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Quantifying the risk of undetected HIV, hepatitis B virus, or hepatitis C virus infection in Public Health Service increased risk donors

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Abstract

To reduce the risk of HIV, hepatitis B virus (HBV), and hepatitis C virus (HCV) transmission through organ transplantation, donors are universally screened for these infections by nucleic acid tests (NAT). Deceased organ donors are classified as “increased risk” if they engaged in specific behaviors during the 12 months before death. We developed a model to estimate the risk of undetected infection for HIV, HBV, and HCV among NAT-negative donors specific to the type and timing of donors’ potential risk behavior to guide revisions to the 12-month timeline. Model parameters were estimated, including risk of disease acquisition for increased risk groups, number of virions that multiply to establish infection, virus doubling time, and limit of detection by NAT. Monte Carlo simulation was performed. The risk of undetected infection was <1/1 000 000 for HIV after 14 days, for HBV after 35 days, and for HCV after 7 days from the time of most recent potential exposure to the day of a negative NAT. The period during which reported donor risk behaviors result in an “increased risk” designation can be safely shortened.

Keywords

donors and donation: deceased; donors and donation: donor-derived infections; ethics and public policy; infection and infectious agents - viral; infectious disease; mathematical model; organ procurement and allocation; organ transplantation in general

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DISCLOSURE

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DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

1 | INTRODUCTION

In 1994, the U.S. Public Health Service recommended interventions to prevent the transmission of human immunodeficiency virus (HIV) through organ and tissue transplantation.[1] These recommendations included designating some donors “high risk” for HIV acquisition based on the report of specific high-risk behaviors within either the previous 12 months (for high-risk sex or exposure to HIV-infected blood) or 5 years (for men who have had sex with men [MSM] behavior, nonmedical injection drug use [IDU], or sex in exchange for money or drugs) prior to organ recovery. In 2013, the guideline was updated and expanded to include identification of hepatitis B virus (HBV) and hepatitis C virus (HCV) risk factors among donors and additional testing of donors and recipients for HIV, HBV, and HCV.[2] Two pertinent changes included adopting new nomenclature (“increased risk” rather than “high risk”) to describe donors with viral blood-borne pathogen infection risk factors and standardizing the period during which reported risky donor behaviors result in an increased risk designation to 12 months preceding death. The guideline recommends specific informed consent for recipients of organs from increased risk donors (IRD) along with additional pre- and post-transplant HIV, HBV, and HCV testing.

Although the 2013 guideline only recommends an HCV nucleic acid test (NAT), since 2017 organ procurement organizations have tested all deceased donors by NAT for HIV, HBV, and HCV,[3] in addition to HIV, HBV, and HCV serological testing. Use of NAT has substantially reduced the period of undetectable infection.[4] However, donor-derived HBV and HCV infections from NAT-negative donors have still been reported since NAT implementation.[5,6] Although HIV transplant-transmission has not been documented in the United States since 2009 (donor was not tested by NAT and had negative HIV antibody test)[3,7] undetected donor infection is still possible during the eclipse period (time during early infection when virus is not detectable in blood).[8]

The IRD designation results in a dichotomous (yes or no) classification based on whether the reported behavior occurred within the 12 months preceding death. Patient or provider fear of viral blood-borne pathogen transmission from IRD organs[9,10] might contribute to underutilization of IRD organs,[11,12] even though the true risk of undetected infection with universal implementation of NAT is likely lower than the risk as perceived among patients and providers.[13-15] A more precise quantification of the risk of undetected HIV, HBV, and HCV infection among donors is warranted.

Previous efforts to model the probability of undetected HIV and HCV infection among IRD relied on the per-act risk of acquiring infection by donors and required knowing the frequency and timing of increased risk behaviors relative to the time of organ recovery.[16] However, these models are limited because of the difficulties of ascertaining donor-specific frequency and timing of increased risk behaviors through donor next-of-kin interviews. Additionally, few data are available to precisely estimate the per-act risk of infection through specific high-risk behaviors (eg, single IDU exposure or MSM encounter). Therefore, we developed a model that utilizes the incidence of disease in place of the per-act risk in order to guide revisions to the 12-month timeline during which reported donor risk behaviors

result in IRD designation. It can also inform patients and providers when discussing informed consent of IRD organ transplantation.

2 | METHODS

2.1 | Model inputs

Similar to previous models,[16] the model described here is based on Monte Carlo analyses and incorporates the following parameters (Tables 1 and 2):

1. Probability of virus acquisition (eg, HIV, HBV, HCV) among persons with a specific reported behavioral risk factor (ie, the incidence of infection among the increased risk population)
2. Initial number of virions in the donor that multiply and result in infection (ie, founder virions)
3. Rate of viral growth in the donor (ie, doubling time)
4. Total donor blood volume and volume of blood used for NAT assay
5. Limit of detection of NAT

Each of these parameters is modeled as a probability distribution.

2.2 | Determining model input values and probability distributions

To determine the annual incidence of HIV infection among MSM and people who inject drugs (PWID), we divided the reported number of incident HIV cases reported in the US population during 2015 attributed to male-to-male sexual contact, IDU, and to both male-to-male sexual contact and IDU[17] by the estimated US population of MSM,[18] PWID in the United States,[19] and MSM who inject drugs (MSM/PWID), respectively. The proportion of HIV-negative MSM who inject drugs was estimated at 2.2%.[20]

Because most HBV and HCV infections are asymptomatic and are not reported, national hepatitis surveillance cannot be used to calculate reliable incidence rates.[21] A literature search was conducted to find studies estimating HBV and HCV incidence in the United States among increased risk groups associated with IRD in the 2013 Public Health Service (PHS) guidelines. The only studies of sufficient size and quality were for estimates of HBV incidence among MSM[22] and HCV incidence among MSM,[23] PWID,[24] and incarcerated persons.[14] The HBV and HCV incidence of other risk groups was estimated to be approximately the same or less than the incidence among MSM or PWID based on published reports,[14,15] prevalence studies, or the consensus opinion of coauthors (Table 1). If the disease prevalence in a risk group was similar or lower, the disease incidence was estimated to be equivalent or lower.

