Estimated Risk of Human Immunodeficiency Virus and Hepatitis C Virus Infection among Potential Organ Donors from 17 Organ Procurement Organizations in the United States

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To prevent unintentional transmission of blood-borne pathogens through organ transplantation, organ procurement organizations (OPOs) screen potential donors by serologic testing to identify human immunodeficiency virus (HIV) and hepatitis C virus (HCV) infection. Newly acquired infection, however, may be undetectable by serologic testing. Our objective was to estimate the incidence of undetected infection among potential organ donors and to assess the significance of risk reductions conferred by nucleic acid testing (NAT) versus serology alone. We calculated prevalence of HIV and HCV—stratified by OPO risk designation—in 13 667 potential organ donors managed by 17 OPOs from 1/1/2004 to 7/1/2008. We calculated incidence of undetected infection using the incidence-window period approach. The prevalence of HIV was 0.10% for normal risk potential donors and 0.50% for high risk potential donors; HCV prevalence was 3.45% and 18.20%, respectively. For HIV, the estimated incidence of undetected infection by serologic screening was 1 in 50 000 for normal risk potential donors and 1 in 11 000 for high risk potential donors; for HCV, undetected incidence by serologic screening was 1 in 5000 and 1 in 1000, respectively. Projected estimates of undetected infection with NAT screening versus serology alone suggest that NAT screening could significantly reduce the rate of undetected HCV for all donor risk strata.

Key words: Donor screening, infection risk, nucleic acid testing, organ transplantation

Abbreviations: HIV, Human immunodeficiency virus; HCV, hepatitis C virus; NAT, nucleic acid-amplification tests; FDA, food and drug administration; OPO, organ procurement organization; RIBA, recombinant immunoblot assay; WB, Western blot.

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Background

Transmission of human immunodeficiency virus (HIV) and hepatitis C virus (HCV) can occur through solid organ transplantation (1–4). Strategies to reduce transmission of these bloodborne pathogens from donor to recipient include assessing donor medical and behavioral risk, and laboratory testing for anti-HIV and anti-HCV seroreactivity in all potential organ donors. For most laboratory tests, there are window periods during which infection cannot be detected in donors with newly acquired infection. Compared with serologic testing, nucleic acid-amplification tests (NAT) shorten the window period through detection of the virus in plasma. In 2007 a donor, who was found to be nonreactive for HIV and HCV by routine serologic screening, was later found to be NAT-positive after four organ recipients were infected with HIV and HCV (5). This incident underscored the need for a better understanding of the prevalence of HIV and HCV among potential organ donors and for evaluation of more sensitive screening tests to reduce the risk of undetected infection.

Estimates of HIV and HCV infection rates during the window period for serologic testing (i.e. undetected infection) were recently reported in US blood and tissue donors but have not been estimated for organ donors. For first-time blood donors, 1 in 3.1 million donations for HIV and 1 in 270 000 for HCV were nonreactive by serology assays, but positive by NAT (6). The estimated risk of undetected
infection among tissue donors for serologic testing is much higher: 1 in 55 000 for HIV and 1 in 42 000 for HCV (7). The US Food and Drug Administration (FDA) currently mandates NAT screening for all blood and tissue donors for HIV and HCV, but no government agency mandates NAT screening for organ donors (8). As of 2008, approximately one-half of the 58 US organ procurement organizations (OPOs) voluntarily performed HIV and HCV NAT on all or at least some subset of their potential donors (9).

