

Prevalence, incidence, and residual risk of human immunodeficiency virus and hepatitis C virus infections among United States blood donors since the introduction of nucleic acid testing

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BACKGROUND: Nucleic acid testing (NAT) for human immunodeficiency virus (HIV) and hepatitis C virus (HCV) was introduced for blood donation screening in the United States in 1999. This study analyzes temporal trends of these two infections since NAT introduction.

STUDY DESIGN AND METHODS: Donation data from 1999 to 2008 were analyzed; each donation was tested for antibodies and viral RNA for HIV and HCV. Incidence for first-time (FT) donors was derived by multiplying that among repeat (RP) donors by the ratio of NAT yield rates between FT and RP donors. Incidence for all donors was the weighted mean based on percentage of FT and RP donors. Residual risk (RR) was determined using the window-period model.

RESULTS: During the 10-year period approximately 66 million donations were screened with 32 HIV (1:2 million) and 244 HCV (1:270,000) NAT yield donations identified. HCV prevalence among FT donors decreased by 53% for 2008 compared to 1999. HIV and HCV incidence among RP donors increased in 2007 through 2008 compared to 2005 through 2006. During 2007 through 2008, HIV incidence was 3.1 per 10⁵ person-years (py), with an RR estimate of 0.68 per 10⁶ (1:1,467,000) donations; HCV incidence was 5.1 per 10⁵ py, with an RR estimate of 0.87 per 10⁶ (1:1,149,000). The increase in HIV incidence was primarily among 16- to 19-year-old, male African American donors and that in HCV was primarily among Caucasian donors of 50 or more years. Donors from the Southern United States had higher incidence rates.

CONCLUSION: HCV prevalence decreased significantly since NAT introduction. The increase in HIV and HCV incidence in 2007 through 2008 warrants continued monitoring and investigation.

The year 1999 marked a significant improvement in ensuring blood safety in the United States with the implementation of universal donation screening for viral ribonucleic acids (RNA) through nucleic acid testing (NAT) for both human immunodeficiency virus (HIV) and hepatitis C virus (HCV).¹ Studies both before and shortly after the implementation of HIV and HCV NAT showed measurable benefits in terms of potential transfusion transmissions prevented attributed to the reduction in infectious window periods.¹⁻¹⁰ This report presents the surveillance results after the implementation of NAT for these two infections as well as the results of investigations regarding the apparent increase of incidence in the period of 2007 through 2008. Based on these results, potential factors that may be associated with fluctuation of marker rates are identified. Further, the need for continuous monitoring and surveillance and the relevant factors that should be considered in examining trends in the post-NAT era are discussed.

ABBREVIATIONS: FT = first-time (donor); py = person-years; RP = repeat; RR = residual risk.

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Received for publication October 21, 2009; revision received January 13, 2010, and accepted January 16, 2010.
doi: 10.1111/j.1537-2995.2010.02622.x

TRANSFUSION 2010;50:1495-1504.

MATERIALS AND METHODS

The American Red Cross (ARC) Blood Services has 36 regions across the United States that collect more than 6 million blood units from more than 4 million donors annually. The regions were grouped into four areas for geographic analysis: New York-Penn, New England, Penn-Jersey, Johnstown, Northeastern Pennsylvania, Connecticut, Greater Chesapeake, and Potomac as "Northeast"; Southern, Carolinas, Tennessee Valley, River Valley, Gulf Coast, South Carolina, Mid-Atlantic, Appalachian, Alabama, Puerto Rico, Southwest, and Greater Ozarks-Arkansas as "South"; Central Plains, Midwest, Missouri-Illinois, Southeastern Michigan, Central Ohio, North Central, Great Lakes, Heart of America, Badger-Hawkeye, Fort Wayne, Northern Ohio, and Western Lake Erie as "Midwest"; and Southern California, Southern Arizona, Lewis and Clark, Pacific Northwest, and Alameda Contra Costa as "West." Collection areas by state within each region may be found at <http://www.redcrossblood.org/our-regions>. All ARC Blood Services regions use standard blood donor recruitment, predonation deferral criteria, and donation testing procedures.⁵ For the purpose of this study, data representing all voluntary and directed blood donations (allogeneic donations) between January 1, 1999, and December 31, 2008, were reviewed and analyzed. All donations were tested for antibodies to HIV (anti-HIV), HIV RNA, antibodies to HCV (anti-HCV), HCV RNA, and other markers as previously described.^{5,8,11,12} For all markers, only reactive screening test results that were confirmed by additional more specific tests were considered confirmed positive.

Prevalence among first-time (FT) donors was defined as the number of confirmed positives over the number of donations tested. NAT yield was defined as the number of NAT confirmed-positive but antibody-negative donations; the NAT yield rate was the number of NAT yield donations divided by the total number of donations tested for both RNA and antibody.⁵ The incidence rate was defined as the number of confirmed seroconverters or viral RNA converters over total number of person-years (py) observed. A converter is defined as a donor who donated a confirmed-positive blood unit during a targeted period with at least one nonreactive donation up to 730 days (2 years) before the confirmed-positive donation. The interdonation interval immediately before the confirmed-positive donation, divided by 2, representing the midpoint for the conversion event, contributes to the calculation of py of evaluation. The total interdonation interval(s) within the previous 730 days of seronegative donors contributed to the calculation of py of evaluation; the combined py was the total number of py of evaluation among the group of repeat (RP) donors that was used for incidence estimation.⁵ To estimate the incidence among FT donors, NAT yield rates, namely, proportions of viral

RNA-positive but antibody-negative (anti-HIV or anti-HCV) donations out of total tested donations, were determined for all FT donations and separately for all RP donations; the ratio of NAT yield rates between donations from FT and RP donors defined the ratio of incidence between FT and RP donors. Multiplication of the incidence estimate for RP donors with the ratio of NAT yield rates gave rise to incidence estimate for FT donors.^{5,9,13} Incidence for all allogeneic donors was then estimated as weighted mean of incidence estimates for both FT donors and RP donors according to proportions of donors of the two donor groups. Residual risk (RR) was derived through the window-period model by multiplying the incidence estimate with the corresponding infectious window period.¹⁴ The infectious window periods for HIV and HCV were, respectively, defined as 9.1 and 7.4 days.⁹

Data analysis was conducted with computer software (SAS, SAS Institute, Cary, NC).¹⁵ Prevalence rates and incidence rates were compared through Poisson regression.¹⁶ A *p* value of less than 0.05 or a 95% confidence interval (95% CI) of an odds ratio (OR) that does not include 1 defines a significant difference for the purpose of this study.