The number of initial virions that multiply to establish infection (or founder virions) is generally lower than the viral load in infectious blood or semen and lower than the infectious dose due to clearance by the host's innate immune system and other nonspecific clearance mechanisms, and the labile nature of the viral particles.[25-27] Two types of studies were utilized to estimate the number of founder virions. In phylogenetic analysis, deep

sequencing technologies can genetically characterize populations of virions within a single host. In HIV-infected individuals, phylogenetic analysis of envelope protein sequences has established the number of founder virions to be from 1 to 5 or more virions, with riskier behaviors resulting in more founder virions.[26] In the second method, animals are infected at a known time, and once the viral load reaches the limit of detection of the assay, the number of founder virions can be inferred from the viral replication rate, the known time of infection, and animal blood volume. Animal studies yield estimates similar to those derived from phylogenetic methods of approximately 10-15 founder virions.[28,29] Both HCV and HBV are more infectious than HIV, with 50% infectious doses estimated to be 4-10 virions.[4,27] The 50% infectious dose in chimpanzees for both viruses has been estimated to be 3-10 particles.[4] The initial number of founder virions for HIV, HBV, and HCV was therefore set to a mean of 10 with a 95% confidence interval (CI) of 4-25 (Table 2).

Viral doubling times were based on prior studies (Table 2).[30]The limit of NAT detection used for these analyses was based on estimates for the Procleix Ultrio (Novartis Diagnostics, Emeryville, CA), a commonly used organ donor screening assay.[31,32] The midpoint of the X_{50} and X_{95} for the Ultrio detection assays was set to the 50th and 95th percentile in a probability density function. Because the 50th percentile is close to zero, a zero-inflated log normal distribution was used to prevent allowing detection of less than one virion per sample in the Monte Carlo simulation. Donor total blood volume is variable and age dependent and was set at a mean of 4.9 L (95% CI: 3.8-6.7).[33] The volume of blood used for NAT assays was estimated at 1.8 mL (95% CI: 1.6-2.0).[31]

2.3 | Statistical methods and risk curve generation

The disease incidence rate was used to estimate the probability of HIV, HBV, or HCV infection among persons with a specific reported risk factor. Other parameters were used to model viral replication once an individual donor is infected and estimate the probability that the limit of detection of the NAT assay threshold has been crossed. Both probabilities are convolved and integrated in time to calculate the total risk probability.

Monte Carlo simulation and statistical methods were performed with the model parameters presented here using Mathematica (Wolfram Research) and JMP software (a SAS visual analytics package).

The analysis proceeded in three steps, each feeding directly into the other, and each centering on the three equations shown here. Each Monte Carlo run simulates the time to cross the limit of detection, as shown in Equation 1,

$$\theta = (V_s / V_b)\, v_0 e^{\lambda \Delta t} \quad (1)$$

where θ is the limit of detection of the NAT assay (number of viral particles), V_s is the sample volume from the blood draw (mL), V_b is the total blood volume (mL), v_0 is the initial viral inoculum, λ is the rate of viral growth (multiples per day), and Δt is the time required for viral growth to exceed the limit of detection. Each of these was sampled from a lognormal distribution as described in Table 2, except that the limit of detection was zero

inflated, and Δt was computed. The 100 000 detection times Δt were then fit to a Johnson S_L distribution, as shown in Equation 2, similar to previous studies.[16]

$$\mathrm{pdf}(t) = \frac{\delta}{\sigma\sqrt{2\pi}} \frac{1}{(t-\xi)} e^{-0.5(\gamma + \delta \mathrm{Log}(t-\xi/\sigma))^2} \quad (2)$$

δ, ξ, and γ are estimated parameters of the distribution, and $\sigma = 1$ for the Johnson S_L. Note that this part of the computation only serves to generate the Johnson S_L function for a distribution of possible infections: it does not imply that timing between NAT testing and risk behavior needs to be known for the incidence-based risk model described here. To compute total absolute risk $R(t)$, the cumulative density function (CDF) of the Johnson S_L function is numerically integrated over time with the known risk rate $r_i(\tau)$, with the integrand limits set as the time since last possible exposure (t) out to a sufficiently large amount of time for the risk to become effectively zero (t_{max}):

$$R(t) = \int_t^{t_{max}} r_i(\tau)[1 - \mathrm{CDF}(\tau)]\, d\tau \quad (3)$$

This integrated risk function yields total absolute risk of undetected infection (ie, NAT negative) in the donor as a function of time in days since the most recent potential exposure, plotted on a semi-log axis in Figures 1-4. Because this integration must be done numerically, the lower limit of integration (t) cannot equal zero, and 0.05 days (about 1 hour) was set as the lower bound of time. The 95% CIs are associated with the incidence-based risk rates $r_i(\tau)$, and these are shown in Figure 1 through 3 as dotted lines. Although the acceptable risk for transmitting HIV, HBV, and HCV through organ transplant has not been defined, a probability of 1/1 000 000 has been suggested to contextualize risk in medical decision-making for other health-related rare events.[34] For this reason, we labeled the risk of 1/1 000 000 of undetected infections on all figures and calculated the number of days from most recent possible increased risk behavior to testing by NAT to reach this threshold (Figures 1-4).

