduce HIV incidence, although these may not be so easy to develop measures specific to at risk individuals. As an example, we have recently analyzed tools like CUE³⁴ and educational material³⁷ but these initiatives were not proven to effective. Perhaps changes in the HIV testing procedures in the general community that would reach less educated males may be more effective than trying to change procedures in the donors screening setting.

Acknowledgments

This work was supported by NHLBI contract HHSN268200417175C

The Retrovirus Epidemiology Donor Study - II (REDS-II), International Component (Brazil) is the responsibility of the following persons: Blood Centers: Fundação Pró-Sangue/Hemocentro São Paulo (São Paulo) - Ester C. Sabino, Cesar de Almeida Neto, Alfredo Mendrone Jr., Ligia Capuani and Nanci Salles; Hemominas (Belo Horizonte, Minas Gerais) - Anna Bárbara de Freitas Carneiro-Proietti, Fernando Augusto Proietti, Claudia Di Lorenzo Oliveira and Carolina Miranda; Fundação Hemope (Recife, Pernambuco) - Divaldo de Almeida Sampaio, Silvana Ayres Carneiro Leão and Maria Inês Lopes. Data Warehouse: University of São Paulo (São Paulo) - João Eduardo Ferreira, Márcio Oikawa and Pedro Losco Takecian. US Investigators: Blood Systems Research Institute and University of California San Francisco - M.P. Busch, E.L. Murphy, B. Custer and T. Gonçalves; Coordinating Center: Westat, Inc - J. Schulman, M. King and K. Kavounis; National Heart, Lung, and Blood Institute, NIH - S.A. Glynn.

References

1. Saude-DST/AIDS Md. Boletim Epidemiologico AIDS DST Boletim Epidemiologico. Vol. 2009. Janeiro a Junho; 2009.
2. Fonseca MG, Bastos FI. Twenty-five years of the AIDS epidemic in Brazil: principal epidemiological findings, 1980–2005. *Cad Saude Publica*. 2007; 23 (Suppl 3):S333–44. [PubMed: 17992340]
3. Caiaffa WT, Bastos FI, Freitas LL, et al. The contribution of two Brazilian multi-center studies to the assessment of HIV and HCV infection and prevention strategies among injecting drug users: the AJUDE-Brasil I and II Projects. *Cad Saude Publica*. 2006; 22:771–82. [PubMed: 16612431]
4. Parker RG. Civil society, political mobilization, and the impact of HIV scale-up on health systems in Brazil. *J Acquir Immune Defic Syndr*. 2009; 52 (Suppl 1):S49–51. [PubMed: 19858939]
5. Franca Junior I, Calazans G, Zucchi EM. Changes in HIV testing in Brazil between 1998 and 2005. *Rev Saude Publica*. 2008; 42 (Suppl 1):84–97. [PubMed: 18660928]
6. Gonzalez TT, Sabino EC, Murphy EL, et al. Human immunodeficiency virus test-seeking motivation in blood donors, Sao Paulo, Brazil. *Vox Sang*. 2006; 90:170–6. [PubMed: 16507016]