RESULTS

NAT yield donors

Figure 1A shows the number of HIV and HCV NAT yield donors by year; all yield donors were allogeneic. For the 10-year period between 1999 and 2008, a total of 32 HIV and 244 HCV RNA-positive but antibody-negative donors were identified. This equates to an HIV yield rate of 1 per 2,060,000 donations screened and an HCV yield rate of 1 per 270,000 for the approximate 66 million donations tested over this time; this is consistent with what has been previously reported.⁸ There appeared to be an increasing trend in the number of NAT yield cases between 2000 and 2007 for HIV¹⁷ and between 2000 and 2002 for HCV (1999 included only 10 months during NAT ramp-up) although the numbers leveled off in recent years for both viruses.

Among the 32 HIV NAT yield donors, males accounted for 28 (88%) and females for 4 (12%), with a mean age of 32 years ranging from 17 to 53 years. Donors of 16 to 19 years comprised 9% of yield, 20- to 24-year-olds were 25%, 25- to 29-year-olds were 16%, 30- to 39-year-olds were 19%, 40- to 49-year-olds were 25%, and 50+-year-olds accounted for 6%. The highest yield rates occurred among donors of 20 to 29 years (Fig. 1B). Donors residing in the Southern United States had the highest yield rate and accounted for the majority of the 32 cases (17, or 53%) whereas only seven (22%) occurred in the Midwest with the fewest reported in the Northeast (five cases, or 16%) and West (three cases, or 9%; Fig. 1B). The median viral load for the confirmed positive donation (index) was 2200 copies/mL (ranging from 100 to 7 million

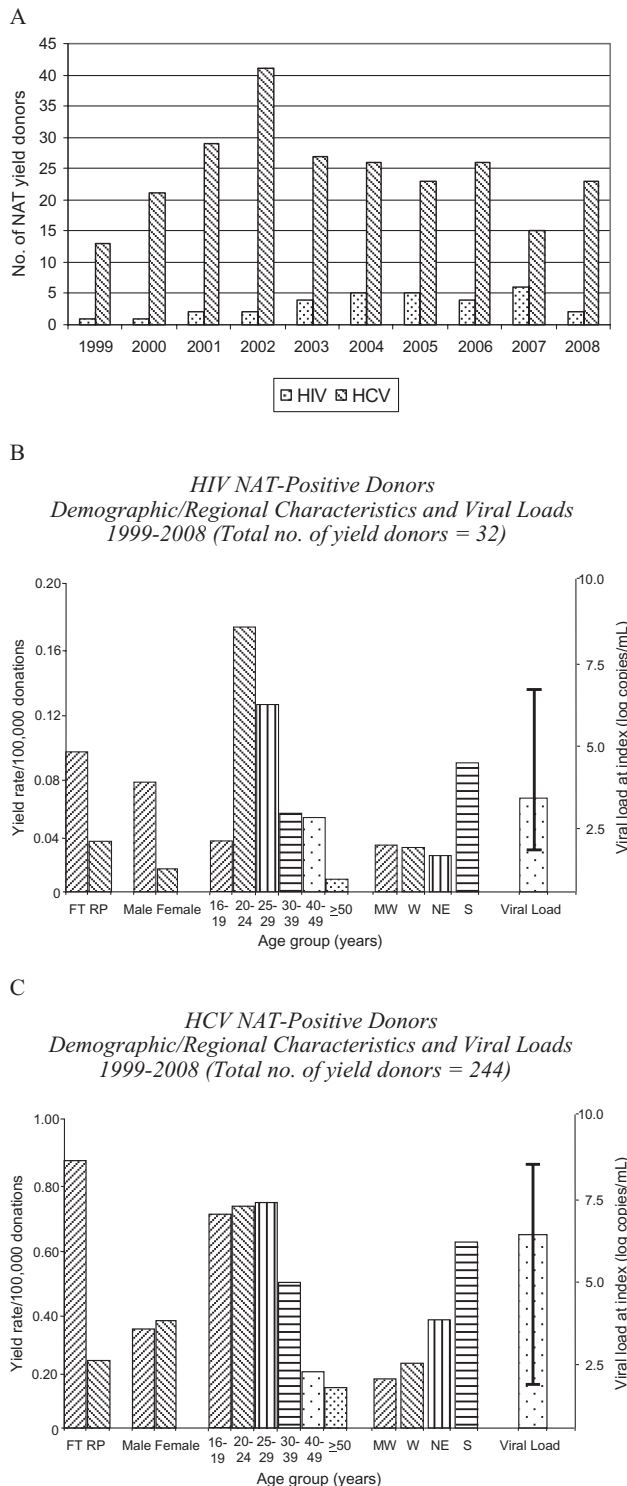


Fig. 1. Number of HIV and HCV NAT yield donors by year from 1999 to 2008. MW = Midwest; NE = Northeast; S = South; W = West.

copies/mL). Among 22 donors who were followed, 16 became enzyme immunoassay (EIA) reactive within a 15-day median (range, 6-64 days) and of those, 12 who continued to be followed became antibody-confirmed-positive within a 21-day median (range, 10-64 days) from index to the first seropositive sample. All donors remained NAT-reactive during their duration of follow-up. Among the remaining donors, six were not observed to seroconvert; their median follow-up time was 7 days (range, 6-33 days); all six donors remained NAT-reactive during their follow-up sampling.