When transplant centers decide whether to accept an organ for transplantation, they rely on serologic test results as well as the ‘high risk’ designation assigned by OPOs during donor evaluations. OPOs are required to document the potential donor’s infectious risk status utilizing risk criteria for HIV transmission outlined in the PHS 1994 guidelines (10). Many OPOs have also used these criteria to evaluate risk for hepatitis virus transmission, as indicated by donor medical-behavioral history questionnaires (Appendix 1). A 2008 survey of US OPOs reported that, on average, 7.7% of an OPO’s donors with organs recovered for transplantation, were designated as high risk, ranging from 2.3 to 26.1% (11). Because transplants can be life saving, recipients and transplant surgeons may accept organs from high risk donors due to the shortage of available organs for transplantation; in 2008, 9465 candidates died or became too ill to benefit from transplantation while waiting for an available organ (12). Organ acceptance may be influenced by type of organ needed, type of risk factor identified, medical health status of the candidate and laboratory testing results.

To appropriately weigh the risk of unintentional infection with HIV or HCV against the risk of delayed transplant, providers and patients must be able to reasonably assess risk. Currently there are no published studies that estimate the risk of undetected infection among potential organ donors by serologic testing in the United States. The objectives of this study were to (1) calculate the prevalence of HIV and HCV among a large subset of potential organ donors in the United States; (2) estimate the incidence of HIV and HCV among potential organ donors during the window periods for serologic and NAT screening.

Materials and Methods

Study population
A sample of 17 of the 58 OPOs in the United States participated voluntarily in this study; these 17 OPOs manage over half of US organ donors (12). Participating OPOs constituted a convenience sample of OPOs that submitted serologic screening results through three large reference laboratories to the CDC for the designated study period. Serologic tests were performed at local OPO, hospital or reference laboratories. The geographic distribution of participating OPOs was concentrated in the northeast, mid-Atlantic and western states, including Alaska (Figure 1). Nucleic acid testing results were not available for the majority of participating OPOs and were available for only a fraction of donors within OPOs performing NAT, thus NAT results were not considered for analysis in this study.

Demographic and serologic data from January 2004 to July 2008 were requested from participating OPOs for all potential organ donors, including those who were consented but subsequently had no organs recovered. Serologic data collected from participating OPOs included anti-HIV and anti-HCV test results. Western blot (WB) confirmatory testing results for anti-HIV and recombinant immunoblot assay (RIBA) confirmatory tests for anti-HCV were also collected when available. Data on high risk designation, as determined by the OPO based on criteria presented in Appendix I, were collected. Participating OPOs also submitted information on the assay and generation of the specific tests used over the study period. All potential donors for whom data were requested had legal consent for organ donation and serologic test results. This study was determined to be exempt from human subjects review by the institutional review board at the Centers for Disease Control and Prevention in August, 2008.

Prevalence of bloodborne pathogens among potential organ donors
To calculate crude prevalence for HIV and HCV among potential donors, the number of positive results for a given serologic test was divided by the total number of potential donors tested. To account for false positive serologic results, adjustment factors were created directly from data submitted by OPOs from subsets of donors with WB or RIBA confirmatory tests available. For example, within the subset of HIV-positive serologic tests with WB availability, the number of positive anti-HIV serologies with positive WB results was divided by the number of all HIV-positive serologies with WB positive, negative or indeterminate results to calculate a conservative adjustment factor; a more liberal adjustment factor using both positive and indeterminate WB results as the numerator was calculated. The same process was followed for HCV, using available RIBA testing to create conservative and liberal adjustment factors. For HIV, there were 11 antibody-reactive cases for which confirmatory WB tests were available; 4 (0.36) had positive WB results, and 2 (0.18) had indeterminate results. For HCV, there were 183 antibody-reactive cases with RIBA confirmatory tests available; 142 (0.78) were RIBA positive, and 11 (0.06) were RIBA indeterminate. The adjustment factors were determined to be the midpoint of the conservative and liberal estimates: 0.45 for HIV and 0.81 for HCV.