2.4 | Sensitivity analyses

Because certain donors might be at a greater risk of an eclipse period infection compared to national surveillance or the included cohort studies, additional donor models were generated, referred to in this study as “greater risk.” These greater risk donor models represent the rare scenario of a donor with extremely high-risk behaviors. For HIV, a greater risk donor was modeled using the reported incidence of HIV among men engaging in unprotected receptive anal intercourse with ejaculation with a HIV-seropositive male partner.[35] For HCV, a greater risk donor was modeled using the incidence of HCV among PWID who shared needles with an HCV-seropositive injecting partner.[36] No study of sufficient quality was found for a greater risk donor of HBV (eg, a study in the United States estimating the incidence of HBV among HBV-serodiscordant MSM couples). Therefore, three times the incidence of HBV among the general HIV-negative MSM population was conservatively used for the HBV greater risk donor.

We also modeled the risk of undetected infection in a donor with a 100% probability of harboring a single virion at the time of most recent increased risk act. This unlikely scenario represents the highest probability of not detecting infection in an infected donor and estimates the longest amount of time required for a NAT to detect infection. To model this scenario, the probability density for the initial viral load was set to a constant (1 virion) and not varied in the Monte Carlo simulation, the incident rate was set to 100%, and all other parameter probability densities were left the same. Because this scenario represents an individual infected with a single virion with 100% certainty and CIs were calculated using the risk of infection, no CIs were generated.

3 | RESULTS

The risks for undetected infection among antibody-negative and NAT-negative MSM, PWID, and MSM who inject drugs (eg, combined risk of MSM and PWID) were grouped by virus.

3.1 | HIV

Among MSM, the risk of undetected HIV infection with a negative NAT 0.05 days after the most recent potential exposure is 1.3/10 000 MSM donors (95% CI: 1.2-1.3/10 000, Figure 1, Table 3). The risk is <1/1 000 000 MSM donors if the NAT is negative ≥10.1 days (95% CI: 10.0-10.2 days) after the most recent potential MSM contact (Table 2). Among PWID, the risk of undetected HIV with a negative NAT 0.05 days after the most recent potential exposure is 0.7/10 000 PWID donors (95% CI: 6-0.9/10 000). The risk is <1/1 000 000 PWID donors if the NAT is negative ≥9.7 days (95% CI: 9.5-9.9 days) after the most recent potential exposure to IDU. Among MSM/PWID, the risk of undetected HIV at 0.05 days after the most recent potential exposure is 10.7/10 000 MSM/PWID donors (95% CI: 10.3-10.8/10 000). The risk is <1/1 000 000 if the NAT is negative ≥10.7 days (95% CI: 10.3-10.8 days) after the most recent potential exposure to both male sexual contact and IDU. Among IRD at “greater risk” for HIV (ie, MSM sexual contact with an HIV-seropositive male partner and having regular unprotected receptive anal intercourse with ejaculation), risk of undetected HIV infection at 0.05 days after the most recent potential exposure is 34.7/10 000 (95% CI: 2.9-218). The risk is <1/1 000 000 donors if the NAT is negative ≥12.4 days (95% CI: 10.7-13.6 days) after the most recent potential male sexual contact. The risk is <1/1 000 000 donors if the NAT is negative ≥21.0 days (95% CI: 21.0-21.0 days) after infection with 1 HIV virion (Figure 4, Table 3).

3.2 | HBV

Among MSM, the risk of undetected HBV infection with a negative NAT 0.05 days after the most recent potential exposure is 4.5/10 000 MSM donors (95% CI: 3.8-5.3/10 000, Figure 2, Table 3). The risk is less than 1/1 000 000 donor if the NAT is negative ≥29.4 days (95% CI: 29.1-29.8 days) after the most recent potential male sexual contact. The risk among PWID was estimated to be the same as the risk among MSM. Among MSM/PWID, the risk of undetected HBV 0.05 days after the most recent potential exposure is 8.9/10 000 MSM/PWID donors (95% CI: 7.6-10.6/10 000). The risk is <1/1 000 000 donors if the NAT is negative ≥30.8 (95% CI: 30.5-31.1 days) after the most recent potential exposure to both male sexual contact and IDU. Among donors at “greater risk” for HBV (ie, estimated at

three times the risk as an average MSM), risk of undetected HBV infection at 0.05 days after the most recent potential exposure is 13.4/10 000 “greater risk” donors (95% CI: 11.5-15.9/10 000). The risk is <1/1 000 000 donors if the NAT is negative ≥31.5 days (95% CI: 31.2-31.8 days) after the most recent potential exposure. The risk is <1/1 000 000 donors beginning 70.9 days (95% CI: 70.9-70.9 days) after infection with 1 HBV virion (Figure 4, Table 3).

3.3 | HCV

Among MSM, the risk of undetected HCV infection at 0.05 days after the most recent potential exposure is 0.06/10 000 MSM donors (95% CI: 0.03-0.09/10 000, Figure 3, Table 3). The risk is less than 1/1 000 000 donors if the NAT is negative ≥3.6 days (95% CI: 3.1-4.0 days) after the most recent potential male sexual contact. Among PWID, the risk of undetected HCV is 0.05 days after the most recent potential exposure is 27.6/10 000 PWID donors (95% CI: 22.7-31.0/10 000). The risk is <1/1 000 000 if the NAT is negative ≥6.6 days (95% CI: 6.5-6.7 days) after the most recent potential exposure to IDU. Among MSM/PWID, the risk of undetected HCV is 0.05 days after the most recent potential exposure is 27.6/10 000 MSM/PWID donors (95% CI: 22.8-31.1/10 000). The risk is <1/1 000 000 donors if the NAT is negative ≥6.6 days (95% CI: 6.5-6.7 days) after the most recent potential exposure to both male sexual contact and IDU Among donors at “greater risk” for HCV (ie, PWID and shared needles with a HCV seropositive injecting partner), risk of undetected HCV infection at 0.05 days after the most recent potential exposure is 27.6/10 000 “greater risk” donors (95% CI: 22.8-31.1/10 000). The risk is <1/1 000 000 donors if the NAT is negative ≥6.6 days (95% CI: 6.5-6.7 days) after the most recent possible exposure. The risk is <1/1 000 000 donors beginning 12.2 days (95% CI: 12.2-12.2 days) after infection with 1 HCV virion (Figure 4, Table 3).