For the 244 HCV NAT yield donors, males accounted for 127 (52%) and females for 117 (48%), with a mean age of 33 years ranging from 17 to 77 years. Donors of 16 to 19 years comprised 24% of yield, 20- to 24-year-olds were 14%, 25- to 29-year-olds were 12%, 30- to 39-year-olds were 22%, and 40- to 49- and 50+-year-old donors both accounted for 14%. The highest yield rates occurred among donors of 16 to 29 years (Fig. 1C). Again, donors residing in the South had the highest yield rate and had the highest number represented of 116 (48%) followed by the Northeast, Midwest, and Western areas, respectively, accounting for 69 (28%), 38 (16%), and 21 (9%) of the donors (Fig. 1C). For 243 donors whose viral load at index donation was available, the median was 2,700,000 copies/mL (ranging from 100 to 380 million copies/mL). Among 92 donors who were followed, 74 became EIA-reactive within a 53-day median (range, 7-207 days) of which 69 remained NAT-reactive during the duration of follow-up. Of the 74 EIA-reactive donors, 58 who continued to be followed became antibody-confirmed-positive within a 74-day median (range, 7-484 days) of which 54 remained NAT-reactive during the duration of follow-up. Thus, fewer than 10% of HCV NAT yield donors who were followed cleared their HCV infection. Ignoring the donor with the longest period to seroconversion reduced the 484-day upper end to seropositivity to 280 days; the donors with the 280- and 484-day antibody-negative periods were sampled regularly for greater than 10 visits each at approximate 30-day intervals during their course of study. Among 15 of the 18 donors who were not observed to seroconvert (i.e., the difference between the 92 total donors who were followed and the 74 who became antibody-reactive), the median follow-up time was 33 days (range, 11-745 days). Three additional longer-term antibody-negative donors who never seroconverted (i.e., immunosilent) were described previously¹⁸ and were not included in the seroconversion analysis presented here.

A total of 12 (38%) HIV and 111 (46%) HCV NAT yield units were identified among FT donations; for the same period, a total of 20 (62%) HIV and 133 (54%) HCV NAT yield units were identified among donations from RP donors. The results represented a NAT yield rate (per 100,000 donations) of 0.094 (12 per 12,733,885 or 1 per 1,060,000) for HIV and 0.872 for HCV (111 per 12,733,883

TABLE 1. Prevalence of HIV and HCV among donations from FT donors, 1999 through 2008

| Year | Number of FT donations | Number of donations confirmed positive for antibody and NAT | | | |
|------|------------------------|---|---------------------------|-----------------|---------------------------|
| | | HIV | | HCV | |
| | | Number positive | /10 ⁵ (95% CI) | Number positive | /10 ⁵ (95% CI) |
| 1999 | 1,390,412 | 165 | 11.9 (10.1-13.7) | 4,795 | 344.9 (335.1-354.6) |
| 2000 | 1,399,881 | 152 | 10.9 (9.1-12.6) | 4,473 | 319.5 (310.2-328.9) |
| 2001 | 1,665,933 | 162 | 9.7 (8.2-11.2) | 5,004 | 300.4 (292.1-308.7) |
| 2002 | 1,270,727 | 152 | 12.0 (10.1-13.9) | 3,265 | 256.9 (248.1-265.7) |
| 2003 | 1,200,307 | 147 | 12.2 (10.3-14.2) | 2,739 | 228.2 (219.7-236.7) |
| 2004 | 1,176,309 | 118 | 10.0 (8.2-11.8) | 2,234 | 189.9 (182.0-197.8) |
| 2005 | 1,173,676 | 133 | 11.3 (9.4-13.3) | 2,165 | 184.5 (176.7-192.2) |
| 2006 | 1,127,287 | 122 | 10.8 (8.9-12.7) | 1,994 | 176.9 (169.1-184.6) |
| 2007 | 1,127,338 | 121 | 10.7 (8.8-12.6) | 1,932 | 171.4 (163.7-179.0) |
| 2008 | 1,202,015 | 114 | 9.5 (7.7-11.2) | 1,964 | 163.4 (156.2-170.6) |

or 1 per 115,000) among FT donations; among donations from RP donors, the corresponding NAT yield rates were 0.038 (20 per 53,203,527 or 1 per 2,660,000) for HIV and 0.250 for HCV (133 per 53,203,527 or 1 per 400,000). Comparison of NAT yield rates among FT donations versus those among RP donations gave a ratio of yield rates of 2.51 for HIV (0.094 for FT donations vs. 0.038 for RP donations) and 3.49 for HCV (0.872 vs. 0.250).

Prevalence of HIV and HCV

Table 1 shows the prevalence of HIV (anti-HIV and/or HIV RNA) and HCV (anti-HCV and/or HCV RNA) among all donations from FT allogeneic donors between 1999 and 2008. Compared to 1999, the prevalence of HCV decreased by 53% in 2008, with an OR at 0.47 (95% CI, 0.45-0.50). Overall between 1999 and 2008, there was an annual decrease of 9% per year compared to each previous year ($p < 0.01$) through Poisson regression analysis. For HIV, there was no significant decline observed for the reporting period (OR, 0.80; 95% CI, 0.63-1.02). The lowest prevalence for both viruses was in calendar year 2008 with a frequency of 1 per 10,550 for HIV and 1 per 612 for HCV.