The prevalence of HIV and HCV among potential organ donors was calculated for all potential donors and for donors stratified by OPO risk designation. Designations included ‘normal risk’ (i.e. actively designated as not ‘high risk’), ‘high risk’ and ‘missing risk’ (i.e. risk status was either not recorded or not available for this study). The raw prevalence was multiplied by an adjustment factor (described above) to reflect prevalence adjusted for false positive serologic tests. Credible intervals surrounding the prevalence estimates were generated using Monte Carlo simulations for each pathogen and risk category. For the simulations, the number of tests reactive by serology was assigned a Poisson distribution. The adjustment factors were assigned triangular distributions with minimum and maximum values reflecting the conservative and liberal adjustment factor calculations: (0.36–0.55) for HIV and (0.78–0.84) for HCV. Values were drawn from these probability distributions for 10 000 repetitions, resulting in 95% credible intervals.

Estimating incidence of undetected infection among potential organ donors
Incidence of undetected HIV and HCV infection in potential organ donors was calculated using the incidence-window period model originally developed for blood donors, which involves multiplying the incidence of infection (i.e. the yearly rate of newly acquired infection) in the donor population by the length of the window period (13–18). The infectious window period is defined as the time after infectivity when the virus reaches a sufficient level in plasma to be transmissible up to the time of detection by NAT or serologic screening methods (14,16,17). The incidence-window period
HIV and HCV among Potential Organ Donors in the United States

Figure 1: Geographic distribution of the 17 organ procurement organizations (OPOs) participating in the study; participating OPOs fully covered states shaded dark gray and partially covered states shaded light gray, representing over 50% of all US organ donors.

Model was recently modified for estimation of undetected infection in the tissue donor population in the United States and to organ and tissue donor populations in Canada (7,16). Incidence in the blood donor population can be determined by examining seroconversion in repeat blood donors (14). Since there are no repeat donations in the deceased potential organ donor population, incidence must be estimated by extrapolating from blood donor data.

Estimating the yearly incidence of HIV and HCV among potential organ donors required making projections from incidence estimates in blood donors during the same time period. It was assumed that prevalence differences between the organ donors in this study and blood donors in published literature would reflect differences in incidence. Thus, the ratio of organ donor prevalence to published blood donor prevalence was multiplied by the published incidence in blood donor population to attain the incidence in the study population of organ donors. Published incidence and prevalence rates from a population of blood donors who had donated to Red Cross Blood Services from 2007 and 2008 were used to make this calculation (18).

To create ranges around incidence calculations, Monte Carlo simulations were used to reflect the combined variation in input parameters, including organ donor prevalence as calculated in this study, blood donor prevalence and incidence as reported in the literature, and window periods for serologic and NAT tests (Table 2). Since the variability surrounding window period inputs was unknown, triangular distributions with 50% variation were assigned to reflect unknown (and thus conservative) distribution and variance parameters. Ranges around incidence estimates were generated from 10,000 repeated calculations resulting in a 95% credible interval around the incidence estimates. All analyses were calculated with SAS 9.2 and in Crystal Ball software applications.

Results

Serologic data were submitted for 13,677 potential donors (n = 13,607 for anti-HIV and n = 13,349 for anti-HCV) (Table 1). For anti-HIV, overall adjusted prevalence was 0.21% with a credible interval (CI) of 0.15–0.29%. Prevalence was lowest for normal risk donors (n = 11,245) at 0.10% (CI = 0.06–0.16%) and highest for donors with missing risk status (n = 1182) at 1.00% (CI = 0.57–1.54%). For high risk donors (n = 1180), prevalence was 0.50% (CI = 0.21–0.86%). The overall adjusted prevalence for anti-HCV was 5.58% (CI = 5.15–6.06%). The adjusted anti-HCV prevalence was lowest for normal risk donors at 3.45% (CI = 3.10–3.85), and highest for high risk donors at 18.20% (CI = 15.74–20.91%). For donors with missing risk status, the adjusted HCV prevalence was 12.88% (CI = 10.83–15.08).

