Solid Organ Transplantation and the Probability of Transmitting HIV, HBV, or HCV: A Systematic Review to Support an Evidence-based Guideline

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Introduction

This systematic review addressed 10 Questions (middle column of Table 1) pertaining to solid organ transplantation and three bloodborne pathogens (HIV, HBV, and HCV). These questions were carefully developed by the Centers for Disease Control and Prevention in consultation with the Center for Evidence-based Practice at the University of Pennsylvania and ECRI Institute. These questions are not intended to encompass *all* important issues related to infectious diseases and organ transplantation. Instead, they were specifically focused to support the development of an evidence-based guideline. The leftmost column of the table shows which section of the guideline pertains to the questions, and the rightmost column provides explanatory comments.

Table 1. Questions for Systematic Review

Major topic area of the guideline	Question for Systematic Review	Comments
I. Probability of transmission of HIV, HBV, or HCV through solid organ transplantation (SOT)	1. What are the prevalence and incidence rates of HIV, HBV, and HCV among potential solid organ donors?	This question addresses the extent of the possible problem. The focus is on the epidemiology rates for each of the three pathogens among people who are being considered for solid organ donation.
	2. What are the rates of transmission to recipients from donors infected with HIV, HBV, or HCV? Do the rates vary by the organ transplanted or when the donor was infected?	A key concern is that a solid organ donor will transmit infection to a recipient. This question concerns the specific situation when the donor is positive for a pathogen but the recipient is not, and what percentage of such recipients become infected after transplantation.
II. Methodology to better estimate donor infection with HIV, HBV, or HCV	3. What behavioral risk factors are associated with an increased probability of infection with HIV, HBV, or HCV? What is the prevalence of these characteristics among potential solid organ donors?	Some behaviors may be associated with infection of HIV, HBV or HCV, and the first half of the question attempts to identify these behaviors. This is accomplished by comparing the rate of infection among those who do engage in a behavior to the rate of infection among those who do not. The second half addresses the frequency of those behaviors among potential solid organ donors.
	4. What nonbehavioral factors are associated with an increased probability of infection with HIV, HBV, or HCV? What is the prevalence of these factors among potential solid organ donors?	This is similar to the previous question, except here the focus is on nonbehavioral factors. Our primary intent was to identify signs and symptoms of incident infections (i.e., recently acquired), but we also included data on signs and symptoms of chronic infection, medical comorbidities, socioeconomic information, and demographic factors.
	5. What are the test characteristics of the screening methods	Numerous tests exist to detect HIV, HBV and/or HCV in potential donors, and this question concerns the diagnostic

Major topic area of the guideline	Question for Systematic Review	Comments
	available to detect HIV, HBV, and HCV in potential solid organ donors? Do test characteristics differ in particular populations and with donor clinical status (i.e., heart beating vs. non-heart beating donors OR adult vs. pediatric donors)?	accuracy of those tests, as well as the length of the window period and the turnaround time. The window period is particularly important in this context, because an infected individual in the window period would not be detectable prior to donation of solid organs.
III. Donor interventions to decrease transmission of HIV, HBV,or HCV from infected donors	6. Which donor interventions reduce the probability of pathogen transmission from an organ donor infected with HIV, HBV, or HCV to a previously uninfected recipient?	Given an infected organ donor, it may be possible to inactivate the virus prior to transplantation into a recipient. This question seeks to identify effective methods for inactivation of viruses in solid organs donors.
IV. Potential risks and benefits of transplanting, or not transplanting, solid organs from donors positive for HIV, HBV, or HCV	7. How do the clinical outcomes of recipients of organs from donors infected with HIV, HBV, or HCV compare to those who remain on the transplant list?	This question concerns whether a patient will live longer after 1) receiving a known infected organ or 2) remaining on the transplant list. Other clinical outcomes of interest include graft survival and quality of life.
V. Potential risks and benefits of transplanting, or not transplanting, organs from donors with risk factors for HIV, HBV, or HCV	8. How do the clinical outcomes of transplant recipients who receive organs from donors with behavioral or nonbehavioral risk factors compare to those who remain on the transplant list?	This question is conceptually similar to question 7. Here, however, the donor is not known to be infected, but the donor is at risk for infection based on a behavioral or clinical factor. As in question 7, the comparison is between implanting or not implanting organs from such donors, with a focus on clinical outcomes (e.g., recipient survival).
	9. What is the impact of excluding potential solid organ donors with behavioral or nonbehavioral risk factors on the organ donor pool?	If at-risk donors are excluded, one negative consequence is a reduction in the organ donor pool. This question attempts to quantify the size of the reduction.
	10. What is the impact of false positive tests on the organ donor pool?	If donors testing positive are excluded from the donor pool, then false positives will result in an inappropriate reduction of the donor pool; this question attempts to quantify the size of the reduction.

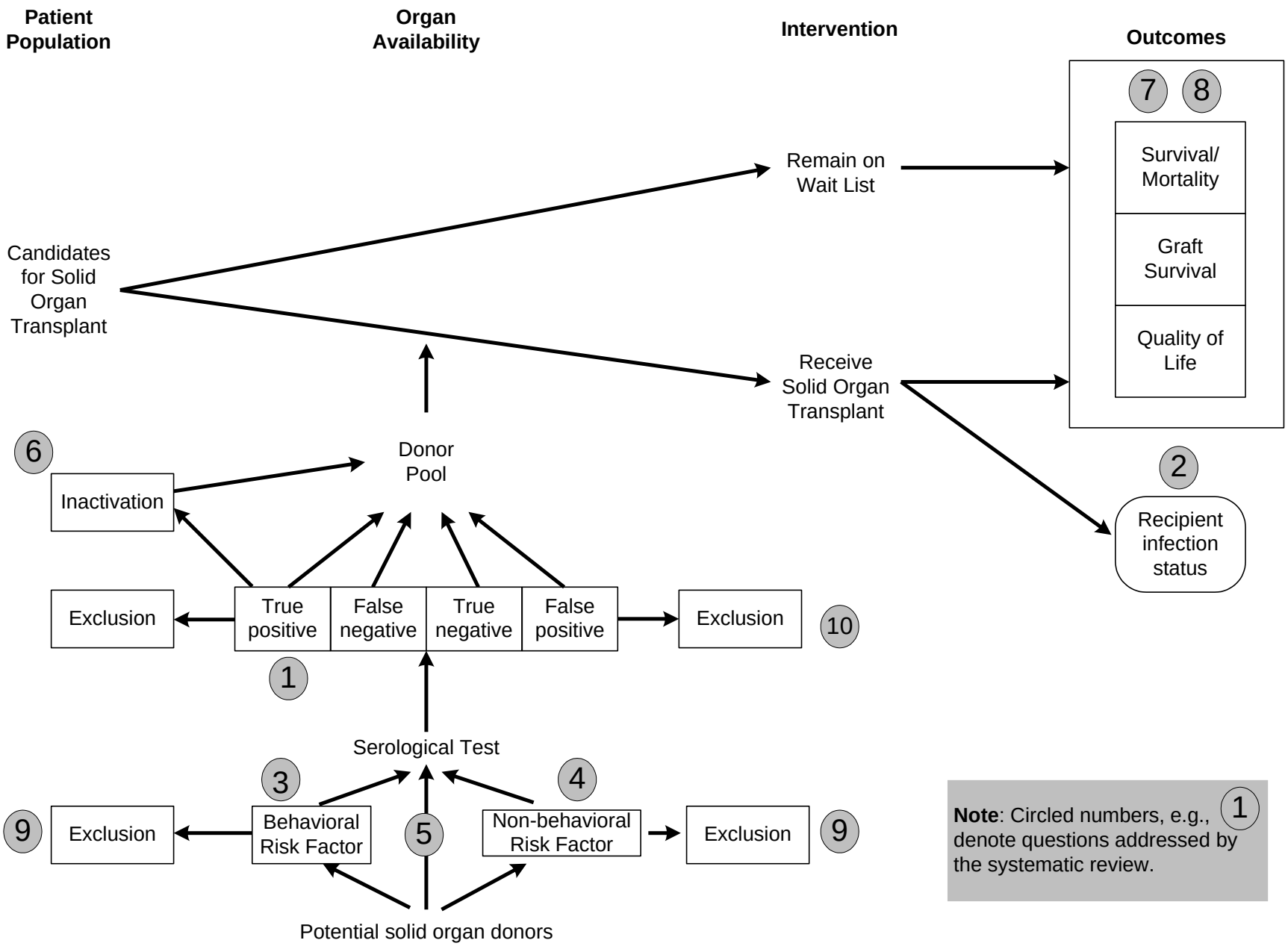
The questions are depicted in an analytic framework (Figure 1) on the next page. The patient population of interest is candidates for solid organ transplantation. The availability of such organs can be influenced by numerous factors depicted in the lower half of the figure, notably the infection status of the donor, and

donor behavioral and nonbehavioral risk factors. In this framework, each candidate either 1) receives an organ or 2) remains on the waitlist. The clinical outcomes of interest include patient survival, graft survival, quality of life and recipient infection status.

The rest of this document is divided into numerous sections, as follows:

- **Methodology**, wherein we describe the methods used for conducting the systematic review
- **Overview of the evidence**, which paints a broad portrait of the included evidence
- **Evidence for each question**, which is divided into 10 sections. All text and evidence tables for a given question are collated together with that question. Thus, there are no appendices of evidence tables.
- **Gaps in the current literature**, which discussed the primary areas where further research is necessary
- **References**, which provides the full bibliography of included evidence
- **Details of literature search,** which provides the search strategies we employed

Figure 1. Analytic Framework



Methodology

Search Strategy

We searched six bibliographic databases including MEDLINE, EMBASE, and the Cochrane Library to identify clinical trials and other relevant publications. (All searched databases are listed in Table 77 of Appendix A.) Separate date limits were used for some questions, although most spanned 1990 through 2009. Mechanisms used to retrieve additional relevant information included review of bibliographies/reference lists from peer reviewed and gray literature. (Gray literature consists of reports, studies, articles, and monographs produced by federal and local government agencies, private organizations, educational facilities, consulting firms, and corporations. These documents do not appear in the peer-reviewed journal literature.) Alphabetical lists of the concepts searched and detailed search strategies are provided in Appendix A (Details of Literature Search).

Inclusion Criteria

The following universal criteria were applied to all Questions for Systematic Review

- English language
- Peer-reviewed, full-length publication with original data
- Multiple publications of the same study were treated as a single study rather than as multiple studies to avoid double-counting patients.
- The study included at least one of the following bloodborne pathogens: HIV, HBV, and HCV.
- The determination of the presence or absence of HIV/HBV/HCV must have been based on laboratory test(s), rather than subjective estimates, physician interviews, or patient interviews.

Additional criteria were applied on a per-question basis, as depicted in Table 2 on the next page. For many questions, an insufficient number of studies was identified to support the development of the guideline. Consequently, in an effort to provide a sufficient amount of relevant information to support the development of the guideline, committee members expanded the inclusion criteria in multiple iterations over several months. The final question-specific inclusion criteria are shown in Table 3. The specific diagnostics tests of interest for Question 5 are listed in Table 4.

Table 2. Original Question-Specific Inclusion Criteria

Inclusion Criteria*	Questions for Systematic Review									
	1	2	3	4	5	6	7	8	9	10
Pertinent data on at least five people	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Data collected in U.S.A.	✓		✓	✓			✓	✓	✓	
Potential organ donors	✓		✓	✓					✓	
Rates not restricted to actual donors	✓									
Not voluntary reporting	✓									
Regardless of symptoms	✓									
Data collected in year 2000 or later	✓		✓	✓					✓	
Donor seropositive pre-transplant		✓				✓	✓			
Recipient seronegative pre-transplant		✓				✓				
Single type of organ, or separated data on different types of organs		✓				✓	✓	✓		
Waitlist control group							✓	✓		
Systematic review					✓					✓
Addressed test sensitivity and specificity					✓					✓
Experimental group with inactivation procedure						✓				
Control group without an inactivation procedure						✓				
Donor+ for behavioral or clinical factor pre-transplant								✓		

*For each Question for Systematic Review, five universal criteria were also applied (see text). A checkmark in a given column means that a study must have met that criterion in order to be included for the numbered Question for Systematic Review.

Table 3. Modified Question-Specific Inclusion Criteria

Inclusion Criteria*	Questions for Systematic Review									
	1	2	3	4	5	6	7	8	9	10
Pertinent data on at least five people	✓	✓	✓	✓	✓		✓	✓	✓	✓
Data collected in U.S.A.	✓		✓						✓	✓
Rates not restricted to actual donors	✓									
At least one of four populations: 1) Potential organ donors; 2) organ donors with samples taken prior to 1992 that were retrospectively tested for HCV; 3) potential tissue donors; or 4) the general population (for this last population, we included only the most up-to-date epidemiological estimates)	✓									
Regardless of symptoms	✓		✓							
Donor seropositive pre-transplant		✓				✓	✓			
Recipient seronegative pre-transplant		✓								
Single type of organ, or separated data on different types of organs		✓					✓	✓		
Waitlist control OR Control is recipients of organs from uninfected donors							✓			
If pre-transplant infected recipients and pre-transplant uninfected recipients were included, the study must have reported separate outcome data on these two types of recipients.							✓			
Reported patient survival, graft survival, or quality of life.							✓	✓		
At least one of four populations, enrolling individuals of any age: 1) Potential organ donors; 2) potential tissue donors; 3) potential blood donors; or 4) a sample representative of the general population (i.e., population unselected for any particular demographic, occupational, or behavioral characteristics, or health status other than HCV, HBV, or HIV infection status)			✓	✓						
A study of a specific *demographic* or *socioeconomic* subpopulation was included for HBV, but excluded for HIV and HCV.			✓	✓						
A study of a specific subpopulation of patients who were all selected for having the same *behavioral* risk factor was excluded for all three pathogens.			✓	✓						

Inclusion Criteria*	Questions for Systematic Review									
	1	2	3	4	5	6	7	8	9	10
Article must have been published in 1990 or later if pertinent to HIV or HCV, or 1966 or later if pertinent to HBV.			✓	✓						
In order to identify risk factors for the pathogen, study must have enrolled people with the risk factor as well as people without the risk factor; similarly, the study must have enrolled people positive for the pathogen as well as people negative for the pathogen.			✓	✓						
For identification of clinical signs and symptoms that may indicate infection, data may be from any country. For identification of co-morbidities or demographic factors that may be associated with infection, data must be from U.S only.				✓						
Reported at least one of the diagnostic tests listed in Table 4.					✓					
Reported at least one of the following: • Sensitivity and specificity • Positive and negative predictive values (clinical populations only) • Positive and negative likelihood ratios (clinical populations only) • Sufficient data to calculate the above • Window period • Turnaround time					✓					
Reported data on an individual test basis rather than multiple tests or algorithms.					✓					
Inactivation procedure performed before transplant on organs obtained from infected individuals.						✓				
Donor positive pre-transplant for behavioral risk factor or signs/symptoms risk factor or comorbidity risk factor.								✓		
Waitlist control OR Control is recipients of organs from donors without that risk factor.								✓		
Reported the number of organs that would not be included in the organ pool if donors with behavioral or nonbehavioral risk factors identified in questions 3 and 4 were excluded.									✓	
Reported the number of organs that would not be included in the organ pool if false positives were excluded.										✓

*For each Question for Systematic Review, five universal criteria were also applied (see text). A checkmark in a given column means that a study must have met that criterion in order to be included for the numbered Question for Systematic Review.

Table 4. Diagnostic Tests of Interest for Question 5

Virus	Test Name	Manufacturer
Tests Currently in Use by U.S. Organ Procurement Organizations		
HIV	Genetics System (GS) HIV-1/HIV-2 Plus 0 EIA	Bio-Rad Laboratories
	HIVAB HIV-1/HIV-2 (rDNA) EIA	Abbott Laboratories
HBV (HBsAg; the surface antigen)	Abbott PRISM HbsAg Assay	Abbott Laboratories
	ADVIA Centaur HbsAg Assay	Siemens Healthcare Diagnostics
	AxSYM HBsAg	Abbott Laboratories
	Genetic Systems (GS) HBsAg EIA 3.0	Bio-Rad Laboratories
HBV (anti-HBs; antibodies to the surface antigen)	Ortho Antibody to HbsAg ELISA Test System 3	Ortho Clinical Diagnostics
HBV (anti-HBc; antibodies to the core antigen)	Abbott PRISM HBcore	Abbott Laboratories
	ADVIA Centaur HBc Total Assay	Siemens Healthcare Diagnostics
	AxSYM Core 2.0	Abbott Laboratories
	CORZYME	Abbott Laboratories
	Ortho HBc ELISA Test System	Ortho Clinical Diagnostics
HCV	Abbott HCV EIA 2.0	Abbott Laboratories
	ADVIA Centaur Anti-HCV	Siemens Healthcare Diagnostics
	AxSYM Anti-HCV	Abbott Laboratories
	Ortho HCV Version 3.0 ELISA Test System	Ortho Clinical Diagnostics
HIV NAT	COBAS AmpliScreen HIV-1 Test v. 1.5	Roche Diagnostics
HCV NAT	COBAS AmpliScreen HCV Test v. 2.0	Roche Diagnostics
HBV NAT	COBAS AmpliScreen HBV Test	Roche Diagnostics
HCV and HIV-1 NAT	ProCleix HIV-1/HCV Assay	Gen-Probe Incorporated
Fourth Generation Tests		
HIV	ARCHITECT HIV Combo	Abbott Laboratories
	AxSYM HIV Ag/Ab Combo	Abbott Laboratories
	COBAS Core HIV Combo	Roche Diagnostics
	Coulter HIV-1 p24 Antigen Assay	Coulter Corporation
	Enzygnost HIV Integral II	Siemens Healthcare Diagnostics
	Genscreen Plus HIV Ag/Ab Combo	Bio-Rad Laboratories
	Genscreen HIV Ultra Ag-Ab Assay	Bio-Rad Laboratories
	Murex HIV Ag/Ab Combo	Abbott Laboratories
	Modular HIV Combo	Roche Diagnostics
	VIDAS DUO ULTRA	bioMerieux Clinical Diagnostics
	VIDAS DUO QUICK	bioMerieux Clinical Diagnostics
	Vironostika HIV Uni-Form II Ag/Ab	bioMerieux Clinical Diagnostics

Virus	Test Name	Manufacturer
HCV	INNOTEST HCV Ab IV	Innogenetics NV
	Monolisa HCV Ag/Ab Ultra	Bio-Rad Laboratories
	Murex 4.0	Abbott Laboratories

EIA or ELISA– Enzyme-linked immunosorbent assay
NAT – Nucleic acid test

Quality Assessment

In order to assess the quality of the data for each Question for Systematic Review, we applied the criteria listed in Table 5. Due to substantial differences among the questions, we generally used different criteria for each question. These criteria were determined after examining existing instruments for quality assessment and selecting the most appropriate items.

Table 5. Quality Assessment Criteria

Question	Quality Criteria
1. What are the prevalence and incidence rates of HIV, HBV, and HCV among potential solid organ donors?	1a. Was the population potential solid organ donors? 1b. For other populations, was the population unselected (i.e., not based on demographic or behavioral characteristics)? (studies of potential solid organ donors were scored as Yes, because they enrolled the population of interest)) 1c. Was infection status determined accurately? (i.e., accuracy of diagnostic test method used to determine infection status)
2. What are the rates of transmission to recipients from donors infected with HIV, HBV, or HCV? Do the rates vary by the organ transplanted or when the donor was infected?	2a. Was the study planned prospectively (i.e., before any data were collected) 2b. Were all consecutive patients enrolled (or a random sample of eligible patients)? 2c. Were laboratory tests performed on recipients regularly in order to monitor antigens/antibodies? (greater frequency means greater accuracy at estimating the rate) 2d. Did all patients receive the same prophylaxis strategy (or none received any prophylaxis)? (a mix of prophylaxis strategies means a less interpretable rate)

Question	Quality Criteria
3. What behavioral risk factors are associated with an increased probability of infection with HIV, HBV, or HCV? What is the prevalence of these characteristics among potential solid organ donors?	3a. Was the population potential solid organ donors? 3b. For other populations, was the population unselected (i.e., not based on demographic or behavioral characteristics)? Were infected and uninfected participants similar on other risk factors? 3c. Were infected and uninfected participants similar on other risk factors? 3d. If not, were statistical adjustments performed to control for other risk factors? 3e. Was risk factor data collected in a valid manner (e.g., confidential or anonymous collection of sensitive risk factor data, collection of personal information from the person directly instead of someone else) 3f. Was infection status determined accurately? (i.e., accuracy of diagnostic test method used to determine infection status)
4. What nonbehavioral factors are associated with an increased probability of infection with HIV, HBV, or HCV? What is the prevalence of these factors among potential solid organ donors?	Same as Question 3
5. What are the test characteristics of the screening methods available to detect HIV, HBV, and HCV in potential solid organ donors? Do test characteristics differ in particular populations and with donor clinical status (i.e., heart beating vs. non-heart beating donors OR adult vs. pediatric donors)?	5a. For measures of diagnostic performance other than window period detection and turnaround time, were the sample sets representative of real-world use in terms of infection prevalence, infection genotypes, and proportion of samples in window period? 5b. For measures of diagnostic performance other than window period detection and turnaround time, was a reference standard with excellent accuracy used? If not, was a reference standard with very good accuracy used? 5c. Were all consecutive patients enrolled (or a random sample of eligible patients)? 5d. Were readers of the diagnostic test of interest blinded to the results of the reference standard? 5e. Were readers of the reference standard blinded to the results of the diagnostic test of interest? 5f. Was the funding for this study derived from a source that would not benefit financially from either data favorable to the test or data unfavorable to the test?

Question	Quality Criteria
6. Which donor interventions reduce the probability of pathogen transmission from an organ donor infected with HIV, HBV, or HCV to a previously uninfected recipient?	6a. Were the patients randomly assigned to treatments? 6b. Was the study planned prospectively (i.e., before any data were collected) 6c. Were all consecutive patients enrolled (or a random sample of eligible patients)? 6d. Were the two groups comparable at baseline? (age, sex, comorbidities, indication for transplant, previous duration on waitlist) 6e. If not, were statistical adjustments performed to control for baseline differences? 6f. Were the two groups treated concurrently? 6g. Did at least 85% of the study enrollees provide data? 6h. Was the between-group difference in study completion rates less than 15%?
7. How do the clinical outcomes of recipients of organs from donors infected with HIV, HBV, or HCV compare to those who remain on the transplant list?	Same as Question 6
8. How do the clinical outcomes of transplant recipients who receive organs from donors with behavioral or nonbehavioral risk factors compare to those who remain on the transplant list?	Same as Question 6
9. What is the impact of excluding potential solid organ donors with behavioral or nonbehavioral risk factors on the organ donor pool?	Same as Question 6
10. What is the impact of false positive tests on the organ donor pool?	Same as Question 6

GRADE Assessment

We used the GRADE evidence rating methodology, which has been developed for treatment comparisons (Questions 6, 7 and 8)[1] and diagnostics (Question 5).[2] The GRADE system determines the quality of the evidence for a single outcome of a single comparison based on nine factors. "Quality" here encompasses not only quality in terms how well the study was designed, but also eight additional factors including inconsistency, indirectness, and imprecision of the evidence base (evidence base being all studies included for that outcome). The first factor (study design) sets the starting GRADE, in which randomized studies start at High, observational studies start at Low, and all other study designs start at Very Low. The next four factors can only be used to downgrade from this starting level (study quality limitations, inconsistency, indirectness, imprecision). The other four factors are grouped under "Other considerations", and they are reporting bias (which can only be used to downgrade), large magnitude of effect, all plausible confounders would have reduced the effect, and dose-response association (these latter three factors can only be used to upgrade, if applicable). Ultimately, the GRADE system yields an overall rating for each outcome, which ranges from "very low" to "high". The interpretation of these ratings is summarized in Table 6.[3] The details of the application of the GRADE system for each question are described in those sections.

Table 6. Interpretation of GRADE Ratings

Quality Rating	Interpretation
High	Further research is very unlikely to change our confidence in the estimate of effect
Moderate	Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate
Low	Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate
Very Low	Any estimate of effect is very uncertain

Note: These interpretations are from Box 2 of Guyatt et al. (2008).[3]

GRADE methodology has not been developed for the questions on epidemiology (Question 1), transmission (Question 2), risk factors (Questions 3 and 4), and the impact of exclusions on the donor pool (Questions 9 and 10). For these, we created GRADE methodology as follows. For Questions 1 and 2, no randomized trials are necessary to address the questions, therefore the starting evidence grade was High, and we applied the other components of the GRADE system as appropriate. For Questions 3 and 4, we used a starting evidence grade of Low because risk factor studies are by nature observational. Portions of Questions 3 and 4 involve the prevalence of risk factors; these were graded similarly as Question 1 (epidemiology). For Questions 9 and 10, it was not necessary to develop new GRADE methodology, because for Question 9 there was only one study and it had already been graded in Question 8, and for Question 10 there were no included studies.

Statistical Analysis

To compute the 95% confidence interval around a single percentage, we used the Wilson score method.[4,5] For comparing pre-transplant characteristics, we computed the size of the between-group difference using Hedges' g for continuous data and the difference in percentages for dichotomous data. We defined a large difference at baseline as a Hedges' g of 0.4 or more for continuous data, or a difference in percentage of 15 percentage points or more for dichotomous data. Where appropriate, we combined the results of multiple studies using DerSimonian and Laird random-effects meta-analysis[6] using specialized software (Comprehensive Meta-Analysis, Biostat Inc., Englewood, New Jersey). We measured heterogeneity using the I^2 statistic.[7] For risk factors, we computed the odds ratio and/or relative risk (and 95% confidence intervals) using standard methods with a 0.5 continuity correction applied to studies with a 0% rate in either group. For diagnostics, we computed sensitivity and specificity (and 95% confidence intervals) using MetaDisc 1.4. Additional statistical methods are described for each question in the text for that question.

Evidence Tables

For each question, we constructed evidence tables displaying numerous details about each study. These varied by question, and included:

- **Question 1 (epidemiology):** Years of data collection, donor population, data sources, relevant viruses, diagnostic methods, whether diagnoses were confirmed, quality assessment criteria, and relevant data
- **Question 2 (transmission):** Country, specific transplantation centers, which organ(s), number of transplantation centers, study funding source, the use of pre-transplant prophylaxis, the frequency of post-transplant testing for infection, duration of follow-up, timing of post-transplant infections, diagnostic methods, pre-transplant patient characteristics, quality assessment criteria, which antigen/antibody was used for defining donor positivity, which antigen/antibody was used for defining recipient positivity after transplant, and the relevant data.
- **Question 3 (behavioral risk factors):** Virus(es), data source(s), country, selection methods, how risk factor data were collected, relevant blood tests used, study funding source, years of data collection, participant characteristics, specific risk factor(s) under investigation, specific population(s) included, how enrollees were selected, which confounders were adjusted for (if applicable), quality assessment criteria, reported statistical test results, and the relevant data
- **Question 4 (nonbehavioral risk factors):** Generally the same as in Question 3
- **Question 5 (diagnostics):** the index test and its category, data source(s), country, whether the infection status of samples was known before the study was conducted, whether the sample was unselected, the reference standard, other tests performed, test manufacturer, FDA approval date (if applicable), test format, whether specimens can be obtained from living donors or deceased donors or both, whether tests are applied to serum of plasma or both, quality assessment criteria, GRADE tables, reported data on diagnostic performance, window period, and turnaround time
- **Question 6 (inactivation):** all steps in the inactivation procedure, when the viral load was measured, quality assessment criteria, GRADE tables, the total viral burden before and after inactivation, the percentage of viral copies that had been removed

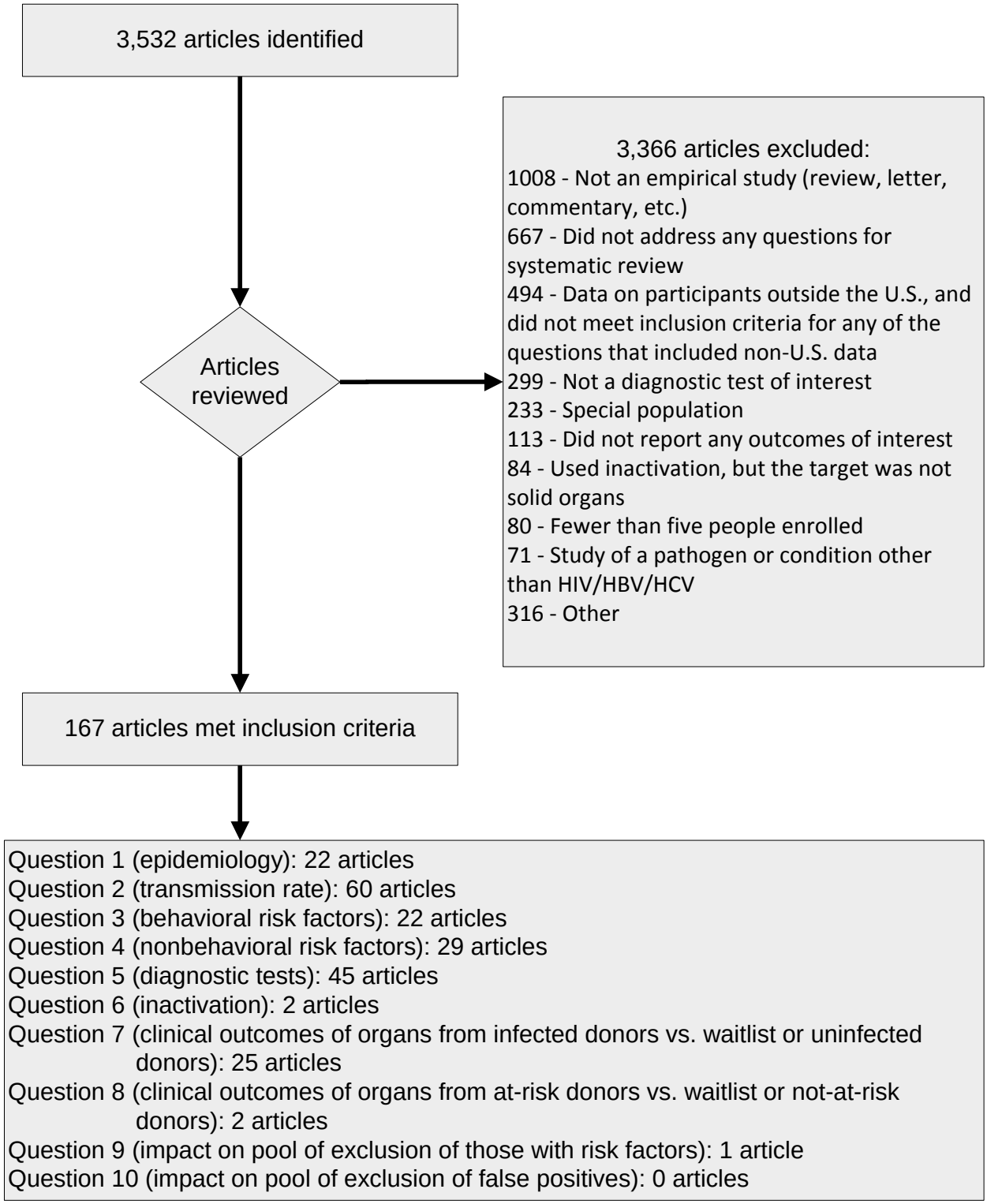
- **Question 7 (clinical outcomes of known positive organs vs. waitlist or known negative organs):** Country, specific transplantation centers, which organ(s), number of transplantation centers, study funding source, pre-transplant patient characteristics, which antigen/antibody was used for defining donor positivity, diagnostic methods, quality assessment criteria, GRADE tables, whether "survival" meant graft survival or patient survival, duration of follow-up for each data point, any adjustments for confounding, reported statistical test results, and the relevant data
- **Question 8 (clinical outcomes of at-risk organs vs. waitlist or not-at-risk organs):** for models, key assumptions about donors/recipients/death rates/costs/QALYS, assumed incidence and prevalence in specific subpopulations, quality assessment criteria, GRADE tables, and relevant data
- **Question 9 (impact of excluding donors with risk factors on the donor pool):** Same as in Question 8
- **Question 10 (impact of false positives on the donor pool):** Same as in Question 8

Overview of the Evidence

A graphical depiction of the process of article identification appears in Figure 2. The three most common reasons for exclusion were: Not an empirical study (review, letter, commentary, etc.), did not address any questions for systematic review, and data on participants outside the U.S., and did not meet inclusion criteria for any of the questions that included non-U.S. data. Of the 167 included articles, the largest evidence bases were for Question 2 on transmission (60 articles) and Question 5 on diagnostic tests (45 articles). The counts for other questions are shown in the figure.

For Question 5 (diagnostics), 99 items from the gray literature were reviewed for potentially useful data. These included literature from manufacturers' Web sites (40), the internet (6), the Food and Drug Administration (FDA) (23), agencies in the United Kingdom (14), agencies from Australia (13), and items from the World Health Organization (3). We included data on window period or turnaround time from 26 of the 99 items.

Figure 2. Study Attrition Diagram



NOTE: The counts add to more than 166 because some articles were included for multiple questions.

Evidence Reviews: I. Probability of transmission of HIV, HBV, or HCV through solid organ transplantation (SOT)

Question 1. What are the prevalence and incidence rates of HIV, HBV, and HCV among potential solid organ donors?

This question involves the frequency of HIV, HBV, and HCV among individuals whose organ(s) are being considered for donation. These rates may differ from rates in the general population or from the rates in individuals who actually did donate organ(s). We considered both the prevalence (the percentage of potential organ donors at a given time who test positive for the pathogen) as well as incidence (the percentage of potential organ donors who newly acquire the pathogen in a one-year period).

Due to the small amount of evidence on potential solid organ donors, we expanded the scope to include other possibly relevant populations. Thus, the evidence for this question is described in separate sections:

1) **Potential solid organ donors** (three studies)
2) **Actual solid organ donors who had donated prior to 1991 and their lab samples were retrospectively tested for HCV** (four studies). Hepatitis C virus (HCV) was discovered in April of 1989, and serological screening for it was not widely performed until 1991. Therefore, another possible source of epidemiological data is studies of stored blood or plasma samples from actual organ donors before 1991. Because of the early donation date, the samples had not been screened for HCV prior to donation.
3) **Potential tissue donors** (two studies). This population may be a reasonable approximation of potential solid organ donors.
4) **The general population** (six studies). This population may also approximate potential solid organ donors.

Potential Organ Donors

Three studies reported prevalence estimates of HIV, HCV, and/or HBV among potential organ donors. The definition of "potential organ donor" involved liver donor referrals in two studies (relatives wishing to donate to children,[8,9] and deceased donors in the other studies.[10,11] Testing methods and diagnostic criteria were not consistently reported and may have varied among the studies. Differences in donor populations and methods used to diagnose and report infection probably contributed to the range in reported prevalence. It is not clear that the antibody tests were confirmed by a more specific method such as Western blot, recombinant immunoblot assay (RIBA), or nucleic acid-amplification tests (NAT) in most of these studies; lack of confirmation may have contributed to overestimation of prevalence due to antibody reaction false-positives. Lack of confirmation could also lead to an underestimation of prevalence if less sensitive antibody are used and if recent infections are missed. One study[10] tested for HBV DNA among those whose serological tests was equivocal or positive for antibodies for the core antigen (anti-HBc) or the surface antigen (HBsAg).

In the study that reported it, the prevalence of HCV was 3.6% among potential living donor relatives.[8] The prevalence of active hepatitis, type unspecified, among deceased potential donors rejected from

donation was reported as 5.3% (95% CI: 2.2% to 12.2%) in a study of potential deceased donors.[11] The remaining study reported the prevalence of unspecified hepatitis at 18.2% (95% CI: 7.0% to 39.6%) among potential living donor relatives excluded at the second stage of evaluation.[9]

HIV prevalence was also reported by two of those studies. A study of living adult potential donors did not detect any cases of HIV out of the 45 individuals screened[9,9], and the study on potential deceased donors reported the prevalence of HIV or syphilis (data for HIV alone not reported) at 2.1% (95% CI: 0.5% to 8.1%).[11]

The quality assessment items are listed in Table 13. Meta-analysis was not performed because there were no instances where at least two studies reported the prevalence of the same virus. These data and additional information regarding the studies they were extracted from are shown in Table 7, below.

Table 7. Prevalence of Hepatitis and HIV among Potential Organ Donors

Citation	Year	Year of Data Collection	Donor Population	Data Collection	Virus	Diagnostic Method	Confirmed?	Prevalence
Hepatitis								
Hidalgo et al.[8]	2001	1990 to 1999	Living adult parents	Retrospective chart review	HCV	Not reported	Not reported	3.6% (95% CI: 1% to 12.3%)¶ (2/55)
Domen et al.[10]	2000	10/94 to 10/98	Potential organ donors	Retrospective chart review	HBV	Unspecified serology	HBV-DNA was also tested in 16 of 22, and it was positive in 1/16.	4.9%* (95% CI: 3.3% to 7.4%)¶ (22/446)
Renz et al.[9]	1995	5/1992 to 5/1994	Living adult relatives	Retrospective review	Hepatitis (both B and C were screened for)	Unspecified serology	Not reported	18.2% (95% CI: 7.0% to 39.6%) (4/22) ¶
Richards[11]	1993	9/1989 to 8/1991	Deceased donors; potential cardiac donors	Retrospective data review	Active viral hepatitis (Authors did not report how many of the 430 potential donors had been *tested* for hepatitis.)	Not reported	Not reported	Of the 94 potential donors excluded from donation for medical reasons, 5.3%; 95% CI: 2.2% to 12.2%)¶ were excluded due to active hepatitis.
HIV								
Renz et al.[9]	1995	5/1992 to 5/1994	Living adult relatives	Retrospective review	HIV	Unspecified serology	Not reported (no positives)	0% (95% CI: 0% to 100%) (0/22) **¶

Citation	Year	Year of Data Collection	Donor Population	Data Collection	Virus	Diagnostic Method	Confirmed?	Prevalence
Richards[11]	1993	9/1989 to 8/1991	Potential deceased cardiac donors	Retrospective data review	HIV or syphilis (not reported separately). Authors did not report how many of the 430 potential donors had been *tested* for HIV.	Not reported	Not reported	Of the 94 potential donors excluded from donation for medical reasons, 2.1%; 95% CI: 0.5% to 8.1%)¶ were excluded due to HIV or syphilis.

* Domen et al.[10] included those with equivocal tests as well as those with positive tests, but did not report the corresponding counts.
95% confidence interval (CI) calculated by ECRI Institute.
¶ **The denominator of 22 is the number of candidates who underwent phase 2 of evaluation for donation, out of 75 total considered for evaluation.