HIV and HCV prevalence rates for males were approximately twofold higher than for females throughout the 10-year period (Fig. 2). While overall HIV prevalence did not show significant change between 1999 and 2008, there was an annual decrease of 5% ($p < 0.01$) among donations from female donors (Fig. 2A). For HCV (Fig. 2B), there were significant decreases in prevalence for both donations from female and male donors, by 8 and 9%, respectively ($p < 0.01$ for both), although most of the decrease occurred between 1999 and 2004.

Figure 3 shows the prevalence of HCV among all allogeneic donations from FT donors by age over the 10-year period. HCV-infected donors in the 40- to 47-year age group in 1999, or the cohort of donors born in 1952 through 1959, had the highest HCV prevalence. The same age group became 49 to 56 years old in 2008 and hence the changes in distribution reflected the aging of the cohort of HCV-positive individuals.

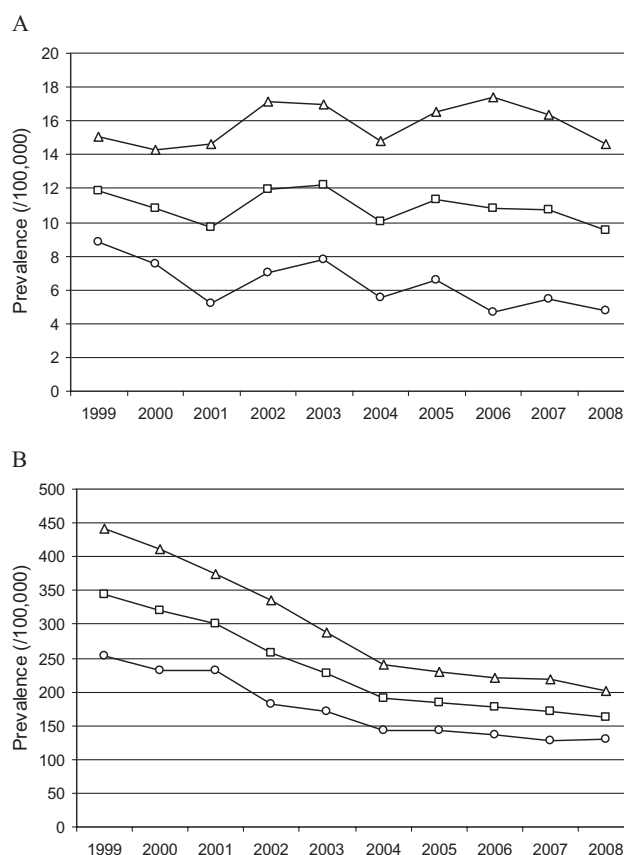


Fig. 2. Prevalence of HIV (A) and HCV (B) among FT donations by donor sex, 1999 through 2008. (○) Female; (△) male; (□) total.

Incidence and RR of HIV and HCV

Due to the small numbers of seroconverters or viral RNA converters, namely, incident cases, incidence rates were estimated for five 2-year periods among RP donors. For HIV, the incidence in 2007 through 2008 (2.2 per 100,000 py) showed a significant increase compared to that in 1999 through 2000 (1.5 per 100,000 py; OR, 1.44; 95% CI, 1.04-1.98; Table 2). For HCV, incidence varied among periods, especially between 2005 through 2006 (2.0 per

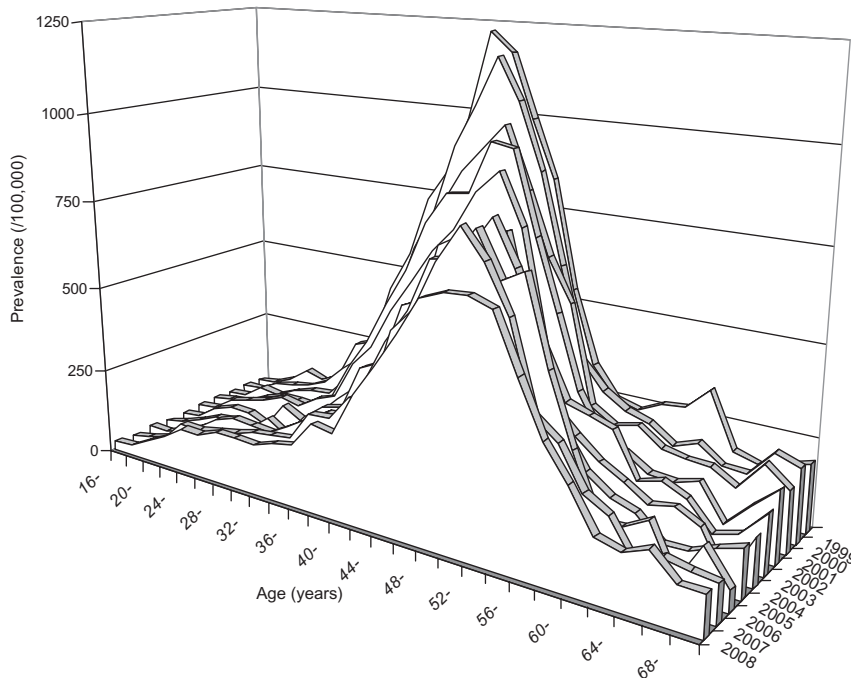


Fig. 3. Prevalence of HCV among donations from FT donors by age, 1999 through 2008. The highest prevalences (/100,000 donations) by age group for each year were 981.6.0 to 1225.3 for 40 to 47 years in 1999, 910.3 to 1165.5 for 40 to 47 years in 2000, 827.1 to 995.8 for 42 to 49 years in 2001, 808.1 to 961.2 for 42 to 49 years in 2002, 730.7 to 904.0 for 44 to 51 years in 2003, 706.0 to 769.9 for 44 to 51 years in 2004, 699.2 to 819.3 for 46 to 53 years in 2005, 682.9 to 804.9 for 46 to 53 years in 2006, 620.4 to 825.5 for 48-55 years in 2007, and 652.8 to 679.6 for 48 to 55 years in 2008.