Out of all potential organ donors tested, 11.3% (n = 1538) did not have any organs recovered. Out of the 64 anti-HIV-positive donors, 58 (90.6%) did not have any organs recovered. Of the six HIV-positive donors with organs
recovered, five were designated as normal risk and one was missing risk status; none were transplanted. Of 924 anti-HCV-positive potential donors, 36.0% (N = 332) did not have any organs recovered. Of the 591 anti-HCV-positive donors who did have organs recovered, 32.3% were considered high risk donors, 63.1% were considered normal risk donors and 4.6% were missing risk status.1

Yearly incidence estimates for HIV among all potential organ donors was approximately 61 per 100 000 person-years; for normal risk, high risk and missing risk donors the incidence was 29, 142 and 283 per 100 000 person-years, respectively. The overall incidence estimate for HCV was approximately 168 per 100 000 person-years; for normal risk, high risk and missing risk donors, incidence was 104, 547 and 387 per 100 000 person-years, respectively.

For normal risk donors, the estimated incidence of undetected HIV infection during the 22-day window period for serologic testing was approximately 1.72 per 100 000 person-years, and 0.55 per 100 000 person-years for the 7-day window period for NAT screening. For high risk donors, undetected HIV incidence per 100 000 person-years during the window periods for serologic and NAT screening were 104.94 and 10.49, respectively. The 95% credible intervals for undetected HIV infection during serologic and NAT window periods did not overlap for any risk strata, indicating significant potential reductions conferred by NAT screening as compared to serology alone for HCV.

**Discussion**

In our prevalence study of over 13 000 potential organ donors, approximately 1 in 500 were positive for anti-HIV after adjusting for false-positive serologic testing, with higher prevalence among high risk donors (1 in 200) versus normal risk donors (1 in 1000). One in 18 of all potential donors were positive for anti-HCV after adjusting for false-positive serologic testing; the prevalence among high risk donors was striking (1 in 5), and that among normal risk donors was substantial (1 in 30).

Findings suggest that organ donors are at higher risk of undetected infection by serologic screening (i.e. incident infection during the window period) compared to tissue donors. In 2004, tissue donors were reported to have a 1 in 55 000 risk of undetected HIV and 1 in 42 000 risk of undetected HCV infection by serologic screening (7). In this study, normal risk organ donors had an estimated 1 in 60 000 risk of undetected HIV infection by serologic screening, which is similar to tissue donors; however, high and missing risk organ donors were at substantially higher risks of undetected HIV infection (1 in 12 000 and 1 in

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**Table 1:** Prevalence of anti-HIV and anti-HCV in potential organ donors stratified by risk status and adjusted for false-positive test results

<table>
<thead>
<tr>
<th>Pathogen</th>
<th>Risk status of potential donors (1)</th>
<th>Number tested</th>
<th>Number reactive by serology</th>
<th>Unadjusted percent reactive (2)</th>
<th>Adjustment factor (3)</th>
<th>Adjusted prevalence (%) (4)</th>
<th>Credible interval for adjusted prevalence (%) (5)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV</td>
<td>Normal risk</td>
<td>11 245</td>
<td>25</td>
<td>0.22</td>
<td>0.45</td>
<td>0.10</td>
<td>0.06–0.16</td>
</tr>
<tr>
<td>HIV</td>
<td>High risk</td>
<td>1 180</td>
<td>13</td>
<td>1.10</td>
<td>0.45</td>
<td>0.50</td>
<td>0.21–0.86</td>
</tr>
<tr>
<td>HIV</td>
<td>Missing risk status</td>
<td>1 182</td>
<td>26</td>
<td>2.20</td>
<td>0.45</td>
<td>1.00</td>
<td>0.57–1.54</td>
</tr>
<tr>
<td>HCV</td>
<td>All potential donors</td>
<td>13 607</td>
<td>64</td>
<td>0.47</td>
<td>0.45</td>
<td>0.21</td>
<td>0.15–0.29</td>
</tr>
<tr>
<td>HCV</td>
<td>Normal risk</td>
<td>10 997</td>
<td>471</td>
<td>4.28</td>
<td>0.81</td>
<td>3.45</td>
<td>3.10–3.85</td>
</tr>
<tr>
<td>HCV</td>
<td>High risk</td>
<td>1 169</td>
<td>264</td>
<td>22.58</td>
<td>0.81</td>
<td>18.20</td>
<td>15.74–20.91</td>
</tr>
<tr>
<td>HCV</td>
<td>Missing risk status</td>
<td>1 183</td>
<td>189</td>
<td>15.98</td>
<td>0.81</td>
<td>12.88</td>
<td>10.83–15.08</td>
</tr>
<tr>
<td>HCV</td>
<td>All potential donors</td>
<td>13 349</td>
<td>924</td>
<td>6.92</td>
<td>0.81</td>
<td>5.58</td>
<td>5.15–6.06</td>
</tr>
</tbody>
</table>