The highest risk for undetected infection of HIV, HBV, or HCV immediately after the most recent potential exposure among MSM and PWID was for HCV among PWID. After 5 days from most recent potential exposure, HBV had the highest risk of undetected infection in all scenarios. HBV had the longest duration from most recent potential increased risk behavior to having <1/1 000 000 risk of undetected infection with a negative NAT for all model scenarios.

4 | DISCUSSION

The results of these analyses suggest that in the setting of universal deceased donor NAT, the risk of undetected HIV, HBV, or HCV infection is low and highly dependent on the duration of time from last possible exposure until testing. The 2013 PHS guideline recommends categorizing donors as IRD if specific behaviors are reported by next of kin within 12 months preceding death.[2] The present model suggests that donors, when tested with NAT, have less than a 1/1 000 000 risk of undetected infection within 14 days of potential increased risk behaviors for HIV and HCV and within 30 days for HBV. Even in the hypothetical situation where the donor is infected with 1 HIV or HCV virion, the probability of undetected HIV or HCV infection 30 days after infection is <1/1 000 000. The risk for undetected HBV infection at 30 days from most recent potential exposure is estimated at

<1/1 000 000 among MSM or PWID and 2/1 000 000 among “greater risk” donors (ie, three times the incidence of HBV among MSM). Donors infected by HBV with few founder virions could be at risk of undetected infection beyond 30 days. The timeline for risk behaviors to categorize an organ donor as increased risk for undetected HIV, HBV, or HCV infection can be safely decreased, resulting in categorizing some donors who are designated IRD under present criteria as standard risk donors.[37]

Previous studies have estimated the absolute risk of undetected HIV and HCV infection among IRD.[13-15] These studies considered both seronegative donors and NAT-negative donors and found risks of undetected infections in the range of ~<1-30 per 10 000 for NAT-negative donors. Because these studies did not compute risk as a function of time and our study did not account for donors only tested by serology, comparing results between the studies is difficult. As expected, compared to the absolute risks previously reported for undetected HCV and HIV infection among NAT-negative donors,[13-15] our models calculated a higher risk immediately after the most recent potential exposure. The present models further calculated a lower risk as the duration of time from the most recent potential risk exposure to testing by NAT increased beyond the eclipse period. Unlike previous studies, our model provides an estimated risk of undetected infection that is specific not only to the donor's risk behavior but also to the timing of the potential disease exposure in relation to the negative NAT. To our knowledge, this model is the first to provide HBV risk estimates. Donor-specific estimates of the risk of undetected infection should improve clinician and patient comfort in utilizing IRD organs.

These findings are subject to the following limitations. First, this study estimates the risk of undetected infection and not the risk of transmission to recipients. Receiving an organ from a recently infected donor with HIV, HBV, or HCV might not result in infection of the recipient. In a case series describing HBV and HCV transmissions to recipients of organs from deceased donors with negative HBV and HCV testing, new HBV infections were detected in seven (47%) of 15 HBV-negative recipients exposed to HBV; new HCV infections were detected in 20 (65%) of 31 HCV-negative recipients exposed to HCV.[35] Second, the threshold for an acceptable risk of HIV, HBV, and HCV transmission through organ transplantation has not been established. We used 1/1 000 000 as a sufficiently low-risk threshold to contextualize risk. However, the acceptable risk of transmission through organ transplantation is likely much higher because of the high mortality rate of patients awaiting organ transplantation. Accepting IRD organs has been shown to result in improved survival among recipients compared to declining these organs and waiting for standard risk donor organs.[38,39] The development of more effective treatments for HIV, HBV, and HCV has resulted in improved outcomes.[40-42] Third, the HIV incidence rates were based on national surveillance and the HBV and HCV incidence rates were based on cohorts to represent the average annual risk of infection among specific increased risk populations. However, some individuals might be at substantially higher or lower risk. Higher risk persons include PWID or other high-risk populations residing in areas experiencing HIV or HCV outbreaks[43] or individuals with particularly risky behaviors, such as those represented in “greater risk donor” sensitivity analyses (eg, serodiscordant sex and needle sharing). Fourth, identification of behavioral risk factors often relies on next-of-kin interviews, which

might be inaccurate. Last, HBV and HIV NAT testing are not currently required and this model is applicable only in the setting of universal NAT testing.

To improve organ utilization and to reflect advances in implementation of transplant-related safety interventions such as NAT, CDC and other federal partners are considering revisions to the 2013 PHS guideline recommendations. In 2019, the Advisory Committee on Blood and Tissue Safety and Availability will assess the findings of this study when considering changes to current recommendations, including reduction of the current 12-month time frame. Although current recommendations categorize donors as IRD if behavior occurred within 12 months prior to death, the present findings suggest that reduction to a shorter interval is possible while preserving recipient safety. Shortening the timeline would likely result in fewer donors designated at risk of undetected HIV, HBV, or HCV infection and might increase organ utilization.[12] Additional considerations include reassessment of the term “increased risk,” which might be currently contributing to underutilization.[12] These findings can improve donor classification criteria and informed consent discussions between providers and recipients.