100,000 py) and 2007 through 2008 (3.0 per 100,000 py; OR, 1.52; 95% CI, 1.16-2.01; Table 2). Incidence rates among RP donors by sex are shown in Fig. 4. For HIV, males clearly had higher incidence than females throughout the five 2-year periods ($p < 0.01$; Fig. 4A). However, the rate of HCV-infected female donors appeared to be higher than that observed for male donors for all 2-year periods (as well as the total) except for 2001 through 2002 (Fig. 4B); however, the overall difference between the five 2-year periods was not significant ($p = 0.22$). The increase in HCV in 2007 through 2008 was primarily among those of age 50 years or older for both sexes (data not shown). By geographic area, the South had higher HIV incidence (Fig. 5A) across the five 2-year periods and also higher HCV incidence (Fig. 5B; $p < 0.01$ for both).

Also shown in Table 2 are incidence estimates for all donors including both FT and RP donors. The overall incidence among all allogeneic donors in 2007 through 2008 was 3.1 per 100,000 py for HIV and 5.1 per 100,000 py for HCV. In 1999 through 2000, the corresponding incidence rates were 2.3 and 4.3 per 100,000 py. Assuming an infectious window period of 9.1 days for HIV and 7.4 days for HCV, the RR for HIV in 2007 through 2008 was 0.68 per

1,000,000 donations, or 1 per 1,466,614, and the RR for HCV was 0.87 per 1,000,000 donations, or 1 per 1,148,577 (Table 3).

Assuming that HIV NAT reduces the infectious window period from 16 days with anti-HIV alone to 9.1 days,^{8,9} the reduced incremental RR due to NAT was estimated at 0.052 per 100,000 donations, which would translate into interdiction of 1 HIV infectious unit per 1,934,230 donations or 34 expected interdicted units out of a total of approximately 66 million donations tested. Similarly, assuming that HCV NAT reduces the infectious window period from 51 days with anti-HCV alone to 7.4 days,⁹ the reduced RR was estimated at 0.513 per 100,000 donations or 1 per 194,942 donations, with an estimated interdiction of 338 units of the approximate 66 million donations tested. The estimated results for HIV were very close to the 32 HIV NAT yield units identified; however, the estimates for HCV were higher than the 244 HCV NAT yield units identified.

Analysis of factors associated with the increase in incidence

To investigate possible factors associated with the increase in incidence among RP donors in the period of 2007 through 2008, HIV and HCV incidence rates were analyzed by various demographic features together with the year of donation. Since the increase was greatest from 2005 through 2006 to 2007 through 2008 (Table 2), incidence data among RP donors for the two periods were examined.

There was a total of 92 HIV incident cases in 2007 through 2008 compared to 67 in 2005 through 2006; for HCV, the numbers were, respectively, 127 and 84 (Table 2). Review of actual numbers of seroconverting or NAT yield cases showed that there were 21 HIV incident cases who were male donors of 16 to 19 years in 2007 through 2008 whereas the same group had only six HIV incident cases in 2005 through 2006 (Table 4); this group alone accounted for 60% of the observed increase in HIV incident cases in 2007 through 2008 compared to 2005 through 2006 $[(21-6)/(92-67) \times 100]$. Through Poisson regression, the increase in HIV incidence density (/py) within this group from 6 per 180,667 py in 2005 through 2006 to 21 per 201,458 py in 2007 through 2008 is significant ($p = 0.01$), with an OR of 3.14 (95% CI, 1.27-7.78). For HCV, the number of incident cases in the 50+ age group of both

TABLE 2. HIV and HCV incidence rates (/100,000 py), from 1999 through 2008

| Years | Incidence in RP donors | | | Incidence rate in FT donors (/10 ⁵ py) | | | Weighted incidence rate all donors (/10 ⁵ py)* | | |
|-----------|-----------------------------|--------|------------------|---|--------------------|-------------------------|---|-------------------|--|
| | HIV | | HCV | HIV† rate (95% CI) | HCV† rate (95% CI) | Percentage of FT donors | HIV rate (95% CI) | HCV rate (95% CI) | |
| | Total py (10 ⁵) | Number | | | | | | | |
| 1999-2000 | 41.66 | 62 | 2.30 (1.89-2.82) | 3.74 (2.91-4.79) | 8.04 (6.58-9.82) | 34.7 | 2.27 (1.77-2.91) | 4.30 (3.52-5.25) | |
| 2001-2002 | 44.61 | 67 | 2.40 (1.98-2.90) | 3.77 (2.97-4.79) | 8.37 (6.93-10.12) | 33.8 | 2.27 (1.79-2.88) | 4.42 (3.66-5.34) | |
| 2003-2004 | 43.90 | 84 | 2.55 (2.12-3.07) | 4.80 (3.88-5.95) | 8.90 (7.40-10.72) | 29.9 | 2.78 (2.24-3.44) | 4.45 (3.70-5.36) | |
| 2005-2006 | 42.96 | 67 | 1.96 (1.58-2.42) | 3.91 (3.08-4.97) | 6.82 (5.51-8.45) | 29.2 | 2.25 (1.77-2.86) | 3.38 (2.73-4.18) | |
| 2007-2008 | 42.68 | 92 | 2.98 (2.50-3.54) | 5.41 (4.41-6.64) | 10.38 (8.73-12.36) | 29.2 | 3.11 (2.53-3.81) | 5.14 (4.32-6.12) | |

* Weighted incidence for all donors was derived by the sum of the incidence rate (IR) among FT donors multiplied by the percentage of FT donors among all donors plus the IR in RP donors times the percentage of RP donors among all donors, or [(FT IR) (%FT/100)] + [(RP IR) (1 - %FT/100)].