Pre-1991 Organ Donors Retrospectively Tested for HCV

We included four such studies, the methods and results are shown in Table 8. All four studies met two of the three quality criteria (not selecting patients on the basis of behavioral or demographic factors, and using a standardized diagnostic test for determining infection status). Two studies only included deceased donors, and the other two did not report whether donors were living. The studies found a wide range of prevalence from 2.4% to 6.8%. Because the studies' methods were sufficiently similar, we combined the results in a random-effects meta-analysis, and this revealed substantial heterogeneity (I^2 = 85%); the combined estimate of HCV prevalence was 4.0% (95% CI: 2.2% to 7.3%).

These rates may be influenced by geography as well as the specific anti-HCV tests used by investigators. Shah et al. (1993)[12] collected data from those who had received transplants in Pittsburgh, and they used a second generation ELISA assay (no further specifics reported). Vincenti et al. (1993)[13] assessed organ donors from California and tested samples for anti-HCV using an ELISA but did not report the generation, and also tested for HCV RNA. Pereira et al. (1992)[14] assessed organ donors from New England using a second generation ELISA assay (the HCV Elisa 2.0 Test System from Ortho Diagnostics) that "detects antibody to four recombinant HCV antigens (5-1-1, c100, c33, and c22)", the RIBA HCV Test system from Chiron, and test for HCV RNA using PCR.[14] Roth et al. (1992)[15] assessed organ donors from Miami "using a commercial ELISA (Ortho Diagnostic Systems)" (unreported generation), "a second generation RIBA" (Chiron Corporation)", and test for HCV RNA via PCR.[15]

Table 8. Prevalence of HCV among Pre-1991 Organ Donors

Citation	Dates of Organ Donation	Donor Population	Data Collection	Diagnostic Method	Confirmed?	Prevalence
Shah et al. (1993)[12,16]	Mar-86 to Mar-90	Liver donors (unreported whether living or deceased)	Retrospective testing of lab samples	Anti-HCV by ELISA2	Not reported	5.8% (95% CI: 4.1% to 8.2%) (30/516) ¶
Vincenti et al. (1993)[13]	Jan-86 to Dec-88	Deceased kidney donors	Retrospective testing of lab samples	Anti-HCV by ELISA (unreported version)	Yes, all four positives were confirmed as HCV RNA+	2.8% (95% CI: 1.1% to 7.0%) (4/143) ¶
Pereira et al. (1992)[14,17-19]	1985 to 1992	Deceased organ donors	Retrospective testing of lab samples	Anti-HCV by ELISA1 and ELISA2	Of those positive by ELISA1, 47% were positive for HCV-RNA.	2.4% (95% CI: 1.9% to 3.0%) (73/3078)[a]¶
Roth et al. (1992)[15,20]	Jan-79 to Feb-91	Deceased organ donors	Retrospective testing of lab samples	ELISA (unreported version) and RIBA	Half of the RIBA+ donors were HCV RNA+	6.8% (95% CI: 4.9% to 9.4%) (33/484) ¶

Citation	Dates of Organ Donation	Donor Population	Data Collection	Diagnostic Method	Confirmed?	Prevalence
Combined prevalence (random-effects meta-analysis; I^2 = 85%)						**4.2% (2.2% to 7.7%)**

¶ 95% confidence interval (CI) calculated by ECRI Institute.

[a] The prevalence in the Pereira et al. study was based on the largest publication, which included 3078 tested donors.[17] The number in the table is the study's estimated prevalence of positivity for HCV RNA, based on the two findings that 5.1% of the 3078 donors were ELISA1 positive, and 47% of those were HCV RNA positive (i.e., 47% of 5.1% is 2.4%)

Potential Tissue Donors

We included one retrospective study on this population. Zou et al. assessed the frequency of HBV, HCV, and/or HIV among tissue donors and estimated both incidence and prevalence.[21] Four of the 5 tissue centers in Zou et al. reported confirmed positive results whereas one center reported screening results only. Zou et al. estimated confirmed positive results for the fourth center using data from the other sites.

Table 9 shows the pertinent data. The prevalence of confirmed HIV was 0.093% (95% CI 0.036% to 0.150%) of donors.. The prevalence of confirmed HBV was 0.229% (95% CI 0.139% to 0.319%) among donors in Zou et al. Zou et al. also used the tissue donor data as well as blood donor data to estimate the incidence of early viral infection undetected during the serologic window period. Their estimated incidence rates per 100,000 person years were 30.11 for anti-HIV, 18.325 for HbsAg, and 12.380 for anti-HCV.

Table 9. Prevalence of Hepatitis and HIV Among Potential Tissue Donors

Citation	Year	Year of Data Collection	Donor Population	Data Collection	Virus	Diagnostic Method	Confirmed?	Prevalence*
Hepatitis								
Zou et al.[21]	2004	2000 through 2002	Tissue donors, no other information provided	Prevalence data retrospectively collected from tissue bank databases of 5 tissue banks; Incidence estimated	HBV	HbsAg	Yes	0.229% (95% CI: 0.139% to 0.319%)¶
					HCV	Anti-HCV	Yes	1.091% (95% CI: 0.896% to 1.286%)¶
HIV								
Zou et al.[21]	2004	2000 through 2002	Tissue donors, no other information provided	Prevalence data retrospectively collected from tissue bank databases of 5 tissue banks; Incidence estimated	HIV	Anti-HIV	Yes	0.093% (95% CI: 0.036% to 0.150%)¶

* Denominator represents all potential donors who were tested for HIV, HBV and HCV.
¶ 95% confidence interval (CI) calculated by ECRI Institute.

General Population

The six included general population studies are listed in Table 10. All six studies met two of the three quality criteria (not selecting patients on the basis of behavioral or demographic factors, and using a standardized diagnostic test for determining infection status).

For HIV in the general population, the CDC has estimated that the annual U.S. incidence in 2006 was 56,300[22,23] and the prevalence was 1,106,400.[24] The U.S. population was approximately 299,000,000 in that year,[25] thus the incidence was approximately 0.019% (1 in 5,308) and the prevalence was approximately 0.37% (1 in 270).

For HBV and HCV in the general population, Table 11 provides the most recently available estimates. The U.S. population was approximately 302,000,000 in 2007,[25], which means the incidence rates for HBV and HCV were 0.014% (1 in 7,023) and 0.0056% (1 in 17,765), respectively. These data are based on estimates from multiple sources including the National Health and Nutrition Examination Survey (NHANES), the National Notifiable Diseases Surveillance System (NNDSS), the Emerging Infection Program, and the American Community Survey.

Table 10. Methods of Studies Included on Incidence and Prevalence in the U.S. General Population

Citation	Year of Data Collection	Data Collection	Virus(es)	Diagnostic Method*	Confirmed?
Hepatitis					
Daniels et al. (2009)[26,27]	2007	NNDSS	HBV, HCV	Various; specifics not reported	Yes
Weinbaum et al. (2008)[28]	2006	NHANES, ACS	HBV	Not reported	NR
McQuillan et al. (1999)[29]	1988-1994	NHANES	HBV	Not reported	NR
Armstrong et al. (2006)[30]	1999-2002	NHANES	HCV	3rd generation ELISA	Yes, using RIBA or HCV-RNA test
HIV					
Prejean et al. (2009)[22,23]	2006	A new national case reporting system	HIV	STARHS	NR
Centers for Disease Control (2008)[24]	2006	A new national case reporting system	HIV	STARHS	NR

* ACS – American Community Survey

ELISA – Enzyme-linked immunosorbent assay
NHANES – National Health and Nutrition Examination Survey
NNDSS – National Notifiable Disease Surveillance System
STARHS – Serological testing algorithm for recent HIV seroconversion

Table 11. Incidence and Prevalence of HBV and HCV in the U.S. General Population

	HBV	HCV
Incidence	43,000 (in 2007)[26,27]	17,000 (in 2007)[26,27]
Number of acute clinical cases[a]	13,000 (in 2007)[26,27]	2,800 (in 2007)[26,27]
Number of people with chronic infection[b]	Between 0.8 million and 1.4 million (in 2006)[28]	Between 2.7 million and 3.9 million (in 1999-2002)[30]
Percentage of people ever infected[c]	Between 4.3% and 5.6% (in 1988-1994)[29]	Between 1.3 and 1.9% (in 1999-2002)[30]

[a] For hepatitis B, the incidence estimates and the estimated number of acute clinical cases are "derived from catalytic modeling of seroprevalence data from the Third National Health and Nutrition Examination Survey (NHANES III) applied to cases reported to the National Notifiable Diseases Surveillance System (NNDSS)."[27] For hepatitis C in 2007, these estimates were based on data from the Emerging Infection Program.[27] The number of acute clinical cases is different from incidence, because most new infections are asymptomatic (and thus not diagnosed or reported)..

[b] For hepatitis B, the number of people with chronic infection was based on the 2006 American Community Survey and a U.S. Department of Justice study of prison and jail inmates.[28] For hepatitis C, the numbers were based on NHANES data from 1999-2002.[30]

[c] For hepatitis B, the percentage of people ever infected was based on NHANES data from 1988-1994.[29] For hepatitis C, the numbers were based on NHANES data from 1999-2002.[30]

GRADE Assessment of Epidemiology

The GRADE table for this question appears in Table 12. We graded the evidence as Low for all three pathogens. This was due to two concerns: varying estimates of epidemiological statistics, and the use of populations other than potential organ donors. The variation in estimates between the different studies was not simply due to their enrollment of different populations. For example, even within the four studies of pre-1991 actual organ donors who were retrospectively tested for HCV, prevalence estimates ranged widely (by a factor of more than three: from 1 in 15 to 1 in 55).

Table 12. GRADE Table for Question 1 (Epidemiology)

Pathogen	Outcome	Quantity and Type of Evidence	Findings	Starting Grade	Decrease GRADE					Increase GRADE			GRADE of Evidence for Outcome	Overall GRADE of Evidence Base
					Study Quality	Consistency	Directness	Precision	Publication Bias	Large Magnitude	Dose-response	Confounders would reduce the effect		
HIV	Incidence	1 study of potential tissue donors[21] 1 study of the U.S. general population[22,23]	In the study of potential tissue donors, incidence of 30.11 per 100,000 person-years In the general population study, incidence of 56,300 in 2006, which corresponds to 18.8 per 100,000 person years	High	0	-1	-1	0	0	0	0	0	Low	Low
	Prevalence	2 studies of potential organ donors[9,11] 1 study of potential tissue donors[21] 1 study of the U.S. general population[24]	In the studies of tested potential organ donors, prevalence of HIV was 0/22 (0%), and prevalence of HIV or syphilis was and 2/94 (2.1% or 1 in 48). In the study of potential tissue donors, prevalence was 10/10,910 (0.093% or 1 in 1,090). In the general population study, prevalence was 1,106,400 in 2006 (0.37%, or 1 in 270)	High	0	-1	-1	0	0	0	0	0	Low	

Pathogen	Outcome	Quantity and Type of Evidence	Findings	Starting Grade	Decrease GRADE					Increase GRADE			GRADE of Evidence for Outcome	Overall GRADE of Evidence Base
					Study Quality	Consistency	Directness	Precision	Publication Bias	Large Magnitude	Dose-response	Confounders would reduce the effect		
HBV	Incidence	1 study of potential tissue donors[21] 1 study of the U.S. general population[26,27]	In the study of potential tissue donors, incidence of 18.325 per 100,000 person-years In the general population study, 43,000 incidence in 2007, which corresponds to 14.4 per 100,000 person-years	High	0	0	-1	0	0	0	0	0	Moderate	
	Prevalence	1 study of HBV in potential organ donors[10] 2 studies of hepatitis(including HBV and HCV) in tested potential organ donors[9,11] 1 study of potential tissue donors[21] 1 study of the U.S. general population[28]	In the study of HBV in potential organ donors, prevalence was 22/446 (4.9%, or 1 in 20). In the two studies of hepatitis in potential organ donors, prevalence of 5/94 (5.3%, or 1 in 19) and4/22 (18.2%, or 1 in 6). The study of potential tissue donors reported a prevalence of 25/10901 (0.229%, or 1 in 436).. In the general population study, prevalence of chronic infection was 1.1 million in 2006 (0.36% or 1 in 274)	High	0	-1	-1	0	0	0	0	0	Low	Low

Pathogen	Outcome	Quantity and Type of Evidence	Findings	Starting Grade	Decrease GRADE					Increase GRADE			GRADE of Evidence for Outcome	Overall GRADE of Evidence Base
					Study Quality	Consistency	Directness	Precision	Publication Bias	Large Magnitude	Dose-response	Confounders would reduce the effect		
HCV	Incidence	1 study of potential tissue donors[21] 1 study of the U.S. general population[26,27]	In the study of potential tissue donors, incidence of 12.38 per 100,000 person-years In the general population study, 17,000 incidence in 2007, which corresponds to 5.7 per 100,000 person-years	High	0	-1	-1	0	0	0	0	0	Low	
	Prevalence	1 study of HCV in potential organ donors[8] 1 study of "hepatitis" in potential organ donors[9] 4 studies of prevalence among pre-1991 organ donors[12-18,20] 1 study of potential tissue donors[21] 1 study of the U.S. general population[30]	In the study of HCV in potential organ donors, prevalence was 2/55 (3.6%, or 1 in 28). In the study of HBV and HCV in potential organ donors, prevalence was 5/430 (1.2%, or 1 in 86) In the studies of pre-1991 organ donors, combined estimate of prevalence of 4.0% or 1 in 25. In the study of potential tissue donors, prevalence of 119/10915 (1.091%, or 1 in 92). In the general population study, prevalence of infection was 4.1 million (1.6% of the U.S. population) in 1999-2002.	High	0	-1	-1	0	0	0	0	0	Low	Low

Additional Evidence Tables for Question 1

Table 13. Question 1: Quality Assessment

Study	1a	1b	1c
Potential Solid Organ Donors			
Hidalgo et al.(2001)[8]	✓	✓	
Domen et al.(2000)[10]	✓	✓	✓
Renz et al. (1995)[9]	✓	✓	
Richards (1993)[11]	✓	✓	
Actual Solid Organ Donors Pre-1991 Retrospectively Tested for HCV			
Shah et al. (1993)[12,16]		✓	✓
Vincenti et al. (1993)[13]		✓	✓
Pereira et al. (1992)[14,17-19]		✓	✓
Roth et al. (1992)[15,20]		✓	✓
Potential Tissue Donors			
Zou et al. (2004)[21]		✓	✓
General Population			
Daniels et al. (2009)[26,27]		✓	✓
Weinbaum et al. (2008)[28]		✓	✓
McQuillan et al. (1999)[29]		✓	✓
Armstrong et al. (2006)[30]		✓	✓
Prejean et al. (2009)[22,23]		✓	✓
Centers for Disease Control (2008)[24]		✓	✓

A checkmark (✓) means that the study met the quality criterion for this Question; the lack of a checkmark means that the study either did not meet the criterion, or it was unclear whether the study met the criterion. The criteria specific to this Question were:

1a. Was the population potential solid organ donors?

1b. For other populations, was the population unselected (i.e., not based on demographic or behavioral characteristics)? (Studies of potential solid organ donors were scored as Yes, because they enrolled the population of interest.)

1c. Was infection status determined accurately? (i.e., accuracy of diagnostic test method used to determine infection status)

Question 2. What are the rates of transmission to recipients from donors infected with HIV, HBV, or HCV? Do the rates vary by the organ transplanted or when the donor was infected?

For this question, the rate of transmission is the chance that an infected organ donor transmits the infection to a previously uninfected recipient. The observed rate of transmission likely depends on numerous factors, including the bloodborne pathogen (HIV, HBV, or HCV), the organ transplanted, the specific antigens or antibodies for which the donor was positive, whether HBV prophylaxis was used, and the type of serologic testing used for detection. Thus, as we tabulated information from the large evidence base for this question, we carefully delineated those facets that could potentially influence the results.

Sixty articles met the inclusion criteria. These contained some duplication of patients, and after careful perusal, the evidence comprised 44 unique studies (a single "study" can involve multiple publications from the same center on the same kinds of patients who were enrolled in overlapping timeframes). All studies addressed either HBV or HCV, and we extracted data on those recipients who were negative before transplant and who had received organs from donors who had tested positive. The lack of evidence on HIV is probably a result of federal regulations that prohibit transplantation of organs from individuals known to be HIV-positive.

The evidence for this question is considered in seven separate sections, according to different pathogens and organs:

- 16 studies of **HBV** transmission from **liver** transplantation
- 9 studies of **HBV** transmission from **kidney** transplantation
- 6 studies of **HBV** transmission from **heart** transplantation
- 1 study of **HBV** transmission from **lung** transplantation
- 2 studies of **HCV** transmission from **liver** transplantation
- 10 studies of **HCV** transmission from **kidney** transplantation
- 4 studies of **HCV** transmission from **heart** transplantation

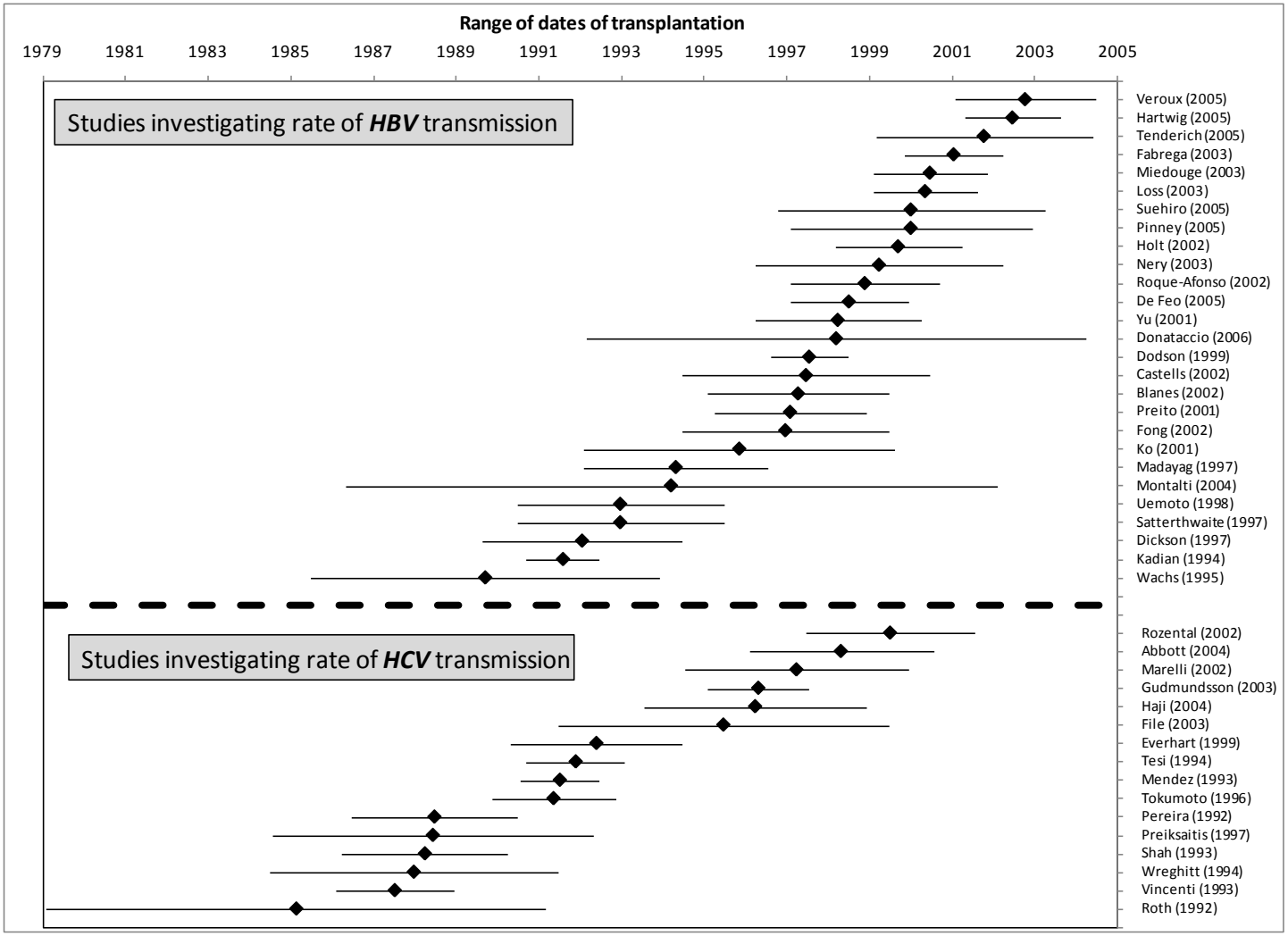
Reported results on transmission can vary greatly based on numerous factors. Obviously, the specific pathogen and the specific organ are critical factors. Also, the type of serological testing will matter, specifically 1) For which antigen/antibody was the donor positive? and 2) For which antigen/antibody was the recipient tested? One study might include organ donors who were anti-HBc+ and HBsAg-, and report the rate of HBsAg positivity among recipients. Another study might include the same types of donors, but report the rate of positive HBV DNA in serum among recipients. These studies are detecting infection in different ways, therefore it would not make sense to consider their results together. Still other important factors include the use of prophylaxis (e.g., lamivudine), specific diagnostic tests used, the frequency and timing of these tests, and the length of follow-up after transplantation. In our presentation of the evidence, we provide information about these factors to aid interpretation of results.

General characteristics of the 44 included studies are listed in Table 22 and Table 23. Twenty-six studies were conducted in the U.S., with the remaining 17 studies conducted in Spain (four studies), Japan (three

studies), Italy (three studies), France (two studies), Latvia, Belgium, Germany, Taiwan, Canada, and the U.K. (one study each). Thirty-five studies were conducted at only a single center. Data were collected retrospectively in 35 studies, prospectively in seven studies, and not reported in the other two studies. Consecutive enrollment was performed in 26 studies. The pre-transplant patient characteristics are listed in Table 24, quality assessments appear in Table 25, and the reported results are listed in Table 26.

A plot of the transplantation dates appears in Figure 3 below. The start dates of organ transplantations ranged from January 1979 to April 2001, with the median at June 1994. The end dates ranged from December 1988 to June 2004, with the median at July 1999. The median length of the transplantation period (the period of time when data were collected) was 4.4 years, with a range from 1.7 to 15.7. Only 13 studies reported information about study funding. These generally involved national funding sources, not corporations with conflicts of interest. The mean or median length of follow-up was reported by 26 studies, and it ranged from five months to 5.25 years, with a median of two years.

Figure 3. Question 2: Plot of Transplantation Dates



Thus, the "typical" study for Question 2 was a single-center U.S. study of unknown funding source that collected data retrospectively on consecutive patients who received an organ transplant in a four-year period in the mid-late 1990's, and were followed for an average of two years.

Pre-transplant characteristics of donors and recipients are listed in Table 24. Most studies (30 of 44, or 68%) did not report any characteristics specifically for those donor-recipient pairs in which the donor was positive and the recipient was negative before transplant. For the 13 studies that did report these characteristics, the following characteristics were reported by three or more studies:

- The mean donor age ranged from 39 to 43 (in the three studies reporting donor age)
- The mean recipient age ranged from 33 to 57 (nine studies)
- The percentage of males among donors ranged from 42% to 74% (three studies)
- The percentage of males among recipients ranged from 33% to 90% (ten studies)
- The percentage or recipients who were UNOS Status 1 ranged from 56% to 100% (three studies; these were studies of HCV transmission after heart transplantation)

Regarding quality assessment (Table 25), 37 of 44 studies (84%) were retrospective, and 26 of 44 studies (59%) enrolled patients consecutively. Twelve of 44 studies (27%) used some form of prophylaxis (e.g., HBIg, lamivudine) for *all* recipients, six used it for some but not all recipients, two used it for no recipients, and the other 23 studies did not report whether prophylaxis had been used. The frequency of post-transplant serology testing was reported by 21 studies, and the methods varied widely:

- Seven studies performed relatively intensive monitoring for hepatitis (e.g., "at weeks 1, 2, 3, 4, then monthly for one year, then every three months.")[31]
- Four studies performed relatively moderate monitoring (e.g., "At months 1, 3, and 6, then yearly")[32]
- Six studies used only sporadic monitoring. (e.g., "When possible, samples were obtained at 4 months, one year, and two years after transplant")[33]
- Three studies reported regular monitoring without stating a frequency (e.g., each patient was "tested on one or more occasions during routine clinical visits")[34]
- One study reported the use of liver biopsy "when clinically indicated"[35]

The next seven subsections describe the study results for this question.

HBV Transmission from Liver Transplantation

Studies measured virus transmission in 14 different ways for the transmission of HBV from liver transplantation (Table 14). As shown in the next to rightmost column, the range of rates was very wide.

The results are shown graphically in Figure 4 and Figure 5. One possible explanation for the differences among studies is the use of prophylaxis, which may result in negative recipient testing despite potential transmission. Studies that used HBV prophylaxis for *all* patients are depicted with open circles; studies that used HBV prophylaxis for *some but not all* patients are depicted with gray circles; studies that used HBV prophylaxis for *no* patients are depicted with black circles; studies that *did not report* whether

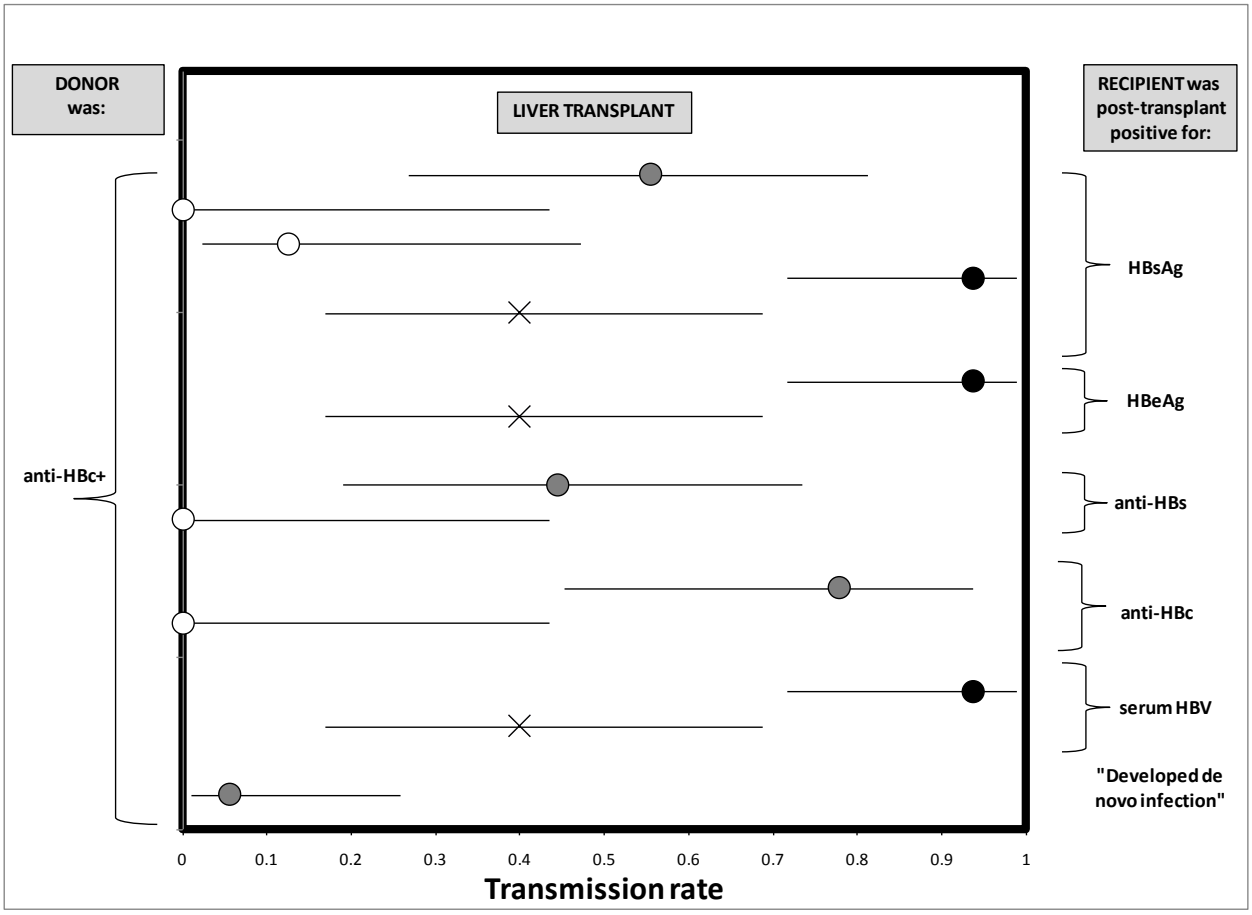
patients received prophylaxis are depicted with X's. The graphs suggest that rates were lower when prophylaxis was used.

Table 14. LIVER Transplantation: Ranges of HBV Results

Donor was:	Recipient was tested for post-transplant positivity of:	# of Studies	Range of Results	Studies
Anti-HBc+	HBsAg	5	0% to 94%	Roque-Afonso et al. (2002)[36], Yu et al. (2001)[35], Dodson et al. (1999)[37], Uemoto et al. (1998)[38-41], Kadian et al. (1994)[42]
Anti-HBc+	HBeAg	2	40% to 94%	Uemoto et al. (1998)[38-41], Kadian et al. (1994)[42]
Anti-HBc+	anti-HBs	2	0% to 44%	Roque-Afonso et al. (2002)[36], Yu et al. (2001)[35]
Anti-HBc+	anti-HBc	2	0% to 78%	Roque-Afonso et al. (2002)[36], Yu et al. (2001)[35]
Anti-HBc+	serum HBV-DNA	2	40% to 94%	Uemoto et al. (1998)[38-41], Kadian et al. (1994)[42]
Anti-HBc+	"Developed de novo infection"	1	6%	Montalti (2004)[43]
Anti-HBc+ and HBsAg-	HBsAg	9	0% to 78%	De Feo et al. (2005)[44,45], Holt et al. (2002)[46], Donataccio et al. (2006)[47], Suehiro et al. (2005)[48], Fabrega et al. (2003)[49], Nery et al. (2003)[50], Preito et al. (2001)[32], Dickson et al. (1997)[33], Wachs et al. (1995)[51]
Anti-HBc+ and HBsAg-	HBeAg	2	13% to 67%	Nery et al. (2003)[50], Preito et al. (2001)[32]
Anti-HBc+ and HBsAg-	anti-HBs	2	0% to 5%	Castells et al. (2002)[52], Wachs et al. (1995)[51]
Anti-HBc+ and HBsAg-	anti-HBc	3	0% to 37%	Holt et al. (2002)[46], Donataccio et al. (2006)[47], Castells et al. (2002)[52]
Anti-HBc+ and HBsAg-	liver HBV-DNA	2	0% to 13%	Holt et al. (2002)[46], Nery et al. (2003)[50]
Anti-HBc+ and HBsAg-	serum HBV-DNA	7	0% to 71%	Holt et al. (2002)[46], Suehiro et al. (2005)[48], Fabrega et al. (2003)[49], Loss et al. (2003)[31,53], Nery et al. (2003)[50], Castells et al. (2002)[52], Preito et al. (2001)[32]

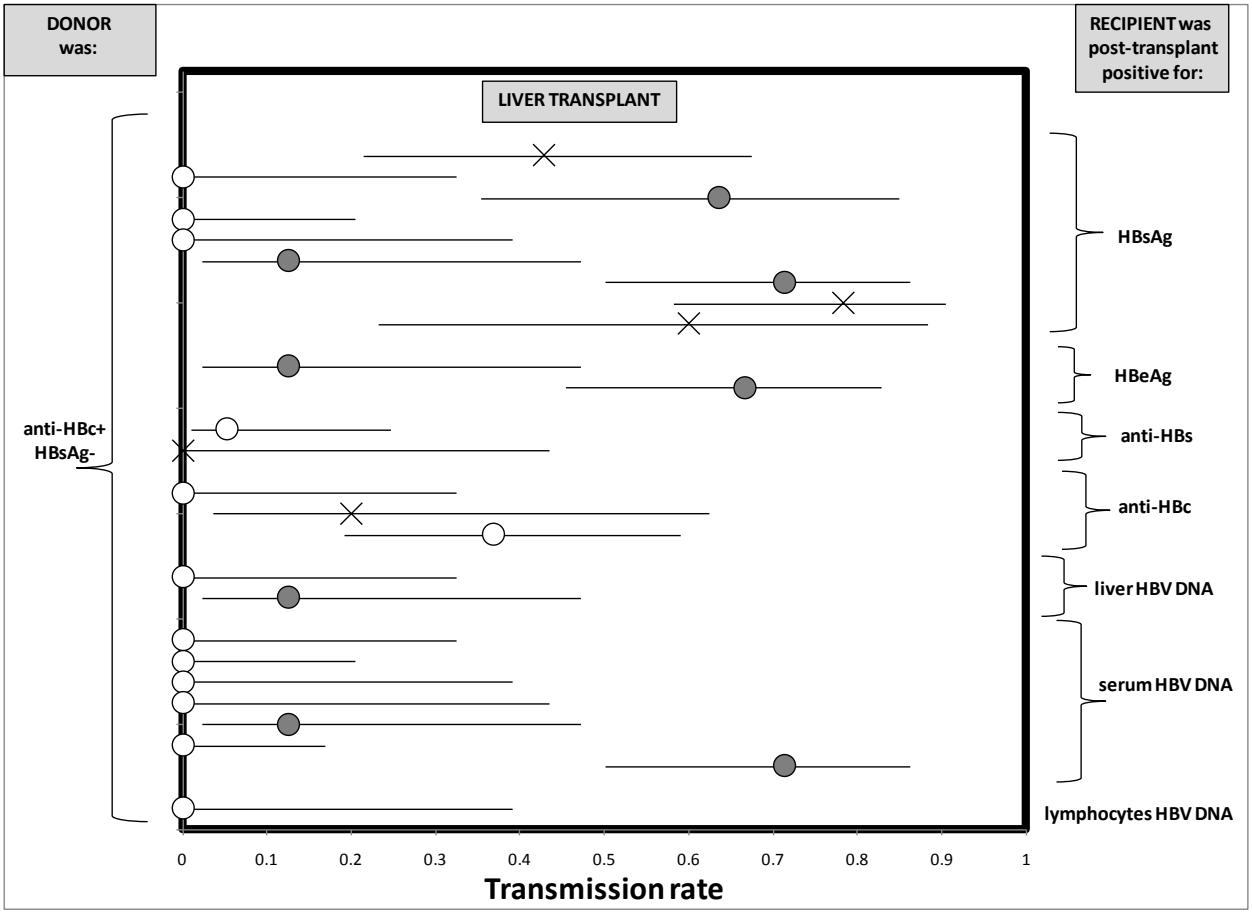
Donor was:	Recipient was tested for post-transplant positivity of:	# of Studies	Range of Results	Studies
Anti-HBc+ and HBsAg-	lymphocytes HBV-DNA	1	0%	Fabrega et al. (2003)[49]

Figure 4. LIVER Transplantation: HBV Positivity in Recipients After the Use of Anti-HBc+ Donors



Note: This figure displays the reported rates of positivity among pre-transplant negative recipients after receiving organs from positive donors.. The title of the figure indicates the relevant pathogen(s) and organ(s). These data also appear in Table 26. The definitions of donor positivity appear on the left side of the figure, and the definitions of recipient post-transplant positivity appear on the right side of the figure. White circles indicate studies where **all** recipients received prophylaxis; gray circles indicate studies where **some but not all** recipients received prophylaxis; black circles indicate studies where **none** of the recipients received prophylaxis; an X indicates studies that did not report whether prophylaxis was used.

Figure 5. LIVER Transplantation: HBV Positivity in Recipients After the Use of Organs from Anti-HBc+ HbsAg- Donors



Note: This figure displays the reported rates of positivity among pre-transplant negative recipients after receiving organs from positive donors. The title of the figure indicates the relevant pathogen(s) and organ(s). These data also appear in Table 26. The definitions of donor positivity appear on the left side of the figure, and the definitions of recipient post-transplant positivity appear on the right side of the figure. White circles indicate studies where **all** recipients received prophylaxis; gray circles indicate studies where **some but not all** recipients received prophylaxis; black circles indicate studies where **none** of the recipients received prophylaxis; an X indicates studies that did not report whether prophylaxis was used.

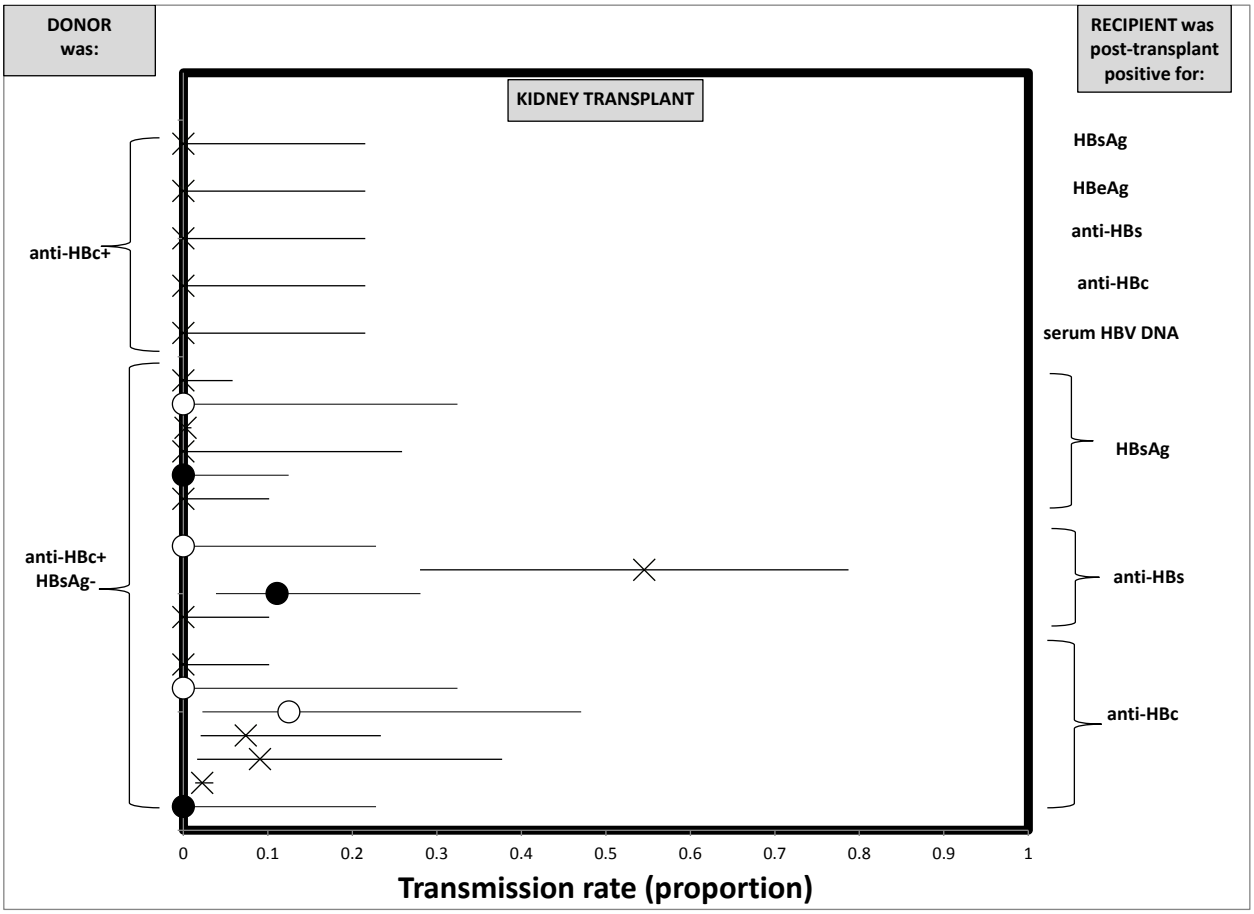
HBV Transmission from Kidney Transplantation

Studies measured virus transmission in 13 different ways for the transmission of HBV from kidney transplantation (Table 15). These rates were very low. The reported resultsare shown graphically in Figure 6 and the top section of Figure 7.