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Abbreviations:

CDC	Centers for Disease Control and Prevention
HBV	hepatitis B virus
HCV	hepatitis C virus
HIV	human immunodeficiency virus
HRSA	Health Resources and Services Administration
IDU	injection drug use
IRD	increased risk donors
MSM	men who have sex with men
NAT	nucleic acid test
PWID	people who inject drugs

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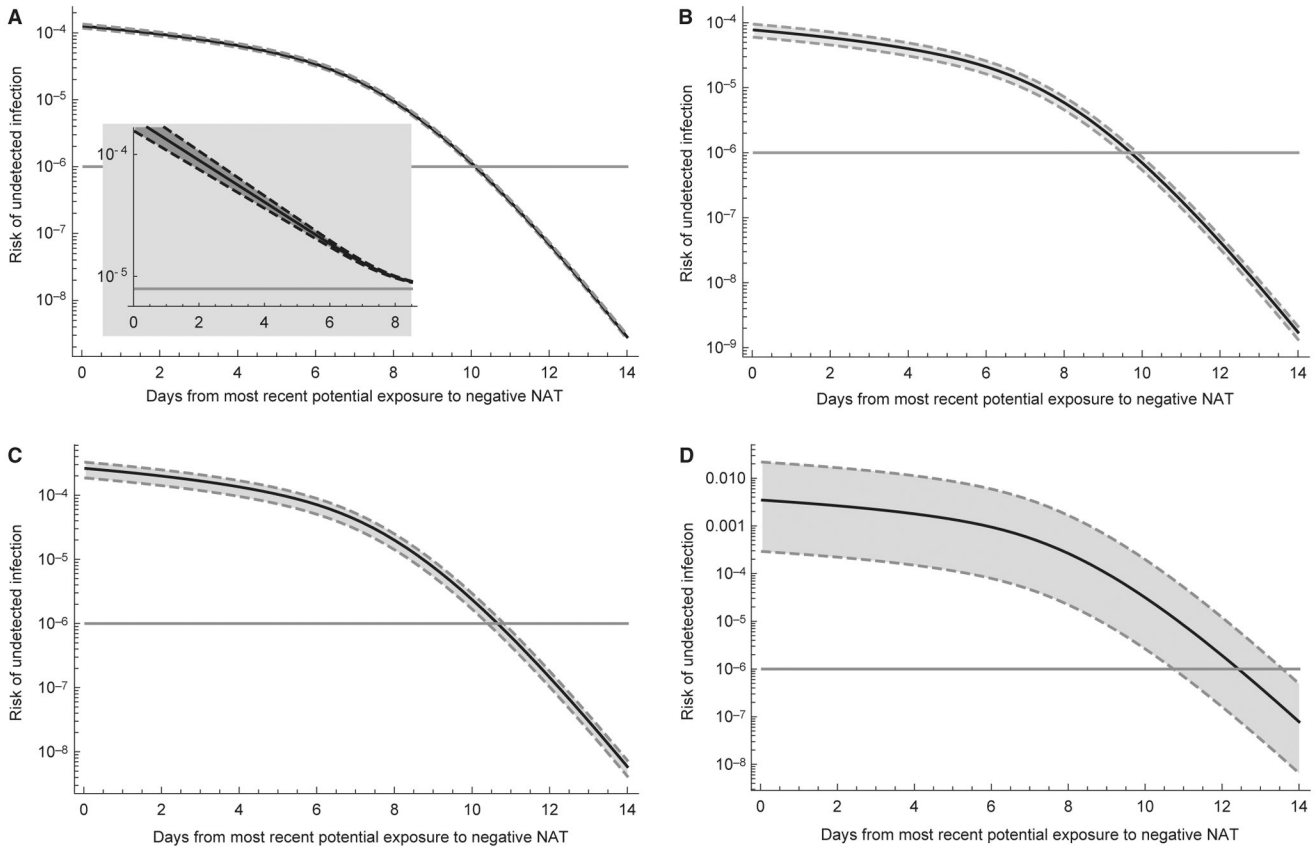

FIGURE 1.

Risk of undetected HIV infection among donors classified as increased risk per Public Health Service criteria with negative nucleic acid testing by risk behavior and time of nucleic acid test from most recent potential exposure. (A) Among men who have sex with men (MSM). (B) Among people who inject drugs. (C) Among MSM who inject drugs. (D) Among MSM with a serodiscordant partner and practicing condomless, receptive anal sex with ejaculation. Black solid line is 50th percentile, gray dashed lines are 5th and 95th percentile, and shaded area represents 95th confidence interval. Gray solid line is 1/1,000,000 risk. Because the confidence intervals are so close to the 50th percentile line (due to very accurate knowledge of the incidence rate among MSM), an inset plot for the non-log transformed risk out to 8 d since potential risk exposure is shown