1 Donors were designated as ‘Normal risk’ if the OPO designated the donor as ‘Not high risk’. Donors with no risk status designated by the OPOs were labeled ‘Missing risk status’. 2 Unadjusted percent reactive = (Number reactive by serology)/Number Tested) × 100%. 3 Adjusted percent reactive was determined by multiplying the percent reactive by an adjustment factor determined by donors with confirmatory tests (western blot for HIV and recombinant immunoblot assay for HCV). The adjustment factor accounts for potential false positive results from serologic testing. 4 Adjusted prevalence (%) = (Adjusted percent reactive) × (Adjustment factor). 5 95% credible intervals for the Adjusted prevalence were generated using Monte Carlo simulation models to account for variation in the number reactive by serology (assuming a Poisson distribution) and in the adjustment factors (assuming a triangular distribution).
### Table 2: Estimated incidence of HIV and HCV for potential organ donors per 100,000 person-years, and estimated incidence of undetected infection during the window period for serologic and NAT screening

<table>
<thead>
<tr>
<th>Pathogen</th>
<th>Risk status</th>
<th>N</th>
<th>Prevalence (%) for organ donors in study</th>
<th>Prevalence (%) for blood donors</th>
<th>Incidence per 100,000 person-years</th>
<th>Incidence per 100,000 person-years of organ donors</th>
<th>Window period (days) for serology</th>
<th>Window period (days) for NAT</th>
<th>Estimated risk of undetected infection among potential donors during window period for serology</th>
<th>Estimated risk of undetected infection among potential donors during window period for NAT</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV</td>
<td>Normal risk</td>
<td>11245</td>
<td>0.10</td>
<td>0.011</td>
<td>3.11</td>
<td>28.55</td>
<td>22</td>
<td>1.72</td>
<td>(0.63–4.40)</td>
<td>(0.20–1.39)</td>
</tr>
<tr>
<td></td>
<td>High risk</td>
<td>1180</td>
<td>0.50</td>
<td>0.011</td>
<td>3.11</td>
<td>141.65</td>
<td>22</td>
<td>8.54</td>
<td>(1.52–23.39)</td>
<td>(0.49–7.44)</td>
</tr>
<tr>
<td></td>
<td>Missing risk</td>
<td>1182</td>
<td>1.00</td>
<td>0.011</td>
<td>3.11</td>
<td>282.73</td>
<td>22</td>
<td>17.04</td>
<td>(6.04–42.18)</td>
<td>(1.94–13.47)</td>
</tr>
<tr>
<td></td>
<td>All potential</td>
<td>13607</td>
<td>0.21</td>
<td>0.011</td>
<td>3.11</td>
<td>60.50</td>
<td>22</td>
<td>3.65</td>
<td>(1.69–8.30)</td>
<td>(0.53–2.61)</td>
</tr>
<tr>
<td>HCV</td>
<td>Normal risk</td>
<td>10997</td>
<td>3.45</td>
<td>0.17</td>
<td>5.14</td>
<td>103.79</td>
<td>70</td>
<td>19.91</td>
<td>(10.75–31.93)</td>
<td>(1.09–3.23)</td>
</tr>
<tr>
<td></td>
<td>High risk</td>
<td>1169</td>
<td>18.20</td>
<td>0.17</td>
<td>5.14</td>
<td>547.19</td>
<td>70</td>
<td>104.94</td>
<td>(56.76–170.78)</td>
<td>(5.55–17.21)</td>
</tr>
<tr>
<td></td>
<td>Missing risk</td>
<td>1183</td>
<td>12.88</td>
<td>0.17</td>
<td>5.14</td>
<td>387.12</td>
<td>70</td>
<td>74.24</td>
<td>(38.57–233.85)</td>
<td>(3.96–12.40)</td>
</tr>
<tr>
<td></td>
<td>All potential</td>
<td>13349</td>
<td>5.58</td>
<td>0.17</td>
<td>5.14</td>
<td>167.73</td>
<td>70</td>
<td>32.17</td>
<td>(17.69–51.71)</td>
<td>(1.77–5.17)</td>
</tr>
</tbody>
</table>