Table 15. KIDNEY Transplantation: Ranges of HBV Results

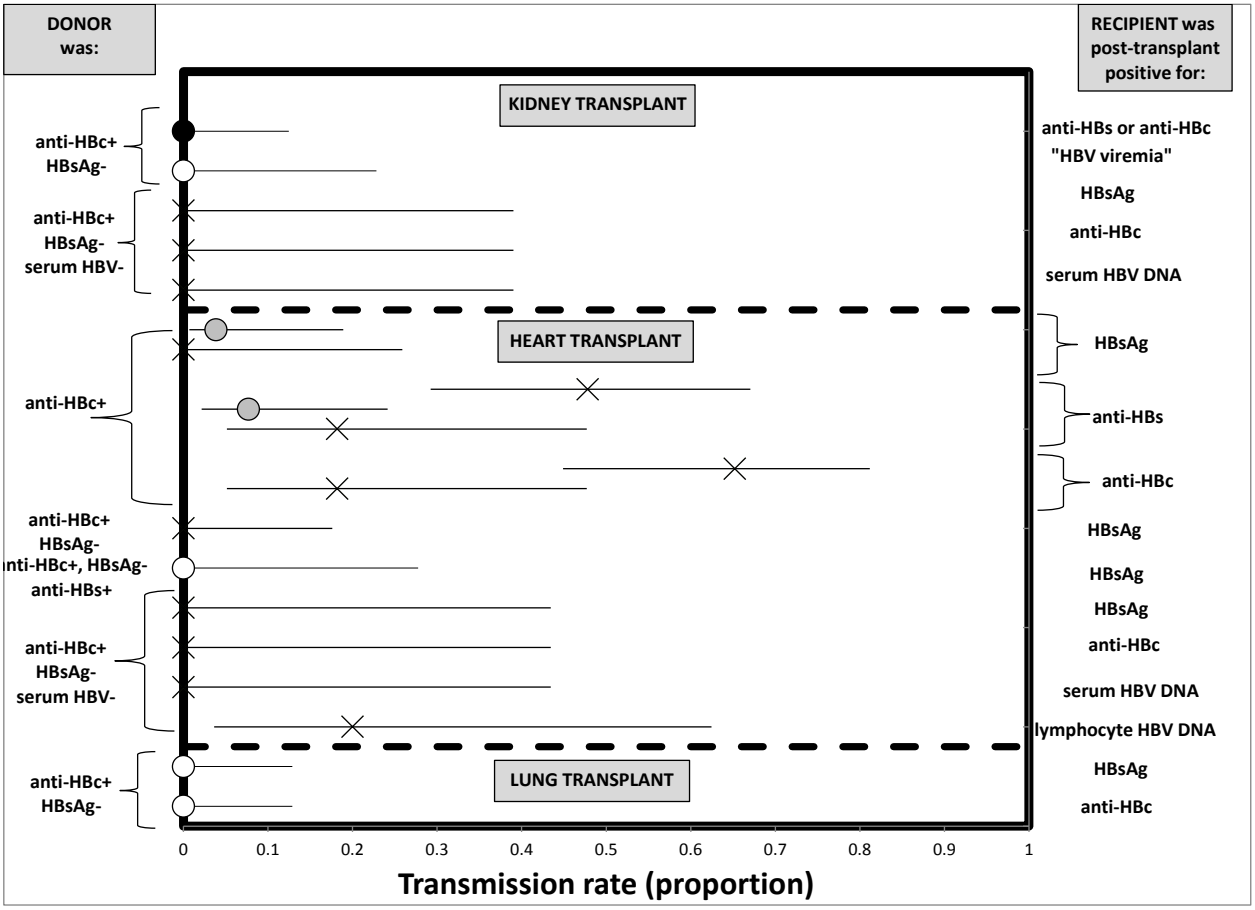
Donor was:	Recipient was tested for post-transplant positivity of:	# of Studies	Range of Results	Studies
anti-HBc+	HBsAg	1	0%	Kadian et al. (1994)[42]
anti-HBc+	HBeAg	1	0%	Kadian et al. (1994)[42]
anti-HBc+	anti-HBs	1	0%	Kadian et al. (1994)[42]
anti-HBc+	anti-HBc	1	0%	Kadian et al. (1994)[42]
anti-HBc+	serum HBV-DNA	1	0%	Kadian et al. (1994)[42]
HBsAg-, anti-HBc+	HBsAg	6	0%	De Feo et al. (2005)[44,45], Veroux et al. (2005)[54], Fong et al. (2002)[55], Madayag et al. (1997)[56], Satterthwaite et al. (1997)[57], Wachs et al. (1995)[51]
HBsAg-, anti-HBc+	anti-HBs	4	0% to 55%	Akalin et al. (2005)[58], Madayag et al. (1997)[56], Satterthwaite et al. (1997)[57], Wachs et al. (1995)[51]
HBsAg-, anti-HBc+	anti-HBc	7	0% to 13%	De Feo et al. (2005)[44,45], Akalin et al. (2005)[58], Veroux et al. (2005)[54], Fong et al. (2002)[55], Madayag et al. (1997)[56], Satterthwaite et al. (1997)[57], Wachs et al. (1995)[51]
HBsAg-, anti-HBc+	anti-HBs and anti-HBc	1	0%	Satterthwaite et al. (1997)[57]
HBsAg-, anti-HBc+	“HBV viremia”	1	0%	Akalin et al. (2005)[58]
HBsAg-, anti-HBc+, serum HBV-DNA-	HBsAg	1	0%	Miedouge et al. (2003)[59]
HBsAg-, anti-HBc+, serum HBV-DNA-	anti-HBc	1	0%	Miedouge et al. (2003)[59]
HBsAg-, anti-HBc+, serum HBV-DNA-	serum HBV-DNA	1	0%	Miedouge et al. (2003)[59]

Figure 6. KIDNEY Transplantation: HBV Positivity in Recipients After the Use of Organs from Anti-HBc+ Donors or Anti-HBc+ HbsAg- Donors



Note: This figure displays the reported rates of positivity among pre-transplant negative recipients after receiving organs from positive donors. The title of the figure indicates the relevant pathogen(s) and organ(s). These data also appear in Table 26. The definitions of donor positivity appear on the left side of the figure, and the definitions of recipient post-transplant positivity appear on the right side of the figure. White circles indicate studies where **all** recipients received prophylaxis; gray circles indicate studies where **some but not all** recipients received prophylaxis; black circles indicate studies where **none** of the recipients received prophylaxis; an X indicates studies that did not report whether prophylaxis was used.

Figure 7. Other Results for HBV



Note: This figure displays the reported rates of positivity among pre-transplant negative recipients after receiving organs from positive donors. The title of the figure indicates the relevant pathogen(s) and organ(s). These data also appear in Table 26. The definitions of donor positivity appear on the left side of the figure, and the definitions of recipient post-transplant positivity appear on the right side of the figure. White circles indicate studies where **all** recipients received prophylaxis; gray circles indicate studies where **some but not all** recipients received prophylaxis; black circles indicate studies where **none** of the recipients received prophylaxis; an X indicates studies that did not report whether prophylaxis was used.

HBV Transmission from Heart Transplantation

Studies measured virus transmission in nine different ways for the transmission of HBV from heart transplantation (Table 16). The reported results are shown graphically in the middle section of Figure 7 above.

Table 16. HEART Transplantation: Ranges of HBV Results

Donor was:	Recipient was tested for post-transplant positivity of:	# of Studies	Range of Results	Studies
anti-HBc+	HBsAg	2	0% to 4%	Pinney et al. (2005)[60], Kadian et al. (1994)[42]
anti-HBc+	anti-HBs	3	8% to 48%	Pinney et al. (2005)[60], Tenderich et al. (2005)[61], Kadian et al. (1994)[42]
anti-HBc+	anti-HBc	2	18% to 65%	Tenderich et al. (2005)[61], Kadian et al. (1994)[42]
HBsAg-, anti-HBc+	HBsAg	1	0%	De Feo et al. (2005)[44,45]
HBsAg-, anti-HBc+, anti-HBs+	HBsAg	1	0%	Ko et al. (2001)[62,63]
HBsAg-, anti-HBc+, serum HBV-DNA-	HBsAg	1	0%	Blanes et al. (2002)[64]
HBsAg-, anti-HBc+, serum HBV-DNA-	anti-HBc	1	0%	Blanes et al. (2002)[64]
HBsAg-, anti-HBc+, serum HBV-DNA-	serum HBV-DNA	1	0%	Blanes et al. (2002)[64]
HBsAg-, anti-HBc+, serum HBV-DNA-	lymphocyte HBV-DNA	1	20%	Blanes et al. (2002)[64]

HBV Transmission from Lung Transplantation

Studies measured virus transmission in two different waysfor the transmission of HBV from lung transplantation (Table 17). Both rates were 0%. The reported resultsare shown graphically in the lower section of Figure 7 (above).

Table 17. LUNG Transplantation: Ranges of HBV Results

Donor was:	Recipient was tested for post-transplant positivity of:	# of Studies	Range of Results	Studies
HBsAg-, anti-HBc+	HBsAg	1	0%	Hartwig et al. (2005)[65]
HBsAg-, anti-HBc+	anti-HBc	1	0%	Hartwig et al. (2005)[65]

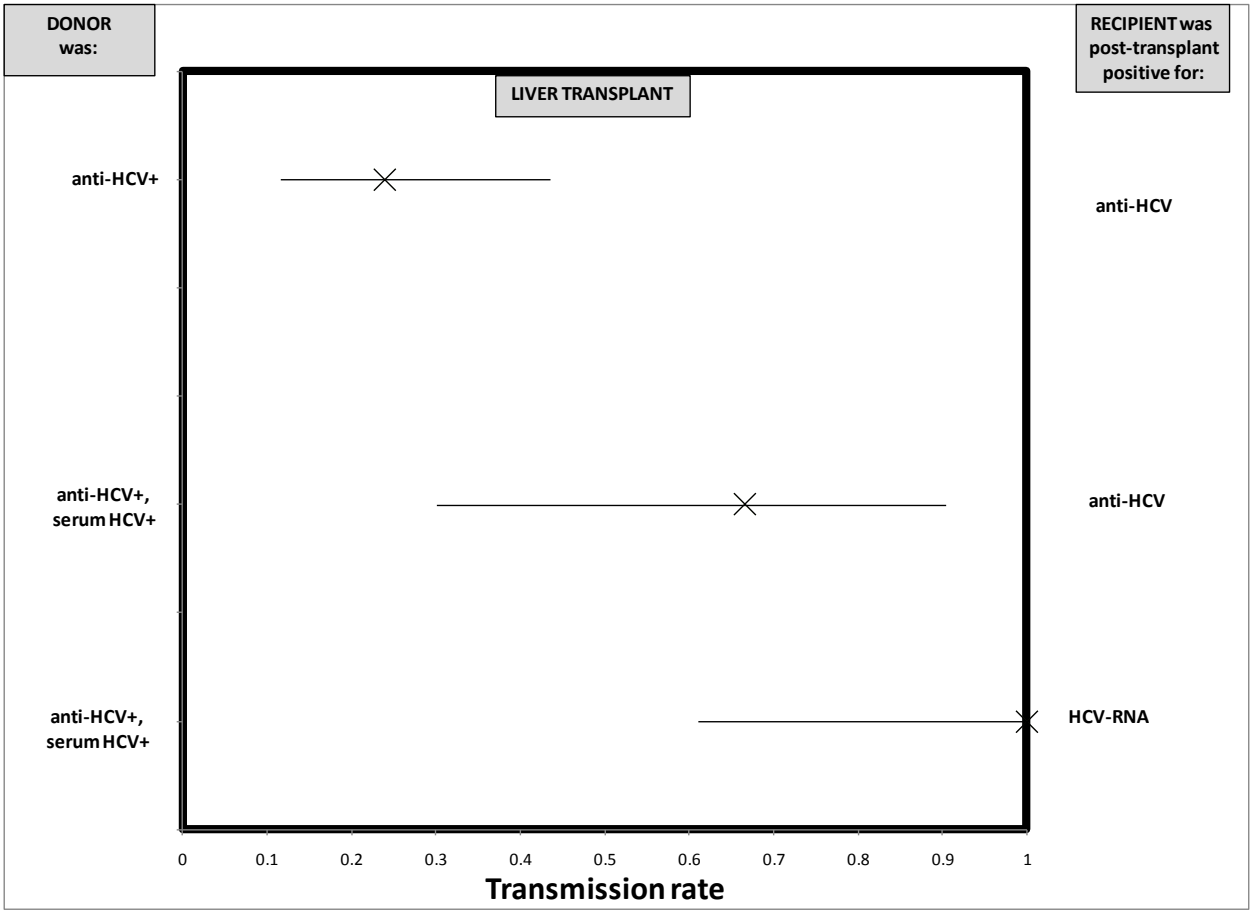
HCV Transmission from Liver Transplantation

Studies measured virus transmission in three different waysfor the transmission of HCV from liver transplantation (Table 18). The reported resultsare shown graphically in Figure 8.

Table 18. LIVER Transplantation: Ranges of HCV Results

Donor was:	Recipient was tested for post-transplant positivity of:	# of Studies	Range of Results	Studies
anti-HCV+	anti-HCV	1	24%	Shah et al. (1993)[12,16]
anti-HCV+, serum HCV-RNA+	anti-HCV	1	67%	Everhart et al. (1999)[66]
anti-HCV+, serum HCV-RNA+	HCV-RNA	1	100%	Everhart et al. (1999)[66]

Figure 8. LIVER transplantation: HCV Positivity in Recipients After the Use of Organs Donors Positive for HCV



Note: This figure displays the reported rates of positivity among pre-transplant negative recipients after receiving organs from positive donors. The title of the figure indicates the relevant pathogen(s) and organ(s). These data also appear in Table 26. The definitions of donor positivity appear on the left side of the figure, and the definitions of recipient post-transplant positivity appear on the right side of the figure. Prophylaxis was not generally applicable to the HCV studies, therefore all studies are represented by X's.

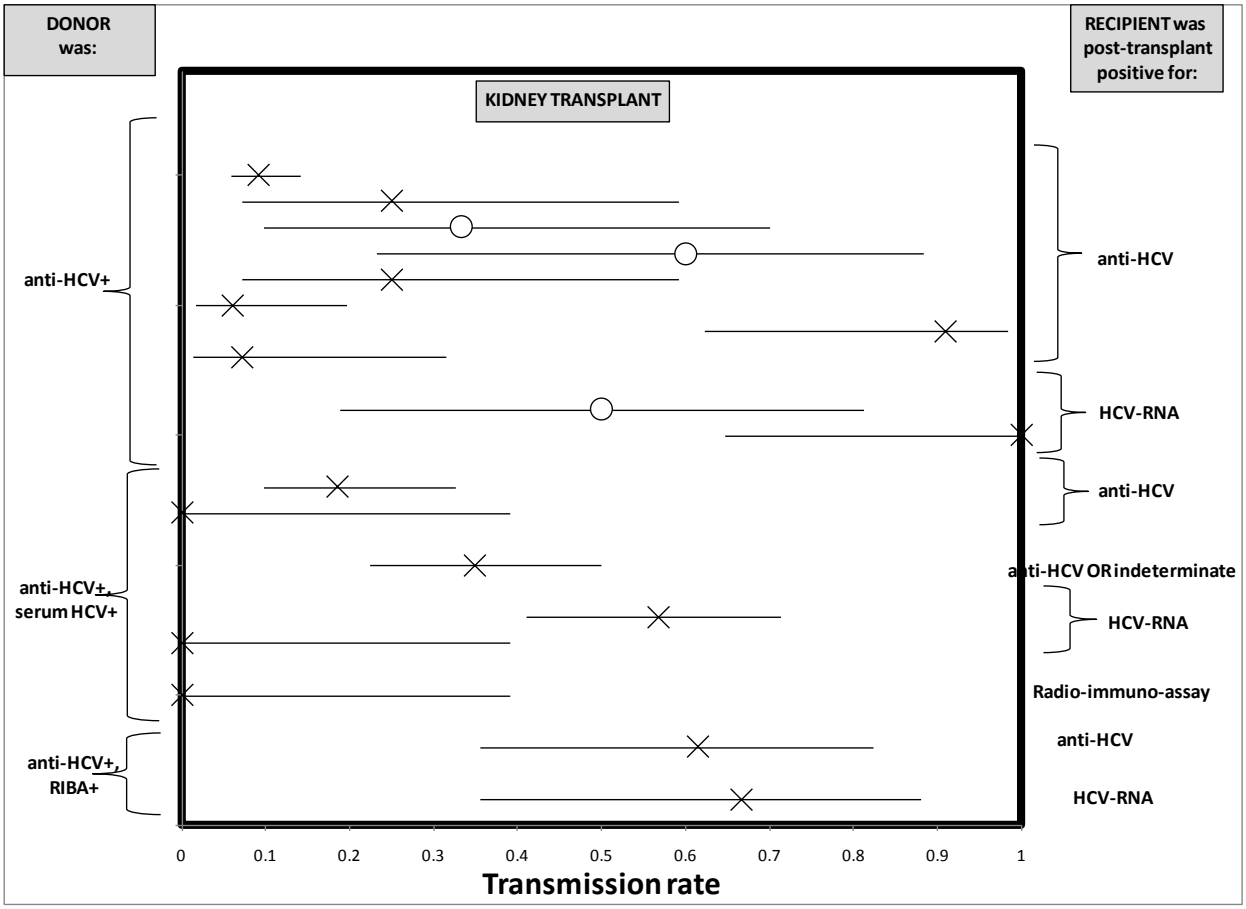
HCV Transmission from Kidney Transplantation

Studies measured virus transmission in eight different ways for the transmission of HCV from kidney transplantation (Table 19). The reported resultsare shown graphically in Figure 9 below.

Table 19. KIDNEY Transplantation: Ranges of HCV Results

Donor was:	Recipient was tested for post-transplant positivity of:	# of Studies	Range of Results	Studies
anti-HCV+	anti-HCV	8	6% to 91%	Abbott et al. (2004)[67,68], Rozental et al. (2002)[69], Tokumoto et al. (1996)[70], Tokumoto et al. (1996)[70], Wreghitt et al. (1994)[71], Mendez et al. (1993)[72,73], Pereira et al. (1992)[14,17-19], Roth et al. (1992)[15,20]
anti-HCV+	HCV-RNA	2	50% to 100%	Tokumoto et al. (1996)[70], Wreghitt et al. (1994)[71]
anti-HCV+, serum HCV-RNA+	anti-HCV	2	0% to 19%	Tesi et al. (1994)[74,75], Vincenti et al. (1993)[13]
anti-HCV+, serum HCV-RNA+	anti-HCV or indeterminate	1	35%	Tesi et al. (1994)[74,75]
anti-HCV+, serum HCV-RNA+	HCV-RNA	2	0% to 57%	Tesi et al. (1994)[74,75], Vincenti et al. (1993)[13]
anti-HCV+, serum HCV-RNA+	RIA	1	0%	Vincenti et al. (1993)[13]
anti HCV+ and RIBA+	anti-HCV	1	62%	Preiksaitis et al. (1997)[76]
anti HCV+ and RIBA+	HCV-RNA	1	67%	Preiksaitis et al. (1997)[76]

Figure 9. KIDNEY Transplantation: HCV Positivity in Recipients After the Use of Organs from Donors Positive For HCV



Note: This figure displays the reported rates of positivity among pre-transplant negative recipients after receiving organs from positive donors. The title of the figure indicates the relevant pathogen(s) and organ(s). These data also appear in Table 26. The definitions of donor positivity appear on the left side of the figure, and the definitions of recipient post-transplant positivity appear on the right side of the figure. Prophylaxis was not generally applicable to the HCV studies, therefore all studies are represented by X's.

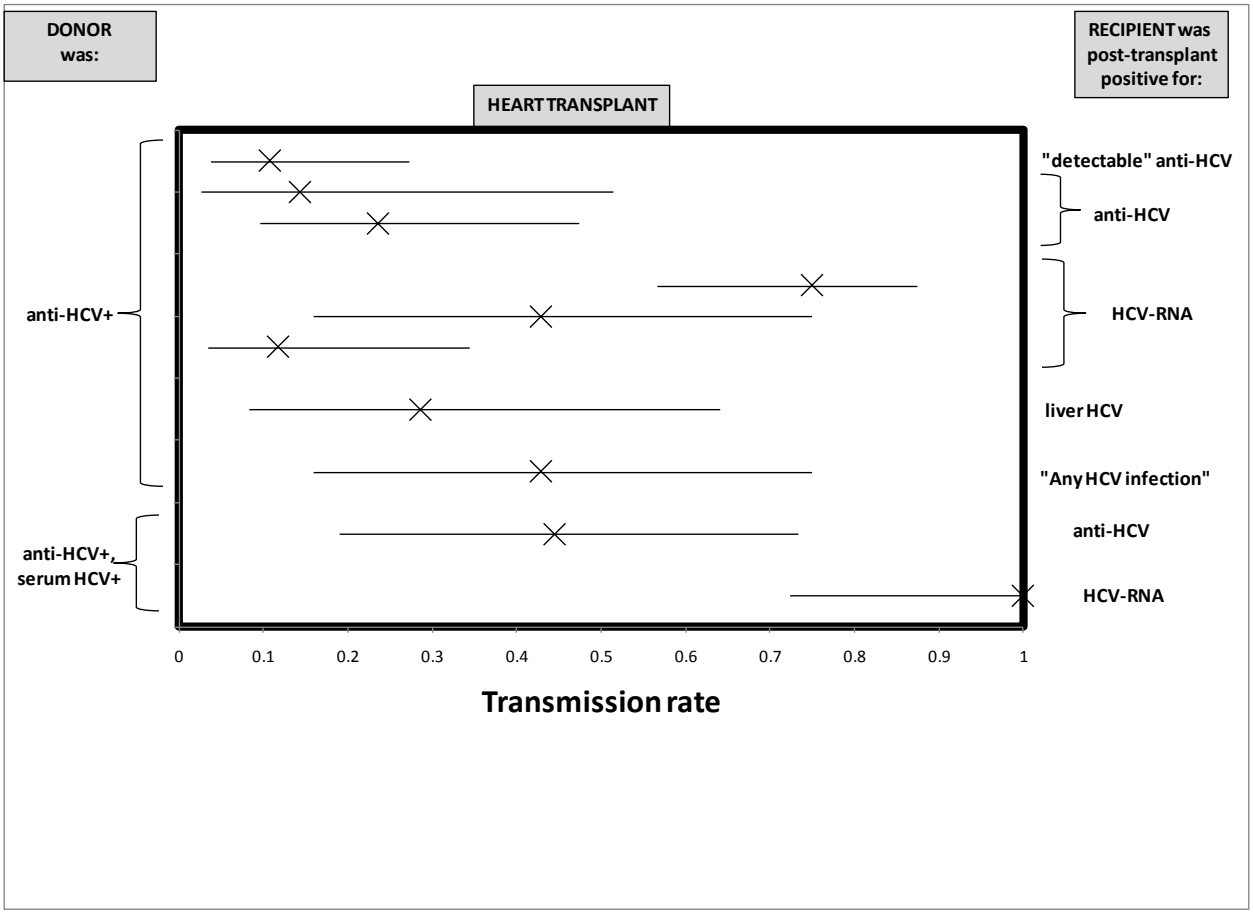
HCV Transmission from Heart Transplantation

Studies measured virus transmission in six different waysfor the transmission of HCV from heart transplantation (Table 20). The reported results are shown graphically in Figure 10.

Table 20. HEART Transplantation: Ranges of HCV Results

Donor was:	Recipient was tested for post-transplant positivity of:	# of Studies	Range of Results	Studies
anti-HCV+	"detectable" anti-HCV	3	11% to 24%	Haji et al. (2004)[77-79], Gudmundsson et al. (2003)[80], Marelli et al. (2002)[81]
anti-HCV+	HCV-RNA	3	12% to 75%	Haji et al. (2004)[77-79], Gudmundsson et al. (2003)[80], Marelli et al. (2002)[81]
anti-HCV+	liver HCV	1	29%	Gudmundsson et al. (2003)[80]
anti-HCV+	"Any HCV infection"	1	43%	Gudmundsson et al. (2003)[80]
anti-HCV+, serum HCV-RNA+	anti-HCV	1	44%	File et al. (2003)[34]
anti-HCV+, serum HCV-RNA+	HCV-RNA	1	100%	File et al. (2003)[34]

Figure 10. HEART Transplantation: HCV Positivity in Recipients After the Use of Organs from Donors Positive for HCV



Note: This figure displays the reported rates of positivity among pre-transplant negative recipients after receiving organs from positive donors. The title of the figure indicates the relevant pathogen(s) and organ(s). These data also appear in Table 26. The definitions of donor positivity appear on the left side of the figure, and the definitions of recipient post-transplant positivity appear on the right side of the figure. Prophylaxis was not generally applicable to the HCV studies, therefore all studies are represented by X's.

GRADE Assessment of Transmission

The GRADE table for this question appears in Table 21; the seven categories of evidence were graded separately. There are numerous permutations of antigens/antibodies, and the committee decided that of these, the most critical HBV results were when the donor was positive for anti-HBc and may or may not have been HBsAg+ (e.g., studies where donor HBsAg status was not reported).The only exception to this was when the recipient was being tested for anti-HBs, which was not considered critical. For HCV, we considered it a critical result whenever the donor was positive for HCV RNA. To acknowledge these priorities, we shaded the rows summarizing and grading the corresponding evidence. The unshaded rows represent less critical results. For the seven categories of evidence, the primary reasons for the Low or Very Low grades involve study quality and consistency. Results were often widely different, even within the specific antigens and antibodies being tested.

Table 21. GRADE Table for Question 2 (Transmission)

Definitions of Donor Positivity	Recipient tested for:	Quantity and Type of Evidence	Range of Results	Starting Grade	Decrease GRADE					Increase GRADE			GRADE of Evidence for Outcome	Overall GRADE of Evidence Base
					Study Quality	Consistency	Directness	Precision	Publication Bias	Large Magnitude	Dose-response	Confounders would reduce the effect		
HBV and Liver Transplantation														
Anti-HBc+	HBsAg	5 OBS[35-42]	0% to 94%	High	-1	-1	0	0	0	0	0	0	Low	Low
Anti-HBc+	HBeAg	2 OBS[38-42]	40% to 94%	High	-2	-1	0	0	0	0	0	0	Very Low	
Anti-HBc+	anti-HBc	2 OBS[35,36]	0% to 78%	High	-1	-1	0	0	0	0	0	0	Low	
Anti-HBc+	serum HBV-DNA	2 OBS[38-42]	40% to 94%	High	-1	-1	0	0	0	0	0	0	Low	
Anti-HBc+	"Developed de novo infection"	1 OBS[43]	6%	High	-2	-1	0	0	0	0	0	0	Very Low	
Anti-HBc+	anti-HBs	2 OBS[35,36]	0% to 44%	High	-1	-1	0	0	0	0	0	0	Low	
Anti-HBc+ and HBsAg-	HBsAg	9 OBS [32,33,44-51]	0% to 78%	High	-2	-1	0	0	0	0	0	0	Very Low	
Anti-HBc+ and HBsAg-	HBeAg	2 OBS[32,50]	13% to 67%	High	-2	-1	0	0	0	0	0	0	Very Low	
Anti-HBc+ and HBsAg-	anti-HBs	2 OBS[51,52]	0% to 5%	High	-1	0	0	0	0	0	0	0	Moderate	
Anti-HBc+ and HBsAg-	anti-HBc	3 OBS[46,47,52]	0% to 37%	High	-1	-1	0	0	0	0	0	0	Low	

Definitions of Donor Positivity	Recipient tested for:	Quantity and Type of Evidence	Range of Results	Starting Grade	Decrease GRADE					Increase GRADE			GRADE of Evidence for Outcome	Overall GRADE of Evidence Base
					Study Quality	Consistency	Directness	Precision	Publication Bias	Large Magnitude	Dose-response	Confounders would reduce the effect		
Anti-HBc+ and HBsAg-	liver HBV-DNA	2 OBS[46,50]	0% to 13%	High	-2	-1	0	0	0	0	0	0	Very Low	
Anti-HBc+ and HBsAg-	serum HBV-DNA	6 OBS [32,46,48-50,52,53]	0% to 71%	High	-1	-1	0	0	0	0	0	0	Low	
Anti-HBc+ and HBsAg-	lymphocytes HBV-DNA	1 OBS[49]	0%	High	0	-1	0	0	0	0	0	0	Moderate	
HBV and Kidney Transplantation														
anti-HBc+	HBsAg	1OBS[42]	0%	High	-2	0	0	0	0	0	0	0	Low	Low
anti-HBc+	HBeAg	1 OBS[42]	0%	High	-2	-1	0	0	0	0	0	0	Very Low	
anti-HBc+	anti-HBc	1OBS[42]	0%	High	-2	0	0	0	0	0	0	0	Low	
anti-HBc+	serum HBV-DNA	1 OBS[42]	0%	High	-2	-1	0	0	0	0	0	0	Very Low	
anti-HBc+	anti-HBs	1 OBS[42]	0%	High	-2	-1	0	0	0	0	0	0	Very Low	
HBsAg-, anti-HBc+	HBsAg	6 OBS [44,45,51,54-57]	0%	High	-1	0	0	0	0	0	0	0	Moderate	
HBsAg-, anti-HBc+	anti-HBs	4 OBS[51,56-58]	0% to 11%	High	-1	0	0	0	0	0	0	0	Moderate	
HBsAg-, anti-HBc+	anti-HBc	7 OBS [44,45,51,54-58]	0% to 13%	High	-1	0	0	0	0	0	0	0	Moderate	

Definitions of Donor Positivity	Recipient tested for:	Quantity and Type of Evidence	Range of Results	Starting Grade	Decrease GRADE					Increase GRADE			GRADE of Evidence for Outcome	Overall GRADE of Evidence Base
					Study Quality	Consistency	Directness	Precision	Publication Bias	Large Magnitude	Dose-response	Confounders would reduce the effect		
HBsAg-, anti-HBc+	anti-HBs and anti-HBc	1 OBS[57]	0%	High	-1	-1	0	0	0	0	0	0	Low	
HBsAg-, anti-HBc+	"HBV viremia"	1 OBS[58]	0%	High	-2	-1	0	0	0	0	0	0	Very Low	
HBsAg-, anti-HBc+, serum HBV-DNA-	HBsAg	1 OBS[59]	0%	High	-2	-1	0	0	0	0	0	0	Very Low	
HBsAg-, anti-HBc+, serum HBV-DNA-	anti-HBc	1 OBS[59]	0%	High	-2	-1	0	0	0	0	0	0	Very Low	
HBsAg-, anti-HBc+, serum HBV-DNA-	serum HBV-DNA	1 OBS[59]	0%	High	-2	-1	0	0	0	0	0	0	Very Low	
HBV and Heart Transplantation														
anti-HBc+	HBsAg	2 OBS[42,60]	0% to 4%	High	-2	0	0	0	0	0	0	0	Low	Very Low
anti-HBc+	anti-HBc	2 OBS[42,61]	18% to 65%	High	-2	-1	0	0	0	0	0	0	Very Low	
anti-HBc+	anti-HBs	3 OBS[42,60,61]	8% to 48%	High	-1	-1	0	0	0	0	0	0	Low	
HBsAg-, anti-HBc+	HBsAg	1 OBS[44,45]	0%	High	-2	-1	0	0	0	0	0	0	Very Low	

Definitions of Donor Positivity	Recipient tested for:	Quantity and Type of Evidence	Range of Results	Starting Grade	Decrease GRADE					Increase GRADE			GRADE of Evidence for Outcome	Overall GRADE of Evidence Base
					Study Quality	Consistency	Directness	Precision	Publication Bias	Large Magnitude	Dose-response	Confounders would reduce the effect		
HBsAg-, anti-HBc+, anti-HBs+	HBsAg	1 OBS[62,63]	0%	High	-1	-1	0	0	0	0	0	0	Low	
HBsAg-, anti-HBc+, serum HBV-DNA-	HBsAg	1 OBS[64]	0%	High	-2	-1	0	0	0	0	0	0	Very Low	
HBsAg-, anti-HBc+, serum HBV-DNA-	anti-HBc	1 OBS[64]	0%	High	-2	-1	0	0	0	0	0	0	Very Low	
HBsAg-, anti-HBc+, serum HBV-DNA-	serum HBV-DNA	1 OBS[64]	0%	High	-2	-1	0	0	0	0	0	0	Very Low	
HBsAg-, anti-HBc+, serum HBV-DNA-	lymphocyte HBV-DNA	1 OBS[64]	20%	High	-2	-1	0	0	0	0	0	0	Very Low	
HBV and Lung Transplantation														
HBsAg-, anti-HBc+	HBsAg	1 OBS[65]	0%	High	-1	-1	0	0	0	0	0	0	Low	Low
HBsAg-, anti-HBc+	anti-HBc	1 OBS[65]	0%	High	-1	-1	0	0	0	0	0	0	Low	

Definitions of Donor Positivity	Recipient tested for:	Quantity and Type of Evidence	Range of Results	Starting Grade	Decrease GRADE					Increase GRADE			GRADE of Evidence for Outcome	Overall GRADE of Evidence Base
					Study Quality	Consistency	Directness	Precision	Publication Bias	Large Magnitude	Dose-response	Confounders would reduce the effect		
HCV and Liver Transplantation														
anti-HCV+	anti-HCV	1 OBS[12,16]	24%	High	-2	-1	0	0	0	0	0	0	Very Low	Low
anti-HCV+, serum HCV-RNA+	anti-HCV	1 OBS[66]	67%	High	-1	-1	0	0	0	0	0	0	Low	
anti-HCV+, serum HCV-RNA+	HCV-RNA	1 OBS[66]	100%	High	-1	-1	0	0	0	0	0	0	Low	
HCV and Kidney Transplantation														
anti-HCV+	anti-HCV	8 OBS[14,15,17-20,67-70,70-73]	6% to 91%	High	-2	-1	0	0	0	0	0	0	Very Low	Very Low
anti-HCV+	HCV-RNA	2 OBS[70,71]	50% to 100%	High	-1	-1	0	0	0	0	0	0	Low	
anti-HCV+, serum HCV-RNA+	anti-HCV	2 OBS[13,75]	0% to 19%	High	-2	-1	0	0	0	0	0	0	Very Low	
anti-HCV+, serum HCV-RNA+	anti-HCV or indeterminate	1 OBS[74,75]	35%	High	-2	-1	0	0	0	0	0	0	Very Low	
anti-HCV+, serum HCV-RNA+	HCV-RNA	2 OBS[13,74,75]	0% to 57%	High	-2	-1	0	0	0	0	0	0	Very Low	

Definitions of Donor Positivity	Recipient tested for:	Quantity and Type of Evidence	Range of Results	Starting Grade	Decrease GRADE					Increase GRADE			GRADE of Evidence for Outcome	Overall GRADE of Evidence Base
					Study Quality	Consistency	Directness	Precision	Publication Bias	Large Magnitude	Dose-response	Confounders would reduce the effect		
anti-HCV+, serum HCV-RNA+	RIA	1 OBS[13]	0%	High	-2	-1	0	0	0	0	0	0	Very Low	
anti-HCV+ RIBA+	anti-HCV	1 OBS[76]	62%	High	-2	-1	0	0	0	0	0	0	Very Low	
anti-HCV+ RIBA+	HCV-RNA	1 OBS[76]	67%	High	-2	-1	0	0	0	0	0	0	Very Low	
HCV and Heart Transplantation														
anti-HCV+	anti-HCV	3 OBS[77-81]	11% to 24%	High	-2	0	0	0	0	0	0	0	Low	Very Low
anti-HCV+	HCV-RNA	3 OBS[77-81]	12% to 75%	High	-2	-1	0	0	0	0	0	0	Very Low	
anti-HCV+	liver HCV	1 OBS[80]	29%	High	-2	-1	0	0	0	0	0	0	Very Low	
anti-HCV+	"Any HCV infection"	1 OBS[80]	43%	High	-2	-1	0	0	0	0	0	0	Very Low	
anti-HCV+, serum HCV-RNA+	anti-HCV	1 OBS[34]	44%	High	-2	-1	0	0	0	0	0	0	Very Low	
anti-HCV+, serum HCV-RNA+	HCV-RNA	1 OBS[34]	100%	High	-2	-1	0	0	0	0	0	0	Very Low	

Note: The shaded rows denote evidence on rates where the donor was positive for anti-HBc but it was not reported whether the donor was positive for HBsAg; these were considered "critical" outcomes. The only expectation to this was when the recipient was being tested for anti-HBs, which was not considered critical. For HCV, we considered the result critical whenever the donor was positive for HCV RNA (thus the row was shaded).