7. Glynn SA, Kleinman SH, Schreiber GB, et al. Trends in incidence and prevalence of major transfusion-transmissible viral infections in US blood donors, 1991 to 1996. *Retrovirus Epidemiology Donor Study (REDS)*. *Jama*. 2000; 284:229–35. [PubMed: 10889598]
8. Seed CR, Kiely P, Keller AJ. Residual risk of transfusion transmitted human immunodeficiency virus, hepatitis B virus, hepatitis C virus and human T lymphotropic virus. *Intern Med J*. 2005; 35:592–8. [PubMed: 16207258]
9. Suligoi B, Raimondo M, Regine V, et al. Epidemiology of human immunodeficiency virus infection in blood donations in Europe and Italy. *Blood Transfus*. 2010; 8:178–85. [PubMed: 20671878]
10. Likatavicius G, Hamers FF, Downs AM, et al. Trends in HIV prevalence in blood donations in Europe, 1990–2004. *Aids*. 2007; 21:1011–8. [PubMed: 17457095]
11. Barreto CC, Sabino EC, Goncalvez TT, et al. Prevalence, incidence, and residual risk of human immunodeficiency virus among community and replacement first-time blood donors in Sao Paulo, Brazil. *Transfusion*. 2005; 45:1709–14. [PubMed: 16271094]
12. Germano FN, da Silva TM, Mendoza-Sassi R, Martinez AM. High prevalence of users who did not return to the Testing and Counseling Center (TCC) for knowing their serological status: Rio Grande, RS, Brazil. *Cien Saude Colet*. 2008; 13:1033–40. [PubMed: 18813597]
13. Carneiro-Proietti AB, Sabino EC, Sampaio D, et al. Demographic profile of blood donors at three major Brazilian blood centers: results from the International REDS-II study, 2007 to 2008. *Transfusion*. 2010; 50:918–25. [PubMed: 20003051]
14. Sabino EC, Salles NA, de Almeida-Neto C, et al. Performance of parallel screening of Brazilian blood donors with two human immunodeficiency virus immunoassays: implications for sequential immunoassay testing algorithms in other countries. *Transfusion*. 51:175–83. [PubMed: 20633245]
15. Kothe D, Byers RH, Caudill SP, et al. Performance characteristics of a new less sensitive HIV-1 enzyme immunoassay for use in estimating HIV seroincidence. *J Acquir Immune Defic Syndr*. 2003; 33:625–34. [PubMed: 12902808]
16. Rawal BD, Degula A, Lebedeva L, et al. Development of a new less-sensitive enzyme immunoassay for detection of early HIV-1 infection. *J Acquir Immune Defic Syndr*. 2003; 33:349–55. [PubMed: 12843746]
17. Keating, SMHD.; Lebedeva, L.; Laeyendecker, O.; Ali-Napo, L.; Contestable, P.; Edwards, S.; Ethridge, S.; Branson, B.; Norris, PJ.; Busch, MP. Optimization and Calibration of Less Sensitive and Avidity Modified Protocols for the Vitros Immunodiagnostic Products Anti-HIV-1+2 for Detection of Early HIV Infections CDC/APHL Diagnostic Conference; Orlando FL. 2010.
18. Busch MP, Glynn SA, Stramer SL, et al. A new strategy for estimating risks of transfusion-transmitted viral infections based on rates of detection of recently infected donors. *Transfusion*. 2005; 45:254–64. [PubMed: 15660836]
19. Kleinman SH, Lelie N, Busch MP. Infectivity of human immunodeficiency virus-1, hepatitis C virus, and hepatitis B virus and risk of transmission by transfusion. *Transfusion*. 2009; 49:2454–89. [PubMed: 19682345]
20. Chiavetta JA, Escobar M, Newman A, et al. Incidence and estimated rates of residual risk for HIV, hepatitis C, hepatitis B and human T-cell lymphotropic viruses in blood donors in Canada, 1990–2000. *Cmaj*. 2003; 169:767–73. [PubMed: 14557314]
21. Lefrere JJ, Dahourouh H, Doekias AE, et al. Estimate of the residual risk of transfusion-transmitted human immunodeficiency virus infection in sub-Saharan Africa: a multinational collaborative study. *Transfusion*. 2011
22. Jayaraman S, Chalabi Z, Perel P, et al. The risk of transfusion-transmitted infections in sub-Saharan Africa. *Transfusion*. 2010; 50:433–42. [PubMed: 19843290]
23. Szwarcwald CL, Castilho EA. Estimated number of HIV-infected individuals aged 15–49 years in Brazil, 1998. *Cad Saude Publica*. 2000; 16:135–41. [PubMed: 10904396]
24. Dodd RY, Notari EP, Stramer SL. Current prevalence and incidence of infectious disease markers and estimated window-period risk in the American Red Cross blood donor population. *Transfusion*. 2002; 42:975–9. [PubMed: 12385406]
25. Goncalvez T, Sabino E, Sales N, et al. Human immunodeficiency virus test-seeking blood donors in a large blood bank in Sao Paulo, Brazil. *Transfusion*. 2010; 50:1806–14. [PubMed: 20456699]