† Incidence rate among FT donors was derived by multiplying that among RP donors with the FT/RP ratio of NAT yield rates (/100,000 donations) during 1999 through 2008: 2.51 for HIV (0.094 for FT donations vs. 0.038 for RP donations) and 3.49 for HCV (0.872 for FT donations vs. 0.250 for RP donations).

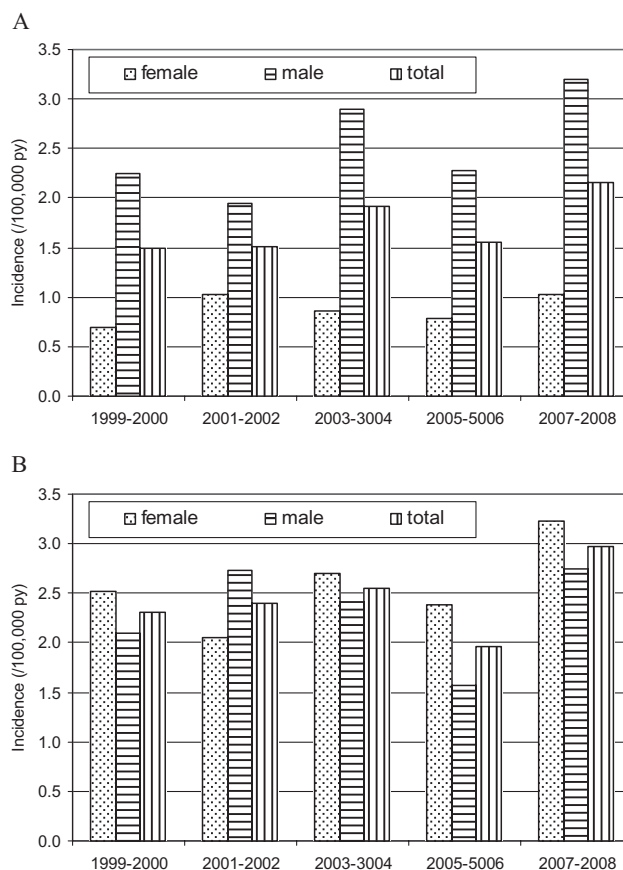


Fig. 4. Incidence (/100,000 py) of HIV (A) and HCV (B) among RP donors by donor sex, 1999 through 2008.

sexes in 2005 through 2006 was 11 and for 2007 through 2008 was 42 (Table 5); this increase accounted for 72% of the total increase in incident cases in 2007 through 2008 [(42-11)/(127-84) × 100]. Comparison of HCV incidence density between the two periods showed an OR of 4.02 (95% CI, 1.35-11.96; $p = 0.01$) for female donors (from 4 per 747,284 py to 17 per 789,209 py) and 3.44 (95% CI, 1.49-7.96; $p < 0.01$) for male donors (from 7 per 951,675 py to 25 per 986,977 py).

Further examination of the 21 HIV cases of male donors aged 16 to 19 years in 2007 through 2008 showed that 11 were African Americans, six were Caucasians, one was "other," and three had unknown race. For 2005 through 2006, four of the six cases were African Americans and two were Caucasians. Incidence density among African Americans increased by 143% from 46.0 per 10⁵ py in 2005 through 2006 to 111.6 per 10⁵ py in 2007 through 2008 (Table 4). The overall increase in this group of donors, as a percentage change from 2005 through 2006 to 2007 through 2008 when all races were combined, was 214%.

For the 42 cases of HCV incident infection in donors 50 years or older in 2007 through 2008, 33 (79%) were Caucasian and then three each were African American, other, and unknown; for 2005 through 2006, the four race

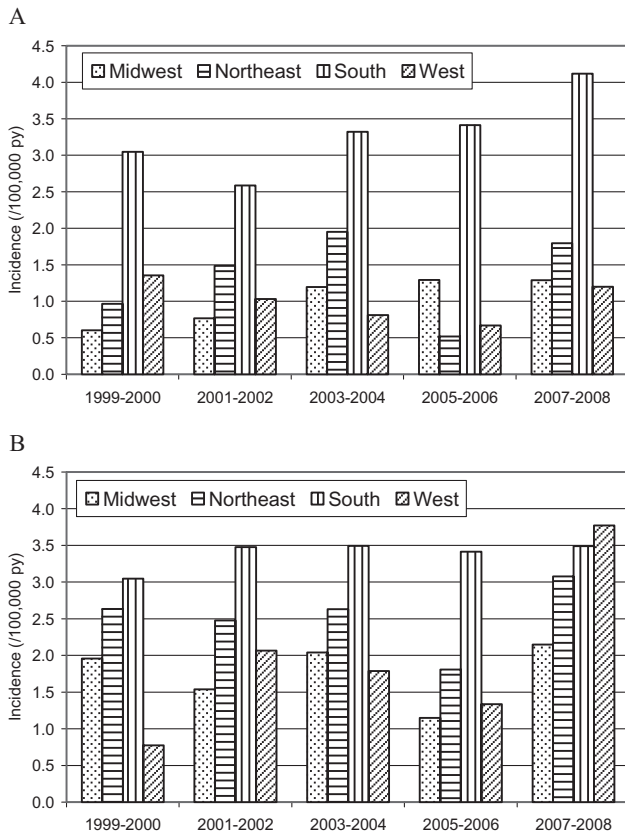


Fig. 5. Incidence (/100,000 py) of HIV (A) and HCV (B) among RP donors by area, 1999 through 2008.

categories accounted for six, one, two, and two cases, respectively, of the 11 total cases (Table 5). Among Caucasian males, incidence density increased by 429% from 0.4 per 10^5 py in 2005 through 2006 to 2.0 per 10^5 py in 2007 through 2008; among Caucasian females, incidence density increased by 331% from 0.5 per 10^5 py in 2005 through 2006 to 2.1 per 10^5 py in 2007 through 2008 (Table 5). The overall increase for all sex and race groups for HCV-infected donors of 50+ years from 2005 through 2006 to 2007 through 2008 was 265%.