Additional Evidence Tables for Question 2

Table 22. Question 2: General Information about Included Studies

Study	Country	Center(s) or Program	Kidney	Liver	Heart	Lung	Centers	Transplantation dates	Funding
Studies of HBV Transmission									
De Feo et al. (2005)[44,45]	Italy	North Italy Transplant program	✓	✓	✓		39	Jan-97 to Dec-99	Supported in part by a grant from the Italian Institute of Health
Kadian et al. (1994)[42]	USA	Mount Sinai Medical Center (NY)	✓	✓	✓		1	Sep-90 to Jun-92	Not reported (NR)
Akalin et al. (2005)[58]	USA	Mt. Sinai School of Medicine, New York, NY	✓				1	NR	NR
Veroux et al. (2005)[54]	Italy	University Hospital of Catania	✓				1	Jan-01 to Jun-04	NR
Miedouge et al. (2003)[59]	France	Toulouse University Hospital	✓				1	Jan-99 to Nov-01	NR
Fong et al. (2002)[55]	USA	UNOS Scientific Renal Transplant Registry	✓				>1	1994 to 1999	NR
Madayag et al. (1997)[56]	USA	University of Maryland, Baltimore, MD	✓				1	Jan-92 to Jul-96	NR
Satterthwaite et al. (1997)[57]	USA	St. Vincent Medical Center, Los Angeles, CA	✓				1	1990 to 1995	NR

Study	Country	Center(s) or Program	Kidney	Liver	Heart	Lung	Centers	Transplantation dates	Funding
Wachs et al. (1995)[51]	USA	University of California (San Francisco, CA)	✓				1	Jun-85 to Dec-93	NR
Donataccio et al. (2006)[47]	Belgium	Universite catholique de Louvain		✓			1	Feb-92 to Mar-04	One author was the recipient of a grant from Associzaone Italiana Trapiantati di Fegato (AITF), First Department of General Surgery, Verona University, Verona Italy
Suehiro et al. (2005)[48]	Japan	Gunma University Hospital or Kyushu University Hospital		✓			2	Oct-96 to Mar-03	Supported in part by a Grant-in-Aid for Scientific Research and the 21st Century COE Program from the Ministry of Education, Culture, Sports Science and Technology, Japan
Montalti et al. (2004)[43]	Italy	University of Bologna		✓			1	Apr-86 to Jan-02	NR
Fabrega et al. (2003)[49]	Spain	University Hospital Marques de Valdecilla		✓			1	Nov-99 to Mar-02	Fundacion Marques del Valdecilla
Loss et al. (2003)[31,53]	USA	Ochsner Clinic Foundation, New Orleans, LA		✓			1	Jan-99 to Aug-01	NR

Study	Country	Center(s) or Program	Kidney	Liver	Heart	Lung	Centers	Transplantation dates	Funding
Nery et al. (2003)[50]	USA	Jackson Memorial Hospital Medical Center, Miami, FL		✓			1	Mar-96 to Mar-02	NR
Castells et al. (2002)[52]	Spain	Hospital General Vall d'Hebron		✓			1	Jun-94 to Jun-00	NR
Holt et al. (2002)[46]	USA	Loyola University Medical Center, Chicago, IL		✓			1	Feb-98 to Mar-01	NR
Roque-Afonso et al. (2002)[36]	France	Hospital Paul Brousse		✓			1	Jan-97 to Sep-00	NR
Preito et al. (2001)[32]	Spain	University Hospital la Fe		✓			1	Mar-95 to Dec-98	NR
Yu et al. (2001)[35]	USA	Cedars-Sinai Medical Center, Los Angeles, CA		✓			1	Mar-96 to Mar-00	NR
Dodson et al. (1999)[37]	USA	Thomas E. Starzl Transplantation Institute, Pittsburgh, PA		✓			1	Aug-96 to Jun-98	NR
Uemoto et al. (1998)[38-41]	Japan	Kyoto University		✓			1	Jun-90 to Jun-95	Scientific Research Fund of the Ministry of Education in Japan

Study	Country	Center(s) or Program	Kidney	Liver	Heart	Lung	Centers	Transplantation dates	Funding
Dickson et al. (1997)[33]	USA	University of Virginia Hospital (Charlottesville, VA), Mayo Clinic (Rochester, MN), University of Nebraska (Omaha, NE), and University of California (San Francisco, CA)		✓			4	Aug-89 to Jun-94	NR
Pinney et al. (2005)[60]	USA	Columbia Presbyterian Medical Center, New York, NY			✓		1	Jan-97 to Dec-02	NR
Tenderich et al. (2005)[61]	Germany	Herz und Diabeteszentrum NRW			✓		1	Feb-99 to May-04	NR
Blanes et al. (2002)[64]	Spain	University Hospital la Fe			✓		1	Jan-95 to Jun-99	NR
Ko et al. (2001)[62,63]	Taiwan	National Taiwan University Hospital			✓		1	Jan-92 to Aug-99	NR
Hartwig et al. (2005)[65]	USA	Duke University Medical Center, Durham, NC				✓	1	Apr-01 to Aug-03	"The authors have no conflict of interest with regard to this work"

Study	Country	Center(s) or Program	Kidney	Liver	Heart	Lung	Centers	Transplantation dates	Funding
Studies of HCV Transmission									
Abbott et al. (2004)[67,68]	USA	United States Renal Data System (USRDS)	✓				>1	Jan-96 to Jul-00	Supported in part by a grant NIDDK. One author had received an award from the American Kidney Fund.
Rozental et al. (2002)[69]	Latvia	P. Stradin Clinical University Hospital	✓				1	1997 to Jul-01	NR
Preiksaitis et al. (1997)[76]	Canada	University of Alberta Hospitals, Alberta	✓				1	1984 to Apr-92	NR
Tokumoto et al. (1996)[70]	Japan	Nigata University	✓				1	Nov-89 to Nov-92	NR
Tesi et al. (1994)[74,75]	USA	Ohio State University, Columbus, OH	✓				1	Sep-90 to Jan-93[a]	NR
Wreghitt et al. (1994)[71]	UK	Cambridge or Papworth	✓				2	1984 to 1991	Bloomsbury and Islington Health Authority
Mendez et al. (1993)[72,73]	USA	St. Vincent Medical Center, Los Angeles, CA	✓				1	Jul-90 to Jun-92	NR
Vincenti et al. (1993)[13]	USA	University of California (San Francisco, CA)	✓				1	Jan-86 to Dec-88	NR

Study	Country	Center(s) or Program	Kidney	Liver	Heart	Lung	Centers	Transplantation dates	Funding
Pereira et al. (1992)[14,17-19]	USA	New England Organ Bank (MA)	✓				14	1986 to 1990	International Society of Nephrology, New England Organ Bank, Nephrology Clinical Research Fellowship Training Program. One author was a stockholder in Ortho Diagnostic Systems, and three authors were stockholders in Chiron Corporation.
Roth et al. (1992)[15,20]	USA	Jackson Memorial Hospital Medical Center, Miami, FL	✓				>1	Jan-79 to Feb-91	Miami Veterans Affairs Hospital Research Support and NIH DK grant
Everhart et al. (1999)[66]	USA	Mayo Clinic (Rochester, MN), University of Nebraska (Omaha, NE), and University of California (San Francisco, CA)		✓			3	Apr-90 to Jun-94	Support from NIH NO1-DK grants
Shah et al. (1993)[12,16]	USA	Presbyterian University Hospital, Pittsburgh, PA		✓			1	Mar-86 to Mar-90	Supported in part by grants from NIDDK
Haji et al. (2004)[77-79]	USA	Cleveland Clinic, Cleveland, OH			✓		1	Jul-93 to Dec-98	NR

Study	Country	Center(s) or Program	Kidney	Liver	Heart	Lung	Centers	Transplantation dates	Funding
File et al. (2003)[34]	USA	Ochsner Clinic Foundation, New Orleans, LA			✓		1	1991 to 1999	NR
Gudmundsson et al. (2003)[80]	USA	Advanced Heart Failure/Heart Transplant Program, Maywood, IL			✓		1	Jan-95 to Jul-97	Robert D. Van Kampen Research Fund
Marelli et al. (2002)[81]	USA	University of California (Los Angeles, CA)			✓		1	Jul-94 to Dec-99	NR

[a] January 1993 is an approximate estimate of the latest transplant date (based on the publication date of the primary publication of March 1994), so that the study could be included in the plot of transplant dates.

NR – Not reported.

Table 23. Question 2: Details of Study Methods

Study	Prospective	Consecutive	Prophylaxis	Frequency of Post-transplant Serological Testing	Duration of Post-transplant Follow-up	If any *de novo* infections occurred, how long after surgery did they occur?	Diagnostic Tests
Studies of HBV Transmission							
De Feo et al. (2005)[44,45]	No	No	NR	NR	NR	NR	Microparticle Enzyme Immunoassay for HBV, and ImxCORE and ImxAVSAB
Kadian et al. (1994)[42]	No	No	NR	NR	Range: 12-33 months	Liver: Range: 8-16 months; Kidney: no positives after transplant; Heart: NR	NR
Akalin et al. (2005)[58]	NR	NR	Lamivudine	NR	Median: 36 months (Range: 6-60)	NA	Tests NR; PCR for HBV-DNA
Veroux et al. (2005)[54]	No	Yes	HBIg	NR	Mean: 17 months (Range: 6-48)	NR	NR
Miedouge et al. (2003)[59]	No	Yes	NR	NR	Mean: 11 months (Range: 6-29)	NA	Abbott Diagnostics and AxSYM for HBV, and Amplicor for HBV-DNA

Study	Prospective	Consecutive	Prophylaxis	Frequency of Post-transplant Serological Testing	Duration of Post-transplant Follow-up	If any *de novo* infections occurred, how long after surgery did they occur?	Diagnostic Tests
Fong et al. (2002)[55]	No	Yes	NR	"The majority of centers do not perform routine HBsAg or anti-HBc testing"	NR	NR	NR
Madayag et al. (1997)[56]	No	Yes	NR	Performed "regularly" after transplant; no frequency reported	Range: 6-36 months	Range: 3-12 months	Abbott Diagnostics for HBV
Satterthwaite et al. (1997)[57]	No	Yes	No HBIg, NR others	NR	NR	NR	NR
Wachs et al. (1995)[51]	No	No	NR	NR	NR	NR	NR
Donataccio et al. (2006)[47]	No	Yes	Of 11 patients, 4 had none, 6 had HBIg, and one had both HBIg and lamivudine	At weeks 1, 2, 3, 4, then at months 2, 3, 6 and 12, and then yearly. Liver biopsy at days 0, 7, and also 6 mo. And 12 mo.	Infections occurred at a median of 27 months (Range: 12-60) after transplant	NR	AxSYM or Abbott Diagnostics for HBV

Study	Prospective	Consecutive	Prophylaxis	Frequency of Post-transplant Serological Testing	Duration of Post-transplant Follow-up	If any *de novo* infections occurred, how long after surgery did they occur?	Diagnostic Tests
Suehiro et al. (2005)[48]	NR	No	HBIg and lamivudine	At weeks 1, 2, 3, 4, then monthly for one year, then every three months.	Mean: 38.5 months (Range: 25-86)	NA	Abbott Diagnostics for HBV, and Amplicor PCR for HBV-DNA
Montalti et al. (2004)[43]	No	Yes	NR for the 18 negative recipients; of 44 total recipients, 11 received no prophylaxis, 13 received HbIg, 19 received both HbiG and lamivudine, and 1 received lamivudine only	NR	NR	NR	NR
Fabrega et al. (2003)[49]	Yes	Yes	HBIg	At weeks 1, 2, 4, and 13; every 13 weeks thereafter	23 months (Range: 9-36)	NA	EIA or Sorin Miomedical for HBV

Study	Prospective	Consecutive	Prophylaxis	Frequency of Post-transplant Serological Testing	Duration of Post-transplant Follow-up	If any *de novo* infections occurred, how long after surgery did they occur?	Diagnostic Tests
Loss et al. (2003)[31,53]	Yes	Yes	Recombivax HB, HBIg, and lamivudine	At weeks 1, 2, 3, 4, then monthly for one year, then every three months.	5 months (Range: 1-12)	NA	Qiagen for HBV, PCR for HBsAg
Nery et al. (2003)[50]	No	No	Of 8 patients, 1 had none, 6 had lamivudine only, and 1 had both HBIg and lamivudine	Every 1-6 months or at discretion of physician	minimum 4 months	NR	Abbott Diagnostics for HBV, and Qiagen for HBV-DNA, also in-house PCR
Castells et al. (2002)[52]	Yes	No	Engerix HB, and lamivudine after transplant if infection detected	At months 1, 3, and 6, then yearly	At least 6 months	Median: 24 months (Range: 6-48)	HBV using Abbott AxSYM; HBeAg and anti-Hbe using Diasorin; HBV-DNA using PCR
Holt et al. (2002)[46]	No	Yes	"Vaccination", HBIg and lamivudine	"All patients have been followed closely in the follow-up period". Liver biopsies at 6 mo., 1 year, and 2 years.	29 months (Range: 6-29)	NA	PCR on liver biopsy for HBV

Study	Prospective	Consecutive	Prophylaxis	Frequency of Post-transplant Serological Testing	Duration of Post-transplant Follow-up	If any *de novo* infections occurred, how long after surgery did they occur?	Diagnostic Tests
Roque-Afonso et al. (2002)[36]	No	Yes	Of 9 patients, 4 had none, and 5 had HBIg	At least once every four months sometimes more often	Median: 24 (Range: 6-45)	At months 8, 9, 11, 15, and 17	anti-HBs using Dade Behring; anti-HBc using Merux Biotech; HBeAg using BioMerieux; HBV-DNA using Quantiplex
Preito et al. (2001)[32]	No	No	Some had lamivudine, but did not report how many	At months 1, 3, and 6, then yearly or when clinically indicated	Mean: 24, SD: 14	Median time: 12 months (Range: 3-24)	HBsAg using Abbott product; antiHBs and anti-HBc and anti-Hbe using Diasiron; HBV-DNA using PCR via Diogene
Yu et al. (2001)[35]	No	Yes	Lamivudine	Did not report frequency of serological test monitoring; only analyzed the most recent serological test result; liver biopsy only when clinically indicated	Mean: 17 months (Range: 2-40)	NA	HBV-DNA with Qiogen and nested PCR
Dodson et al. (1999)[37]	Yes	Yes	Of 8 patients, 1 had HBIg only, and the other 7 had both HBIg and lamivudine	Daily for 7 days, then monthly for 6 months, then every six months	Median: 15 months (Range: 7-20)	At 6 months	NR

Study	Prospective	Consecutive	Prophylaxis	Frequency of Post-transplant Serological Testing	Duration of Post-transplant Follow-up	If any *de novo* infections occurred, how long after surgery did they occur?	Diagnostic Tests
Uemoto et al. (1998)[38-41]	No	Yes	None	NR	NR	The 15 new infections were found at a mean of one year (Range: 5-26 months)	Dinabot for HBV, and nested PCR for HBV-DNA
Dickson et al. (1997)[33]	No	No	NR	When possible, samples were obtained at 4 months, one year, and two years after transplant	Mean: 19 months (Range: 4-60)	Median: 12 months (Range: 2-37)	HBV using Abbott product; HBV-DAN by PCR via National Genetics Institute
Pinney et al. (2005)[60]	No	Yes	Some had lamivudine, but did not report how many	Every year after transplant	NR	The one infection occurred at 10 months after transplant	NR

Study	Prospective	Consecutive	Prophylaxis	Frequency of Post-transplant Serological Testing	Duration of Post-transplant Follow-up	If any *de novo* infections occurred, how long after surgery did they occur?	Diagnostic Tests
Tenderich et al. (2005)[61]	No	Yes	NR	Within four months before transplant, and between six hours and one year after transplant; did not report a standard monitoring frequency	NR	HBV was "already detectable in several blood samples within 6-10 hours after heart transplant"; others detected at 5 weeks and 4 months after transplant	HBV using Abbott AxSYM; also analyzed two samples of Flebogamma
Blanes et al. (2002)[64]	No	No	NR	NR	Mean: 37.7	NR	HBcAg using AxSYM; anti-HBc and anti-HBs using Diasorin; HBV-DNA by nested PCR
Ko et al. (2001)[62,63]	No	No	HBIg	At least once every four weeks, sometimes more often	32 months (Range: 6-98)	NA	Well-cozyme or Chatillon for HBV, and Qiagen for HBV-DNA
Hartwig et al. (2005)[65]	No	Yes	Recombivax HB	NR	Median: 21.5 months	NA	NR

Study	Prospective	Consecutive	Prophylaxis	Frequency of Post-transplant Serological Testing	Duration of Post-transplant Follow-up	If any *de novo* infections occurred, how long after surgery did they occur?	Diagnostic Tests
Studies of HCV Transmission							
Abbott et al. (2004)[67,68]	No	Yes	NR	NR	Range: 6-36 months	NR	ELISA2 or ELISA3
Rozental et al. (2002)[69]	No	Yes	NR	NR	18 months (did not report whether this was a mean or median)	NR	HCV using MEIA

Study	Prospective	Consecutive	Prophylaxis	Frequency of Post-transplant Serological Testing	Duration of Post-transplant Follow-up	If any *de novo* infections occurred, how long after surgery did they occur?	Diagnostic Tests
Preiksaitis et al. (1997)[76]	No	Yes	NR	One year after transplant, and/or the time of latest followup	Overall median followup of kidney recipients was 54 months (range 9-154).	Positive anti-HCV tests occurred in 8 kidney recipients at an average of 22 months after transplant (median 6.5 months, range 2 to 60.5). Positive HCV RNA tests occurred in 7 kidney recipients at an average of 5.9 years after transplant (median 5.3 years, range 2 to 60.5).	Anti-HCV using Ortho HCV 3.0 ELISA, RIBA using Chiron RIBA HCV 3.0 strip immunoblot assay, and HCV RNA by PCR using the Amplicor HCV virus test.
Tokumoto et al. (1996)[70]	Yes	Yes	Interferon	Weeks 2, 4, 6, 8, 10, 12, 16, 20, and 24	Mean: 40 months (Range: 30-65)	NR	RIBA1; HCV-RNA using PCR
Tesi et al. (1994)[74,75]	Yes	No	NR	NR	Mean: 20 months (Range: 2-38)	NR	ELISA1, ELISA 2, Matrix (Abbott) and PCR

Study	Prospective	Consecutive	Prophylaxis	Frequency of Post-transplant Serological Testing	Duration of Post-transplant Follow-up	If any *de novo* infections occurred, how long after surgery did they occur?	Diagnostic Tests
Wreghitt et al. (1994)[71]	No	No	NR	Only the latest serological test results were analyzed	Mean: 41 (Range: 12-72)	Two at 7 months and 9 months after transplantation; timing of other de novo infections were not reported	NR
Mendez et al. (1993)[72,73]	No	Yes	NR	NR	Range: 12-23 months	At 4 and 11 months after transplant	ELISA2
Vincenti et al. (1993)[13]	No	Yes	NR	NR	Range: 36-40 months	NA	HCV using Chiron-Orth; if reactive, then tested for HCV-RNA
Pereira et al. (1992)[14,17-19]	No	No	NR	Only the most recent serological test was analyzed	Median: 29 months (Range: 12-39)	NR	ELISA2 and RIBA2; HCV-RNA using PCR
Roth et al. (1992)[15,20]	No	No	NR	NR	Median: 55 months (Range: 3-73)	At 10 weeks after transplant	ELISA1, and if reactive, RIBA2
Everhart et al. (1999)[66]	Yes	No	NR	At 4 months, one year, two years and at study end (which was 2-5 years after transplant)	NR	NR	ELISA2, and if that was reactive, then RIBA2; HCV-RNA using Amplicor

Study	Prospective	Consecutive	Prophylaxis	Frequency of Post-transplant Serological Testing	Duration of Post-transplant Follow-up	If any *de novo* infections occurred, how long after surgery did they occur?	Diagnostic Tests
Shah et al. (1993)[12,16]	No	No	NR	At six months, one year, and two years	NR	Mean: 21 months (plus or minus 16; did not report whether the plus or minus meant SD, or SE, or CI, or IQR, or SIQR, or range)	ELISA2
Haji et al. (2004)[77-79]	No	No	NR	NR	Mean: 50 months (SD: 23)	NR	ELISA2; HCV-RNA using PCR
File et al. (2003)[34]	No	Yes	NR	Each patient was "tested on one or more occasions during routine clinical visits"; nothing else reported about monitoring frequency	NR	NR	ELISA2; HCV-RNA using PCR (Amplicor)
Gudmundsson et al. (2003)[80]	No	Yes	NR	NR	Mean: 63 months (Range: 28-86)	At 19, 39, and 55 months after transplant	ELISA2; HCV-RNA using PCR (Roche)

Study	Prospective	Consecutive	Prophylaxis	Frequency of Post-transplant Serological Testing	Duration of Post-transplant Follow-up	If any *de novo* infections occurred, how long after surgery did they occur?	Diagnostic Tests
Marelli et al. (2002)[81]	No	Yes	NR	NR	Median: 22 months (Range: 7-112)	NR	ELISA2; HCV-RNA using PCR (Amplicor)

NA – Not applicable
NR – Not reported

Table 24. Question 2: Pre-transplant Patient Characteristics

Study	Patient Characteristics Pre-transplant	Mean (SD) or % (N/N)	Comments
Studies of HBV Transmission			
De Feo et al. (2005)[44,45], Kadian et al. (1994)[42], Akalin et al. (2005)[58], Veroux et al. (2005)[54], Miedouge et al. (2003)[59], Madayag et al. (1997)[56], Wachs et al. (1995)[51], Donataccio et al. (2006)[47], Montalti et al. (2004)[43], Fabrega et al. (2003)[49], Loss et al. (2003)[31,53], Nery et al. (2003)[50], Castells et al. (2002)[52], Preito et al. (2001)[32], Dodson et al. (1999)[37], Uemoto et al. (1998)[38-41], Dickson et al. (1997)[33], Pinney et al. (2005)[60], Blanes et al. (2002)[64], Ko et al. (2001)[62,63], Hartwig et al. (2005)[65]	These studies did not report pre-transplant characteristics for pre-transplant negative patients who received organs from positive patients		
Fong et al. (2002)[55]	Cold ischemia time (hours)	22.1 (SD: 8.5)	
	Donor % African-American	17% (130/763)	
	Donor % death due to stroke	51% (389/763)	
	Donor % HCV+	11% (84/763)	
	Donor % male	42% (320/763)	
	Donor mean age	40.5 (SD: 16)	
	Num. of HLA mismatches	3.7 (SD: 1.6)	

Study	Patient Characteristics Pre-transplant	Mean (SD) or % (N/N)	Comments
	Recipient % African-American	34% (259/763)	
	Recipient % Asian-American	5% (38/763)	
	Recipient % being retransplanted	12% (92/763)	
	Recipient % HCV+	11% (84/763)	
	Recipient % male	63% (481/763)	
	Recipient mean age	47.8 (SD: 13.1)	
	Recipient duration of dialysis (months)	38.1 (SD: 34.6)	
	Recipient Peak Panel Reactive Antibody	13.2 (SD: 24.3)	
Satterthwaite et al. (1997)[57]	“Avermean age match” (not defined)	1.6 (SD: NR)	
	% with Cold ischemia time >36 hours	41% (11/27)	
	Recipient % age <12	7% (2/27)	
	Recipient % being retransplanted	11% (3/27)	
	Recipient % African-American	15% (4/27)	
	Recipient % Caucasian-American	44% (12/27)	
	Recipient % Hispanic-American	30% (8/27)	
	Recipient % Other race	4% (1/27)	
	Recipient % male	63% (17/27)	
	Recipient % with diabetes	15% (4/27)	
	Recipient panel reactive antibody <40	0% (0/27)	
Suehiro et al. (2005)[48]	Donor % male	53% (8/15)	
	Donor mean age	43.3 (SD: 10.2)	
	Recipient % male	33% (5/15)	
	Recipient mean age	35.3 (SD: 14.4)	

Study	Patient Characteristics Pre-transplant	Mean (SD) or % (N/N)	Comments
Holt et al. (2002)[46]	Recipient % indication for transplant was active hepatitis, IgA deficiency	13% (1/8)	
	Recipient % indication for transplant was acute Budd-Chiari syndrome	13% (1/8)	
	Recipient % indication for transplant was alcoholic cirrhosis	13% (1/8)	
	Recipient % indication for transplant was chronic active HCV	13% (1/8)	
	Recipient % indication for transplant was fulminant liver failure	13% (1/8)	
	Recipient % indication for transplant was liver failure secondary to amyloidosis	13% (1/8)	
	Recipient % indication for transplant was primary biliary cirrhosis	13% (1/8)	
	Recipient % indication for transplant was primary biliary cirrhosis and scleroderma	13% (1/8)	
	Recipient % male	50% (4/8)	
	Recipient mean age	48.9 (SD: 13.5)	
Roque-Afonso et al. (2002)[36]	Recipient % blood type A+	56% (5/9)	
	Recipient % blood type B+	11% (1/9)	
	Recipient % blood type O+	33% (3/9)	
	Recipient % indication for transplant was alcoholic cirrhosis	44% (4/9)	
	Recipient % indication for transplant was Budd-Chiari syndrome	11% (1/9)	
	Recipient % indication for transplant was HCV+ alcoholic cirrhosis	11% (1/9)	

Study	Patient Characteristics Pre-transplant	Mean (SD) or % (N/N)	Comments
	Recipient % indication for transplant was primary biliary cirrhosis	11% (1/9)	
	Recipient % indication for transplant was symptomatic amyloidosis	22% (2/9)	
Yu et al. (2001)[35]	Recipient % indication for transplant was HCC (NR what this meant)	60% (3/5)	
	Recipient % indication for transplant was HCV cirrhosis	100% (5/5)	
Tenderich et al. (2005)[61]	Recipient % indication for transplant was coronary heart disease	43% (10/23)	
	Recipient % indication for transplant was dilated cardiomyopathy	48% (11/23)	
	Recipient % male	83% (19/23)	
	Recipient % other indication for transplant	9% (2/23)	
	Recipient mean age	53.5 (“+/- 5.4”; NR what this meant)	
	Serum creatinine	1.25 (“+/- 0.49”; NR what this meant)	
	Recipient height (cm)	171 (“+/- 21”; NR what this meant)	
	Recipient left ventricular ejection fraction (%)	29.6 (“+/- 12.9”; NR what this meant)	
	Recipient serum creatinine	72.4 (“+/- 20.6”; NR what this meant)	

Study	Patient Characteristics Pre-transplant	Mean (SD) or % (N/N)	Comments
Studies of HCV transmission			
Abbott et al. (2004)[67,68], Rozental et al. (2002)[69], Preiksaitis et al. (1997)[76], Tesi et al. (1994)[74,75], Wreghitt et al. (1994)[71], Vincenti et al. (1993)[13], Pereira et al. (1992)[14,17-19], Everhart et al. (1999)[66], Shah et al. (1993)[12,16]	These studies did not report pre-transplant characteristics for pre-transplant negative patients who received organs from positive patients		
Tokumoto et al. (1996)[70]	Recipient HLA AB mismatch	1.3 (SD: 0.8)	
	Recipient HLA DR mismatch	0.7 (SD: 0.8)	
	Recipient % male	50% (3/6)	
	Recipient % received organs from deceased donors	50% (3/6)	
	Recipient mean age	36.7 (SD: 13.3)	
Mendez et al. (1993)[72,73]	Donor % CMV+	85% (28/33)	
	Recipient % CMV+	76% (25/33)	
	Recipient % etiology diabetes	27% (9/33)	
	Recipient % etiology hypertension	18% (6/33)	
	Recipient % male	45% (15/33)	
	Recipient mean age	33 (SD: 11)	
	Recipient pre-transplant dialysis tie (months)	25 (SD: 6)	
	Recipient prior number of blood transfusions	9 (SD: 4)	

Study	Patient Characteristics Pre-transplant	Mean (SD) or % (N/N)	Comments
Roth et al. (1992)[15,20]	Donor % chronic active hepatitis	45% (5/11)	3 of the 14 donors' pre-transplant CMV status was not reported
	Donor % chronic persistent hepatitis	9% (1/11)	3 of the 14 donors' pre-transplant CMV status was not reported
	Donor % CMV+	50% (7/14)	
	Donor % normal liver histology	45% (5/11)	3 of the 14 donors' pre-transplant CMV status was not reported
	Recipient % CMV+	69% (9/13)	1 of the 14 recipients' pre-transplant CMV status was not reported
Haji et al. (2004)[77-79]	% "Cause" was dilated cardiomyopathy	32% (11/34)	
	% "Cause" was ischemic cardiomyopathy	62% (21/34)	
	% "Cause" was something else	5% (2/34)	
	Donor % male	74% (25/34)	
	Donor mean age	39 (SD: 9)	
	Recipient % male	76% (26/34)	
	Recipient mean age	57 (SD: 10)	
	Recipient mean age biopsy score	1.31 (SD: 0.65)	
	Recipient episodes of acute rejection before this transplant	1.7 (SD: 1.5)	
File et al. (2003)[34]	Recipient % history of alcohol abuse	10% (1/10)	
	Recipient % ischemic cardiomyopathy	100% (10/10)	
	Recipient % male	90% (9/10)	
	Recipient % UNOS status I	100% (10/10)	
	Recipient mean age	52 (SD: 7.1)	SD calculated by ECRI Institute based on Table 1 of the article

Study	Patient Characteristics Pre-transplant	Mean (SD) or % (N/N)	Comments
Gudmundsson et al. (2003)[80]	Recipient % anti-HBs+	13% (1/8)	
	Recipient % indication for transplant was idiopathic dilation	25% (2/8)	
	Recipient % indication for transplant was ischemia	50% (4/8)	
	Recipient % indication for transplant was restrictive cardiomyopathy	13% (1/8)	
	Recipient % indication for transplant was valvular	13% (1/8)	
	Recipient % male	88% (7/8)	
	Recipient % UNOS status I	88% (7/8)	
	Recipient % with HCV+ serology	0% (0/8)	
	Recipient % with other positive HBV serology	0% (0/8)	
	Recipient mean age	55 (SD: NR)	
Marelli et al. (2002)[81]	Recipient % UNOS status 1	56% (10/18)	

SD – Standard deviation

Table 25. Question 2: Quality Assessment

Study	2a	2b	2c	2d
Studies of HBV Transmission				
De Feo et al. (2005)[44,45]				
Kadian et al. (1994)[42]				
Akalin et al. (2005)[58]				✓
Veroux et al. (2005)[54]		✓		✓
Miedouge et al. (2003)[59]		✓		
Fong et al. (2002)[55]		✓		
Madayag et al. (1997)[56]		✓	✓	
Satterthwaite et al. (1997)[57]		✓		✓
Wachs et al. (1995)[51]				
Donataccio et al. (2006)[47]		✓	✓	
Suehiro et al. (2005)[48]			✓	✓
Montalti et al. (2004)[43]		✓		
Fabrega et al. (2003)[49]	✓	✓	✓	✓
Loss et al. (2003)[31,53]	✓	✓	✓	✓
Nery et al. (2003)[50]			✓	
Castells et al. (2002)[52]	✓		✓	✓
Holt et al. (2002)[46]		✓	✓	✓
Roque-Afonso et al. (2002)[36]		✓	✓	
Preito et al. (2001)[32]			✓	
Yu et al. (2001)[35]		✓		✓
Dodson et al. (1999)[37]	✓	✓	✓	✓
Uemoto et al. (1998)[38-41]		✓		✓
Dickson et al. (1997)[33]			✓	
Pinney et al. (2005)[60]		✓	✓	
Tenderich et al. (2005)[61]		✓	✓	
Blanes et al. (2002)[64]				
Ko et al. (2001)[62,63]			✓	✓
Hartwig et al. (2005)[65]		✓		✓

Study	2a	2b	2c	2d
Studies of HCV Transmission				
Abbott et al. (2004)[67,68]		✓		
Rozental et al. (2002)[69]		✓		
Preiksaitis et al. (1997)[76]		✓		
Tokumoto et al. (1996)[70]	✓	✓	✓	✓
Tesi et al. (1994)[74,75]	✓			
Wreghitt et al. (1994)[71]				
Mendez et al. (1993)[72,73]		✓		
Vincenti et al. (1993)[13]		✓		
Pereira et al. (1992)[14,17-19]				
Roth et al. (1992)[15,20]				
Everhart et al. (1999)[66]	✓		✓	
Shah et al. (1993)[12,16]			✓	
Haji et al. (2004)[77-79]				
File et al. (2003)[34]		✓		
Gudmundsson et al. (2003)[80]		✓		
Marelli et al. (2002)[81]		✓		

A checkmark (✓) means that the study met the quality criterion for this Question; the lack of a checkmark means that the study either did not meet the criterion, or it was unclear whether the study met the criterion. The criteria specific to this Question were:

2a. Was the study planned prospectively (i.e., before any data were collected)?

2b. Were all consecutive patients enrolled (or a random sample of eligible patients)?

2c. Were laboratory tests performed on recipients regularly in order to monitor antigens/antibodies? (Greater frequency means greater accuracy at estimating the rate.)

2d. Did all patients receive the same prophylaxis strategy (or none received any prophylaxis)? (A mix of prophylaxis strategies means a less interpretable rate.)

Table 26. Question 2: Data Table of Results

Study	Specific Test Results in these Donors	The rate applies to recipient positivity for what specific antigen/antibody?	Percentage of recipients who tested positive (95% CI) ¶ (Number of Recipients Positive Post-transplant/ Number of Recipients Negative Pre-transplant)
HBV Transmission from LIVER Transplantation			
Roque-Afonso et al. (2002)[36]	anti-HBc+	HBsAg	56% (95% CI: 27% to 81%) (5/9)
Yu et al. (2001)[35]	anti-HBc+	HBsAg	0% (95% CI: 0% to 43%) (0/5)
Dodson et al. (1999)[37]	anti-HBc+	HBsAg	13% (95% CI: 2% to 47%) (1/8)
Uemoto et al. (1998)[38-41]	anti-HBc+	HBsAg	94% (95% CI: 72% to 99%) (15/16)
Kadian et al. (1994)[42]	anti-HBc+	HBsAg	40% (95% CI: 17% to 69%) (4/10)
Uemoto et al. (1998)[38-41]	anti-HBc+	HBeAg	94% (95% CI: 72% to 99%) (15/16)
Kadian et al. (1994)[42]	anti-HBc+	HBeAg	40% (95% CI: 17% to 69%) (4/10)
Roque-Afonso et al. (2002)[36]	anti-HBc+	anti-HBs	44% (95% CI: 19% to 73%) (4/9)
Yu et al. (2001)[35]	anti-HBc+	anti-HBs	0% (95% CI: 0% to 43%) (0/5)
Roque-Afonso et al. (2002)[36]	anti-HBc+	anti-HBc	78% (95% CI: 45% to 94%) (7/9)
Yu et al. (2001)[35]	anti-HBc+	anti-HBc	0% (95% CI: 0% to 43%) (0/5)
Uemoto et al. (1998)[38-41]	anti-HBc+	serum HBV-DNA	94% (95% CI: 72% to 99%) (15/16)

Study	Specific Test Results in these Donors	The rate applies to recipient positivity for what specific antigen/antibody?	Percentage of recipients who tested positive (95% CI) ¶ (Number of Recipients Positive Post-transplant/ Number of Recipients Negative Pre-transplant)
Kadian et al. (1994)[42]	anti-HBc+	serum HBV-DNA	40% (95% CI: 17% to 69%) (4/10)
Montalti (2004)[43]	anti-HBc+	"Developed de novo infection"	6% (95% CI: 1% to 26%) (1/18)
De Feo et al. (2005)[44,45]	HBsAg-, anti-HBc+	HBsAg	43% (95% CI: 21% to 67%) (6/14)
Holt et al. (2002)[46]	HBsAg-, anti-HBc+	HBsAg	0% (95% CI: 0% to 32%) (0/8)
Donataccio et al. (2006)[47]	HBsAg-, anti-HBc+	HBsAg	64% (95% CI: 35% to 85%) (7/11)
Suehiro et al. (2005)[48]	HBsAg-, anti-HBc+	HBsAg	0% (95% CI: 0% to 20%) (0/15)
Fabrega et al. (2003)[49]	HBsAg-, anti-HBc+	HBsAg	0% (95% CI: 0% to 39%) (0/6)
Nery et al. (2003)[50]	HBsAg-, anti-HBc+	HBsAg	13% (95% CI: 2% to 47%) (1/8)
Preito et al. (2001)[32]	HBsAg-, anti-HBc+	HBsAg	71% (95% CI: 50% to 86%) (15/21)
Dickson et al. (1997)[33]	HBsAg-, anti-HBc+	HBsAg	78% (95% CI: 58% to 90%) (18/23)
Wachs et al. (1995)[51]	HBsAg-, anti-HBc IgM+	HBsAg	60% (95% CI: 23% to 88%) (3/5)
Nery et al. (2003)[50]	HBsAg-, anti-HBc+	HBeAg	13% (95% CI: 2% to 47%) (1/8)
Preito et al. (2001)[32]	HBsAg-, anti-HBc+	HBeAg	67% (95% CI: 45% to 83%) (14/21)

Study	Specific Test Results in these Donors	The rate applies to recipient positivity for what specific antigen/antibody?	Percentage of recipients who tested positive (95% CI) ¶ (Number of Recipients Positive Post-transplant/ Number of Recipients Negative Pre-transplant)
Castells et al. (2002)[52]	HBsAg-, anti-HBc+	anti-HBs	5% (95% CI: 1% to 25%) (1/19)
Wachs et al. (1995)[51]	HBsAg-, anti-HBc IgM+	anti-HBs	0% (95% CI: 0% to 43%) (0/5)
Holt et al. (2002)[46]	HBsAg-, anti-HBc+	anti-HBc	0% (95% CI: 0% to 32%) (0/8)
Donataccio et al. (2006)[47]	HBsAg-, anti-HBc IgM+	anti-HBc	20% (95% CI: 4% to 62%) (1/5)
Castells et al. (2002)[52]	HBsAg-, anti-HBc+	anti-HBc	37% (95% CI: 19% to 59%) (7/19)
Holt et al. (2002)[46]	HBsAg-, anti-HBc+	liver HBV-DNA	0% (95% CI: 0% to 32%) (0/8)
Nery et al. (2003)[50]	HBsAg-, anti-HBc+	liver HBV-DNA	13% (95% CI: 2% to 47%) (1/8)
Holt et al. (2002)[46]	HBsAg-, anti-HBc+	serum HBV-DNA	0% (95% CI: 0% to 32%) (0/8)
Suehiro et al. (2005)[48]	HBsAg-, anti-HBc+	serum HBV-DNA	0% (95% CI: 0% to 20%) (0/15)
Fabrega et al. (2003)[49]	HBsAg-, anti-HBc+	serum HBV-DNA	0% (95% CI: 0% to 39%) (0/6)
Loss et al. (2003)[31,53]	HBsAg-, anti-HBc+	serum HBV-DNA	0% (95% CI: 0% to 43%) (0/5)
Nery et al. (2003)[50]	HBsAg-, anti-HBc+	serum HBV-DNA	13% (95% CI: 2% to 47%) (1/8)
Castells et al. (2002)[52]	HBsAg-, anti-HBc+	serum HBV-DNA	0% (95% CI: 0% to 17%) (0/19)