1. Donors were designated as 'Normal risk' if the OPO designated the donor as 'Not high risk'. Donors with no risk status designated by the OPOs were labeled 'Missing risk status'.
2. Prevalence estimates for organ donors generated from OPO data (Table 1).
3. Prevalence estimates for blood donors with 95% confidence intervals, 2007 (published by Zou et al. (18)). Reported here as a percent.
4. Incidence estimates per 100,000 person-years for blood donors and 95% confidence intervals, 2007–2008 (published by Zou et al. (18)).
5. Incidence per 100,000 Person-Years in Organ Donors = (Prevalence among Organ Donors in Study) / (Prevalence in Blood Donors Reported in 2007) * (Incidence in Blood Donors Reported in 2007–2008). Incidence is reported with 95% credible intervals generated using Monte Carlo simulation models.
6. Window periods determined from published studies.
7. Estimated risk of undetected infection among organ donors = (Incidence in Organ Donors per 100,000 person-years) * (Window Period in Days) / 365). Incidence is reported with 95% credible intervals generated using Monte Carlo simulation models.
6000, respectively). Organ donors of all risk strata had a higher risk of undetected HCV infection by serologic testing compared to tissue donors. In this study, normal risk organ donors had an estimated 1 in 5000 risk of undetected HCV infection by serologic testing, and high risk donors had a 1 in 1000 risk. For HCV, reduction in the window period for NAT screening decreased the risk by 90% of undetected infection to 1 in 50,000 for normal risk donors and 1 in 10,000 for high risk donors. Credible intervals for HCV incidence during the window period for serologic versus NAT screening did not overlap for any of the risk strata; this is potentially a result of low HIV prevalence and incidence rates, wide variation in input parameters, and a smaller change in the window period for serology versus NAT for HIV compared with HCV (i.e. a 15 day difference vs. a 63 day difference).

The prevalence estimates of anti-HCV in high and normal risk donors demonstrated in this study are similar to those reported in a nation-wide analysis of donors reported to UNOS during the same time period (9). Rates of anti-HIV in this study were higher, likely because most HIV-positive potential donors do not have organs recovered, and thus may not be reported to UNOS. This study included potential donors who had consent for testing, but who had no organs recovered likely because of their HIV status. Both this study and the nation-wide UNOS study are likely to underestimate the true prevalence of HIV among potential organ donors because HIV-positive persons are excluded from donation by law; therefore, known HIV positive persons are less likely to be consented for testing.

A nontrivial proportion (approximately 9%) of donors tested for anti-HIV and anti-HCV were missing risk status designations by OPOs. This phenomenon was not limited to one or few OPOs; 13 of the 17 participating OPOs submitted serologic testing results for donors with missing risk status. Donors with ‘missing risk’ status had a high prevalence of HIV (1.0%). A possible explanation is that this study included all potential donors who received serologic testing including those whose organs were not recovered due to HIV positivity. Donors no longer considered for transplantation are rarely reported to UNOS, which requires that the OPO report the risk designation, and thus OPO may not assign risk designations for these donors.