DISCUSSION

The results from this study describe the prevalence and incidence of HIV and HCV infections among allogeneic donors since the implementation of NAT in the United States for blood donor screening. Recently, we reported on the prevalence and incidence of hepatitis B virus infections among donors and donations.¹² Due to the large size of our donor population and standardized system procedures, these results represent the most reliable assessments of viral risks of the US blood supply using currently implemented safety measures.

Further, the results of this study provide direct evidence of the benefits of HIV and HCV NAT during the qualification of approximately 66 million donations. A total of 32 HIV NAT yield units (yield of 1 per 2 million) and 244 HCV NAT yield units (yield of 1 per 270,000) were interdicted during the 10-year period. Most NAT yield

TABLE 3. HIV and HCV RRs (/1,000,000 donations), from 1999 through 2008*

| Period | RP donations | | FT donations | | Percent† | All donations | |
|-----------|-------------------|-------------------|-------------------|-------------------|----------|-------------------|-------------------|
| | HIV risk (95% CI) | HCV risk (95% CI) | HIV risk (95% CI) | HCV risk (95% CI) | | HIV risk (95% CI) | HCV risk (95% CI) |
| 1999-2000 | 0.37 (0.29-0.48) | 0.47 (0.38-0.57) | 0.93 (0.73-1.19) | 1.63 (1.34-1.99) | 21.7 | 0.49 (0.38-0.63) | 0.72 (0.59-0.88) |
| 2001-2002 | 0.37 (0.29-0.48) | 0.49 (0.40-0.59) | 0.94 (0.74-1.19) | 1.70 (1.40-2.05) | 21.5 | 0.50 (0.39-0.63) | 0.75 (0.62-0.90) |
| 2003-2004 | 0.48 (0.39-0.59) | 0.52 (0.43-0.62) | 1.20 (0.97-1.48) | 1.81 (1.50-2.17) | 17.9 | 0.61 (0.49-0.75) | 0.75 (0.62-0.90) |
| 2005-2006 | 0.39 (0.31-0.49) | 0.40 (0.32-0.49) | 0.98 (0.77-1.24) | 1.38 (1.12-1.71) | 17.7 | 0.49 (0.39-0.63) | 0.57 (0.46-0.71) |
| 2007-2008 | 0.54 (0.44-0.66) | 0.60 (0.51-0.72) | 1.35 (1.10-1.65) | 2.11 (1.77-2.51) | 17.8 | 0.68 (0.56-0.84) | 0.87 (0.73-1.04) |

* RR was derived by incidence multiplied by window period in year, 9.1/365 or 0.025 for HIV and 7.4/365 or 0.020 for HCV.

† Percentage of donations from FT donors; RR for all donations was derived by the sum of RR for FT donations multiplied by the percentage of donations from FT donors plus RR for RP donations multiplied by the percentage of donations from RP donors.

TABLE 4. HIV incidence among male, RP donors of 16 to 19 years by race, 2007 through 2008 versus 2005 through 2006

| Race | 2005-2006 | | | | 2007-2008 | | | | Percentage change | |
|-------------------|------------------|-----------------|----------|---------------------|------------------|-----------------|----------|---------------------|-------------------|-----------|
| | Number of donors | Number of cases | Total py | /10 ⁵ py | Number of donors | Number of cases | Total py | /10 ⁵ py | Number of donors | Incidence |
| African Americans | 10,711 | 4 | 8,687 | 46.0 | 11,973 | 11 | 9,853 | 111.6 | 11.8 | 142.5 |
| Caucasians | 129,511 | 2 | 116,819 | 1.7 | 160,352 | 6 | 147,083 | 4.1 | 23.8 | 138.3 |
| Other | 15,903 | 0 | 12,991 | 0.0 | 21,047 | 1 | 17,383 | 5.8 | 32.3 | N/A |
| Unknown | 50,744 | 0 | 42,170 | 0.0 | 33,015 | 3 | 27,139 | 11.1 | -34.9 | N/A |
| Total | 206,869 | 6 | 180,667 | 3.3 | 226,387 | 21 | 201,458 | 10.4 | 9.4 | 213.9 |

TABLE 5. HCV incidence among male and female, RP donors of 50+ years by race, 2007 through 2008 versus 2005 through 2006

| Sex | Race | 2005-2006 | | | | 2007-2008 | | | | Percentage change | |
|-------------------------|-------------------|------------------|-----------------|-----------|---------------------|------------------|-----------------|-----------|---------------------|-------------------|-----------|
| | | Number of donors | Number of cases | Total py | /10 ⁵ py | Number of donors | Number of cases | Total py | /10 ⁵ py | Number of donors | Incidence |
| | | | | | | | | | | | |
| Male | Caucasians | 510,945 | 3 | 779,267 | 0.4 | 582,923 | 18 | 883,444 | 2.0 | 14.1 | 429.2 |
| | African Americans | 13,493 | 1 | 19,325 | 5.2 | 14,374 | 2 | 20,551 | 9.7 | 6.5 | 88.1 |
| | Other | 20,891 | 2 | 29,115 | 6.9 | 21,776 | 3 | 30,511 | 9.8 | 4.2 | 43.1 |
| | Unknown | 91,456 | 1 | 123,969 | 0.8 | 41,324 | 2 | 52,472 | 3.8 | -54.8 | 372.5 |
| | Total | 636,785 | 7 | 951,675 | 0.7 | 660,397 | 25 | 986,977 | 2.5 | 3.7 | 244.4 |
| Female | Caucasians | 417,697 | 3 | 605,052 | 0.5 | 489,066 | 15 | 702,783 | 2.1 | 17.1 | 330.5 |
| | African Americans | 14,950 | 0 | 20,243 | 0.0 | 16,099 | 1 | 21,845 | 4.6 | 7.7 | N/A |
| | Other | 14,290 | 0 | 18,712 | 0.0 | 15,643 | 0 | 20,501 | 0.0 | 9.5 | N/A |
| | Unknown | 79,908 | 1 | 103,277 | 1.0 | 36,128 | 1 | 44,080 | 2.3 | -54.8 | 134.3 |
| | Total | 526,845 | 4 | 747,284 | 0.5 | 556,936 | 17 | 789,209 | 2.2 | 5.7 | 302.4 |
| All sex and race groups | | 1,163,630 | 11 | 1,698,959 | 0.6 | 1,217,333 | 42 | 1,776,186 | 2.4 | 4.6 | 265.2 |