Study	Specific Test Results in these Donors	The rate applies to recipient positivity for what specific antigen/antibody?	Percentage of recipients who tested positive (95% CI) ¶ (Number of Recipients Positive Post-transplant/ Number of Recipients Negative Pre-transplant)
Preito et al. (2001)[32]	HBsAg-, anti-HBc+	serum HBV-DNA	71% (95% CI: 50% to 86%) (15/21)
Fabrega et al. (2003)[49]	HBsAg-, anti-HBc+	lymphocytes HBV-DNA	0% (95% CI: 0% to 39%) (0/6)
HBV Transmission from KIDNEY Transplantation			
Kadian et al. (1994)[42]	anti-HBc+	HBsAg	0% (95% CI: 0% to 22%) (0/14)
Kadian et al. (1994)[42]	anti-HBc+	HBeAg	0% (95% CI: 0% to 22%) (0/14)
Kadian et al. (1994)[42]	anti-HBc+	anti-HBs	0% (95% CI: 0% to 22%) (0/14)
Kadian et al. (1994)[42]	anti-HBc+	anti-HBc	0% (95% CI: 0% to 22%) (0/14)
Kadian et al. (1994)[42]	anti-HBc+	serum HBV-DNA	0% (95% CI: 0% to 22%) (0/14)
De Feo et al. (2005)[44,45]	HBsAg-, anti-HBc+	HBsAg	0% (95% CI: 0% to 6%) (0/62)
Veroux et al. (2005)[54]	HBsAg-, anti-HBc+	HBsAg	0% (95% CI: 0% to 32%) (0/8)
Fong et al. (2002)[55]	HBsAg-, anti-HBc+	HBsAg	0% (95% CI: 0% to 1%) (2/763)
Madayag et al. (1997)[56]	HBsAg-, anti-HBc+	HBsAg	0% (95% CI: 0% to 26%) (0/11)
Satterthwaite et al. (1997)[57]	HBsAg-, anti-HBc+	HBsAg	0% (95% CI: 0% to 12%) (0/27)
Wachs et al. (1995)[51]	HBsAg-, anti-HBc IgM+	HBsAg	0% (95% CI: 0% to 10%) (0/34)

Study	Specific Test Results in these Donors	The rate applies to recipient positivity for what specific antigen/antibody?	Percentage of recipients who tested positive (95% CI) ¶ (Number of Recipients Positive Post-transplant/ Number of Recipients Negative Pre-transplant)
Akalin et al. (2005)[58]	HBsAg-, anti-HBc+	anti-HBs	0% (95% CI: 0% to 23%) (0/13)
Madayag et al. (1997)[56]	HBsAg-, anti-HBc+	anti-HBs	55% (95% CI: 28% to 79%) (6/11)
Satterthwaite et al. (1997)[57]	HBsAg-, anti-HBc+	anti-HBs	11% (95% CI: 4% to 28%) (3/27)
Wachs et al. (1995)[51]	HBsAg-, anti-HBc IgM+	anti-HBs	0% (95% CI: 0% to 10%) (0/34)
Veroux et al. (2005)[54]	HBsAg-, anti-HBc+	anti-HBc	0% (95% CI: 0% to 32%) (0/8)
Akalin et al. (2005)[58]	HBsAg-, anti-HBc+	anti-HBc	0% (95% CI: 0% to 23%) (0/13)
Veroux et al. (2005)[54]	HBsAg-, anti-HBc+	anti-HBc	13% (95% CI: 2% to 47%) (1/8)
Fong et al. (2002)[55]	HBsAg-, anti-HBc+	anti-HBc	2% (95% CI: 1% to 4%) (17/763)
Madayag et al. (1997)[56]	HBsAg-, anti-HBc+	anti-HBc	9% (95% CI: 2% to 38%) (1/11)
Satterthwaite et al. (1997)[57]	HBsAg-, anti-HBc+	anti-HBc	7% (95% CI: 2% to 23%) (2/27)
Wachs et al. (1995)[51]	HBsAg-, anti-HBc IgM+	anti-HBc	0% (95% CI: 0% to 10%) (0/34)
Satterthwaite et al. (1997)[57]	HBsAg-, anti-HBc+	anti-HBs and anti-HBc	0% (95% CI: 0% to 12%) (0/27)
Akalin et al. (2005)[58]	HBsAg-, anti-HBc+	“HBV viremia”	0% (95% CI: 0% to 23%) (0/13)

Study	Specific Test Results in these Donors	The rate applies to recipient positivity for what specific antigen/antibody?	Percentage of recipients who tested positive (95% CI) ¶ (Number of Recipients Positive Post-transplant/ Number of Recipients Negative Pre-transplant)
Miedouge et al. (2003)[59]	HBsAg-, anti-HBc+, serum HBV-DNA-	HBsAg	0% (95% CI: 0% to 39%) (0/6)
Miedouge et al. (2003)[59]	HBsAg-, anti-HBc+, serum HBV-DNA-	anti-HBc	0% (95% CI: 0% to 39%) (0/6)
Miedouge et al. (2003)[59]	HBsAg-, anti-HBc+, serum HBV-DNA-	serum HBV-DNA	0% (95% CI: 0% to 39%) (0/6)
HBV Transmission from HEART Transplantation			
Pinney et al. (2005)[60]	anti-HBc+	HBsAg	4% (95% CI: 1% to 19%) (1/26)
Kadian et al. (1994)[42]	anti-HBc+	HBsAg	0% (95% CI: 0% to 26%) (0/11)
Pinney et al. (2005)[60]	anti-HBc+	anti-HBs	8% (95% CI: 2% to 24%) (2/26)
Tenderich et al. (2005)[61]	anti-HBc+	anti-HBs	48% (95% CI: 29% to 67%) (11/23)
Kadian et al. (1994)[42]	anti-HBc+	anti-HBs	18% (95% CI: 5% to 48%) (2/11)
Tenderich et al. (2005)[61]	anti-HBc+	anti-HBc	65% (95% CI: 45% to 81%) (15/23)
Kadian et al. (1994)[42]	anti-HBc+	anti-HBc	18% (95% CI: 5% to 48%) (2/11)
De Feo et al. (2005)[44,45]	HBsAg-, anti-HBc+	HBsAg	0% (95% CI: 0% to 18%) (0/18)
Ko et al. (2001)[62,63]	HBsAg-, anti-HBc+, anti-HBs+	HBsAg	0% (95% CI: 0% to 28%) (0/10)
Blanes et al. (2002)[64]	HBsAg-, anti-HBc+, serum HBV-DNA-	HBsAg	0% (95% CI: 0% to 43%) (0/5)

Study	Specific Test Results in these Donors	The rate applies to recipient positivity for what specific antigen/antibody?	Percentage of recipients who tested positive (95% CI) ¶ (Number of Recipients Positive Post-transplant/ Number of Recipients Negative Pre-transplant)
Blanes et al. (2002)[64]	HBsAg-, anti-HBc+, serum HBV-DNA-	anti-HBc	0% (95% CI: 0% to 43%) (0/5)
Blanes et al. (2002)[64]	HBsAg-, anti-HBc+, serum HBV-DNA-	serum HBV-DNA	0% (95% CI: 0% to 43%) (0/5)
Blanes et al. (2002)[64]	HBsAg-, anti-HBc+, serum HBV-DNA-	lymphocyte HBV-DNA	20% (95% CI: 4% to 62%) (1/5)
HBV Transmission from LUNG Transplantation			
Hartwig et al. (2005)[65]	HBsAg-, anti-HBc+	HBsAg	0% (95% CI: 0% to 13%) (0/26)
Hartwig et al. (2005)[65]	HBsAg-, anti-HBc+	anti-HBc	0% (95% CI: 0% to 13%) (0/26)
HCV Transmission from KIDNEY Transplantation			
Abbott et al. (2004)[67,68]	anti-HCV+	anti-HCV	9% (95% CI: 6% to 14%) (17/187)
Rozental et al. (2002)[69]	anti-HCV+	anti-HCV	25% (95% CI: 7% to 59%) (2/8)
Tokumoto et al. (1996)[70]	anti-HCV+	anti-HCV-1	33% (95% CI: 10% to 70%) (2/6)
Tokumoto et al. (1996)[70]	anti-HCV+	anti-HCV-2	60% (95% CI: 23% to 88%) (3/5)
Wreghitt et al. (1994)[71]	anti-HCV+	anti-HCV	25% (95% CI: 7% to 59%) (2/8)
Mendez et al. (1993)[72,73]	anti-HCV+	anti-HCV	6% (95% CI: 2% to 20%) (2/33)
Pereira et al. (1992)[14,17-19]	anti-HCV+	anti-HCV	91% (95% CI: 62% to 98%) (10/11)
Roth et al. (1992)[15,20]	anti-HCV+	anti-HCV	7% (95% CI: 1% to 31%) (1/14)

Study	Specific Test Results in these Donors	The rate applies to recipient positivity for what specific antigen/antibody?	Percentage of recipients who tested positive (95% CI) ¶ (Number of Recipients Positive Post-transplant/ Number of Recipients Negative Pre-transplant)
Tokumoto et al. (1996)[70]	anti-HCV+	HCV-RNA	50% (95% CI: 19% to 81%) (3/6)
Wreghitt et al. (1994)[71]	anti-HCV+	HCV-RNA	100% (95% CI: 65% to 100%) (7/7)
Tesi et al. (1994)[74,75]	anti-HCV+, serum HCV-RNA+	anti-HCV	19% (95% CI: 10% to 33%) (8/43)
Vincenti et al. (1993)[13]	anti-HCV+, serum HCV-RNA+	anti-HCV	0% (95% CI: 0% to 39%) (0/6)
Tesi et al. (1994)[74,75]	anti-HCV+, serum HCV-RNA+	anti-HCV or indeterminate	35% (95% CI: 22% to 50%) (15/43)
Tesi et al. (1994)[74,75]	anti-HCV+, serum HCV-RNA+	HCV-RNA	57% (95% CI: 41% to 71%) (21/37)
Vincenti et al. (1993)[13]	anti-HCV+, serum HCV-RNA+	HCV-RNA	0% (95% CI: 0% to 39%) (0/6)
Vincenti et al. (1993)[13]	anti-HCV+, serum HCV-RNA+	RIA	0% (95% CI: 0% to 39%) (0/6)
Preiksaitis et al. (1997)[76]	anti HCV+ and RIBA+	anti-HCV	62% (95%CI 36% to 82%) (8/13)
Preiksaitis et al. (1997)[76]	anti HCV+ and RIBA+	HCV-RNA	67% (95% CI: 35% to 88%) (6/9)
HCV Transmission from LIVER Transplantation			
Shah et al. (1993)[12,16]	anti-HCV+	anti-HCV	24% (95% CI: 11% to 43%) (6/25)
Everhart et al. (1999)[66]	anti-HCV+, serum HCV-RNA+	anti-HCV	67% (95% CI: 30% to 90%) (4/6)
Everhart et al. (1999)[66]	anti-HCV+, serum HCV-RNA+	HCV-RNA	100% (95% CI: 61% to 100%) (6/6)
HCV Transmission from HEART Transplantation			

Study	Specific Test Results in these Donors	The rate applies to recipient positivity for what specific antigen/antibody?	Percentage of recipients who tested positive (95% CI) ¶ (Number of Recipients Positive Post-transplant/ Number of Recipients Negative Pre-transplant)
Haji et al. (2004)[77-79]	anti-HCV+	"detectable" anti-HCV	11% (95% CI: 4% to 27%) (3/28)
Gudmundsson et al. (2003)[80]	anti-HCV+	anti-HCV	14% (95% CI: 3% to 51%) (1/7)
Marelli et al. (2002)[81]	anti-HCV+	anti-HCV	24% (95% CI: 10% to 47%) (4/17)
Haji et al. (2004)[77-79]	anti-HCV+	HCV-RNA	75% (95% CI: 57% to 87%) (21/28)
Gudmundsson et al. (2003)[80]	anti-HCV+	HCV-RNA	43% (95% CI: 16% to 75%) (3/7)
Marelli et al. (2002)[81]	anti-HCV+	HCV-RNA	12% (95% CI: 3% to 34%) (2/17)
Gudmundsson et al. (2003)[80]	anti-HCV+	liver HCV	29% (95% CI: 8% to 64%) (2/7)
Gudmundsson et al. (2003)[80]	anti-HCV+	"Any HCV infection"	43% (95% CI: 16% to 75%) (3/7)
File et al. (2003)[34]	anti-HCV+, serum HCV-RNA+	anti-HCV	44% (95% CI: 19% to 73%) (4/9)
File et al. (2003)[34]	anti-HCV+, serum HCV-RNA+	HCV-RNA	100% (95% CI: 72% to 100%) (10/10)

¶ The 95% confidence interval (CI) around each rate was calculated by ECRI Institute.

Evidence Reviews: II. Methodology to better estimate donor infection with HIV, HBV, or HCV

Question 3. What behavioral risk factors are associated with an increased probability of infection with HIV, HBV, or HCV? What is the prevalence of these characteristics among potential solid organ donors?

And

Question 4. What nonbehavioral risk factors are associated with an increased probability of infection with HIV, HBV, or HCV? What is the prevalence of these factors among potential solid organ donors?

As most of the included studies address both Questions 3 and 4, information regarding study populations and protocols, study risk of bias, and our methods of analysis are reported together for both questions in this section. Findings regarding behavioral risk factors are reported in *Question 3: Results*, and findings regarding nonbehavioral risk factors (e.g., signs and symptoms suggestive of infection, co-morbidity, socioeconomic factors, demographic factors) are reported in *Question 4: Results.*

The CDC document *Guidelines for Preventing Transmission of Human Immunodeficiency Virus Through Transplantation of Human Tissue and Organs* (1994),[100] listed seven "Behavior/History Exclusionary Criteria." According to the guideline, any potential donor with any of these characteristics should not donate organs regardless of HIV test results:

1. "Men who have had sex with another man in the preceding 5 years."
2. "Persons who report nonmedical intravenous, intramuscular, or subcutaneous injection of drugs in the preceding 5 years."
3. "Persons with hemophilia or related clotting disorders who have received human-derived clotting factor concentrates."
4. "Men and women who have engaged in sex in exchange for money or drugs in the preceding 5 years."
5. "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."
6. "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."
7. "Inmates of correctional systems. (This exclusion is to address issues such as difficulties with informed consent and increased prevalence of HIV in this population.)"

The 1994 guideline also excludes children with certain risk factors from donating, regardless of HIV test result status. The guideline states:

1. "Children meeting any of the exclusionary criteria listed above for adults should not be accepted as donors.
2. 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) should not be accepted as donors unless HIV infection can be definitely excluded in the child as follows:

   Children >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.

3. Children ≤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."

The purpose of Questions 3 and 4 is to search and summarize evidence regarding potential risk factors for the transmission of HIV, and also HBV and HCV. Behavioral factors are presented in Question 3, and nonbehavioral factors are presented in Question 4. Nonbehavioral factors include signs and symptoms suggestive of acute or chronic infection, co-morbidity, socioeconomic factors, and demographic factors.

To be included in these questions, studies had to meet inclusion criteria, as discussed in the *Introduction*. Although data restricted to potential solid organ donors were initially sought to identify risk factors, the paucity of evidence motivated the inclusion of data from three additional populations: potential tissue donors, blood donors, and the general population. Because there was still little data on the identification of risk factors for HBV infection, for HBV only the criteria were expanded to include demographic and socioeconomic subpopulations. Such subpopulation studies may have limited enrollment to people with a particular ethnic heritage or occupation. Risk factors identified in these populations may not be generalizable to other populations, including potential solid organ donors. In addition, they cannot be used to determine whether the characteristic all participants were selected for is a risk factor, unless there is a control or comparison group in the study.

Inclusion criteria for prevalence and incidence of identified risk factors were stricter. We did not include prevalence estimates from populations with pre-screened blood donors (which would underestimate prevalence), special demographic or socioeconomic subpopulations (which could overestimate or underestimate prevalence, depending on the population), or populations that over-selected for infected individuals in case-control study designs (which would overestimate prevalence). We also did not extract demographic prevalence (e.g., race or sex) or infection incidence or prevalence data (e.g., proportion co-infected) because there are other, more accurate, sources of this type of information available than the studies included for this question provide (such as in Question 1). Some data on the *prevalence* of risk factors appeared to overlap between Armstrong et al.[30] and McQuillan et al.[101], as both used NHANES IV (1992 to 2002) data. In these instances we used the prevalence data from Armstrong et al. because the data set they used was larger. No studies that assessed risk factors associated with incident infection were identified.

Thirty studies comprise the evidence base for Questions 3 and 4, with 22 addressing Question 3 and 29 addressing Question 4. Of the 29 studies that associated behavioral and/or nonbehavioral risk factors

with infection, 12 addressed HBV, 12 addressed HCV, and 6 addressed HIV (one study addressed both HBV and HCV). Twenty one studies reported identification of behavioral factors (such as drug use or sexual activities) and are included in Question 3. Only eight studies reported the prevalence of identified behavioral risk factors in potential donors or the general population, including one study that did not provide data for the identification of risk factors.[8] (One additional study reported information on prevalence of risk factors from the National Health and Nutrition Examination Surveys (NHANES)-III (1988-1994)[29] but this information was superseded by NHANES-IV (1992-2002) data from other studies.[30,101] Twenty-nine studies reported on the identification of nonbehavioral risk factors. Of those, only four reported prevalence of identified factors. Although we sought information on signs and symptoms that may be associated with infection, extremely little information on this was identified. Included studies and the Questions they address are listed below in Table 27.

Table 27. Included Studies, Questions 3 and 4

Citation	Year	Virus(es)	Question 3		Question 4	
			Identification	Prevalence	Identification	Prevalence
Potential and Actual Organ Donors						
Gasink et al.[102]	2006	HCV	✓	✓	✓	
Hidalgo et al.[8]	2001	Not Applicable*		✓		
Potential Tissue Donors						
Sanchez et al.[103]	2006	HBV	✓	✓	✓	
Blood Donors						
Orton et al.[104]	2004	HCV	✓		✓	
Murphy et al.[105]	2000	HCV	✓		✓	
Conry-Cantilena et al.[106]	1996	HCV	✓		✓	
Murphy et al.[107]	1996	HCV			✓	
General Population						
McGinn et al.[108]	2008	HCV			✓	
McQuillan et al.[29]	1999	HBV	✓		✓	
Mehta et al.[109]	2008	HIV	✓	✓	✓	✓
Nguyen et al.[110]	2008	HIV	✓	✓	✓	✓
Zetola et al.[111]	2008	HIV			✓	
Armstrong et al.[30]	2006	HCV	✓	✓	✓	✓
McQuillan et al.[101]	2006	HIV	✓		✓	
Hand and Vasquez[112]	2005	HCV	✓		✓	
Nguyen et al.[113]	2005	HCV	✓		✓	
Fischer et al.[114]	2000	HCV	✓		✓	

Citation	Year	Virus(es)	Question 3		Question 4	
			Identification	Prevalence	Identification	Prevalence
Alpert et al.[115]	1996	HIV	✓		✓	
Kaur et al.[116]	1996	HBV, HCV	✓	✓	✓	✓
Alter et al.[117]	1989	HBV	✓		✓	
Children and Adolescents						
Luban et al.[118]	2007	HCV			✓	
D'Angelo et al.[119]	1991	HIV			✓	
Demographic and Socioeconomic Subpopulation (HBV Only)						
Lee et al.[120]	2008	HBV			✓	
Tabibian et al.[121]	2008	HBV	✓		✓	
Hann et al.[122]	2007	HBV			✓	
Lin et al.[123]	2007	HBV			✓	
Hwang et al.[124]	2006	HBV	✓		✓	
Butterfield et al.[125]	2004	HBV	✓		✓	
Butterfield et al.[126]	1990	HBV	✓		✓	
Turner et al.[127]	1989	HBV	✓		✓	

* Hidalgo et al. assessed the prevalence of a general risk factor only (unspecified substance abuse), and did not attempt associate the factor with any particular infection.

Studied Populations and Study Methods

This section provides a brief description of the enrollees and methods in the included studies. The studies are organized by population type (as divided in Table 27). Additional information regarding study protocols, including setting and location of study, method of data collection, relevant blood test used to determine infection status, funding source, and year(s) of data collection, are shown in Table 28. Details regarding participant characteristics, including methods of participant selection and selection criteria, demographic descriptors (e.g., percent male, race, age), are shown in Table 29.

Data on potential or actual solid organ donors were very limited. Two retrospective studies, each with few factors reported, were identified. Only one of those studies focused on potential solid organ donors, Hidalgo et al.[8] This study provides reasons for donor ineligibility among a cohort of 55 potential living who were able to provide data regarding their health status. A second study, Gasink et al.[102], statistically assessed the association between donor characteristics and HCV infection to indentify risk factors for HCV in a cohort of 10,915 actual heart donors, including 261 with HCV, using data from the Scientific Registry of Transplant Recipients (SRTR). Prevalence of some factors was also reported.

Potential Tissue Donors

One study on risk factors for HCV among potential cornea donors, Sanchez et al., was also included.[103] Eighty three potential donors with positive serological result(s) and 56 randomly selected controls were included. In this study, infection status was retrospectively tested for association with behavioral and clinical factors in a questionnaire completed by next of kin. This study is unique in that the identification of risk factors relied upon next-of-kin interviews rather than medical record review or self-report.

Actual Blood Donors

Also included were four studies that examined risk factors for HCV among actual blood donors, Conry-Cantilena et al.,[106] Murphy et al. (2000),[105] Murphy et al. (1996),[107] and Orton et al.[104] We included these studies with the intent of examining factors other than those that potential donors are screened for (e.g., other than men having sex with men or injection drug use). However, in all four studies, some donors who were followed-up with questionnaires or interviews admitted to exclusionary behaviors. Therefore, it was possible to investigate these factors for association with HCV. However, because potential donors who were not deceptive about these factors were screened out and not permitted to donate, we did not consider the prevalence of these factors among actual donors because the prevalence would be underestimated. We did not identify any studies on potential (i.e., pre-screened) blood donors, or potential donors who were eliminated from the donor pool as a result of the screening process.

The four studies used different approaches to identifying risk factors. Conry-Cantilena et al. and Murphy et al. (2000) were case-control studies that enrolled samples of infected and uninfected donors and compared the factors among them.[105,106] Conry-Cantilena et al. enrolled 248 individuals with HCV and 131 without. Murphy et al. (2000) enrolled 758 infected individuals and 1,039 uninfected individuals. Both of these studies identified participants by retrospective assessment of their HCV status and prospectively collected data on risk factors using questionnaires. Orton et al. recalled blood donors who initially tested anti-HCV positive for further testing and collection of risk factor data and prospectively re-tested them using nucleic acid tests, and administered in-person questionnaires. Of those who completed follow-up at the time of donation, the factors of 65 participants who were confirmed as positive by nucleic acid tests were compared to the factors among the 225 participants who were

ultimately deemed uninfected (initial false-positives). Murphy et al. (1996) was a much larger (n = 862,398) study that examined consecutive blood donors and retrospectively evaluated infection status and demographic information collected at this time of donation.[107]

General Population

Thirteen additional studies enrolled participants representative of a general population. By "general population," we mean a population unselected for any particular demographic, occupational, or behavioral characteristics, or health status other than HCV, HBV, or HIV infection status. These studies recruited participants from various settings including emergency departments,[111,115] primary care clinics,[108] medical centers,[109,112,113,117] health plan enrollees,[114] using advertisements to the public,[116] or NHANES data.[29,30,101,110] (When extracting data we were careful to ensure that duplicate NHANES data were not included. Where data from probably overlapping pools of participants were reported, we used the statistic from the study with the larger sample size. We only collected prevalence information from the most recent NHANES data.)

The general design of these studies was to collect blood samples to test for infection and administer questionnaires or interviews regarding potential risk factors. Most of these studies were prospective. The studies were generally large, with only four enrolling under 1,000 participants. Five of these studies addressed HIV, five addressed HCV, and one addressed both HCV and HBV.

Children

Two included studies specifically assessed children. Luban et al. performed a record review of 2,758 children who had received a blood transfusion and targeted factors for HCV.[118] D'Angelo et al. reviewed records of 3,520 adolescents with leftover serum from other tests and considered factors for HIV infection.[119]

Demographic and Socioeconomic Subpopulations

A total of eight subpopulation studies that evaluated risk factors and HBV were included. Populations assessed in these studies include mentally ill veterans in inpatient Veterans Administration (VA) Hospital psychiatric care,[121,125] women registered for obstetric care at a military hospital,[126] college students,[124] embalmers,[127] Asian Americans,[123] and Korean-American church-goers.[120,122] Most of the Asian Americans and Korean American church-goers were foreign-born. All of these studies were prospective. On the whole, these studies were smaller than the general population studies: Half enrolled fewer than 1,000 people, with the smallest study enrolling 108 individuals.[127]

Table 28. Study Protocols for Questions 3 and 4

Citation	Year	Question 3	Question 4	Virus(es)	Setting(s) Selected From	Location	Selection Methods	Method of Risk Factor Data Collection	Relevant Blood Test Used	Clearly States Adjusted / Controlled Statistics Reported	Prospective or Retrospective	Funding	Year(s) Data Collected
Potential and Actual Organ Donors													
Gasink et al.[102]	2006	✓	✓	Hepatitis C Virus (HCV)	Hospitals – heart transplant donors	Nationwide	All actual heart donations during time period	Scientific Registry of Transplant Recipients (SRTR) record review, including blood test results	Patients considered positive if medical chart marked "recipient anti-HCV," or "recipient RIBA [recombinant immunoblot assay)," or "recipient RNA" positive	No (for outcomes of interest)	Retrospective	Academic division of cardio-vascular unit. No disclosures reported.	1994 to 2003
Hidalgo et al.[8]	2001	✓		Not Applicable (prevalence of risk factors only)	Relatives of children with end-stage renal disease	Brooklyn, NY	Potential related donors of all children <21 with end stage renal disease (ESRD) and surviving transplant between 1990 and 1999	Retrospective chart review and interview	Not reported (and not relevant because only included for prevalence of risk factors)	Not applicable	Retrospective	Not reported. Authors affiliated with and data collected from academic hospital.	1990 to 1999

Citation	Year	Question 3	Question 4	Virus(es)	Setting(s) Selected From	Location	Selection Methods	Method of Risk Factor Data Collection	Relevant Blood Test Used	Clearly States Adjusted / Controlled Statistics Reported	Prospective or Retrospective	Funding	Year(s) Data Collected
Potential Tissue Donors													
Sanchez et al.[103]	2006	✓	✓	All	Potential corneal donors	Dallas, TX	All potential donor corneas with positive serological results for infectious disease	Retrospective review of next-of-kin questionnaire	HIV 1/2, HIV p24 antigen (Ag), HIV DNA, HIV nucleic acid test (NAT), HbsAg, HB Core, HCV, HCV-NAT	No	Retrospective	Not reported. Authors affiliated with university medical centers.	2002 to 2004
Blood Donors													
Conry-Cantilena et al.[106]	1996	✓	✓	HCV	Actual volunteer blood donors	Greater Chesapeake and Potomac area	Blood donors to American Red Cross with positive EIA results, including those with false positives as determined by RIBA	Medical history taken by physician, private drug use questionnaire	Enzyme linked immunosorbent assay (EIA) 1.0 Ortho Diagnostics, EIA 2.0 Ortho diagnostics, RIBA 2.0 Chiron	Yes	Prospective questionnaire of donors identified retro-spectively by initial positive EIA result	Not reported. Most authors affiliated with National Institutes of Health.	1991 to 1994

Citation	Year	Question 3	Question 4	Virus(es)	Setting(s) Selected From	Location	Selection Methods	Method of Risk Factor Data Collection	Relevant Blood Test Used	Clearly States Adjusted / Controlled Statistics Reported	Prospective or Retrospective	Funding	Year(s) Data Collected
Murphy et al.[105]	2000	✓	✓	HCV	Actual blood donors	Baltimore/ Washington, Southeast Michigan, Oklahoma City, San Francisco, Los Angeles	Cases were all HCV positive donors during time period, Controls by HCV negativity and matched to controls	Mailed anonymous questionnaire	Not reported, but tested through U.S. blood donation centers so should be valid	Yes	Prospective questionnaire of donors identified retro-spectively by initial positive EIA result	National Heart Lung and Blood Institute	1994 to 1995
Murphy et al.[107]	1996		✓	HCV	Actual blood donors	Baltimore, Washington DC, Detroit, Oklahoma City, San Francisco, Los Angeles	All donations in a time period	Demographic information collected at donation time	Second-generation HCV EIA with RIBA HCV 2.0 EIA (Abbott) or Matrix (Unlicensed) for confirmation	Yes	Retrospective	National Heart, Lung, and Blood Institute	1992 though 1993
Orton et al.[104]	2004	✓	✓	HCV	Actual blood donors	Apparently nationwide	Blood donors to American Red Cross	Questionnaire administered in person by donation counselor or physician	ProCleix HIV-1 and HCV assay (Chiron Corporation) with confirmation with RT-PCR (reverse-transcriptase polymerase chain reaction) (NCI)	Yes	Prospective questionnaire of donors identified retro-spectively by initial EIA negative and NAT reactive result	Not reported, but appears to be American Red Cross, Centers for Disease Control and Prevention	1999 to 2003

Citation	Year	Question 3	Question 4	Virus(es)	Setting(s) Selected From	Location	Selection Methods	Method of Risk Factor Data Collection	Relevant Blood Test Used	Clearly States Adjusted / Controlled Statistics Reported	Prospective or Retrospective	Funding	Year(s) Data Collected
General Population													
Alpert et al.[115]	1996	✓	✓	Human Immuno-deficiency Virus (HIV)	Inner-city emer-gency depart-ment	Bronx, NY	Consecu-tive adult noncritical medical patients	In-person interview by physician	EIA (Genetic systems) with Western blot confirmation (Cambridge-Biotech)	Yes	Prospective	In part by Centers for Disease Control (CDC) and National Institute of Allergy and Infectious Diseases	1993 to 1994
Alter et al.[117]	1989	✓	✓	HBV	Cases reported to health depart-ment, controls from general population	Alabama, Washington State	Cases selected by reporting to county health department and had no known cause of hepatitis, Controls selected by randomly dialing other county residents	Interviews by nurses	HBV core antigen test	Yes	Prospective	Not reported, appears to have been publically funded	1985 to 1986

Citation	Year	Question 3	Question 4	Virus(es)	Setting(s) Selected From	Location	Selection Methods	Method of Risk Factor Data Collection	Relevant Blood Test Used	Clearly States Adjusted / Controlled Statistics Reported	Prospective or Retrospective	Funding	Year(s) Data Collected
Armstrong et al.[30]	2006	✓	✓	HCV	General population	Nation-wide	Participants in National Health and Nutrition Examina-tions Surveys (NHANES) IV	National Center for Health Statistics (NHANES) IV survey with sensitive items on computer	Ortho HCV ELISA v. 3.0 (Ortho-Clinical Diagnostics); Repeatedly reactive samples tested with Chiron RIBA HCV Strip Immunoblot Assay v. 3.0 (Chiron Corp). RIBA positive or indeterminate tested for RNA with COBAS Amplicor HCV Monitor Test v. 2.0 (Roche Molecular Diagnostics)	Yes	Prospective	National Centers for Disease Control (CDC)	1999 to 2002
Fischer et al.[114]	2000	✓	✓	HCV	HMO enrollees	Twin Cities metro area of Minnesota	Health plan patients identified as being at elevated or normal risk though database (plus health care workers)	Anonymous risk profile questionnaire	Polymerase chain reaction (PCR)	Yes	Prospective	Contract with Integrated Thera-peutic Group of Schering-Plough	1996 to 1997

Citation	Year	Question 3	Question 4	Virus(es)	Setting(s) Selected From	Location	Selection Methods	Method of Risk Factor Data Collection	Relevant Blood Test Used	Clearly States Adjusted / Controlled Statistics Reported	Prospective or Retrospective	Funding	Year(s) Data Collected
Hand and Vasquez[112]	2005	✓	✓	HCV	General population	Patients at university medical center	Patients who had HCV test and positive (case) or negative (control) results	Interview in person in hospital setting or by telephone if not available in person	Abbott HCV EIA 2.0	Yes	Prospective interview based upon retrospective review of lab results	State of Texas Tobacco Settlement Endow-ment for Texas Tech University Health Sciences Center	2000 to 2002
Kaur et al.[116]	1996	✓	✓	Hepatitis B Virus (HBV), HCV	General population	Nationwide, primarily urban	Volunteers responding to advertise-ment	Risk profile questionnaire. Details not reported.	HbsAg and anti-HBC (Abbott Diagnostics) and HCV EIA 2.0 (Abbott Laboratories) confirmed by MATRIX HCV dot-blot immunoassay (Abbott Laboratories)	Yes	Prospective	Schering Pharma-ceuticals, Abbott Labora-tories, American Liver Foundation	1992
McGinn et al.[108]	2008		✓	HCV	Adult primary care clinic	Inner city New York, NY	Random selection	Survey by in person interview and medical record review	HCV EIA 2.0 Recombinant c100-3, HC31, and HC-34, (Abbott Laboratories)	No (only univariate used)	Prospective	No disclosures reported	2002 to 2003

Citation	Year	Question 3	Question 4	Virus(es)	Setting(s) Selected From	Location	Selection Methods	Method of Risk Factor Data Collection	Relevant Blood Test Used	Clearly States Adjusted / Controlled Statistics Reported	Prospective or Retrospective	Funding	Year(s) Data Collected
McQuillan et al.[101]	2006	✓	✓	HIV	General population	Nationwide	Participants in National Health and Nutrition Examinations Surveys (NHANES) versions 1988 to 1994 and 1999 to 2002	Confidential surveys	ELISA (Genetic Systems, or Organon-Teknika Corporation) and confirmed by Western blot (Biotech/DuPont) or HIV-1/HIV-2 peptide EIA (Genetic Systems) confirmed by Western blot (Calypte Biomedical Corporation) or urinalysis (Calypte HIV01 Peptide EIA confirmed by Western blot (Calpype Biomedical)	No (ECRI Institute calculated univariate analyses)	Prospective	Federal	1999 to 2002 for risk factors

Citation	Year	Question 3	Question 4	Virus(es)	Setting(s) Selected From	Location	Selection Methods	Method of Risk Factor Data Collection	Relevant Blood Test Used	Clearly States Adjusted / Controlled Statistics Reported	Prospective or Retrospective	Funding	Year(s) Data Collected
McQuillan et al.[29]	1999	✓	✓	HBV	General population	Nationwide	Participants in National Health and Nutrition Examina-tions Surveys (NHANES)	Confidential surveys	NHANES II Antibody to HBV surface antigen or core antigen and HBV surface antigen by EIA (AUSAB, CORZYME, AUSZYME, Abbott) NHANES III HBC core antibodies radio-immunoassay (CORAB) and confirmation by surface antigen and surface antigen antibody (AUSRIA and AUSAB, Abbott)	Yes	Prospective	Not specifically stated. All authors employed by National Center for Infectious Diseases, Centers for Disease Control (CDC)	1976 through 1994

Citation	Year	Question 3	Question 4	Virus(es)	Setting(s) Selected From	Location	Selection Methods	Method of Risk Factor Data Collection	Relevant Blood Test Used	Clearly States Adjusted / Controlled Statistics Reported	Prospective or Retrospective	Funding	Year(s) Data Collected
Mehta et al.[109]	2008	✓	✓	HIV	Hospital urgent care center, inpatient floors, outpatient primary care, non-clinical drop-in center, emer-gency depart-ment	Boston, MA	Consecu-tive (all) or self-selected for HIV test, depending on setting where sample was drawn from	Personal interview in medical center	OraQuick Rapid HIV-1 Antibody Test (Orasure Technologies) with confirmation by both ELISA and Western blot	No	Retrospective	Public health department and CDC	2002 to 2004
Nguyen et al.[110]	2008	✓	✓	HIV	General population	New York City	Random selection from NYC households	In-person interview plus computer-assisted survey for sensitive information	Unnamed HIV-1/HIV-2 EIA with Western blot confirmation, Remnants tested for HIV-1 RNA by PCR.	No	Prospective	CDC	2004
Nguyen et al.[113]	2005	✓	✓	HCV	General internal medicine clinic (controls) and hepa-tology clinic (cases) at urban medical university	Philadelphia, PA	Not reported	Anonymous written questionnaire	HCV antibody (Home Access Health Corp, Hoffman Associates)	Yes	Prospective	In part by Schering-Plough; no financial disclosure	Not reported

Citation	Year	Question 3	Question 4	Virus(es)	Setting(s) Selected From	Location	Selection Methods	Method of Risk Factor Data Collection	Relevant Blood Test Used	Clearly States Adjusted / Controlled Statistics Reported	Prospective or Retrospective	Funding	Year(s) Data Collected
Zetola et al.[111]	2008		✓	HIV	Patients in general hospital emergency department	San Francisco, CA	Emergency department patients who had blood drawn and were not known to be HIV+	Record review of demographic and medical records	All screened by EIA (Genetic Systems HIV-1/HIV-2 plus O EIA, Bio-Rad Laboratories); positives confirmed with immunofluorescent assay (IFA) (Fluorognost HIV-1 IFA, Sanochemia Pharmazeutika AG), and discordant results resolved with RNA transcription mediated amplification test (TMA Aptima HIV-1 RNA Quantitative Assay, Gen-Probe Inc.)	Yes	Retrospective	Division of Research Resources of National Institutes of Health (NIH), California HIV Research Program Grant, San Francisco Department of Health	2007

Citation	Year	Question 3	Question 4	Virus(es)	Setting(s) Selected From	Location	Selection Methods	Method of Risk Factor Data Collection	Relevant Blood Test Used	Clearly States Adjusted / Controlled Statistics Reported	Prospective or Retrospective	Funding	Year(s) Data Collected
Children and Adolescents													
Luban et al.[118]	2007		✓	HCV	Tertiary-care urban university childrens' hospital and commun-ity controls	Washington, D.C.	Record identification of children who had blood transfusion	Record review	Abbott anti-HCV EIA with confirmation by Chiron RIBA-2 and COBAS AmpliCore HCV PCR test	No	Retrospective	NIH	Transfusions administered between 1982 and 1992
D'Angelo et al.[119]	1991		✓	HIV	Children's National Medical Center	Washington, D.C.	Leftover serum from other tests	Record review	Abbott EIA, DuPont Western Blot and another EIA for confirmation	No	Retrospective	Not reported, authors either affiliated with a university hospital or federal health agency	1987 to 1989