Differences in regulatory restrictions for organ donation versus blood and tissue donation may be attributed to differences in the degree of risk acceptable for the respective recipient group of each allograft. Allowing organs from high risk donors to be transplanted is one of several policies aimed at increasing the availability for life-saving organs; increasingly, organs are transplanted from donors with underlying chronic illnesses as well as donation after circulatory determination of death. Transplanting organs from these clinically suboptimal donors is presumably accepted because of the potential life years gained by the recipient or recipients (20). In contrast, donors with behavioral risk factors are routinely excluded from the blood and tissue supply.

Decisions to recover and transplant organs are made based on several factors. Donors designated as high risk may not have their organs recovered or transplanted because of their high risk designation or because of other known medical or anatomical issues. However, because organs are in such high demand, the high risk designation may or may not dissuade a transplant center from accepting an organ. A recent survey of transplant surgeons showed that NAT screening enhanced surgeons’ comfort in accepting organs from high risk donors, presumably because concerns about undetected infection were allayed (11). Still, a recently published expert consensus concluded that there exists insufficient evidence to recommend routine NAT because the benefit may not outweigh the possibility of disqualifying organs for transplantation because of false-positive NAT results (20). Our study suggests that adoption of NAT screening for HCV could significantly reduce the incidence of undetected infection during the window period with a particularly high yield for high risk donors; thus NAT screening could potentially improve organ acceptance from high risk donors with negative results. The question remains as to whether expanding the donor pool through enhanced acceptance of NAT-negative organs would balance or exceed organ loss from false-positive NAT. False-positive rates for NAT screening are poorly understood. False-positive NAT screening could be detrimental to the organ supply if noninfected organs are rejected. Given the concerns about false-positive NAT results, more research on the frequency and causes of false-positives is needed and protocols for NAT screening should promote maximum specificity. While this study was not designed to assess the rate of false-positive NAT screens, we do believe this phenomenon should be considered in parallel with the results from this study when making policy decisions related to NAT screening.

This study is subject to a number of limitations. Importantly, the geographic distribution of OPOs participating in this study is focused mainly on the areas of highest population density, so that results may not be generalizable nationally. Also, interpretation of the results should be predicated on the fact that most of the serologic tests used in this study (between 2004 and 2008) were third-generation tests. The introduction of more sensitive fourth-generation serologic assays would also shorten window periods and thus may be a suitable alternative to NAT screening for purposes of reducing window periods if approved by FDA. Additionally, when considering the validity of serology results, differences may exist between large reference labs and smaller production labs and may influence the relative rate of false-positive results.
The results of our study suggest that undetected infection, and potentially transmission, can occur with current testing methods, although relatively few transmission events have been reported. There may be several reasons for this discrepancy. First, it is possible that transmissions occur unnoticed because a recipient dies before the infection is detected. Under-reporting may also occur because a transplant physician is unable to identify the donor as the source of recipient infection, particularly if discovered months after the transplant. Finally, reporting of suspected disease transmissions to UNOS was not part of OPTN policy until 2005, and that policy has remained voluntary.

This study is also subject to the inherent limitations of the incidence window-period methodology in which the incidence of undetected infection among potential organ donors is estimated from incidence in the blood donor population multiplied by an organ-to-blood donor prevalence ratio. This methodology assumes that the organ-to-blood donor prevalence ratio accurately reflects the organ-to-blood donor incidence ratio. This limitation was minimized by using prevalence and incidence estimates from the same time period; all estimates used to calculate the probability of undetected infection of HIV and HCV among potential organ donors—blood donor incidence data, blood donor prevalence data and organ donor prevalence data—were collected from 2004 through 2008.