donors were in their early 30s and were primarily from the Southern portion of the United States; for HIV, males comprised a disproportionate number of cases. Assuming that a mean of 1.5 transfusable components are generated from each donated unit, HIV and HCV NAT prevented the release of 48 HIV RNA-positive components and 366 HCV RNA-positive components. The viral loads of the donations (100 copies/mL or greater) supported their likely infectivity. While the number of interdicted units may not represent large numbers considering the costs of implementing the test, other public health impacts should be considered, such as secondary transmissions from these infected asymptomatic individuals.^{6,19}

The observed number of HIV NAT yield units at 32 was almost identical to the 34 that were estimated; however, the 244 HCV NAT yield units were less than the estimated number of 338. The discrepancy in HCV modeled versus observed yield likely reflects an overestimate of the HCV NAT window-period reduction. Our observations suggest that the time between the first observed NAT-positive sample and the first observed seropositive follow-up sample was 51 days; however, the relatively long spacing between follow-up samples does not permit precise definition of the actual time to seroconversion and thus the published 51-day window period from NAT reactivity to seropositivity may be an overestimate. The number of NAT yield cases showed an apparent increase between 1999 and 2004 for HIV and between 1999 and 2002 for HCV, although the numbers for both viruses have leveled off in recent years (Fig. 1). A recent study suggests that there was an increase in the number of HIV variants and drug-resistant mutants observed from 1999 to 2005 but the frequency of these is still less than 10% of all HIV infections in blood donors, with very few drug-resistant mutations identified in newly infected donors versus donors with established HIV infections.¹⁷ It is important to monitor viral variants and mutants as well as their possible association with trends in NAT yield.²⁰

The ratios of NAT yield rates obtained in this study, 2.51 for HIV and 3.49 for HCV, were consistent with earlier estimates also among ARC blood donors,⁵ 2.08 for HIV and 2.42 for HCV. As they were derived from 66 million donations over the 10-year period, the current ratio estimates should better reflect the relative levels of incidence for the two infections among FT and RP blood donors to the ARC.

Surveillance and monitoring of test results may contribute to blood safety by identifying adverse trends and by defining their underlying causes. During this study, significantly increased incidence rates of both HIV and HCV were observed in 2007 through 2008 compared to 2005 through 2006. Interestingly, the change in incidence was not reflected in the number of NAT yield donations. Demographic analysis of the population of donors with incident HIV infection showed that most of the excess of

cases could be attributed to male donors in the 16- to 19-year age group. Further, within that group, the major contribution (11 of 21) came from African American donors, even though they represented only approximately 5% of the subpopulation. In addition, incidence rates among both young African American and Caucasian donors were about 2.4-fold higher in 2007 through 2008 than in the preceding 2 years (Table 4).

In contrast, the major contribution to increased incident cases of HCV was found among male and female blood donors more than 50 years old with the large majority from Caucasian donors. Although this group had the lowest incidence rate, they nevertheless showed the greatest increase in HCV incidence and represent the largest proportion of all donors in the age group (Table 5). The proportional increase in the actual number of donors between 2005 through 2006 and 2007 through 2008 was very much smaller than the increase in incidence rates.

The increase in the incidence of HIV and HCV is a matter of concern, because it reflects an increase in residual infection risk. For HIV, the risk is disproportionately focused among young donors. The incidence rate for HIV among young African American donors was 112 per 100,000 py, approximately the same as that reported by the CDC for all African American males in 2006 (CDC: HIV/AIDS Surveillance Report 2007, <http://www.cdc.gov/hiv/topics/surveillance/resources/reports/>). This is particularly alarming, as the donors identified in this study were RP donors, who have usually been shown to have a much lower incidence rate than that for the population at large. The finding suggests that donor selection procedures may have been unsuccessful, and more attention may need to be given to risk-factor questioning and perhaps other factors such as privacy and peer pressure among the growing population of young donors.

The increased incidence of HCV infection among older donors is not readily explained and requires further investigation. In the past, studies have suggested that the majority of recently HCV-infected donors who acknowledge a risk behavior have injected illicit drugs.²¹ It seems unlikely that this explains the increased incidence among these older donors. On the other hand, it has recently been noticed that increased use of nonhospital health care facilities may contribute to HCV infections.²² It is also of interest to note that, in some European countries, endoscopy is a risk factor for HCV infection and there has been recent concern about such risk in a number of well-publicized clusters in the United States.^{23,24} Given that endoscopy is recommended for those aged 50 or more, this is a possible contributor to the observations in this study.

The very low levels of viral infections in blood donors and the dynamic nature of our donor population dictate the need for continuous monitoring of data from large blood programs to establish if trends exist and to identify

risk factors in such donor groups if trends are identified. Although the data from 2007 through 2008 demonstrate an increase in the incidence rates for both HIV and HCV, the results in Tables 2 and 3 showed clear fluctuations from period to period. If upward trends continue to be observed, recruitment and screening practices in donor groups that contribute to these increases may need to be examined and modified, including the use of community outreach and education.

CONFLICT OF INTEREST

None of the authors had a conflict of interest.

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