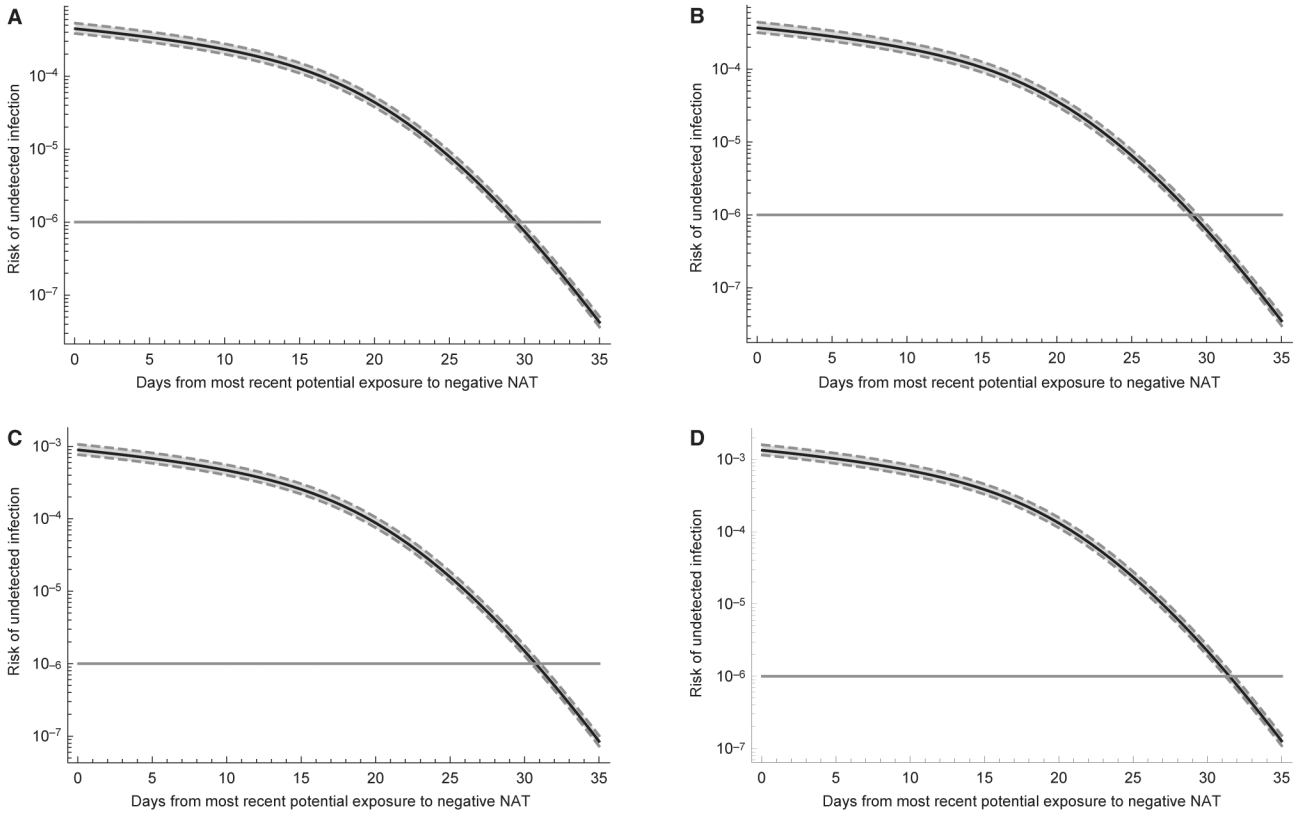

FIGURE 2.

Risk of undetected hepatitis B virus infection among donors classified as increased risk per Public Health Service criteria with negative nucleic acid testing by risk behavior and time of nucleic acid test from most recent potential exposure. (A) Among men who have sex with men (MSM). (B) Among people who inject drugs. (C) Among MSM who inject drugs. (D) Among MSM with a serodiscordant partner and practicing condomless, receptive anal sex with ejaculation. Black solid line is 50th percentile, gray dashed lines are 5th and 95th percentile, and shaded area represents 95th confidence interval. Gray solid line is 1/1,000,000 risk

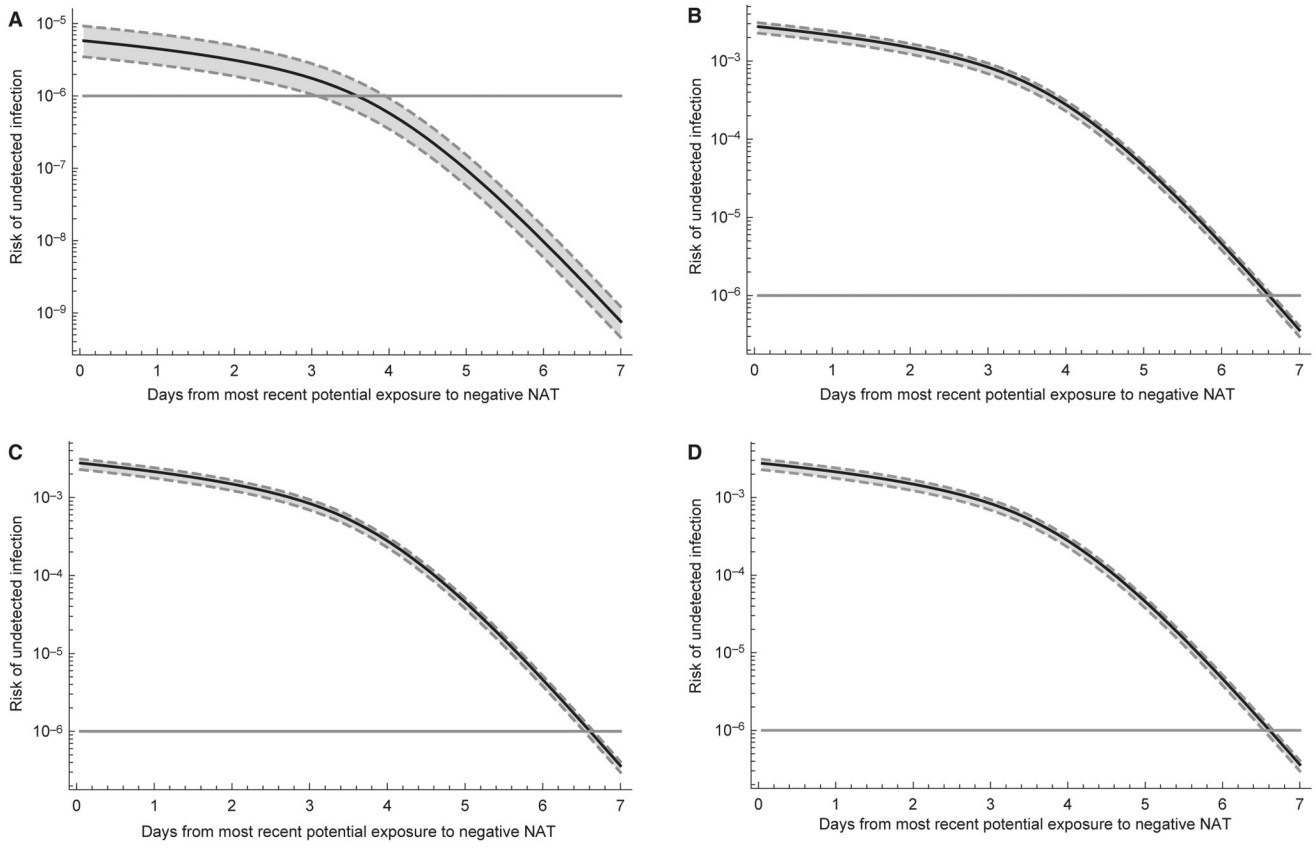

FIGURE 3.