26. Busch MP, Pilcher CD, Mastro TD, et al. Beyond detuning: 10 years of progress and new challenges in the development and application of assays for HIV incidence estimation. *Aids*. 2010; 24:2763–71. [PubMed: 20975514]
27. Pillonel J, Le Marrec N, Girault A, et al. Epidemiological surveillance of blood donors and residual risk of blood-borne infections in France, 2001 to 2003. *Transfus Clin Biol*. 2005; 12:239–46. [PubMed: 15963749]
28. WHO WHO. Universal access to safe blood [monograph on the internet]. 2009. Available from: <http://www.who.int/bloodsafety/en/>
29. WHO WHO. Screening Donated Blood for Transfusion-Transmissible Infections [monograph on the internet]. 2009. Available from: <http://www.who.int/bloodsafety/ScreeningTTI.pdf>
30. Allain JP, Sarkodie F, Asenso-Mensah K, Owusu-Ofori S. Relative safety of first-time volunteer and replacement donors in West Africa. *Transfusion*. 2010; 50:340–3. [PubMed: 19843284]
31. Mbanya DN. Volunteer or family/replacement donations: are the tides changing? *Transfusion*. 2010; 5:1849–50. [PubMed: 20883253]
32. Andre L. Relatively safety of first-time volunteer and replacement donors in Guinea. *Transfusion*. 2010; 5:1850–51.
33. Pereira A, Sanz C, Tassies D, Ramirez B. Do patient-related blood donors represent a threat to the safety of the blood supply? *Haematologica*. 2002; 87:427–33. [PubMed: 11940488]
34. de Almeida Neto C, McFarland W, Murphy EL, et al. Risk factors for human immunodeficiency virus infection among blood donors in Sao Paulo, Brazil, and their relevance to current donor deferral criteria. *Transfusion*. 2007; 47:608–14. [PubMed: 17381618]
35. Lau JT, Thomas J, Lin CK. HIV-related behaviours among voluntary blood donors in Hong Kong. *AIDS Care*. 2002; 14:481–92. [PubMed: 12204151]
36. Lefrere JJ, Elghouzzi MH, Paquez F, et al. Interviews with anti-HIV-positive individuals detected through the systematic screening of blood donations: consequences on predonation medical interview. *Vox Sang*. 1992; 62:25–8. [PubMed: 1580063]
37. Gonzalez TT, Sabino EC, Salles NA, et al. The impact of simple donor education on donor behavioral deferral and infectious disease rates in Sao Paulo, Brazil. *Transfusion*. 2010; 50:909–17. [PubMed: 20003056]

Calculation of incidence among repeat donors, REDS II study in Brazil, 2007-2008

Figure 1.

Calculation of incidence among donations from repeat donors, REDS II study in Brazil, 2007–2008.

*Incident represents probability that HIV incident occurs during the REDS – II study period (assuming incident is equally likely to occur on any date within the inter-donation interval)

Table 1

Correlates of HIV infection among first time blood donors, REDS II study in Brazil, 2007–2008.

HIV Prevalence per 100,000 donation								
Characteristics	N (Donations)	N (Positive)	Prevalence	(95%CI)	p-value	AOR ^α	95% CI	p-value
Overall	189802	175	92.20	(78.55–105.86)				
Blood Center								
Recife	58751	70	119.15	(91.25–147.04)	0.03	1		0.77
Belo Horizonte	45081	32	70.98	(46.40–95.57)		1.20	(0.74 – 1.97)	
São Paulo	85970	73	84.91	(65.44–104.38)		1.31	(0.72 – 2.39)	
Type of Donation								
Community	101529	112	110.31	(89.89–130.73)	0.02	1		0.002
Replacement	88237	63	71.40	(53.77–89.02)		0.48	(0.30 – 0.75)*	
Age								
age <2–5	74742	53	70.91	(51.83–89.99)	0.01	1		0.11
age ≥ 25 – <35	62779	74	117.87	(91.03–144.71)		1.58	(0.96 – 2.58)	
age ≥ 35 – <45	31774	37	116.45	(78.95–153.95)		1.10	(0.58 – 2.10)	
age ≥ 45 – <55	16016	6	37.46	(7.49–67.43)		0.54	(0.18 – 1.58)	
age ≥ 55	4420	5	113.12	(14.02–212.22)		2.01	(0.68 – 5.98)	
Gender								
Female	75119	30	39.94	(25.65–54.22)	<0.01			<0.0001
Male	114683	145	126.44	(105.87–147.00)		3.44	(1.97 – 6.02)*	
Education								
< 8years	12947	19	146.75	(80.81–212.69)	0.02	1		0.04
Complete 8 years	17138	21	122.53	(70.16–174.91)		0.80	(0.42 – 1.50)	
Complete 11 years	63291	41	64.78	(44.96–84.60)		0.46	(0.25 – 0.82)*	
Complete College	15776	12	76.06	(33.04–119.09)		0.64	(0.30 – 1.36)	
Race								
Black	16083	15	93.27	(46.09–140.44)	0.01	1		0.43
Mixed	68449	76	111.03	(86.08–135.98)		0.71	(0.36 – 1.42)	
White	69093	42	60.79	(42.41–79.17)		1.14	(0.61 – 2.15)	

HIV Prevalence per 100,000 donation									
Characteristics	N (Donations)	N (Positive)	Prevalence	(95%CI)	p-value	AOR ^a	95% CI	p-value	
Other	2460	0	0.00	---					
Year									
2007	95179	81	85.10	(66.58–103.63)	0.30	1			0.22
2008	94623	94	99.34	(79.27–119.41)		0.73	(0.44 – 1.21)		

N= number

^a AOR = adjusted odds ratio

Table 2

Incidence* per 100,000 donations among first time and repeat donors, REDS II study in Brazil, 2007–2008.