Citation	Year	Question 3	Question 4	Virus(es)	Setting(s) Selected From	Location	Selection Methods	Method of Risk Factor Data Collection	Relevant Blood Test Used	Clearly States Adjusted / Controlled Statistics Reported	Prospective or Retrospective	Funding	Year(s) Data Collected
Demographic and Socioeconomic Subpopulations (HBV only)													
Butterfield et al.[125]	2004	✓	✓	HBV	Veterans Administration (VA) psychiatric inpatient unit	Durham, NC	Consecutive admissions	Standardized in-person risk interview	Abbott Corzyme test for HBV core antibody	Yes	Prospective	VA research grants	1998 to 2000
Butterfield et al.[126]	1990	✓	✓	HBV	Women registered for obstetric care at military hospital	El Paso, TX	Consecutive enrollment	Questionnaire at initial physician consultation	AUSRIA II-125 radio-immunoassay kit, Abbott	No	Prospective	Not reported	1987 and 1988
Hann et al.[122]	2007		✓	HBV	Korean-American church-goers	Northeastern U.S.	Recruited from church	Questionnaire completed by family (no highly sensitive or personal information)	HbsAg, anti-HBs, HbeAg, anti-HBe tests by Abbott	No	Prospective	Not reported	1988 to 1990
Hwang et al.[124]	2006	✓	✓	HBV	College students	Houston, TX	Recruited from large classes of required courses and public areas of universities	Anonymous self-administered questionnaire	Abbott anti-HBc, anti-HBs, and HbsAg	Yes	Prospective	CDC	1999

Citation	Year	Question 3	Question 4	Virus(es)	Setting(s) Selected From	Location	Selection Methods	Method of Risk Factor Data Collection	Relevant Blood Test Used	Clearly States Adjusted / Controlled Statistics Reported	Prospective or Retrospective	Funding	Year(s) Data Collected
Lee et al.[120]	2008		✓	HBV	Korean-American church-goers	Colorado	Recruited from church	Collection of demographic data and vaccination history	HBsAg, anti-HBs, brand unspecified but run on Advia Centaur XP immunoassay system	No	Prospective	University school of nursing research grant, Shil-IL Overseas Korean Health Founda-tion, Equality Fund from Colorado Trust	2004 to 2007
Lin et al.[123]	2007		✓	HBV	Recruited Through advertise ments and screened at commun-ity-based events	San Francisco bay area	None reported other than Asian-American and signed informed consent	Questionnaire about demographic information and vaccination history	HBsAg, plus in some cases, HBs, brands unspecified	Yes	Prospective	Not explicitly reported, possibly Asian Liver Center at Stanford University	2001 through 2006
Tabibian et al.[121]	2008	✓	✓	HBV	Veterans acutely and voluntarily hospital-ized in psych-iatric ward	West Los Angeles	Consecu-tive admissions	Interview using standardized questionnaire, VA risk assessment tool	HbsAg, HBsAb, HbcAg, brands unspecified	Yes	Prospective	Not reported	2002 to 2003

Citation	Year	Question 3	Question 4	Virus(es)	Setting(s) Selected From	Location	Selection Methods	Method of Risk Factor Data Collection	Relevant Blood Test Used	Clearly States Adjusted / Controlled Statistics Reported	Prospective or Retrospective	Funding	Year(s) Data Collected
Turner et al.[127]	1989	✓	✓	HBV	Embalm-ers in an urban area	Boston and Worcester MA metro-politan areas	Not reported	Oral questionnaire	HBV surface antigen and antibody and core tests using Abbott brand tests. Confirmation by Western blot	Yes	Prospective	Biomedical research grant from National Institutes of health and National Institute for Occupation al Health and Safety	1986 to 1987

Table 29. Participant Characteristics for KQ 4 and 5

Citation	Year	KQ4	KQ5	Virus(es)	Participant Selection	Selection Criteria	Number of Participants	Percent Male	Race (as reported in study)	Age
Potential and Actual Organ Donors										
Gasink et al.[102]	2006	✓	✓	Hepatitis C Virus (HCV)	Actual heart donors registered in Scientific Registry of Transplant Recipients	All heart donors of transplant recipients at least 18 years who received their transplant between 4/1/1994 and 7/31/2003	18,618 initially considered eligible, 10,915 met inclusion criteria, 261 with HCV+ donor	69%	White: 86%; Black: 12%; Other: 2%	Median: 29 years
Hidalgo et al.[8]	2001	✓		Not applicable (prevalence of risk factors only)	Potential living donor parents of child transplant candidates	Potential related donors of all children <21 years with end-stage renal disease and surviving transplant between 1990 and 1999	55 potential donors screened	36%	Race of potential donors not reported. Their children transplant candidates were: Black: 60% Hispanic: 30% Caucasian: 7% Asian: 3%	Mean: 38.8 years
Potential Tissue Donors										
Sanchez et al.[103]	2006	✓	✓	All	All donor corneas with positive serological results for infectious disease plus negative controls	Consecutive tissues with positive serological results in time period	83 donors with positive serological results plus 56 randomly selected seronegative controls	62%	White: 75%; Black: 17%; Other: 4%	Mean: 54 years

Citation	Year	KQ4	KQ5	Virus(es)	Participant Selection	Selection Criteria	Number of Participants	Percent Male	Race (as reported in study)	Age
Blood Donors										
Conry-Cantilena et al.[106]	1996	✓	✓	HCV	Blood donors with positive enzyme linked immunosorbent assay (EIA) enrolled consecutively until target enrollment attained	Consecutive volunteer whole blood donors who donated between 1991 and 1994 and had positive EIA	4,585 donors screened positive, 481 of them enrolled. 248 enrolled as positive and 131 as negative (and 102 indetermin-ate)	57%	Black: 12.7%	Mean: 40 years
Murphy et al.[105]	2000	✓	✓	HCV	All HCV positive and during time period and matched HCV negative blood donors	By serostatus; cases and controls matched by age, sex, race/ethnicity, first time vs. repeat donor status	2,316 HCV+ invited, 758 participated. 2,316 HCV- invited, 1039 participated	54%	White non-Hispanic: 73%, Black non-Hispanic: 10%, Hispanic: 8%, Asian: 2%, Other: 2%	Most aged 30 to 49 years
Murphy et al.[107]	1996		✓	HCV	All blood donors	Consecutive blood donors	862,398	53%	White: 81%, Black: 7%, Hispanic: 6%, Asian: 3%, Other: 1%, Missing: 2%	Majority between 20 and 49 years, Range: 11 to 93 years

Citation	Year	KQ4	KQ5	Virus(es)	Participant Selection	Selection Criteria	Number of Participants	Percent Male	Race (as reported in study)	Age
Orton et al.[104]	2004	✓	✓	HCV	Blood donors anti-HCV- but unconfirmed nucleic acid test (NAT) reactive results	Blood donors anti-HCV- but unconfirmed reactive NAT results who donated blood in time period and completed questionnaire	810 potential participants, of whom 116 confirmed positive. 65 cases and 225 controls completed study.	54%	88% White non-Hispanic, rest "other"	Mean: 39 years
General Population										
Alpert et al.[115]	1996	✓	✓	Human Immunodeficiency Virus (HIV)	Consecutive noncritical adults in emergency department	Consecutive	1,744 patients, with 988 having blood drawn and 875 with adequate amount for testing and no known HIV	Not reported (NR)	NR	NR

Citation	Year	KQ4	KQ5	Virus(es)	Participant Selection	Selection Criteria	Number of Participants	Percent Male	Race (as reported in study)	Age
Alter et al.[117]	1989	✓	✓	HBV	Cases reported to county health department, controls selected randomly	Cases had acute HBV infection and none of the following factors within last six months: blood transfusion, IV drug use, male homosexual activity, health care employment requiring frequent contact with blood, hemodialysis, sexual or household contact with HBV carrier. Controls were HBV-uninfected and were matched by age within 5 years, sex, race, area code, and telephone exchange.	76 cases, 152 controls	Not reported	Not reported	Not reported
Armstrong et al.[30]	2006	✓	✓	HCV	Nationally representative sample of civilians and non-institutionalized population	Selected to be representative of general population	21,509 eligible, 17,548 interviewed, and 15,079 gave sufficient blood sample and were included	48%	Non-Hispanic White: 40%; Non-Hispanic Black: 23%; Mexican-American: 29%	NR

Citation	Year	KQ4	KQ5	Virus(es)	Participant Selection	Selection Criteria	Number of Participants	Percent Male	Race (as reported in study)	Age
Fischer et al.[114]	2000	✓	✓	HCV	Health plan patients identified as being at elevated or normal risk though database, (or health care workers, not included in this analysis).	Based upon diagnostic codes suggestive of Hepatitis C, plus controls without any liver-related diagnoses	8,800 identified in database. 1,380 total completed study, including 454 at higher risk and 926 controls.	34%	NR	NR, 26% less than 50 years
Hand and Vasquez[112]	2005	✓	✓	HCV	Clinic or hospital patients selected by HCV test result	For cases, positive HCV test, for controls, negative HCV test. Patients were tested due to suspected liver disease, planned hemodialysis, or hepatitis risk factors People who participated in interview could be included.	627	70%	Hispanic: 87%, Non-Hispanic: 13%	Mean age: 45.5, Range: 14 to 99
Kaur et al.[116]	1996	✓	✓	Hepatitis B Virus (HBV), HCV	Volunteers responding to advertisement	None reported	8581	42%	White: 77%, African American: 14%, Asian: 3%, Other: 6%	Mean: 45 (Standard error [SE] 15) years

Citation	Year	KQ4	KQ5	Virus(es)	Participant Selection	Selection Criteria	Number of Participants	Percent Male	Race (as reported in study)	Age
McGinn et al.[108]	2008		✓	HCV	A stochastically randomized sample of all patients attended primary care were invited to participate	Age 18 or older, English or Spanish language proficient	1,485 invited, 1,000 enrolled	27%	Latino: 54%; Black: 32%; White: 10%; Other: 4%	Mean: 50.1 (SD: 14.7) years
McQuillan et al.[101]	2006	✓	✓	HIV	"Stratified multi-staged probability cluster design that selected a sample representative of the U.S. civilian non-institutionalized population."	Participants aged 18 to 59 who were anonymously tested for HIV antibody	NHANES III: 15,141 participants total, 13,022 agreed to interview, 11,203 agreed to exam and had sufficient serum NHANES 99-'02: 6,458 invited, 5,926 agreed to exam and had HIV test	NR	NR	NR
McQuillan et al.[29]	1999	✓	✓	HBV	Stratified, multistage, probability cluster design of U.S. households	Random selection	Analysis of risk factors "generally restricted" to NHANES III, which enrolled 40,000 people	NR	NR	NR

Citation	Year	KQ4	KQ5	Virus(es)	Participant Selection	Selection Criteria	Number of Participants	Percent Male	Race (as reported in study)	Age
Mehta et al.[109]	2008	✓	✓	HIV	Consecutive patients in hospital system were approached for participation	All patients who consented	17,594 pretest counseling sessions and 16,750 HIV tests, 229 new HIV diagnoses	59%	Black: 39%; White: 23%; Hispanic: 19%; Haitian: 8%	Median age: 36 years
Nguyen et al.[110]	2008	✓	✓	HIV	Random selection or representative households of adults aged at least 20 years	Not institutionalized or homeless	4,026 randomly selected, 3,388 screened, 3,047 eligible, 1,999 completed interview and at least one component of physical exam, and 1,626 provided blood	46.2%	White: 30% Black: 21% Asian: 13% Hispanic: 36%	Mean age NR; 57.3% at least 40 years old
Nguyen et al.[113]	2005	✓	✓	HCV	Patients with known HCV under care at hepatology clinic (cases) and asymptomatic patients with unknown status in general medical clinic (controls)	Aged 18 to 60 years English proficient	429 total, 225 HCV positive; 204 HCV negative	42%	White: 63%; African-American: 27%; Asian: 4%; Latino: 3%; Other: 3%	NR; wide range of decades of birth

Citation	Year	KQ4	KQ5	Virus(es)	Participant Selection	Selection Criteria	Number of Participants	Percent Male	Race (as reported in study)	Age
Zetola et al.[111]	2008		✓	HIV	All patients seeking emergency medical attention who had blood drawn and were not known to be infected with HIV	Consecutive patients	1,820 had blood drawn, 1,674 were of unknown or negative HIV status and met inclusion criteria	62.3%	White: 27.4%, Black: 28.4%, Latino: 22.6%, Other: 17.6%, Unknown: 4%	Mean: NR, 24.9% 18-30 years, 29.1% 31-45 years, 44.1% >45 years
Children and Adolescents										
Luban et al.[118]	2007		✓	HCV	Children who had blood or blood product transfusions	Under 15 years at time of transfusion, no perinatal transmission, and no malignancy, hemophilia, rheumatologic disease, HIV, or organ or marrow transplantation or dialysis	5,473 identified as potentially eligible, 4,726 locatable, 2,758 tested	59%	African-American: 38%, Asian: 1.5%, Caucasian: 48.3%, Hispanic: 3.4%, Other/unknown: 8.8%	NR, age at time of transfusion less than one year on average
D'Angelo et al.[119]	1991		✓	HIV	Children attending ambulatory care hospital services with leftover serum	Appears to be all children with leftover serum	3,520	33%	NR	Mean NR, all patients 20 years and younger

Citation	Year	KQ4	KQ5	Virus(es)	Participant Selection	Selection Criteria	Number of Participants	Percent Male	Race (as reported in study)	Age
Demographic and Socioeconomic Subpopulations (HBV only)										
Butterfield et al.[125]	2004	✓	✓	HBV	Inpatients in Veterans Administration (VA) psychiatric unit	Consecutively admitted veterans with severe mental illness who were either African American or Caucasian and had blood test results	399 consecutive recruits, 376 included	90%	Caucasian: 41%, African-American: 59%	NR
Butterfield et al.[126]	1990	✓	✓	HBV	Consecutive women seeking prenatal care	All patients included	1,466	0%	NR	NR
Hann et al.[122]	2007		✓	HBV	Korean-American church-goers	None reported besides participant selection method	6,130	48%	Korean-American: 100%	NR
Hwang et al.[124]	2006	✓	✓	HBV	College students	For HBV risk assessment, U.S. or Canada born and no evidence of immunization	7,960, of whom 4,328 were U.S. or Canada born and had no evidence of immunization	39.2%	Non-Hispanic white: 41.5%, non-Hispanic black: 26.1%, Hispanic: 22.2%, Asian: 6.8%, Other :3.5%	Median age: 21 years
Lee et al.[120]	2008		✓	HBV	Korean-Americans attending church	Adult, literate Korean-Americans (18 to 70 years old) willing to sign informed consent	609	46%	Korean-American: 100%, 98% of adults born in Korea	Mean age: 49 years
Lin et al.[123]	2007		✓	HBV	Asian Americans	Adults (at least 18 years old) willing to sign informed consent	3,279 tested. 3,163 included	39.7%	Asian Americans: 100%, 93.4% born in Asia	Median age: 52.9 years

Citation	Year	KQ4	KQ5	Virus(es)	Participant Selection	Selection Criteria	Number of Participants	Percent Male	Race (as reported in study)	Age
Tabibian et al.[121]	2008	✓	✓	HBV	Voluntarily admitted veteran psychiatric inpatients	Consecutive voluntary admissions with consent	234 admissions, with 129 participants	98%	Caucasian: 50.3%, African-American: 33.3%, Hispanic: 9.3%, Other, including Asian and Native American: 7%	Mean age: 48.9 years (SD: 8.9 years)
Turner et al.[127]	1989	✓	✓	HBV	Have embalmed more than 20 bodies	Not reported	108	NR	NR	NR

Analysis Methods

We extracted all data on the identification of risk factors from the included literature, including factors that were investigated but not found to be associated with infection. For Question 3 these data are presented in Table 33 (HBV), Table 34 (HCV), and Table 35 (HIV). For Question 4 these data are shown in Table 39 (HBV), Table 40 (HCV), and Table 41 (HIV). We grouped the extracted data by category as listed in the 1994 CDC document *Guidelines for Preventing Transmission of Human Immunodeficiency Virus Through Transplantation of Human Tissue and Organs*[100], and qualitatively summarized the evidence for each of the risk factors listed in the guideline by describing which studies identified associations for which infection in which population type. Following that, in the same manner we summarized the evidence for additional risk factors not listed in the 1994 guideline. Information on behavioral risk factors is presented first (Question 3), followed by information on nonbehavioral factors (Question 4).

We performed the analysis qualitatively (i.e., using narrative descriptive analysis) because the methodologic and reporting differences among the studies made combining them in quantitative analysis (i.e., meta-analysis) inappropriate. These fundamental between-study differences fell into four main categories:

1. Population: We included data from organ, tissue and blood donors, as well as from general populations drawn from various settings, and, for HBV, various special subpopulations
2. Outcomes: Potential risk factors were often reported in different ways. For instance, studies used different numbers to define "multiple" sex partners or gathered data regarding different time spans (i.e., lifetime drug use, drug use within past 6 months).
3. Comparators: Some studies used different bases of comparison. For instance, in assessing whether MSM is a risk factor, one study compared the prevalence of infection in MSM to heterosexual men, and another compared it to the prevalence of infection among men who have never had sex.
4. Analysis type: Although use of various metrics can be dealt with in secondary quantitative analysis, most of these studies differed with respect to whether univariate or multivariate analyses were used. Some reported one but not the other. Data reporting methods did not provide sufficient information to make standardization possible. Not having information on both clouds the independence of the relationship between the factor of interest and the infection in question, especially since data from various populations were considered. For more information on this, please see the following text.

We considered data calculated in two main ways, through univariate analyses and multivariate analysis. Univariate analyses look at the association between the factor of interest and infection. These may be the only type of analysis performed in a study, or it may be the first step in identifying which potentially important factors should be included in the multivariate model. Multivariate models look at the association between the factor of interest and infection while taking into consideration additional confounding factors. This is the type of analysis required to determine if the risk factor is an *independent* risk factor. This is important because many of the behavioral risk factors are found together in individuals. For instance, among individuals who have been incarcerated, is exposure during incarceration itself or the illicit activity that led to incarceration (e.g., sex work, drug use) that is the true risk factor?

Demographic and socioeconomic factors are not risk factors in and of themselves but proxies for other risk factors. On the other hand, dependent factors identified by univariate analyses may be useful for identifying at-risk potential donors. To provide as much information as possible about these factors, we extracted information on *both* univariate and multivariate analyses where both were provided. Where ECRI Institute calculated effect sizes and p-values, unadjusted univariate analyses were performed by necessity because that is what the reported data permits.

Assessment of Risk of Bias (Quality of Study Design): Identification of Risk Factors

To assess the risk of bias of the included studies, we asked the questions listed in Table 30. (Itemized quality assessment for each study for both questions is provided in Table 31.) Following Table 30 we provide a discussion of each of the quality domains assessed.

Table 30. Risk of Bias Assessment Items for Questions 3 and 4: Identification of Risk Factors

Domain	Question Item	Question
Comparability of uninfected and infected participants	Identification (I)-A	Were infected and uninfected participants similar on other risk factors?
	I-B	If not, were statistical adjustments performed to control for other risk factors?
Validity of risk factor data collection	I-C	Was risk factor data collected in a valid manner (e.g., confidential or anonymous collection of sensitive risk factor data, collection of personal information from the person directly instead of someone else)?
Validity of method used to determine infection status	I-D	Was infection status determined accurately? (i.e., accuracy of diagnostic test method used to determine infection status)

Comparability of Uninfected and Infected Participants (Quality Items I-A and I-B)

Regarding item A, none of the studies were uninfected and infected groups of participants similar on all risk factors besides the one being investigated at the time (most studies investigated multiple factors). That is, infected and uninfected participants differed in many ways. Therefore, none of the studies can be considered to satisfy these items. However, many of the studies did perform statistical adjustments to control for confounding factors. Whether controlled or adjusted analyses were performed for each study is reported in the table of study protocols (Table 28), in the data extraction tables, and in the text of the results section.

Although not all studies met items A or B, all of these studies drew all of their participants from a single pool, either selecting them from the pool based upon their infection status or including all participants in the pool and subdividing them by infection status.

Validity of Risk Factor Data Collection (Quality Item I-C)

Much of the data collected for Question 3, regarding behavioral risk factors, is very private and highly sensitive. Much of these data also pertain to illicit activity. Therefore, to promote reliable reporting of risk factor data, confidentiality and anonymity are preferable. Although not all studies went to great pains to ensure privacy (e.g., anonymous questionnaires, interview given through computer interface only), all of the included studies for Question 4 offered confidentiality, at the very least within the context of medical care. In addition, because behavioral risk factors are nearly always personal matters, the most reliable information will come from the individual about him or herself.

Although objective record and database reviews are generally regarded as being more reliable than patient interview, most types of information of interest, especially behavioral risk factors, are unlikely to be catalogued in such records. The applicability of these interview and questionnaire self-report data to potential solid organ donors is unclear, since most solid organ donors are deceased.

Data on deceased actual organ donors in Gasink et al. were collected from a registry and record review, but most of the items inquired about were not highly sensitive, and this is unlikely to compromise the integrity of their findings. However, sensitive data for Sanchez et al. was collected from next of kin of deceased potential tissue donors. Findings from Sanchez et al. suggest that next-of-kin may be unaware of (or unwilling to report) important factors including high-risk sexual activities, or history of sexually transmitted infection (STI). Although the data in Sanchez et al. were not verified against objective records, it is unlikely that the prevalence of these items was actually zero, as the next-of-kin reported. The next-of-kin data in Sanchez et al. may be inaccurate. This was the only study that did not satisfy quality item c.

Although not all studies that only addressed Question 4 appear to have explicitly offered confidentiality, most of these studies investigated factors that are less sensitive (e.g., country of birth, race, age) and so it is unlikely that the validity of the findings will be affected, and this should not be considered a threat to the validity of Question 4.

Validity of Infection Status Determination (Quality Item I-D)

In accord with the general inclusion criteria for this review, the infection status of all participants had to be determined using objective laboratory testing methods. The validity of infection status determination therefore is based upon the accuracy of diagnostic test used (see Table 28 for which test(s) were used in each study; nearly all studies reported it). Most studies confirmed antibody or antigen tests with more specific methods such as Western blot, nucleic acid tests, or immunoblots. These studies should have fewer false positives than studies that did not confirm positives. On the whole, the validity of infection status determination is good. Studies nearly universally used reputable commercially-available diagnostic tests. No studies relied upon rapid or oral tests or home brew (i.e., noncommercial, unregulated) tests alone. Only one study, Nguyen et al., used a test with potentially compromised accuracy. In this study, participants were given a kit to take home and test themselves with. Although the test may be accurate with appropriate use, because the test was not administered under supervision and were not verified with follow-up testing, it is not possible to be as confident in the results.

Itemized quality assessment for each of the studies is shown in Table 31, below.

Table 31. Quality Assessment for Questions 3 and 4: Identification of Risk Factors

Study	Year	Question 3				Question 4			
		I-A	I-B	I-C	I-D	I-A	I-B	I-C	I-D
Potential and Actual Organ Donors									
Gasink et al.[102]	2006			✓	✓				✓
Hidalgo et al.[8]	2001			✓	✓	Not applicable			
Potential Tissue Donors									
Sanchez et al.[103]	2006				✓				✓
Blood Donors									
Conry-Cantilena et al.[106]	1996		✓	✓	✓		✓	✓	✓
Murphy et al.[105]	2000		✓	✓	✓		✓	✓	✓
Murphy et al.[107]	2000	Not applicable					✓	✓	✓
Orton et al.[104]	2004		✓	✓	✓		✓	✓	✓
General Population									
Alpert et al.[115]	1996		✓	✓	✓		✓	✓	✓
Alter et al.[117]	1989		✓	✓	✓		✓	✓	✓
Armstrong et al.[30]	2006		✓	✓	✓		✓	✓	✓
Fischer et al.[114]	2000		✓	✓	✓		✓	✓	✓
Hand and Vasquez[112]	2005		✓	✓	✓		✓	✓	✓
Kaur et al.[116]	1996		✓	✓	✓		✓	✓	✓
McGinn et al.[108]	2008	Not applicable						✓	✓
McQuillan et al.[101]	2006			✓	✓			✓	✓
McQuillan et al.[29]	1999		✓	✓	✓		✓	✓	✓
Mehta et al.[109]	2008			✓	✓			✓	✓
Nguyen et al.[110]	2008			✓	✓			✓	✓
Nguyen et al.[113]	2005		✓	✓			✓	✓	
Zetola et al.[111]	2008	Not applicable					✓	✓	✓
Children and Adolescents									
Luban et al.[118]	2007	Not applicable						✓	✓
D'Angelo et al.[119]	1991	Not applicable						✓	✓

Study	Year	Question 3				Question 4			
		I-A	I-B	I-C	I-D	I-A	I-B	I-C	I-D
Demographic and Socioeconomic Subpopulations (HBV only)									
Butterfield et al.[125]	2004		✓	✓	✓		✓	✓	✓
Butterfield et al.[126]	1990			✓	✓			✓	✓
Hann et al.[122]	2007	Not applicable						✓	✓
Hwang et al.[124]	2006		✓	✓	✓		✓	✓	✓
Lee et al.[120]	2008	Not applicable						✓	✓
Lin et al.[123]	2007	Not applicable					✓	✓	✓
Tabibian et al.[121]	2008		✓	✓	✓		✓	✓	✓
Turner et al.[127]	1989		✓	✓	✓		✓	✓	✓

A checkmark (✓) means that the study met the quality criterion for this Question; the lack of a checkmark means that the study either did not meet the criterion, or it was unclear whether the study met the criterion. The criteria specific to this Question were:

3/4 I-A. Was the population potential solid organ donors?

3/4 I-B. For other populations, was the population unselected (i.e., not based on demographic or behavioral characteristics)? Were infected and uninfected participants similar on other risk factors?

3/4 I-C. If not, were statistical adjustments performed to control for other risk factors?

3/4 I-D. Was risk factor data collected in a valid manner (e.g., confidential or anonymous collection of sensitive risk factor data, collection of personal information from the person directly instead of someone else)

3/4 I-E. Was infection status determined accurately? (i.e., accuracy of diagnostic test method used to determine infection status)

Assessment of Risk of Bias (Quality of Study Design): Prevalence of Risk Factors

To assess the risk of bias of the included studies, we used the same quality assessment instrument as was used in Question 1. One modification was made for the third item. Rather than ask about the accuracy of determining infection status, we ask about the accuracy of determining the prevalence of the risk factor. Specifically, highly personal information should be reported by the person in question. Ideally, medical history (e.g., history of STD) would be collected using objective data, but we considered subject self-report acceptable as well. Studies meeting 2 or 3 criteria were not penalized for quality in the GRADE system. Studies meeting only 0 or 1 criterion were penalized one level.

Table 32. Quality Assessment for Questions 3 and 4: Prevalence of Risk Factors

Study	Year	Question 3			Question 4		
		P*-A	P-B	P-C	P-A	P-B	P-C
Potential Organ Donors							
Hidalgo et al.[8]	2001	✓	✓	✓	Not applicable		
Actual Organ Donors							
Gasink et al.[102]	2006	-	-	✓	Not applicable		
General Population							
Armstrong et al.[30]	2006	-	✓	✓	-	✓	✓
Kaur et al.[116]	1996	-	✓	✓	-	✓	✓
McQuillan et al.[101]	2006	-	✓	✓	Not Applicable		
Mehta et al.[109]	2008	-	✓	✓	-	✓	✓
Nguyen et al.[110]	2008	-	✓	✓	-	✓	✓

*P: Prevalence

A checkmark (✓) means that the study met the quality criterion for this Question; the lack of a checkmark means that the study either did not meet the criterion, or it was unclear whether the study met the criterion. The criteria specific to this Question were:

3/4 P-A. Was the population potential solid organ donors?

3/4 P-B. For other populations, was the population unselected (i.e., not based on demographic or behavioral characteristics)? (studies of potential solid organ donors were scored as Yes, because they enrolled the population of interest)

3/4 P-C. Was risk factor prevalence determined accurately? (i.e., were personal factors reported by subject themselves?)

GRADE Assessment of Identification of Risk Factors

To assess the strength of the evidence regarding the identification of risk factors, we applied a GRADE system modified for this purpose. We assigned GRADE ratings for evidence bases comprised of at least two studies addressing a certain factor, divided by virus. The steps used to assign a rating are described in this section. The GRADE table for Question 4 is Table 36, and the table for Question 5 is Table 42, which appear following the results sections.

Because all of these studies are observational, they were all assigned a starting grade of "Low," per convention. The following factors could be used to decrease this grade: Overall quality, consistency, directness, and precision. Large magnitude of effect could be used to increase one grade. Criteria for these are provided in the following text. If a direct relationship between infection and the factor was suggested (e.g., higher number of sex partners associated with higher odds of infection), the GRADE was increased by one. Explanation of all plausible confounders could also increase the GRADE. These steps are described in the following subsections. We did not assess publication bias.

Overall Risk of Bias

Overall quality was determined in two steps. First, each study was assessed for risk of bias, as shown in Table 31. Then, the overall risk of bias of the evidence base was determined using the median number of quality items. Evidence bases with a median of 3 or 4 criteria were considered "moderate," those with a median of 2 criteria were considered "low," and those with only 1 criterion were considered "very low." Evidence bases with a "very low" quality rating were decreased by one grade.

Consistency

Consistency was determined based upon how well the qualitative findings of the studies agreed with each other. If studies were consistent with the exception of a special population study or a very low-quality study; or if all studies (two or more) had large magnitudes of effect (OR>5) with the exception of one study, the evidence base was still considered consistent because these studies are least reliable. Other inconsistency that was easily explained for a single reason (with no other possible explanation) would not be downgraded. Evidence bases with only one study were downgraded due to lack of demonstrated consistency, because scientific replication is an important component of evidence.

Directness

Only one study[8] examined potential organ donors, and this was a very small study of living relative donors, who comprise the minority of potential donors. One study on actual heart donors that did not exclude donors with HCV was included.[102] Although a large number of donors were examined in this study, it is not possible to determine how highly selected they were (i.e., how many potential donors were excluded and for what reasons) because these data are not reported.

Most of the remaining studies studied potential tissue donors, actual blood donors, or members of the general population. These studies were not downgraded due to indirectness, despite the fact that they did not enroll potential organ donors. This is because the identification of a risk factor in these populations may be generalizable to potential organ donors. By contrast, studies of demographic and socioeconomic subpopulations are probably not very representative of potential organ donors. Some of the populations have high prevalence of multiple high-risk behaviors and a relatively high prevalence of

HBV (e.g., psychiatric inpatient veterans with co-morbid substance abuse problems), while others had few high-risk behaviors and a relatively low prevalence of HBV (e.g., women receiving prenatal care). We therefore downgraded evidence bases that predominately had this type of study (i.e., -1).

Precision

We considered all evidence bases with three or more studies to be precise (and therefore did not downgrade for imprecision). When there were only two studies, we considered the factor precise if one of two criteria were met. We considered the evidence base precise if both effects were statistically significant. If this criterion was not met, we evaluated the evidence base for precision by combining the two studies' data in a summary effect size and evaluating the confidence intervals around the point estimate. We considered the evidence base precise if the confidence intervals were sufficiently narrow, defined as a maximum difference of 0.4 between the estimated log odds ratio and the upper bound of its 95% confidence interval. For example, if the summary effect size was 1.1 with a 95% CI from 0.86 to 1.4, this was deemed sufficiently precise (because ln(1.4)-ln(1.1) is less than 0.4), whereas if the summary effect size was 1.1 with a 95% CI from 0.6 to 2.0, this was considered imprecise (because ln(2)-ln(1.1) is greater than 0.4, and the evidence is consistent with important effects in either direction). When there was only a single study, we considered the evidence base precise if either the effect was statistically significant, or if the confidence interval around the effect size was sufficiently narrow (defined in the same way as with two studies).

Large Magnitude of Effect

We upgraded the rating for any evidence base in which the studies consistently showed a large magnitude of effect. We defined this as any statistically significant odds ratio with a point estimate of 2.0 or higher. We did not require that the confidence intervals around the effect size point estimate be fully above 2.0.

Dose-Response Association

Evidence of a dose-response association is suggested if increasing levels of the factor corresponded to increasing risk of infection. Although studies could have measured such outcomes using continuous reporting (e.g., total number of lifetime sex partners), in this evidence base studies measured a risk factor on a categorical basis. For example, Nguyen et al. (2005)[113] examined the risk factor of number of lifetime sex partners by placing each respondent into one of five categories: 0, 1, 2-9, 10-49, or 50+. If the risk of infection increased along with the number of sex partners, we considered this a dose-response association. We upgraded some evidence bases +1 where the dose-response association was clear multiple studies.

Significant Association Found Despite Confounders

If the studies in an evidence base found a factor to have a statistically significant relationship with infection despite the fact that the evidence base was clearly biased against finding such a relationship, we upgraded +1 GRADE Assessment of Prevalence of Risk Factors

GRADE Assessment of Prevalence of Risk Factors

To assess the prevalence of behavioral and nonbehavioral risk factors, we used the system described in Question 1.

Question 3: Results

The results on identification of risk factors are presented in this section. Information pertinent to the exclusionary factors listed in the 1994 guideline is presented first, and then information regarding additional factors is presented. Text was prepared for all factors that were reported by at least two studies. All of the data used to produce this section is provided in Table 33 (HBV), Table 34 (HCV), Table 35 (HIV), and Table 37 (prevalence of factors), which follow the text.

Exclusionary Behavioral Criteria from 1994 Guideline

The following sections present all data identified as relevant to the exclusion criteria from the 1994 guideline. Specifically, we did not restrict the information provided to original timeframes (e.g., engaged in a particular behavior "*within 5 preceding years*," "*currently"* incarcerated.). We also included additional very relevant information in these sections, such as sex partners not identified in the original guideline.

Men Who Have Sex with Men

The 1994 guideline excludes from donating "Men who have had sex with another man in the preceding 5 years." We identified zero studies that inquired whether men engaged in sex with other men (MSM) in this particular time frame. However, several studies addressed lifetime history of having sex with other men. Briefly, two studies found associations with HBV, two did not find associations with HCV, and two studies found an association with HIV.

HBV: In a sample of men aged 17 to 59 years drawn from the general population, McQuillan et al. compared the prevalence of HBV among men who reported having sex with other men to those who did not and found a significantly increased prevalence of HBV among MSM.[29] Hwang et al. compared HBV infection rates among MSM compared to men who have never had sex in a population of college students and found that the rate of HBV was higher among MSM in both univariate and multivariate analyses.[124]

HCV: Murphy et al. (2000) compared HCV prevalence between homosexual or bisexual men to men who had never had sex among blood donors and did not find an increased prevalence when the comparison was controlled for intravenous drug use (IDU). However, the unadjusted risk was elevated.[105] Hand and Vasquez compared the rates of HCV among MSM and non-MSM among adults tested for HCV because of clinical suspicion and did not find a significant difference in a univariate analysis.[112]

HIV: McQuillan et al. reported the prevalence of HIV among MSM to non-MSM in a sample drawn from the general population (using NHANES data), and the unadjusted rate shows MSM have a significantly higher prevalence of HIV.[101]Using New York City (NYC) HANES data from a later year, Nguyen et al.[110] also found a significantly higher rate of HIV among MSM in a univariate analysis.

GRADE Summary: The evidence associating MSM with HBV and HIV was moderate. For both the evidence bases consistently found an association, and the magnitude of the effect was large. However, the strength of evidence associating MSM with HCV infection in blood donor and general populations studies was very low due to inconsistent findings. Neither pertinent study found MSM to be an independent risk factor for HCV (although MSM may be an important proxy factor; the evidence is insufficient to tell).

Prevalence: Reported prevalence of MSM in the included studies were 3.7%[101] and 9.3%.[110]

GRADE Summary of Prevalence: The evidence for the prevalence data was rated as low due to indirectness and inconsistency.

Injection Drug Users

The 1994 guideline excludes from donating "Persons who report nonmedical intravenous, intramuscular, or subcutaneous injection of drugs in the preceding 5 years." We identified zero studies that investigated the risk of injection drug use (IDU) within this time frame. Most identified studies associated lifetime IDU with infection, and one considered the association with IDU greater or less than 6 months before the blood draw. Some studies reported IDU, and others reported intravenous drug use (IVU). In general, studies did not report both or distinguish between the two. Briefly, IDU/IVU was associated with HBV by three studies but not in a fourth (the fourth study being a smaller study of a special obstetric population), HCV in seven studies, and HIV in two of three studies.

HBV: Kaur et al. associated IDU with HBV in a multivariate analysis of volunteers from the general population.[116] Tabibian et al.[121] and Butterfield et al. (2004)[125] identified an increased risk of HBV among IVU veterans in inpatient psychiatric hospitals, and Hwang et al. identified an increased risk of HBV among IDU college students.[124] Butterfield et al. (1990)[126] did not find an elevated risk in an obstetric population. However, it appears that this is probably due to the low prevalence of HBV and IDU in this population. Only one individual in the population reported IDU, and she was HBV negative. Rather than contradict the association between IDU and HBV, the study was probably underpowered to detect an association given the low prevalence of both in this special low-risk subpopulation.

HCV: Among blood donors, Orton et al.[104] and Murphy et al.[105] detected an association between IDU and HCV, and Conry-Cantilena et al.[106] detected an association between IVU and HCV. Orton et al., use within the last six months only was associated with infection.[104] Among people in a study group drawn from the general population, an increased prevalence of HCV was associated with IDU in Armstrong et al.,[30] Fischer et al.,[114] and Hand and Vasquez,[112] and with IVU in Kaur et al.[116]

HIV: McQuillan et al.[101] studied IDU and the national general population, and Nguyen et al.[110] assessed ever having used a needle for drugs, and in univariate analyses both found an increased rate of HIV. Mehta et al.[109] did not find an association between IDU and HIV among hospital patients; the reason for this is unclear.

Two studies specifically investigated the association between infection and injection steroid use, and neither found any association. Hwang et al. did not detect an increased risk of HBV among college students who injected steroids,[124] and Orton et al. did not find an increased risk of HCV among blood donors.[104] However, the Orton study did find a trend toward higher infection rate among blood donors who had injected steroids longer than six months ago ($P = 0.07$), and a larger study might detect an association.

GRADE Summary: The strength of the evidence associating IDU with HCV was "moderate" due to the consistently large effect sizes found in all studies that associated this factor (with the exception of one small study on steroid use only that did not find an association with infection). For HBV, the evidence was "low." All but one special population study found an association, but not all of the studies found a

large magnitude of effect (not including the findings of one study that injection steroid use was not associated with HBV). For HIV, the evidence was "low."

Prevalence: Prevalence of injection drug use reported in the general population studies were 1.4%,[110] 1.7%,[30] 3.5%,[116] and 7.9%.[109] Of the IDUs in one of those studies, 63.2% reported that they did not use a needle exchange program.[109]

GRADE Summary of Prevalence: The prevalence data for injection drug abuse was rated as low due to inconsistency and indirectness.