Risk of undetected hepatitis C virus infection among donors classified as increased risk per Public Health Service criteria with negative nucleic acid testing risk behavior and time of nucleic acid test from most recent potential exposure. (A) Among men who have sex with men (MSM). (B) Among people who inject drugs. (C) Among MSM who inject drugs. (D) Among MSM with a serodiscordant partner and practicing condomless, receptive anal sex with ejaculation. Black solid line is 50th percentile, gray dashed lines are 5th and 95th percentile, and shaded area represents 95th confidence interval. Gray solid line is 1/1,000,000 risk

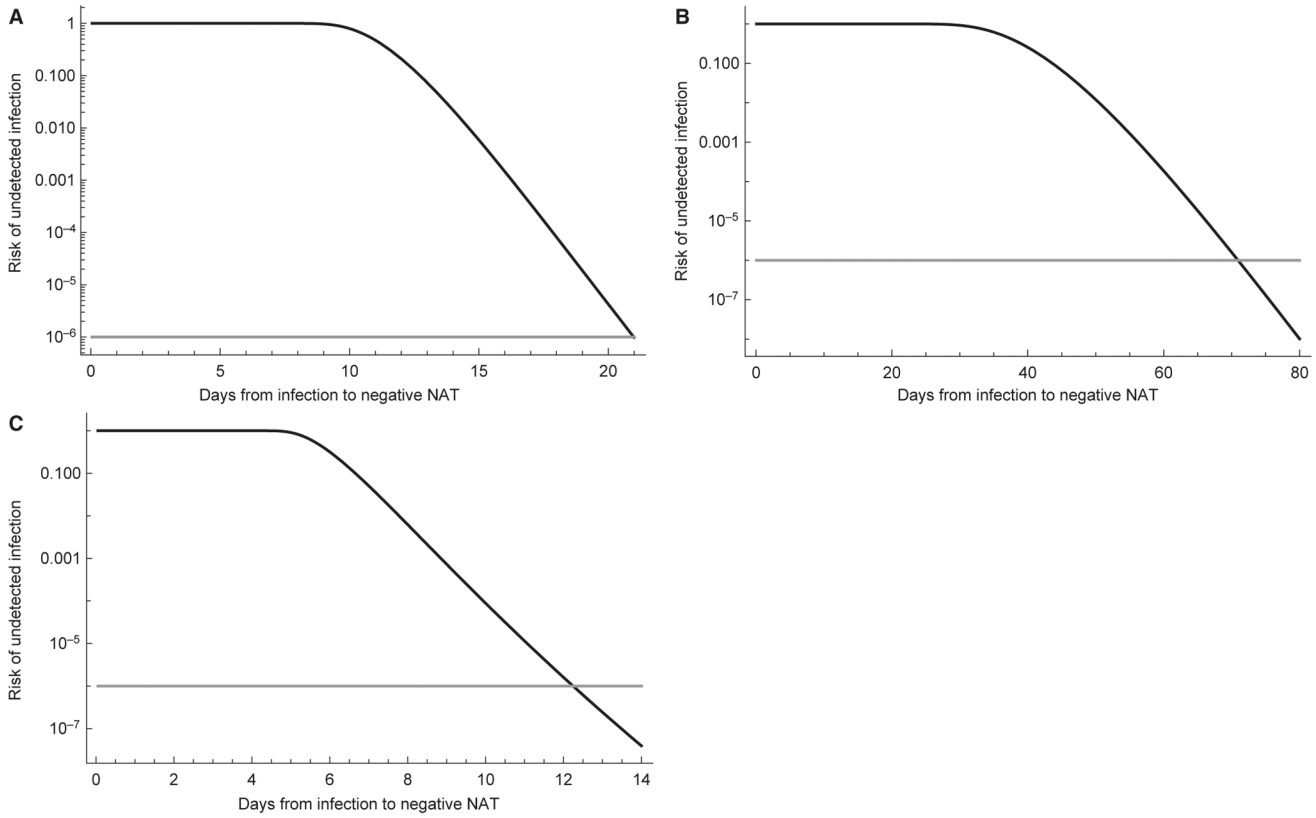

FIGURE 4.