Characteristics	First Time Donors			Repeat Donors		
	Incidence	95% CI	p value	Incidence	95% CI	p value
Overall	38.49	(25.55 – 51.42)		22.55	(17.05 – 28.04)	
Blood Center			0.84			0.55
Recife	43.88	(19.06 – 68.71)		26.98	(18.54 – 35.43)	
Belo Horizonte	33.36	(8.65 – 58.07)		20.09	(11.07 – 29.11)	
São Paulo	37.49	(18.52 – 56.46)		20.48	(13.98 – 26.99)	
Type of Donation			0.006			0.10
Community	55.02	(33.87 – 76.17)		25.51	(19.90 – 31.11)	
Replacement	19.48	(5.98 – 32.98)		15.83	(8.53 – 23.13)	
Age			0.02			0.03
age <25	28.75	(10.93–46.56)		27.10	(14.82 – 39.38)	
age ≥ 25 – <35	61.60	(33.15–90.06)		27.96	(19.75 – 36.16)	
age ≥ 35 – <45	27.05	(0.54–53.55)		23.68	(14.89 – 32.46)	
age ≥ 45 – <55	0	(0.00–40.24)		8.22	(1.08 – 15.36)	
age ≥ 55	97.22	(0.00–231.93)		0.00	(0.00 – 25.45)	
Gender			0.06			0.04
Female	22.88	(7.03–38.74)		13.09	(6.39 – 19.78)	
Male	48.71	(29.99–67.43)		26.11	(20.46 – 31.77)	
Education			0.42			0.73
< 8 years	16.59	(0.00–49.12)		14.64	(1.61 – 27.67)	
Complete 8 years	50.15	(1.01–99.28)		27.87	(11.76 – 44.00)	
Complete 11 years	16.97	(2.10–31.85)		21.50	(13.52 – 29.48)	
Complete College	13.62	(0.00–40.31)		20.07	(6.35 – 33.78)	
Race			0.15			0.79
Black	26.72	(0.00–63.74)		21.99	(4.62 – 39.35)	
Mixed	53.36	(28.00–78.72)		18.31	(10.18 – 26.44)	
White	18.66	(3.73–33.59)		23.66	(14.39 – 32.94)	
Other	0.00	(0.00–262.02)		47.80	(0.00 – 126.10)	

Characteristics	First Time Donors			Repeat Donors		
	Incidence	95% CI	p value	Incidence	95% CI	p value
Year						
2007	51.92	(34.50–78.12)	0.04	22.50	(14.63–34.60)	0.99
2008	24.98	(13.83–45.10)		22.57	(16.78–30.34)	

* First time donor incidence rate based on 34 recently HIV infected cases (as determined by 'detuned' assay); repeat donor incidence rate based on estimated 64.6 incident HIV cases within the 2 year study period.

Table 3

Composite incidence and residual risk (and 95% confidence intervals) according to blood center, REDS II study in Brazil, 2007–2008.

Blood Center	Composit incidence per 100,000 person year (95%CI)	Residual risk per 1,000,000 (95%CI)		
		According to window phase		
		Ag+Ab IA (15.0 days)	ID NAT (5.6 days)	MP-NAT (9.0 days)
Recife	31.8 (21.5, 42.2)	13.1 (8.3, 17.8)	4.9 (3.2, 6.6)	7.8 (5.1, 10.6)
Belo Horizonte	24.2 (13.8, 34.9)	10.0 (5.4, 14.6)	3.7 (2.0, 5.4)	6.0 (3.3, 8.7)
São Paulo	25.9 (17.8, 33.9)	10.6 (6.9, 14.4)	4.0 (2.6, 5.3)	6.4 (4.2, 8.5)
Brazil	27.5 (22.0, 33.0)	11.3 (8.4, 14.2)	4.2 (3.2, 5.2)	6.8 (5.1, 8.4)

CI = confidence interval

Ag+Ab IA = immunoassay that detect antigen p24 and antibody anti-HIV.