Related Factors: In addition, reporting living with an IDU was associated with HCV among blood donors, even when IDU was controlled for,[105] as was living with an IDU in the last six months.[104] Alter et al. grouped household and sexual contact with an IDU during the last six months and found it was associated with recent HBV infection in a univariate, but not multivariate, analysis.[117] Among the general population, both being at a social gathering with injection drugs and witnessing the use of injection drugs were associated with HCV.[113] See the section *High Risk Sex Partners* for information on infection risk among people who have sex with IDUs.

We also identified information on other types of substance abuse. For information, under *Risk Factors Identified in the Literature as of 2009* see "Non-injection substance use and abuse."

Sex Work

The 1994 guideline excludes from donating "Men and women who have engaged in sex in exchange for money or drugs in the preceding 5 years." We did not find any literature that studied the association between this factor and the given time frame, but we did find literature that studied lifetime sex work and infection risk. Briefly, sex work was not associated with HBV in three studies (one was the next-of-kin tissue donor interview study, the other two enrolled special subpopulations of psychiatric inpatient veterans) or with HIV in one study (the next-of-kin interview study) but was associated with HCV in three studies.

HBV: In their study of tissues donors, Sanchez et al. did not find any association between sex work and infection with HBV upon univariate analysis. However, their data came from next-of-kin interviews, and none of the relatives of infected potential donors reported sex work.[103] Among psychiatric inpatient veterans, Tabibian et al.[121] did not detect an association between "sex bartering" in a multivariate analysis. In that population rates of sex bartering were high among both HBV negative (30%) and HBV positive (37%) participants. Unprotected sex for drugs was not associated with HBV infection upon multivariate analysis in the other study that enrolled psychiatric inpatient veterans, Butterfield et al. (2004).[125]

HCV: Sanchez et al. did not find any association between sex work and infection with HBV among tissue donors, with sex work as reported by next of kin.[103] Sex work was associated with HCV among blood donors in Murphy et al. in a multivariate analysis[105] and in general populations studies by Hand and Vasquez[112] and Nguyen et al. in univariate analyses.[113] (In Hand and Vasquez, all women who reported sex work also reported IDU.)

HIV: In the study of tissues donors, Sanchez et al. did not find any association between sex work and infection with HIV.[103]

GRADE Summary: The evidence relating sex work and HBV and HIV infection was rated as very low. For HBV this was due to indirectness; the data were from primarily special populations. For HIV, this was due to having only one study of very low quality. In the HBV and HIV studies, no relationship was detected. For HCV, the evidence was rated as low. Three studies found associations. A fourth study did not, but we did not downgrade the evidence due to inconsistency because it was of very poor quality.

Prevalence: One study reported the prevalence of exchanging sex for drugs or money among patients in an urban medical care center at 2.3%.[109]

GRADE Summary of Prevalence: The prevalence of sex work was rated as low due to indirectness and lack of proof of consistency.

High-Risk Sex Partners

The 1994 guideline excludes from donating "Persons who have had sex in the preceding 12 months with any person described in items 1–4 above [refers to MSM, IDU, sex workers, and people with clotting disorders, who are covered in Question 4] or with a person known or suspected to have HIV infection." We did not identify any literature on infection risk in people with high-risk sex partners during this time frame, but we did identify literature on infection risk associated with having high-risk sex partners at some point in life. As the scope of this evidence report encompasses HBV and HCV in addition to HIV, we have also included data on infection risk among people having sex with a person with known or suspected hepatitis. Briefly, having a high-risk or infected sex partner was associated with HBV in six of seven studies (the seventh being a special subpopulation study of psychiatric inpatient veterans), with HCV in ten studies, and with HIV in one study.

Sex with IDU

HBV: Sex with an IDU was associated with HBV in general population groups (including when use of IDU was controlled for) by Kaur et al.[116] and in univariate analyses among college students by Hwang et al.,[124] but not among psychiatric inpatient veterans in Tabibian et al.[121] Sex *or* household contact with an IDU was associated with HBV infection in Alter et al.[117] upon univariate investigation, but not when use of IDU was controlled for.

HCV: Sex with an IDU or IVU was found to be associated with HCV in blood donors by Murphy et al. (2000)[105] in univariate analysis and Orton et al.,[104] in multivariate analysis, and in the general population by Nguyen et al.[113] in univariate analysis and Kaur et al.[116] in multivariate analysis. In Orton et al. the time frame was limited to the six months prior to donation.

GRADE Summary: The evidence associating HBV infection with having a sex partner who uses injection drugs was rated as very low due to inconsistent findings. For HCV, the evidence was moderate due to the consistent findings of association with large magnitude of effect.

Prevalence: In one study, 5% of respondents reported having sex with an IDU.[116]

GRADE Summary of Prevalence: The evidence of prevalence of having an IDU sex partner was low due to indirectness and lack of proof of consistency.

Sex with a Sex Worker

HBV: Sex with a sex worker was not associated with HBV among psychiatric inpatient veterans in a univariate analysis in Tabibian et al.[121]

HCV: Sex with a sex worker was associated with HCV among blood donors in a multivariate analysis in Murphy et al.[105] and in univariate analyses of general population studies by Ngyuen et al.[113] and Hand and Vasquez.[112] However, in Hand and Vasquez the relationship was no longer significant in the multivariate analysis.

GRADE Summary: A single special population study did not associate HBV with sex with a sex worker, but this evidence is rated as "very low" due to indirectness and lack of proof of consistency of evidence. Three studies associated having sex with a sex worker with HCV in univariate analyses. This evidence was rated as "very low."

Prevalence: In one study, 7.4% of respondents indicated they had had sex with a sex worker.[109]

GRADE Summary of Prevalence: The estimate of prevalence of having sex with a sex worker was graded as low due to indirectness and lack of proof of consistency.

Sex with People Known to Have Infection

HBV: Sex with a partner with hepatitis was found to be a risk factor for HBV in college students in Hwang et al.,[124] but not in an obstetric population in Butterfield et al. (1990).[126] Both of these analyses were univariate.

HCV: Among blood donors, sex with someone with hepatitis at any point in life in Murphy et al. (2000)[105] in a multivariate analysis, or during the last six months in Orton et al.[104]in a univariate analysis, was associated with HCV.

HIV: Having sex with someone known to have HIV was associated with having HIV by Mehta et al. in a group of patients from a general population using univariate analysis.[109]

GRADE Summary: The evidence associating HBV and having a sex partner with a known infection was rated as very low due to low quality, inconsistency, and indirectness. The evidence associating the factor with HIV was also rated as low, for having no proof of consistency but a large effect size magnitude. For HCV the evidence was rated as low for consistently identifying sex with people known to have infection as a risk factor for HCV.

Prevalence: On study stated that 3.6% of participants reported having sex with someone known to be infected with HIV.[109]

GRADE Summary of Prevalence: The estimate of prevalence of having sex with someone known to be HIV-positive was graded as low due to indirectness and lack of proof of consistency.

Other High-Risk Sex Partners

Some miscellaneous types of high-risk sex partners pertinent to high-risk sex partners not mentioned in the original guideline were also reported. Sexual promiscuity (defined as history of STD, sex with a sex worker, or at least five sex partners per year) was associated with HCV infection in blood donors in Conry-Cantilena et al.[106] Alter et al. did not associate HBV infection with sex with a blood transfusion recipient, with a health care worker, or a person with a foreign birth in an endemic area.[117] Sex with a transfusion recipient was associated with HCV in blood donors in Murphy et al.[105] We report these other high-risk sex partners here because they are germane to the larger issue of having high-risk sex partners. However, we did not grade this evidence because these factors were reported by one study only.

Inmates

The 1994 guideline excludes from donating "Inmates of correctional systems. (This exclusion is to address issues such as difficulties with informed consent and increased prevalence of HIV in this population.)" No studies that examined the association between present incarceration and infection were identified. However, the searches did identify studies that examined the association between recent or lifetime history of incarceration. In brief, a history of incarceration was associated with HBV in three of four studies, with HCV in four of five studies, and was not associated with HIV in one study. The study that did not detect an association of incarceration and HBV, HCV, or HIV infection was Sanchez et al., the tissue donor study based upon information provided by next of kin.

HBV: A history of incarceration as reported by next-of-kin was not associated with HBV in potential tissue donors in Sanchez et al.[103] In general population studies, imprisonment within the last six months was associated with recent HBV infection in a univariate analysis, but not a multivariate analysis in Alter et al.[117] Incarceration was also associated with HBV upon univariate analysis among psychiatric inpatient veterans in Tabibian et al.[121] and among college students incarcerated for at least 24 hours in Hwang et al.[124]

HCV: A history of incarceration as reported by next-of-kin was not associated with HCV infection in potential tissue donors in Sanchez et al.[103] Incarceration was associated with HCV in three studies of blood donors, Orton et al.,[104] Murphy et al. (2000),[105], and Conry-Cantilena et al.[106] Two of those studies also tested whether incarceration was an independent risk factor; in both of those studies incarceration was associated with IDU. Murphy et al. (2000) found that incarceration for more than three days was an independent risk factor (although, compared with the unadjusted odds, odds were not as large once IDU was controlled for in the multivariate model),[105] while Conry-Cantilena et al. found that, once adjusted for IDU, it was not.[106] In addition, having been arrested was associated with HCV infection in a general population sample by Nguyen et al.[113]

HIV: A history of incarceration as reported by next-of-kin was not associated with HIV infection in potential tissue donors in Sanchez et al.[103]

GRADE Summary: Aside from one very low-quality study, a history of incarceration was consistently associated with HCV, and rated as low in strength overall. The association with HBV was inconsistent due to conflicting findings, and the association with HIV is unclear because only one very low-quality study addressed this outcome. The ratings for HBV and HIV were therefore both very low.

Risk Factors in Children

We identified no literature on any behavioral risk factors in children, or on the risk of infection from mothers who engage in those risk behaviors. While vertical transmission is generally recognized as a mode of hepatitis or HIV transmission, this body of literature lacks the evidence to assess the 1994 criteria as risk factors. This may be because of the relative infrequency of this mode of transmission, and because of the lack of data on children. For instance, although they used NHANES data from the general nationwide population, Armstrong et al. reported identifying only three people under the age of 20 years that were infected with HCV, which precluded the investigation of risk factors in children and adolescents in their study.[30] In the literature base analyzed in this report, only one individual, a 17-year-old first-time blood donor with HCV RNA but not anti-HCV, had perinatal exposure as a possible mode of transmission.[104] Her mother had an HCV infection during her pregnancy, and no other likely causes exposure were identified.

Additional Potential Risk Factors Identified in the 2009 Literature Search

In addition to the factors identified in the 1994 guideline, we extracted data on all other reported behavioral risk factors identified in the literature and describe the findings regarding factors reported by at least two studies.

Other Sex Practices

Multiple Partners

Having multiple partners, including heterosexual partners, was associated with increased risk of infection across different populations. In brief, various measures of having multiple partners were associated with HBV in five studies, with HCV in six studies, and with HIV in one of three studies.

HBV: HBV infection was associated with sex with multiple partners in general populations in Kaur et al.[116] in multivariate analysis. In multivariate analyses, multiple partners within the last six months was associated with recent HBV infection in a general population in Alter et al.[117] and among psychiatric inpatient veterans in Butterfield et at. (2004).[125] In a sample of people representative of the general population, compared to individuals with zero or one lifetime sex partners, having at least two lifetime sex partners was associated with HBV in McQuillan et al. in a multivariate analysis, and the odds of infection increased with greater numbers of partners.[29] Among college students in the study by Hwang et al., both having at least 50 lifetime heterosexual partners and having at least 5 heterosexual partners in the preceding four months were associated with HBV infection in univariate analyses.[124]

HCV: HCV infection in women blood donors was associated with having at least 11 male sexual partners (compared to having zero sexual partners) in Murphy et al. (2000)[105] in multivariate analysis. Having the same number of lifetime female partners among men was not associated with HCV in the same study. Having two or more sexual partners, whether same sex or not, in the last six months was associated with an increased rate of HCV infection overall in Orton et al.[104] in a univariate analysis. In general population univariate analyses, HCV was also associated with having "frequent" sex partners in Fischer et al.,[114] "multiple" sex partners in Kaur et al.,[116] and at least 20 sexual partners in Armstrong et al.[30] Greater numbers of sex partners was also associated with HCV infection in Nguyen et al.[113] Hand and Vasquez noted the strong association between greater numbers of sex partners and IDU in their study. Of the 18.5% of their patients who reported having at least 10 sex partners in their sample, 84% also reported IDU.[112]

HIV: In the general population, having multiple sex partners in the past year was not associated with HIV in Nguyen et al.,[110] nor was having at least 10 lifetime sex partners in Mehta et al.[109], but having 50 or more lifetime sex partners was associated with HIV in McQuillan et al.[101] All of these analyses were univariate.

GRADE Summary: Studies used different thresholds to define "multiple sex partners," (ranging from as few as 2 to as many as 50 or more) so identifying the minimum number of partners associated with an increased risk of infection is not possible based upon this evidence base. However, using their various definition, HBV and HCV studies did (with the exception of heterosexual men in one HCV study) consistently associate infection with having multiple sex partners. For HBV and HCV, the strength of this association was moderate due to a positive "dose" response association. For HIV there was also a dose-response relationship in two studies (one study found a relationship with having at least 50 partners, the other did not find a relationship with having at least 10 partners). The third study did not find a relationship with having "multiple" sex partners in the past year. The evidence was rated as low for having a dose-response relationship but inconsistent findings.

Prevalence: In a national general population, 29% of survey respondents indicated having had at least 10 sex partners,[30] and 3.5% reported having at least 50 sex partners.[101] Among New Yorkers, 6.6% reported at least 50 sex partners.[110] 22% of New Yorkers reported having sex with multiple partners during the previous year,[110] and 26% of volunteers from an urban area reported sex with multiple partners.[116]

GRADE Summary of Prevalence: Prevalence estimates of having "multiple" sex partners (number undefined) and having at least 2 sex partners (but not more than 49 in one study) were both rated as moderate due to indirectness. The prevalence of having at least 50 partners was rated as low due to indirectness and lack of consistency.

Same-Sex Partners, Not Restricted to Men

Three studies investigated having same sex partners but did not restrict the analysis to MSM. Two associated this factor with HCV, and the other associated it with HIV.

HCV: Having same-sex partners among women was associated with an increased risk of HCV among women blood donors in Murphy et al. (2000)[105] in multivariate analysis. For women who had had only one same-sex partner, this risk was no longer significant when adjusted for IDU, but it remained significant if there were two or more same-sex partners. Among outpatients, Nguyen did not find any association between having sex with a person of the same sex and HCV infection.[113]

HIV: Mehta et al. detected a univariate association between having a same-sex partner and HIV, including both men and women in the sample.[109]

GRADE Summary: The evidence for HCV was rated as very low due to inconsistency and imprecision. The evidence for HIV was rated as low because the single study had large magnitude of effect but could provide no proof of consistency for the evidence base.

Prevalence: One study asked both men and women if they had same-sex sex partners, and 8.2% reported that they did.[109]

GRADE Summary of Prevalence: This evidence was rated as low due to indirectness and lack of proof of consistency.

Age at First Sexual Intercourse

Younger age at the time of first sexual experience was also associated with infection among adults in univariate analyses. One study associated it with HBV, two associated it with HCV, and one associated it with HIV.

HBV: Age of 18 years or younger was not associated with HBV in McQuillan et al. (1990) in a multivariate analysis.[29] Age at first intercourse of 15 years or younger was associated with HBV infection among college students in Hwang et al. in a univariate analysis.[124]

HCV: In the general population, age of 17 years or younger was associated with HCV in Armstrong et al. in a univariate analysis. The study stratified age at first intercourse by age younger than 11, age 12-15, and age 16-17 years. The groups of people who were younger at the time of their first sexual intercourse had the highest risk of HCV.[30]

HIV: Age of 18 years or younger was associated with HIV in McQuillan et al. (2006) in a univariate analysis. The size of this effect was large.[101]

GRADE Summary: For HBV, one study associated HBV with age at first intercourse 15 or younger, and another did not find a relationship with age at first intercourse 18 or younger. This evidence was rated as low because, although the findings were not necessarily consistent, they do suggest a 'dose-dependent' relationship between younger age at first intercourse and increased risk of HBV. For HCV, one study found that younger age was associated with infection in a dose-dependent relationship, and the evidence rating for it was 'low.' For HIV, age younger than 18 was associated with increased risk of infection, and the evidence for this was rated as 'low' for having a large magnitude of effect despite no proof of consistency.

Prevalence: The proportion of adults who reported having sex at age 18 or younger were 58%[30] and 59%[101] in two studies.

GRADE Summary of Prevalence: This estimate was rated as moderate due to lack of directness to potential organ donors.

Additional Various Associations

We report additional reported associations between sexual practices and infection below because they are relevant to this overall section. However, we did not assign Grade ratings because these factors were reported by so few studies.

- Unprotected sex was associated with HCV infection in a general population by Fischer et al.[114], although not using condoms consistently was not associated with HIV infection in a general population by Mehta et al.[109] or Nguyen et al.[110]
- Anal-insertive sex that occurred at least six weeks ago was associated with HIV infection among men in a general population, and anal-receptive sex at least six weeks ago among women and men in a general population in Mehta et al.[109]

- Having vaginal sex was associated with a reduced risk in HIV compared with people who did not have vaginal sex (but may have been having anal sex) in the general population study by Mehta et al.[109]

Non-injection Substance

Other Illicit Drugs

Of the studies that inquired about the association between non-injection illicit drug use (mostly inhaled drugs, predominantly intranasal cocaine), two of five found an association with HBV and seven of eight found an association with HCV. Two of the studies that did not find an association with HBV both enrolled a special subpopulation (psychiatric inpatient veterans). The other study that did not find an association with either HBV or HCV was the next-of-kin interview study of tissue donors, Sanchez et al.[103]

HBV: Illicit drug use was not associated with HBV in the tissue donor study by Sanchez et al.[103] Ever having used cocaine was associated with HBV in the general population by McQuillan et al.[29] in a multivariate analysis. HBV infection was associated with intranasal drug use among the college students in Hwang et al.[124] However, in Tabibian et al.[121] and Butterfield et al.[125], who enrolled psychiatric inpatient veterans, HBV infection was not associated with inhaled or 'snorted' drugs.

HCV: Any illicit drug use was not associated with HCV in the tissue donor study by Sanchez et al.[103] Intranasal drugs were associated with HCV infection in blood donors in Orton et al.,[104] Conry-Cantilena et al.[106] and Murphy et al.[105], including when adjusted for IDU or other factors in two of those studies (the third study did not perform adjusted analyses.[104] In a general population, use of snorting or inhaling nonprescription drugs,[113] inhaling cocaine,[114] using intranasal cocaine,[112] and use of non-injection drugs other than marijuana[30] were all associated with increased prevalence of HCV. Two of the studies investigated whether this factor was independently associated with HCV, and Armstrong et al. found it was using NHANES data[30] while Hand and Vasquez found it was not based upon a smaller set of data on adults tested for HCV because of clinical suspicion.[112] However, Hand and Vasquez note that cocaine use in the absence of IDU or tattoos was unusual in their sample. Although 39% of patients admitted to intranasal cocaine, only 2% of whom did not have tattoos or IDU used cocaine.

Being at a social gathering with cocaine was associated with HCV in Nguyen et al.[113] Having friends who use "street drugs" was associated with an increased risk of HCV among blood donors Orton et al.[104]

HIV: HIV was associated with ever using cocaine or street drugs in a univariate analysis by McQuillan et al. (2006)[101] and in a multivariate analysis by Alpert et al.[115] among members of the general population.

GRADE Summary: The evidence associating non-injection illicit drug use and HBV was inconsistent and graded as "very low" due to this inconsistency. Aside from one very low-quality study, studies consistently associated non-injection drug use with HCV. The evidence associating HCV with non-injection drugs was rated as low. Two studies associated HIV with non-injection drug use, and this evidence was rated also rated as low.

Prevalence: Among potential living organ donors in one smaller study, 5.5% reported having ongoing drug abuse problems.[8] In the general population, 17% reported lifetime use of drugs other than marijuana,[30] 18% reported ever having used street drugs,[110] and 21% reported using street drugs/cocaine.[101]

GRADE Summary of Prevalence: The estimate of ongoing drug use prevalence in living potential organ donors was rated as low due to imprecision and lack of proof of consistency. The estimates of drug use in the general population were rated as moderate due to indirectness.

Alcohol

The association between alcohol intake and infection was less consistent.

HBV: Alcohol use, as reported by next-of-kin, was not associated with HBV infection among potential tissue donors in a univariate analysis in Sanchez et al.[103] HBV was not associated with alcohol use disorder among psychiatric inpatient veterans in Butterfield et al. in a multivariate analysis (2004).[125]

HCV: HCV was associated with "heavy" alcohol use in heart donors in Gasink et al.[102], and with having at least two units of alcohol per day among adults tested for HCV because of clinical suspicion in Hand and Vasquez.[112] However, HCV was not associated with alcohol use among tissue donors in Sanchez et al.,[103] having at least 5 alcoholic drinks weekly in patients in Nguyen et al.[113] or alcoholism in HMO enrollees in Fischer et al.[114] All of these analyses were univariate.

HIV: HIV was associated with having an alcohol and/or (unspecified) drug problem among HMO enrollees in Fischer et al.[114] (as identified in a claims database), but not with alcohol use among potential tissue donors in Sanchez et al.[103] Both of these analyses were univariate.

GRADE Summary: Alcohol use was not associated with HBV and was inconsistently associated with HCV and HIV. These evidence bases were all rated as "very low" due to inconsistency and/or imprecision.

Prevalence: In a database study of actual organ donors, 20% reportedly drank heavily.[102]

GRADE Summary of Prevalence: The estimate of heavy alcohol abuse was rated as low due to low study quality and lack of proof of consistency. The directness to potential donors is also unclear.

Tobacco

HBV: No association was found between cigarette smoking and HBV among tissue donors in the study by Sanchez et al.[103]

HCV: A history of tobacco use was associated with HCV in heart donors in Gasink et al.,[102] and cigarette smoking was associated with HCV (but not HBV or HIV) in tissue donors in Sanchez et al.[103] Both of these associations were made using univariate analyses.

HIV: The same tissue donor study that did not find an association between cigarette smoking and HBV or HCV also did not find one between cigarette smoking and HIV.[103]

GRADE Summary: One organ donor study associated tobacco with HCV, but the tissue donor study did not; the strength of the evidence base as very low. For HBV and HIV the evidence was rated as very low because only one study that did not find a relationship was identified.

Prevalence: Among actual heart donors, 36% had a history of tobacco use.[102]

GRADE Summary of Prevalence: The estimate of tobacco use was rated as low due to low study quality and lack of proof of consistency. The directness to potential donors is also unclear.

Tattoos and Piercing

Tattoos and piercings were not associated with HBV in any of five studies or with HIV in one study, but tattoos were associated with HCV in six studies and piercings were associated with HCV in three of six studies. We report on tattoos and piercing because the tissue donor study, Sanchez et al.[103] reported on them together.

HBV: Tattoos, piercing, and acupuncture (as collectively analyzed as one outcome and reported by next-of-kin) were not associated with HBV in tissue donors in Sanchez et al.[103]

Tattoos were not associated with HBV infection among psychiatric inpatient veterans in Tabibian et al.,[121] women receiving prenatal care in Butterfield et al. (1990),[126] or among college students in Hwang et al.,[124] unless the college students were tattooed with reused non-autoclaved needles. Having a tattoo in the last six months was not associated with acute HBV infection by Alter et al.[117]

Piercings were not associated with HBV among psychiatric inpatient veterans in Tabibian et al.[121], and body piercings (other than ears) were not associated with HBV among college students in Hwang et al.[124] Piercings within the last six months were not associated with acute HBV in the general population either in Alter et al.[117]

HCV: Tattoos, piercing, and acupuncture (as collectively analyzed as one outcome and reported by next-of-kin) were not associated with HCV in potential tissue donors in Sanchez et al.[103]

Tattoos were associated with HCV in three univariate analyses of blood donors, Orton et al.,[104] Conry-Cantilena et al.,[106] and Murphy et al. (2000)[105] Orton et al. focused on having had a tattoo within the last six months and the appearance of acute HCV. Two of these studies also performed multivariate analyses. Conry-Cantilena found that tattoos were not significantly associated with infection once other factors are controlled for.[106] Murphy et al. found that, although the odds of infection were reduced once IDU was controlled for, tattoos were an independent predictor of HCV.[105] Three general populations studies, Nguyen et al.,[113] Fischer et al.,[114] and Hand and Vasquez et al.,[112] also detected significant associations between tattoos and HCV. Only Hand and Vasquez investigated further and found that tattoos were an independent predictor. In that study, adults were enrolled based upon clinical suspicion of hepatitis. Most patients enrolled in the Hand and Vasquez study reported that their tattoos had been applied by friends, fellow gang members, or fellow inmates (as opposed to professional tattooists working from commercial parlors).

Among blood donors, HCV was not associated with body piercing in the last 6 months by Orton et al.,[104] but was associated with ear piercing among men in Conry-Cantilena et al.,[106] and with pierced ears or body parts in Murphy et al. (2000).[105] Fischer et al.[114] and Hand and Vasquez[112] considered the association between body piercing and HCV in general population patients and did not find an association. Nguyen et al.[113] and Hand and Vasquez[112] investigated ear piercing in adult patients, and while Nguyen et al. detected an association Hand and Vasquez did not.

HIV: Tattoos, piercing, and acupuncture (as collectively analyzed as one outcome and reported by next-of-kin) were not associated with HIV in potential tissue donors in Sanchez et al.[103]

GRADE Summary: Tattoos and piercings were consistently not assocated with HBV. The rating of this evidence is low. Aside from one very low-quality study, tattoos were consistently associated with HCV, and piercings were inconsistently associated with HCV. The rating of this evidence is also low. Only one very low study considered piercing and tattoos and HIV, and did not find an association. This evidence was rated as very low due to low quality, lack of proof of consistency, and imprecision.

International Travel

Several studies inquired whether participants had traveled outside the U.S. but none detected an association with infection. Among potential tissue donors in Sanchez et al., international travel was not associated with HBV, HCV, or HIV.[103] International travel within the last six months was not associated with acute HBV in a general population by Alter et al.[117] Among blood donors, traveling outside the U.S. during the last six months was not found to be significantly associated with HCV in Orton et al.,[104] and having ever lived outside the U.S. was not found to be significantly associated with HCV in Murphy et al.[105]

GRADE Summary: International travel was not associated with any of the viruses. For HBV and HIV the evidence was rated as very low due to imprecision and, for HIV, low quality. For HCV the evidence was rated as low.

Evidence Tables for Question 3

Table 33. HBV Identification of Behavioral Risk Factors Data

Category	Factor	Citation	Year	Percentage of Infected with Factor	Total Number Infected	Percentage of Uninfected with Factor	Total Number Uninfected	Effect Size*	p-Value**	Comparison Made	Associated in Study?	Population
Potential Tissue Donors												
Sex Work	Prostitution, history of	Sanchez et al.[103]	2006	Not repor-ted (NR)	47	NR	56	NR	Not significant (NS)†	Proportion in HBV+ vs. HBV-	No	Potential tissue donors, as reported by next of kin
Incarceration	Incarceration, history of	Sanchez et al.[103]	2006	NR	47	NR	56	NR	NS †	Proportion in HBV+ vs. HBV-	No	Potential tissue donors, as reported by next of kin
Non-IDU Drugs	Illicit drug use (any)	Sanchez et al.[103]	2006	NR	47	NR	56	NR	NS †	Proportion in HBV+ vs. HBV-	No	Potential tissue donors, as reported by next of kin
	Alcohol use	Sanchez et al.[103]	2006	NR	47	NR	56	NR	NS †	Proportion in HBV+ vs. HBV-	No	Potential tissue donors, as reported by next of kin
	Smoking history	Sanchez et al.[103]	2006	NR	47	NR	56	NR	NS †	Proportion in HBV+ vs. HBV-	No	Potential tissue donors, as reported by next of kin
Tattoos/ Piercing	Tattoos, body piercing, or acupuncture	Sanchez et al.[103]	2006	NR	47	NR	56	NR	NS †	Proportion in HBV+ vs. HBV-	No	Potential tissue donors, as reported by next of kin

Category	Factor	Citation	Year	Percentage of Infected with Factor	Total Number Infected	Percentage of Uninfected with Factor	Total Number Uninfected	Effect Size*	p-Value**	Comparison Made	Associated in Study?	Population
Other	Foreign travel	Sanchez et al.[103]	2006	NR	47	NR	56	NR	NS†	Proportion in HBV+ vs. HBV-	No	Potential tissue donors, as reported by next of kin
General Population												
MSM	Men who have had sex with men	McQuillan et al.[29]	1999	6.5%	323	1.2%	5,058	5.7 (3.4 to 9.5)†¶	<0.001†	Proportion in HBV+ vs. HBV-	Yes	General population aged 17 to 59 years
IDU	Intravenous drug use	Kaur et al.[116]	1996	62.6%	6,121	17.2%	1,417	8.11 (5.47 to 12.03)‡	SS	Proportion in HBV+ vs. HBV-	Yes	Volunteers from general population
High-risk Sex Partner	Sex with intravenous drug user	Kaur et al.[116]	1996	44.7%	1,189	16.7%	5,373	2.57 (1.78 to 3.17)‡	SS	Proportion in HBV+ vs. HBV-	Yes	Volunteers from general population
	Household/ sexual contact with someone with history of IV drug use, last 6 months	Alter et al.[117]	1989	9%	76	0.7%	152	NR	<0.01†; NS‡	Proportion in HBV+ vs. HBV-	Yes (uni-variate only)	General population adults with no obvious cause of acute HBV and matched controls
	Sexual contact with blood transfusion recipient	Alter et al.[117]	1989	3%	76	5%	152	NR	NS†	Proportion in HBV+ vs. HBV-	No	General population adults with no obvious cause of acute HBV and matched controls

Category	Factor	Citation	Year	Percentage of Infected with Factor	Total Number Infected	Percentage of Uninfected with Factor	Total Number Uninfected	Effect Size*	p-Value**	Comparison Made	Associated in Study?	Population
	Sexual contact with person employed in health care	Alter et al.[117]	1989	0%	76	5%	152	NR	NS†	Proportion in HBV+ vs. HBV-	No	General population adults with no obvious cause of acute HBV and matched controls
	Sexual contact with person of foreign birth in area with high endemic HBV rate	Alter et al.[117]	1989	3%	76	0%	152	NR	NS†	Proportion in HBV+ vs. HBV-	No	General population adults with no obvious cause of acute HBV and matched controls
Incarceration	Imprisonment last 6 months	Alter et al.[117]	1989	7%	76	0%	152	NR	<0.01†; NS‡	Proportion in HBV+ vs. HBV-	Yes (uni-variate only)	General population adults with no obvious cause of acute HBV and matched controls
Other Sex Practices	Sex with multiple partners	Kaur et al.[116]	1996	22.6%	1,402	17.9%	5,923	1.33 (1.08 to 1.64)‡	NR	Proportion in HBV+ vs. HBV-	Yes	Volunteers from general population
	Multiple (>1) sexual partners, last 6 months	Alter et al.[117]	1989	26%	76	7%	152	6.0‡ (confidence intervals not reported)	<0.01	Proportion in HBV+ vs. HBV-	Yes	General population adults with no obvious cause of acute HBV and matched controls

Category	Factor	Citation	Year	Percentage of Infected with Factor	Total Number Infected	Percentage of Uninfected with Factor	Total Number Uninfected	Effect Size*	p-Value**	Comparison Made	Associated in Study?	Population
	Lifetime sex partners 2 to 9	McQuillan et al.[29]	1999	47%	505	50%	10,613	2.1 (1.4 to 3.2)‡	SS	Prevalence HBV+ vs. HBV- vs. 0 to 1	Yes	General population aged 17 to 59 years
	Lifetime sex partners 10 to 49	McQuillan et al.[29]	1999	26%	505	20%	10,613	2.9 (1.9 to 4.3)‡	SS	Prevalence HBV+ vs. HBV- vs. 0 to 1	Yes	General population aged 17 to 59 years
	Lifetime sex partners 50+	McQuillan et al.[29]	1999	4%	505	11%	10,613	6.5 (3.5 to 12.2)‡	SS	Prevalence HBV+ vs. HBV- vs. 0 to 1	Yes	General population aged 17 to 59 years
	Age at first intercourse <18	McQuillan et al.[29]	1999	69%	496	60%	9,978	1.2 (0.9 to 1.6)	NS	Prevalence HBV+ vs. HBV- vs. >18 years	No	General population aged 17 to 59 years
Non-Injection Drugs	Ever used cocaine	McQuillan et al.[29]	1999	22%	541	11%	10,773	1.8 (1.2 to 2.7)‡	SS	Proportion in HBV+ vs. HBV-	Yes	General population aged 17 to 59 years
Tattoo	Tattoo, last six months	Alter et al.[117]	1989	1%	76	1%	152	NR	NS†	Proportion in HBV+ vs. HBV-	No	General population adults with no obvious cause of acute HBV and matched controls

Category	Factor	Citation	Year	Percentage of Infected with Factor	Total Number Infected	Percentage of Uninfected with Factor	Total Number Uninfected	Effect Size*	p-Value**	Comparison Made	Associated in Study?	Population
Piercing	Ear piercing, last six months	Alter et al.[117]	1989	3%	76	3%	152	NR	NS†	Proportion in HBV+ vs. HBV-	No	General population adults with no obvious cause of acute HBV and matched controls
Travel	International travel, last six months	Alter et al.[117]	1989	1%	76	<1%	152	NR	NS†	Proportion in HBV+ vs. HBV-	No	General population adults with no obvious cause of acute HBV and matched controls
Other	Raw shellfish, ingesting, last six months	Alter et al.[117]	1989	15%	76	8%	152	NR	NS†	Proportion in HBV+ vs. HBV-	No	General population adults with no obvious cause of acute HBV and matched controls
	Raw shellfish, shucking, last six months	Alter et al.[117]	1989	4%	76	3%	152	NR	NS†	Proportion in HBV+ vs. HBV-	No	General population adults with no obvious cause of acute HBV and matched controls
	Sharing a razor or toothbrush with someone in household	Alter et al.[117]	1989	22%	76	27%	152	NR	NS†	Proportion in HBV+ vs. HBV-	No	General population adults with no obvious cause of acute HBV and matched controls

Category	Factor	Citation	Year	Percentage of Infected with Factor	Total Number Infected	Percentage of Uninfected with Factor	Total Number Uninfected	Effect Size*	p-Value**	Comparison Made	Associated in Study?	Population
Demographic and Socioeconomic Subpopulation												
MSM	Men who have sex with men	Hwang et al.[124]	2006	6%	245	3%	3,824	Relative risk (RR): 2.06 (1.17 to 3.61)† OR: 3.54 (1.31 to 9.59)‡	p <0.05 for both	Prevalence HBV+ vs. HBV- vs. never had sex	Yes	College students
IDU	Intravenous drug use	Tabibian et al.[121]	2008	62.5%	40	27%	89	4.51 (2.04 to 9.96)†¶	<0.001	Prevalence in HBV+ vs. HCV-	Yes	Psychiatric inpatient veterans
	Intravenous drug use	Butterfield et al.[125]	2004	NR	80	NR	276	4.54 (2.28 to 9.04)‡	<0.001	Prevalence HBV+ vs. HBV-	Yes	Psychiatric inpatient veterans
	Intravenous drug use	Butterfield et al.[126]	1990	0%	12	0.2%	1,454	16.59 (0.81 to 338.24)†¶	0.07¶	Prevalence HBV+ vs. HBV-	No	Obstetric population
	Injected illegal drugs	Hwang et al.[124]	2006	6%	266	2%	3,968	RR: 3.02 (1.91 to 4.77)†	<0.05	Prevalence HBV+ vs. HBV-	Yes	College students
	Injected steroids	Hwang et al.[124]	2006	1%	268	1%	4,013	RR: 0.98 (0.32 to 2.94)†	NS	Prevalence HBV+ vs. HBV-	No	College students
Sex Work	Sex bartering	Tabibian et al.[121]	2008	30%	40	37%	89	NR	NS†	Prevalence in HBV+ vs. HBV-	No	Psychiatric inpatient veterans

Category	Factor	Citation	Year	Percentage of Infected with Factor	Total Number Infected	Percentage of Uninfected with Factor	Total Number Uninfected	Effect Size*	p-Value**	Comparison Made	Associated in Study?	Population
	Unprotected sex for drugs	Butterfield et al.[125]	2004	NR	80	NR	276	1.25 (0.60 to 2.61)‡	NS	Prevalence HBV+ vs. HBV-	No	Psychiatric inpatient veterans
High-Risk Sex Partners	Sex with intravenous drug user	Tabibian et al.[121]	2008	17.5%	40	11%	89	NR	NS†	Prevalence in HBV+ vs. HBV-	No	Psychiatric inpatient veterans
	Sex with injection drug user	Hwang et al.[124]	2006	8%	267	4%	4,006	RR: 2.05 (1.36 to 3.09)†	<0.05	Prevalence HBV+ vs. HBV-	Yes	College students
	Sex with prostitute	Tabibian et al.[121]	2008	32.5%	40	18%	89	NR	NS†	Prevalence in HBV+ vs. HBV-	No	Psychiatric inpatient veterans
	Sexual partner with hepatitis	Hwang et al.[124]	2006	4%	268	2%	4,010	RR: 2.28 (1.30 to 3.99)†	p <0.05	Prevalence HBV+ vs. HBV-	Yes	College students
	Sexual contact with partner with hepatitis	Butterfield et al.[126]	1990	0%	12	0.1%	1,454	0.36 (0.02 to 6.09)†¶	0.48¶	Prevalence HBV+ vs. HBV-	No	Obstetric population
Incarceration	Previous Incarceration	Tabibian et al.[121]	2008	85.0%	40	67%	89	NR	<0.05†	Prevalence in HBV+ vs. HBV-	Yes	Psychiatric inpatient veterans
	Incarcerated >24 hours	Hwang et al.[124]	2006	13%	268	8%	4,026	RR: 1.71 (1.22 to 2.41)†	<0.05	Prevalence HBV+ vs. HBV-	Yes	College students