Risk of undetected blood-borne viral infection among theoretical donors infected with one virion with negative nucleic acid testing by virus and time of nucleic acid test from time of infection. (A) HIV. (B) Hepatitis B Virus. (C) Hepatitis C Virus. Gray solid line is the 1/1 000 000 risk

TABLE 1

Model parameters for incidence of HIV, hepatitis B virus, and hepatitis C virus among donors classified as increased risk per Public Health Service criteria

	Virus		
	HIV	**HBV**	**HCV**
Behavioral group	**Annual incidence per 100 person-years (95% CI)**		
Men who have sex with men	0.56 (0.52-0.56)[17,18]	0.78 (0.67-0.93)[22]	0.05 (0.03-0.08)[23]
People who inject drugs	0.34 (0.27-0.42)[17,19]	Approximate to MSM risk[44]	24 (20-27)[24]
MSM who inject drugs	1.0 (0.7-1.2)[17,18,20]	1.6 (1.3-1.9)[22]	24 (20-27)[23,24]
People who have had sex in exchange for money or drugs	Equal to or less risky than PWID risk	Approximate to MSM risk	Approximate to MSM risk
People who have had sex with a person known or suspected to have HIV, HBV, or HCV infection	Approximate to MSM risk	Equal to or lower MSM risk	Approximate to MSM risk
Women who have had sex with a man with a history of MSM behavior	Equal to or lower MSM risk	Equal to or lower MSM risk	Approximate to MSM risk
People who have had sex with a person who had sex in exchange for money	Equal to or lower MSM risk	Equal to or lower MSM risk	Approximate to MSM risk
People who have had sex with a person who injected drugs by intravenous, intramuscular, or subcutaneous route for nonmedical reasons	Equal to or lower MSM risk	Equal to or lower MSM risk	Approximate to MSM risk
People who have been in lockup, jail, prison, or a juvenile correctional facility for more than 72 consecutive hours	Equal to or lower MSM risk	Equal to or lower MSM risk	0.4 (0.04-1.3)[14]
People who have been newly diagnosed with, or have been treated for, syphilis, gonorrhea, Chlamydia, or genital ulcers	Equal to or lower MSM risk	Approximate to MSM risk	Approximate to MSM risk
People who have sex for money or drugs	Approximate to MSM risk	Equal to or lower MSM risk	Approximate to MSM risk
Greater risk donor	15.5 (1.30-97.3) among MSM with a serodiscordant partner and practicing condomless, receptive anal sex with ejaculation[35]	2.3 (2.0-2.8), three times the incidence among MSM	24 (20-27) among PWID with seropositive injection partner[36]

Abbreviations: HIV, human immunodeficiency virus; HBV, hepatitis B virus; HCV, hepatitis C virus; MSM, men who have sex with men; PWID, people who inject drugs.

TABLE 2

Model parameters to quantify the risk of undetected HIV, hepatitis B virus, or hepatitis C virus infection among donors classified as increased risk per Public Health Service

	Virus		
Model parameter	**HIV**	**HBV**	**HCV**
Number of founder virions (95% CI)	10 virions (4-25)[4,27-29]	10 virions (4-25)[4,27-29]	10 virions (4-25)[4,27-29]
Viral doubling time (95% CI)	0.85 d (0.76-0.97)[30]	2.56 d (2.26-3.06)[30]	0.45 d (0.41-0.50)[30]
Donor blood volume (95% CI)	4.9 L (3.8-6.7)[33]	4.9 L(3.8-6.7)[33]	4.9 L (3.8-6.7)[33]
Volume of blood used for viral nucleic acid test (95% CI)	1.8 mL (1.6-2.0)[31]	1.8 mL (1.6-2.0)[31]	1.8 mL (1.6-2.0)[31]
Limit of detection of viral nucleic acid test (95% CI)	2.7 virions (1-18.4)[32]	7.5 virions (1-80.3)[32]	2.3 virions (1-20.2)[32]

Abbreviations: HIV, human immunodeficiency virus; HBV, hepatitis B virus; HCV, hepatitis C virus; CI, confidence interval; d, days.

TABLE 3

Risk of undetected HIV, hepatitis B virus, and hepatitis C virus infection among donors classified as increased risk per Public Health Service criteria with negative nucleic acid testing by virus, risk behavior, and time of nucleic acid test from most recent potential exposure

	Virus					
	HIV		HBV		HCV	
Risk group	Risk of undetected infection 0.05[a] d after most recent potential exposure per 10 000 donors (95% CI)	Days to reach risk of undetected infection of 1/1 000 000 (95% CI)	Risk of undetected infection 0.05[a] d after most recent potential exposure per 10 000 donors (95% CI)	Days to reach risk of undetected infection of 1/1 000 000 (95% CI)	Risk of undetected infection 0.05[a] d after most recent potential exposure per 10 000 donors (95% CI)	Days to reach risk of undetected infection of 1/1 000 000 (95% CI)
Men who have sex with men	1.3 (1.2-1.3)	10.1 (10.0-10.2)	4.5 (3.8-5.3)	29.4 (29.1-29.8)	0.06 (0.03-0.09)	3.6 (3.1-4.0)
People who inject drugs	0.7 (0.6-0.9)	9.7 (9.5-9.9)	4.5 (3.8-5.3)	29.4 (29.1-29.8)	27.6 (22.7-31.0)	6.6. (6.5-6.7)
MSM who inject drugs	2.6 (1.9-3.3)	10.7 (10.3-10.8)	8.9 (7.6-10.6)	30.8 (30.5-31.1)	27.6 (22.8-31.1)	6.6. (6.5-6.7)
"Greater risk" donors[b]	34.7 (2.9-218)	12.4 (10.7-13.6)	13.4 (11.5-15.9)	31.5 (31.2-31.8)	27.6 (22.8-31.1)	6.6. (6.5-6.7)
Infected with 1 virion	n/a	21.0 (21.0-21.0)	n/a	70.9 (70.9-70.9)	n/a	12.2 (12.2-12.2)

Abbreviations: HIV, human immunodeficiency virus; HBV, hepatitis B virus; HCV, hepatitis C virus; MSM, men who have sex with men; 95% CI, 95% confidence interval.

[a]Because the risk of undetected infection is calculated from an integrated risk function, the lower limit of integration (time) cannot equal zero, and 0.05 d was set as the lower bound of time.

[b]"Greater risk" donor defined for HIV as MSM donors with serodiscordant partner and practicing condomless receptive anal sex with ejaculation, for HBV as donors with three times the incidence of HBV among MSM, and for HCV as PWID with HCV-positive injection partners.