Although recent surveys indicate that NAT is feasible, as it is performed by many OPOs on some donors for at least one bloodborne pathogen, the practice is variable (11). This is of particular concern as high risk donor recovery also is highly variable, and may not be correlated with use of NAT. Because the risk of transmitting bloodborne infections through transplantation is unlikely to be completely eliminated and can be difficult to predict for each individual donor, recipients and providers should have a clear understanding of the risk and benefits through standardized informed consent at appropriate points in the transplantation listing and offering process (21). Through ongoing collection and analysis of donor testing results as performed in our study, a better definition of transmission risk is possible, resulting in a decision process that allows for most effective use of a limited organ supply.

The Organ Procurement Organization
Nucleic Acid Testing Yield Project Team

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Disclosure

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References

Behavior/History Criteria for 'High Risk' Donor Status:

- Men who have had sex with another man in the preceding 5 years.
- Persons who report nonmedical intravenous, intramuscular, or subcutaneous injection of drugs in the preceding 5 years.
- Persons with hemophilia or related clotting disorders who have received human-derived clotting factor concentrates
- Men and women who have engaged in sex in exchange for money or drugs in the preceding 5 years.
- Persons who have had sex in the preceding 12 months with any person described in items 1–4 above or with a person known or suspected to have HIV infection.
- Persons who have been exposed in the preceding 12 months to known or suspected HIV-infected blood through percutaneous inoculation or through contact with an open wound, nonintact skin, or mucous membrane.
- Inmates of correctional systems.

Pediatric Donors Criteria for 'High Risk' Donor Status:

- Children meeting any of the exclusionary criteria listed above for adults.
- Children born to mothers with HIV infection or mothers who meet the behavioral or laboratory exclusionary criteria for adult donors (regardless of their HIV status) unless HIV infection can be definitely excluded in the child as follows:
  - Children greater than 18 months of age who are born to mothers with or at risk for HIV infection, who have not been breast fed within the last 12 months, and whose HIV antibody tests, physical examination, and review of medical records do not indicate evidence of HIV infection can be accepted as donors.
  - Children less than or equal to 18 months of age who are born to mothers with or at risk for HIV infection or who have been breast fed within the past 12 months should not be accepted as donors regardless of their HIV test results.

Medical Criteria for 'High Risk' Donor Status:

- Unexplained weight loss, night sweats, blue or purple spots on the skin or mucous membranes typical of Kaposi’s sarcoma, unexplained lymphadenopathy lasting greater than 1 month, unexplained temperature greater than 100.5°F (38.6°C) for greater than 10 days, unexplained persistent cough and shortness of breath, opportunistic infections, unexplained persistent diarrhea, sexually transmitted diseases, or needle tracks or other signs of parenteral drug abuse.

Examples of reported inconsistencies in application of PHS criteria by OPO:

- Some OPOs included viral hepatitis as a risk factor (e.g., addition of the question “Had sex in the past 12 months with any person known or suspected to have viral hepatitis or HIV infection?”)
- The PHS adult behavior/history section recommended excluding persons who participated in risk behavior during the preceding 12 months or 5 years, depending on the question. For these first six PHS criteria, some OPOs list 5 years instead of 12 months, 12 months instead of 5 years; others used “ever” as the timeframe for behavioral risk factors.
- Regarding the PHS adult behavior/history criteria “Inmates of correctional systems,” OPOs typically applied one or more specific parameters, such as whether the person was a current inmate; incarcerated greater than 72 consecutive hours in the past 12 months; currently greater than 72 hours; released in the past 12 months; or housed in one or more of the following institutions (correctional facility, jail, prison, lock-up, juvenile detention, mental institution).
- Medical criteria, such as unexplained weight loss, night sweats or unexplained lymphadenopathy lasting greater than one month are considered in the broader context of the donor’s medical and behavioral history to determine risk status.