Category	Factor	Citation	Year	Percentage of Infected with Factor	Total Number Infected	Percentage of Uninfected with Factor	Total Number Uninfected	Effect Size*	p-Value**	Comparison Made	Associated in Study?	Population
Other Sex Practices	Lifetime heterosexual partners >0 ≤50	Hwang et al.[124]	2006	67%	243	74%	3,824	RR 0.89 (0.65 to 1.24)†	NS	Prevalence HBV+ vs. HBV- vs. no hetero-sexual partners	No	College students
	Lifetime heterosexual partners ≥50	Hwang et al.[124]	2006	4%	243	1%	3,824	RR 3.08 (1.60 to 5.93)†	<0.05	Prevalence HBV+ vs. HBV- vs. no hetero-sexual partners	Yes	College students
	Heterosexual partners last 4 months ≥5	Hwang et al.[124]	2006	3%	240	1%	3,790	RR: 2.02 (1.00 to 4.10)†; OR: 2.61 (0.91 to 7.47)‡	NS†, <0.05‡	Prevalence HBV+ vs. HBV- vs. <5	Yes	College students
	Multiple sex partners last 6 months	Butterfield et al.[125]	2004	NR	80	NR	276	2.01 (1.06 to 3.78‡	<0.05	Prevalence HBV+ vs. HBV-	Yes	Psychiatric inpatient veterans
	Age at first intercourse ≤15 years	Hwang et al.[124]	2006	20%	249	13%	3,810	RR: 1.52 (1.01 to 2.27)†	<0.05	Prevalence HBV+ vs. HBV- vs. never had sex	Yes	College students

Category	Factor	Citation	Year	Percentage of Infected with Factor	Total Number Infected	Percentage of Uninfected with Factor	Total Number Uninfected	Effect Size*	p-Value**	Comparison Made	Associated in Study?	Population
	Age at first intercourse ≥15 years	Hwang et al.[124]	2006	65%	249	70%	3,810	RR: 0.97 (0.69 to 1.36)†	NS	Prevalence HBV+ vs. HBV- vs. never had sex	No	College students
Non-Injection Substance	Intranasal drug use	Tabibian et al.[121]	2008	80%	40	66%	89	NR	NS†	Prevalence in HBV+ vs. HBV-	No	Psychiatric inpatient veterans
	Intranasal drug use	Hwang et al.[124]	2006	19%	262	14%	3,921	RR: 1.39 (1.03 to 1.86)†	<0.05	Prevalence HBV+ vs. HBV-	Yes	College students
	Sniffed/ snorted drugs	Butterfield et al.[125]	2004	NR	80	NR	276	1.06 (0.51 to 2.21)‡	NS	Prevalence HBV+ vs. HBV-	No	Psychiatric inpatient veterans
	Smoked crack cocaine	Butterfield et al.[125]	2004	NR	80	NR	276	1.18 (0.55 to 2.54)‡	NS	Prevalence HBV+ vs. HBV-	No	Psychiatric inpatient veterans
	Alcohol use disorder	Butterfield et al.[125]	2004	NR	80	NR	276	0.93 (0.52 to 1.69)‡	NS	Prevalence HBV+ vs. HBV-	No	Psychiatric inpatient veterans
Tattoo	Tattoo	Tabibian et al.[121]	2008	40%	40	30%	89	NR	NS†	Prevalence HBV+ vs. HBV-	No	Psychiatric inpatient veterans
	Tattoo	Hwang et al.[124]	2006	25%	274	26%	4,047	RR: 0.96 (0.73 to 1.25)†	NS	Prevalence HBV+ vs. HBV-	No	College students

Category	Factor	Citation	Year	Percentage of Infected with Factor	Total Number Infected	Percentage of Uninfected with Factor	Total Number Uninfected	Effect Size*	p-Value**	Comparison Made	Associated in Study?	Population
	Tattoo	Butterfield et al.[126]	1990	0	12	4.6%	1,454	0.82 (0.05 to 14.06)†¶	0.893¶	Prevalence HBV+ vs. HBV-	No	Obstetric population
	Tattoo, number of, 1-2	Hwang et al.[124]	2006	20%	274	20%	4,039	RR: 0.99 (0.74 to 1.32)†	NS	Prevalence HBV+ vs. HBV- vs. no tattoo	No	College students
	Tattoo, number of ≥3	Hwang et al.[124]	2006	5%	274	5%	4,039	RR: 0.87 (0.50 to 1.50)†	NS	Prevalence HBV+ vs. HBV- vs. no tattoo	No	College students
	Tattooed in professional setting	Hwang et al.[124]	2006	21%	274	22%	4,035	RR: 0.93 (0.70 to 1.23)†	NS	Prevalence HBV+ vs. HBV- vs. no tattoo	No	College students
	Tattooed in non-professional setting	Hwang et al.[124]	2006	4%	274	3%	4,035	RR: 1.24 (0.69 to 2.23)†	NS	Prevalence HBV+ vs. HBV- vs. no tattoo	No	College students
	Tattooed with new or autoclaved needles only	Hwang et al.[124]	2006	18%	267	21%	3,920	RR: 0.87 (0.65 to 1.18)†	NS	Prevalence HBV+ vs. HBV- vs. no tattoo	No	College students
	Tattooed with reused non-autoclaved needles	Hwang et al.[124]	2006	4%	267	2%	3,920	RR: 1.91 (1.11 to 3.30)†	<0.05	Prevalence HBV+ vs. HBV- vs. no tattoo	Yes	College students

Category	Factor	Citation	Year	Percentage of Infected with Factor	Total Number Infected	Percentage of Uninfected with Factor	Total Number Uninfected	Effect Size*	p-Value**	Comparison Made	Associated in Study?	Population
	Tattooed with ink in single wells only	Hwang et al.[124]	2006	12%	242	15%	3,646	RR: 0.79 (0.55 to 1.15)†	NS	Prevalence HBV+ vs. HBV- vs. no tattoo	No	College students
	Tattooed with ink in common wells	Hwang et al.[124]	2006	2%	242	2%	3,646	RR: 1.10 (0.50 to 2.41)†	NS	Prevalence HBV+ vs. HBV- vs. no tattoo	No	College students
Piercing	Piercing	Tabibian et al.[121]	2008	37.5%	40	30%	89	NR	NS†	Prevalence in HBV+ vs. HBV-	No	Psychiatric inpatient veterans
	Body piercing (other than ears)	Hwang et al.[124]	2006	16%	268	21%	4,008	RR: 0.74 (0.54 to 1.02)†	NS	Prevalence HBV+ vs. HBV-	No	College students
	Number of body piercings 1-2	Hwang et al.[124]	2006	14%	266	17%	3,975	RR: 0.77 (0.55 to 1.08)†	NS	Prevalence HBV+ vs. HBV- vs. no piercing	No	College students
	Number of body piercings ≥3	Hwang et al.[124]	2006	2%	266	3%	3,975	RR: 0.55 (0.23 to 1.30)†	NS	Prevalence HBV+ vs. HBV- vs. no piercing	No	College students

Category	Factor	Citation	Year	Percentage of Infected with Factor	Total Number Infected	Percentage of Uninfected with Factor	Total Number Uninfected	Effect Size*	p-Value**	Comparison Made	Associated in Study?	Population
Other	Professional manicure	Hwang et al.[124]	2006	56%	272	54%	4,033	RR: 1.08 (0.86 to 1.37)†	NS	Prevalence HBV+ vs. HBV- vs. no manicure	No	College students
	Do not always wear gloves while embalming	Turner et al.[127]	1989	NR	14	NR	94	RR: 9.8 (3.4 to 28.5)†	NR	Prevalence HBV+ vs. HBV- vs. wears gloves	Yes	Embalmers in high-prevalence urban area
	Do not always wear gowns, aprons, shoe coverings, goggles, glasses, or face masks	Turner et al.[127]	1989	NR	14	NR	94	NR	NR	Prevalence HBV+ vs. HBV- vs. does wear	No	Embalmers in high-prevalence urban area
	Eat or drink while embalming	Turner et al.[127]	1989	NR	14	NR	94	RR: 1.8 (0.66 to 4.7)†	NR	Prevalence HBV+ vs. HBV- vs. does not	No	Embalmers in high-prevalence urban area
	Smoke while embalming	Turner et al.[127]	1989	NR	14	NR	94	RR: 1.6 (0.58 to 4.3)†	NR	Prevalence HBV+ vs. HBV- vs. does not	No	Embalmers in high-prevalence urban area

* Odds ratios as reported in publication, unless otherwise specified
** As reported in publication, unless otherwise specified

† Univariate, unadjusted
‡ Multivariate, adjusted for other factors
¶ Calculated by ECRI Institute
NR – Not reported

Table 34. HCV Identification of Behavioral Risk Factors Data

Category	Factor	Citation	Year	Percentage of Infected with Factor	Total Number Infected	Percentage of Uninfected with Factor	Total Number Uninfected	Effect Size*	p-Value**	Comparison Made	Associated in Study?	Population
Potential Organ Donors												
Non-injection Drugs	Alcohol - 'Heavy' use	Gasink et al.[102]	2006	49.2%	261	19.9%	10,654	Not reported (NR)	<0.001†	Proportion in HCV+ vs. HCV-	Yes	Heart donors
	Tobacco use, history of	Gasink et al.[102]	2006	69.0%	261	35.4%	10,654	NR	<0.001†	Proportion in HCV+ vs. HCV-	Yes	Heart donors
Potential Tissue Donors												
Sex Work	Prostitution, history of	Sanchez et al.[103]	2006	NR	18	NR	56	NR	NS	Proportion in HCV+ vs. HCV-	No	Potential tissue donors, as reported by next of kin
Incarceration	Incarceration, history of	Sanchez et al.[103]	2006	NR	18	NR	56	NR	NS	Proportion in HCV+ vs. HCV-	No	Potential tissue donors, as reported by next of kin

Category	Factor	Citation	Year	Percentage of Infected with Factor	Total Number Infected	Percentage of Uninfected with Factor	Total Number Uninfected	Effect Size*	p-Value**	Comparison Made	Associated in Study?	Population
Non-injection Drugs	Illicit drug use	Sanchez et al.[103]	2006	NR	18	NR	56	4.65 (1.21 to 17.91)	$X^2 = 0.016$	Proportion in HCV+ vs. HCV-	Yes	Potential tissue donors, as reported by next of kin
	Alcohol use	Sanchez et al.[103]	2006	NR	18	NR	56	NR	NS	Proportion in HCV+ vs. HCV-	No	Potential tissue donors, as reported by next of kin
	Cigarette smoking	Sanchez et al.[103]	2006	NR	18	NR	56	4.01 (1.11 to 14.65)	$X^2 = 0.024$	Proportion in HCV+ vs. HCV-	Yes	Potential tissue donors, as reported by next of kin
Tattoos and Piercing	Tattoos, body piercing, or acupuncture	Sanchez et al.[103]	2006	NR	18	NR	56	NR	NS	Proportion in HCV+ vs. HCV-	No	Potential tissue donors, as reported by next of kin
Travel	Foreign travel	Sanchez et al.[103]	2006	NR	18	NR	56	NR	NS	Proportion in HCV+ vs. HCV-	No	Potential tissue donors, as reported by next of kin

Category	Factor	Citation	Year	Percentage of Infected with Factor	Total Number Infected	Percentage of Uninfected with Factor	Total Number Uninfected	Effect Size*	p-Value**	Comparison Made	Associated in Study?	Population
Blood Donors												
MSM	Men: Number of lifetime male partners 1	Murphy et al.[105]	2000	3%	400	1%	568	0.9 (0.2 to 4.4)‡	NS	Proportion in HCV+ vs. HCV- Adjusted for IDU with reference to 0 partners	No	Blood donors
	Men: Number of lifetime male partners 2+	Murphy et al.[105]	2000	6%	400	1%	568	1.1 (0.2 to 5.4)‡	NS	Proportion in HCV+ vs. HCV- Adjusted for IDU with reference to 0 partners	No	Blood donors
	Men: Bisexual/ homosexual	Murphy et al.[105]	2000	8%	758	2%	1,039	1.0 (0.3 to 3.0)‡	NS	Proportion in HCV+ vs. HCV- Adjusted for IDU with reference to hetero-sexual	No	Blood donors

Category	Factor	Citation	Year	Percentage of Infected with Factor	Total Number Infected	Percentage of Uninfected with Factor	Total Number Uninfected	Effect Size*	p-Value**	Comparison Made	Associated in Study?	Population
IDU	Injection drug use in last 6 months	Orton et al.[104]	2004	29.2%	65	0%	225	61.46 (7.81 to 483.67)†¶ (Reported as undefined in original publication due to absence of factor in uninfected group)	<0.001†	Proportion in HCV+ vs. HCV-	Yes	Blood donors
	Intravenous drug use	Conry-Cantilena et al.[106]	1996	42%	248	2%	131	12.5 (2.7 to 57.1)‡	0.001	Proportion in HCV+ vs. HCV-	Yes	Blood donors initially positive on enzyme linked immunosorbent assay (EIA)
	Injected drugs	Murphy et al.[105]	2000	51%	758	1%	1,039	49.6 (20.3 to 121.1)‡	Statisti-cally significant (SS)	Proportion in HCV+ vs. HCV- final multivariable logistic regression model	Yes	Blood donors
	Injection drug use longer than 6 months ago only	Orton et al.[104]	2004	4.9%	46	0.5%%	225	10.9 (0.6 to 647)†	0.07	Proportion in HCV+ vs. HCV-	No	Blood donors

Category	Factor	Citation	Year	Percentage of Infected with Factor	Total Number Infected	Percentage of Uninfected with Factor	Total Number Uninfected	Effect Size*	p-Value**	Comparison Made	Associated in Study?	Population
	Injection steroid use longer than 6 months ago only	Orton et al.[104]	2004	3.5%	65	0.5%	225	7.6 (0.4 to 448)†	0.12	HCV-	No	Blood donors
	Lived with injection drug user	Murphy et al.[105]	2000	38%	758	1%	1,039	5.1 (2.9 to 8.8)‡	SS	Proportion in HCV+ vs. HCV- Adjusted for IDU	Yes	Blood donors
	Reside with an injection drug user in last 6 months	Orton et al.[104]	2004	7.7%	65	0%	225	Undefined (because zero controls reported this factor)	<0.001†	Proportion in HCV+ vs. HCV-	Yes	Blood donors
Sex Work	Received money for sex	Murphy et al.[105]	2000	7%	758	1%	1,039	3.0 (0.9 to 9.7)‡	SS	Proportion in HCV+ vs. HCV- Adjusted for IDU	Yes	Blood donors
High-risk Sex Partners	Sex with injection drug user in last 6 months	Orton et al.[104]	2004	18.5%	65	1.8%	225	12.5 (3.6 to 54)†	<0.001	Proportion in HCV+ vs. HCV-	Yes	Blood donors

Category	Factor	Citation	Year	Percentage of Infected with Factor	Total Number Infected	Percentage of Uninfected with Factor	Total Number Uninfected	Effect Size*	p-Value**	Comparison Made	Associated in Study?	Population
	Sex with injection drug user in last 6 months	Murphy et al.[105]	2000	41%	758	3%	1,039	6.3 (3.3 to 12.0)‡	SS	Proportion in HCV+ vs. HCV- Adjusted for IDU	Yes	Blood donors
	Gave money for sex	Murphy et al.[105]	2000	15%	758	6%	1,039	1.5 (0.9 to 2.5)‡	SS	Proportion in HCV+ vs. HCV- Adjusted for IDU	Yes	Blood donors
	Sex with hepatitis case	Murphy et al.[105]	2000	7%	758	3%	1,039	2.2 (1.1 to 4.5)‡	SS	Proportion in HCV+ vs. HCV- Adjusted for IDU	Yes	Blood donors
	Sex partner had hepatitis in last 6 months	Orton et al.[104]	2004	7.7%	65	1.8%	225	4.6 (1.0 to 24)†	0.03	Proportion in HCV+ vs. HCV-	Yes	Blood donors
	Sex with transfusion recipient	Murphy et al.[105]	2000	5%	758	3%	1,039	2.5 (1.3 to 5.0)‡	SS	Proportion in HCV+ vs. HCV- Adjusted for IDU	Yes	Blood donors

Category	Factor	Citation	Year	Percentage of Infected with Factor	Total Number Infected	Percentage of Uninfected with Factor	Total Number Uninfected	Effect Size*	p-Value**	Comparison Made	Associated in Study?	Population
Incarceration	Been in jail within 6 months of donation	Orton et al.[104]	2004	30.9%	65	12.0%	225	3.3 (1.6 to 6.6)†	<0.001	Proportion in HCV+ vs. HCV-	Yes	Blood donors
	Been in jail at least 6 months before donation	Orton et al.[104]	2004	30.9%	65	12.0%	225	3.3 (1.6 to 6.6)†	<0.001	Proportion in HCV+ vs. HCV-	Yes	Blood donors
	In jail more than 3 days	Murphy et al.[105]	2000	22%	758	2%	1,039	5.0 (2.6 to 9.8)‡	SS	Proportion in HCV+ vs. HCV- Adjusted for IDU	Yes	Blood donors
	Imprisonment (history of)	Conry-Cantilena et al.[106]	1996	25%	248	2%	131	NR	<0.001†; NS‡	Proportion in HCV+ vs. HCV-	Yes; Uni-variate only	Blood donors initially positive on EIA
Other Sex Practices	Sexual promiscuity (history of STD, sex with prostitute, >5 partners/ year)	Conry-Cantilena et al.[106]	1996	53%	248	24%	131	3.0 (1.5 to 5.9)‡	0.002	Proportion in HCV+ vs. HCV-	Yes	Blood donors initially positive on EIA

Category	Factor	Citation	Year	Percentage of Infected with Factor	Total Number Infected	Percentage of Uninfected with Factor	Total Number Uninfected	Effect Size*	p-Value**	Comparison Made	Associated in Study?	Population
	Men: Number of lifetime female partners 1	Murphy et al.[105]	2000	8%	400	24%%	568	0.8 (0.3 to 2.6)‡	NS	Proportion in HCV+ vs. HCV- Adjusted for IDU with reference to 0	No	Blood donors
	Men: Number of lifetime female partners 2-10	Murphy et al.[105]	2000	38%	400	44%	568	1.5 (0.6 to 4.0)‡	NS	Proportion in HCV+ vs. HCV- Adjusted for IDU with reference to 0 partners	No	Blood donors
	Men: Number of lifetime female partners 11+	Murphy et al.[105]	2000	51%	400	24%	568	1.7 (0.6 to 4.8)‡	NS	Proportion in HCV+ vs. HCV- Adjusted for IDU with reference to 0 partners	No	Blood donors
	Men: Not sexually active	Murphy et al.[105]	2000	3%	400	6%	568	0.7 (0.2 to 2.0)‡	NS	Proportion in HCV+ vs. HCV- with reference to hetero-sexual	No	Blood donors

Category	Factor	Citation	Year	Percentage of Infected with Factor	Total Number Infected	Percentage of Uninfected with Factor	Total Number Uninfected	Effect Size*	p-Value**	Comparison Made	Associated in Study?	Population
	Women: Number of lifetime male partners 1	Murphy et al.[105]	2000	13%	351	32%	463	1.2 (0.5 to 3.3)‡	NS	Proportion in HCV+ vs. HCV- Adjusted for IDU with reference to 0 partners	No	Blood donors
	Women: Number of lifetime male partners 2-10	Murphy et al.[105]	2000	46%	351	50%	463	1.9 (0.7 to 5.0)‡	NS	Proportion in HCV+ vs. HCV- Adjusted for IDU with reference to 0 partners	No	Blood donors
	Women: Number of lifetime male partners 11-49	Murphy et al.[105]	2000	28%	351	11%	463	3.2 (1.1 to 9.1)‡	SS	Proportion in HCV+ vs. HCV- Adjusted for IDU with reference to 0 partners	Yes	Blood donors
	Women: Number of lifetime male partners 50+	Murphy et al.[105]	2000	8%	351	1%	463	8.8 (2.0 to 39.4)‡	SS	Proportion in HCV+ vs. HCV- with reference to 0 partners	Yes	Blood donors

Category	Factor	Citation	Year	Percentage of Infected with Factor	Total Number Infected	Percentage of Uninfected with Factor	Total Number Uninfected	Effect Size*	p-Value**	Comparison Made	Associated in Study?	Population
	Women: Not sexually active	Murphy et al.[105]	2000	3%	351	4%	463	0.9 (0.3 to 2.4)‡	NS	Proportion with HCV+ vs. HCV- adjusted for IDU and compared to hetero-sexual	No	Blood donors
	Two or more sexual partners in last 6 months	Orton et al.[104]	2004	21.5%	65	4.9%	225	5.3 (2.3 to 13)†	<0.001	Proportion in HCV+ vs. HCV-	Yes	Blood donors
	Women: Number of lifetime female partners >1	Murphy et al.[105]	2000	6%	351	2%	463	1.3 (0.4 to 4.4)‡	NS‡ (Un-adjusted was SS)	Proportion with HCV+ vs. HCV- adjusted for IDU and compared to 0 lifetime female partners	No (Once adjusted for IDU)	Blood donors
	Women: Number of lifetime female partners >2	Murphy et al.[105]	2000	9%	351	2%	463	3.7 (1.2 to 11.1)‡	SS	Proportion with HCV+ vs. HCV- adjusted for IDU and compared to 0 lifetime female partners	Yes	Blood donors

Category	Factor	Citation	Year	Percentage of Infected with Factor	Total Number Infected	Percentage of Uninfected with Factor	Total Number Uninfected	Effect Size*	p-Value**	Comparison Made	Associated in Study?	Population
	Women: Sexual orientation bisexual/ homosexual	Murphy et al.[105]	2000	16%	351	4%	463	2.3 (1.0 to 5.2)‡	NS	Proportion with HCV+ vs. HCV- adjusted for IDU and compared to heterosexual	No (when adjusted for IDU)	Blood donors
Non-injection Drugs	Snort drugs in last 6 months	Orton et al.[104]	2004	20.0%	65	0%	225	Undefined (because zero controls reported this factor)	<0.001†	Proportion in HCV+ vs. HCV-	Yes	Blood donors
	Intranasal drugs longer than 6 months ago	Orton et al.[104]	2004	17.4%	52	6.6%	225	3.0 (1.0 to 8.2)†	0.04†	Proportion in HCV+ vs. HCV-	Yes	Blood donors
	Intranasal cocaine use	Conry-Cantilena et al.[106]	1996	68%	248	11%	131	8.0 (3.9 to 16.5)‡	<0.001	Proportion in HCV+ vs. HCV-	Yes	Blood donors initially positive on EIA
	Inhaled drugs	Murphy et al.[105]	2000	63%	758	21%	1,039	2.2 (1.6 to 3.1)‡	SS	Proportion in HCV+ vs. HCV- Adjusted for IDU	Yes	Blood donors
	Friends use street drugs in last 6 months	Orton et al.[104]	2004	38.5%	65	6.7%	225	8.8 (4.2 to 18)†	<0.001	Proportion in HCV+ vs. HCV-	Yes	Blood donors

Category	Factor	Citation	Year	Percentage of Infected with Factor	Total Number Infected	Percentage of Uninfected with Factor	Total Number Uninfected	Effect Size*	p-Value**	Comparison Made	Associated in Study?	Population
Tattoo	Tattoo in last 6 months	Orton et al.[104]	2004	4.6%	65	0.5%	225	11 (0.8 to 566)†	0.04	Proportion in HCV+ vs. HCV-	Yes	Blood donors
	Tattoo	Conry-Cantilena et al.[106]	1996	21%	248	4%	131	NR	p <0.001†; NS‡	Proportion in HCV+ vs. HCV-	Yes; uni-variate only	Blood donors initially positive on EIA
	Tattoo	Murphy et al.[105]	2000	27%	758	5%	1,039	3.9 (2.5 to 6.1)‡	SS	Proportion in HCV+ vs. HCV- adjusted for IDU	Yes	Blood donors
Piercing	Had body piercing in last 6 months	Orton et al.[104]	2004	4.6%	65	2.2%	225	2.1 (0.3 to 11)†	0.38	Proportion in HCV+ vs. HCV-	No	Blood donors
	Ear piercing among men	Conry-Cantilena et al.[106]	1996	30%	139	0%	83	NR	<0.05‡	Proportion in HCV+ vs. HCV-	Yes	Blood donors initially positive on EIA (male only; factor not significant among women)
	Pierced ears/ body parts	Murphy et al.[105]	2000	56%	758	40%	1,039	2.0 (1.1 to 3.7)‡	SS	Proportion in HCV+ vs. HCV- final multivariable logistic regression model	Yes	Blood donors

Category	Factor	Citation	Year	Percentage of Infected with Factor	Total Number Infected	Percentage of Uninfected with Factor	Total Number Uninfected	Effect Size*	p-Value**	Comparison Made	Associated in Study?	Population
Travel	Travel outside U.S. in last 6 months	Orton et al.[104]	2004	1.5%	65	6.7%	225	0.2 (0.01 to 1.5)†	0.13	Proportion in HCV+ vs. HCV-	No	Blood donors
	Lived outside the U.S.	Murphy et al.[105]	2000	17%	758	15%	1,039	1.0 (0.7 to 1.5)‡	NS	Proportion in HCV+ vs. HCV- adjusted for IDU	No	Blood donors
Other	Religious scarification	Murphy et al.[105]	2000	8%	758	2%	1,039	2.8 (1.2 to 7.0)‡	SS	Proportion in HCV+ vs. HCV- final multivariable logistic regression model	Yes	Blood donors
	Shared toothbrush/ razor	Murphy et al.[105]	2000	16%	758	7%	1,039	1.6 (1.0 to 2.5)‡	SS	Proportion in HCV+ vs. HCV- adjusted for IDU	Yes	Blood donors

Category	Factor	Citation	Year	Percentage of Infected with Factor	Total Number Infected	Percentage of Uninfected with Factor	Total Number Uninfected	Effect Size*	p-Value**	Comparison Made	Associated in Study?	Population
	Electrolysis hair removal	Murphy et al.[105]	2000	3%	758	3%	1,039	1.2 (0.6 to 2.6)‡	NS	Proportion in HCV+ vs. HCV- adjusted for IDU	No	Blood donors
General Population												
MSM	Men who have sex with men	Hand and Vasquez[112]	2005	5%	320	6%	307	NR	0.658†	Proportion HCV+ vs. HCV-	No	Adults tested for HCV in health system because of clinical suspicion
IDU	Drug use – Injection, lifetime	Armstrong et al.[30]	2006	45%	114	0.7%	5,254	148.9 (44.9 to 49.4)‡	SS	No use (or marijuana only) HCV+	Yes	General population aged 20 to 59 years
	Injected drugs	Fischer et al.[114]	2000	27%	11	2%	1,369	26.47 (8.39 to 83.55)‡¶	<0.001†	Proportion in HCV+ vs. HCV-	Yes	Adults enrolled in HMO
	Injection drug use	Hand and Vasquez[112]	2005	53%	320	5%	307	20.1 (10.3 to 39.4)‡	<0.0001	Proportion in HCV+ vs. HCV-	Yes	Adults tested for HCV in health system because of clinical suspicion
	Intravenous drug use	Kaur et al.[116]	1996	66.6%	6,121	5.2%	528	23.34 (15.21 to 35.81)‡	SS	Proportion in HCV+ vs. HCV-	Yes	Volunteers from general population

Category	Factor	Citation	Year	Percentage of Infected with Factor	Total Number Infected	Percentage of Uninfected with Factor	Total Number Uninfected	Effect Size*	p-Value**	Comparison Made	Associated in Study?	Population
	Being at a social gathering with injecting drugs	Nguyen et al.[113]	2005	45.0%	225	7.4%	204	NR	<0.001	Proportion HCV+ vs. HCV-	Yes	Adults at general internal medicine clinic (controls) and hepatology clinic (cases)
	Seeing use of injecting drugs	Nguyen et al.[113]	2005	55.0%	225	10.8%	204	NR	<0.001	Proportion HCV+ vs. HCV-	Yes	Adults at general internal medicine clinic (controls) and hepatology clinic (cases)
Sex Work	Female prostitutes	Hand and Vasquez[112]	2005	2%	320	0%	307	NR	0.028†	Proportion HCV+ vs. HCV-	Yes	Adults tested for HCV in health system because of clinical suspicion
	Exchanging sex for money	Nguyen et al.[113]	2005	17.1%	225	2.0%	204	NR	<0.001†	Proportion HCV+ vs. HCV-	Yes	Adults at general internal medicine clinic (controls) and hepatology clinic (cases)
High-risk Sex Partners	Sex with injecting drug users	Nguyen et al.[113]	2005	37.8%	225	3.4%	204	5.39 (2.01 to 14.42)†	<0.001	Proportion HCV+ vs. HCV-	Yes	Adults at general internal medicine clinic (controls) and hepatology clinic (cases)
	Sex with intravenous drug users	Kaur et al.[116]	1996	45.7%	408	4.7%	5,373	7.29 (4.74 to 11.21)‡	NR	Proportion in HCV+ vs. HCV-	Yes	Volunteers from general population

Category	Factor	Citation	Year	Percentage of Infected with Factor	Total Number Infected	Percentage of Uninfected with Factor	Total Number Uninfected	Effect Size*	p-Value**	Comparison Made	Associated in Study?	Population
	Sex with prostitute	Nguyen et al.[113]	2005	20.7%	225	1.5%	204	9.76 (2.50 to 38.13)†	<0.01†	Proportion HCV+ vs. HCV-	Yes	Adults at general internal medicine clinic (controls) and hepatology clinic (cases)
	Sex with prostitutes	Hand and Vasquez[112]	2005	3%	320	0.7%	307	NR†; 3.4 (0.6 to 18.9)‡	0.014†; 0.169‡	Proportion in HCV+ vs. HCV-	Yes; uni-variate only	Adults tested for HCV in health system because of clinical suspicion
Incarceration	Arrested, having been	Nguyen et al.[113]	2005	33.3%	225	6.9%	204	NR	<0.001†	Prevalence in HCV+ vs. HCV-	Yes	Adults at general internal medicine clinic (controls) and hepatology clinic (cases)
Additional Sex Practices	Unprotected sex	Fischer et al.[114]	2000	45%	11	12%	1,369	NR	<0.001†	Proportion in HCV+ vs. HCV-	Yes	Adults enrolled in HMO
	Number of sex partners – 0	Nguyen et al.[113]	2005	11.7%	225	8.8%	204	NR	<0.01†	Proportion with factor HCV+ vs. HCV-	Yes	Adults at general internal medicine clinic (controls) and hepatology clinic (cases)
	Number of sex partners – 1	Nguyen et al.[113]	2005	7.2%	225	17.2%	204					
	Number of sex partners – 2-9	Nguyen et al.[113]	2005	32.4%	225	46.6%	204					

Category	Factor	Citation	Year	Percentage of Infected with Factor	Total Number Infected	Percentage of Uninfected with Factor	Total Number Uninfected	Effect Size*	p-Value**	Comparison Made	Associated in Study?	Population
	Number of sex partners – 10-49	Nguyen et al.[113]	2005	37.8%	225	25.0%	204					
	Number of sex partners – At least 50	Nguyen et al.[113]	2005	10.8%	225	2.5%	204					
	Number of sex partners 2-19	Armstrong et al.[30]	2006	27%	179	63%	5,178	1.4 (0.3 to 6.0)‡	NR	0-1 partners prevalence of HCV+	No	General population aged 20 to 59 years
	Number of sex partners ≥20	Armstrong et al.[30]	2006	39%	179	14%	5,178	5.2 (1.5 to 18.2)‡	NR	0-1 partners prevalence of HCV+	Yes	General population aged 20 to 59 years
	Frequent sex partners	Fischer et al.[114]	2000	36%	11	7%	1,369	NR	<0.001†	Proportion in HCV+ vs. HCV-	Yes	Adults enrolled in HMO
	Sex with multiple partners	Kaur et al.[116]	1996	13.5%	542	6.5%	5,923	2.24 (1.87 to 2.69)†	NR	Proportion in HCV+ vs. HCV-	Yes	Volunteers from general population
	Sex with person of same sex (not restricted to MSM)	Nguyen et al.[113]	2005	8.6%	225	8.8%	204	NR	>0.99†	Proportion HCV+ vs. HCV-	No	Adults at general internal medicine clinic (controls) and hepatology clinic (cases)

Category	Factor	Citation	Year	Percentage of Infected with Factor	Total Number Infected	Percentage of Uninfected with Factor	Total Number Uninfected	Effect Size*	p-Value**	Comparison Made	Associated in Study?	Population
	Age at first sexual intercourse 16-17 years (participants aged 20 to 59 years)	Armstrong et al.[30]	2006	27%	126	30%	4,928	NR	<0.05†	HCV+ with first sexual intercourse ≥18 years	Yes	General population aged 20 to 59 years
	Age at first sexual intercourse 12-15 years (participants aged 20 to 59 years)	Armstrong et al.[30]	2006	47%	126	26%	4,928	NR	<0.005†	HCV+ with first sexual intercourse ≥18 years	Yes	General population aged 20 to 59 years
	Age at first sexual intercourse ≤11 years (participants aged 20 to 59 years)	Armstrong et al.[30]	2006	11%	126	2.5%	4,928	NR	<0.05†	HCV+ with first sexual intercourse ≥18 years	Yes	General population aged 20 to 59 years
Non-injection Drugs	Drug use – noninjection (except marijuana)	Armstrong et al.[30]	2006	29%	114	2.2%	5,254	3.7 (1.7 to 7.9)‡	NR	No drug use or only marijuana, HCV+	Yes	General population aged 20 to 59 years

Category	Factor	Citation	Year	Percentage of Infected with Factor	Total Number Infected	Percentage of Uninfected with Factor	Total Number Uninfected	Effect Size*	p-Value**	Comparison Made	Associated in Study?	Population
	Snorting or inhaling non-prescription drugs	Nguyen et al.[113]	2005	55.4%	225	18.1%	204	NR	<0.00†	Proportion HCV+ vs. HCV-	Yes	Adults at general internal medicine clinic (controls) and hepatology clinic (cases)
	Inhaled cocaine	Fischer et al.[114]	2000	18%	11	2%	1,369	NR	<0.05†	Proportion in HCV+ vs. HCV-	Yes	Adults enrolled in HMO
	Intranasal cocaine	Hand and Vasquez[112]	2005	39%	320	14%	307	NR†, 1.4 (0.8 to 2.4)‡	<0.0001†; 0.283‡	Proportion in HCV+ vs. HCV-	Yes; uni-variate only	Adults tested for HCV in health system because of clinical suspicion
	Being at a social gathering with cocaine	Nguyen et al.[113]	2005	66.2%	225	28.4%	204	NR	<0.001†	Proportion HCV+ vs. HCV-	Yes	Adults at general internal medicine clinic (controls) and hepatology clinic (cases)
	Alcohol use – none/missing weekly	Nguyen et al.[113]	2005	15.3%	225	11.8%	204	NR	0.12†	Prevalence of factor in HCV+ vs. HCV-	No	Adults at general internal medicine clinic (controls) and hepatology clinic (cases)
	Alcohol use – <1 drink weekly	Nguyen et al.[113]	2005	59.0%	225	52.5%	204					
	Alcohol use – 1-5 drinks weekly	Nguyen et al.[113]	2005	15.3%	225	27.9%	204					

Category	Factor	Citation	Year	Percentage of Infected with Factor	Total Number Infected	Percentage of Uninfected with Factor	Total Number Uninfected	Effect Size*	p-Value**	Comparison Made	Associated in Study?	Population
	Alcohol use – More than 5 drinks weekly	Nguyen et al.[113]	2005	10.4%	225	7.8%	204					
	Alcoholism	Fischer et al.[114]	2000	18%	11	9%	1,369	NR	NS †	Proportion in HCV+ vs. HCV-	No	Adults enrolled in HMO
	Moderate to heavy alcohol use (at least 2 units per day)	Hand and Vasquez[112]	2005	58%	320	49%	307	NR	0.034†	Proportion in HCV+ vs. HCV-	Yes	Adults tested for HCV in health system because of clinical suspicion
Tattoo	Tattoo	Nguyen et al.[113]	2005	28.4%	225	16.2%	204	NR	0.003†	Proportion HCV+ vs. HCV-	Yes	Adults at general internal medicine clinic (controls) and hepatology clinic (cases)
	Tattoo	Fischer et al.[114]	2000	36%	11	6%	1,369	NR	<0.001†	Proportion in HCV+ vs. HCV-	Yes	Adults enrolled in HMO
	Tattoo	Hand and Vasquez[112]	2005	57%	320	22%	307	NR†; 2.9 (1.9 to 4.6)‡	<0.0001†; <0.001‡	Proportion in HCV+ vs. HCV-	Yes	Adults tested for HCV in health system because of clinical suspicion

Category	Factor	Citation	Year	Percentage of Infected with Factor	Total Number Infected	Percentage of Uninfected with Factor	Total Number Uninfected	Effect Size*	p-Value**	Comparison Made	Associated in Study?	Population
Piercing	Pierced ears	Nguyen et al.[113]	2005	59.0%	225	73.5%	204	NR	0.002†	Proportion HCV+ vs. HCV-	Yes	Adults at general internal medicine clinic (controls) and hepatology clinic (cases)
	Pierced ears	Hand and Vasquez[112]	2005	38%	320	38%	307	NR	0.998†	Proportion HCV+ vs. HCV-	No	Adults tested for HCV in health system because of clinical suspicion
	Body piercing	Fischer et al.[114]	2000	45%	11	33%	1,369	NR	NS†	Proportion HCV+ vs. HCV-	No	Adults enrolled in HMO
	Body piercing	Hand and Vasquez[112]	2005	2%	320	3%	307	NR	0.737†	Proportion in HCV+ vs. HCV-	No	Adults tested for HCV in health system because of clinical suspicion
Other	No lifestyle risks	Fischer et al.[114]	2000	0%	11	32%	1,369	NR	<0.05†	Proportion in HCV+ vs. HCV-	Yes	Adults enrolled in HMO

* Odds ratios as reported in publication, unless otherwise specified

** As reported in publication, unless otherwise specified

† Univariate, unadjusted

‡ Multivariate, adjusted for other factors

¶ Calculated by ECRI Institute

Table 35. HIV Identification of Behavioral Risk Factors Data

Category	Factor	Citation	Year	Percentage of Infected with Factor	Total Number Infected	Percentage of Uninfected with Factor	Total Number Uninfected	Effect Size*	p-Value**	Comparison Made	Associated in Study?	Population
Potential Tissue Donors												
Sex Work	Prostitution, history of	Sanchez et al.[103]	2006	Not reported (NR)	10	NR	56	NR	Not significant (NS)	Proportion in HIV+ vs. HIV	No	Potential tissue donors, as reported by next of kin
Incarceration	Incarceration, history of	Sanchez et al.[103]	2006	NR	10	NR	56	NR	NS	Proportion in HIV+ vs. HIV	No	Potential tissue donors, as reported by next of kin
Non-IDU	Illicit drug use	Sanchez et al.[103]	2006	NR	10	NR	56	NR	NS	Proportion in HIV+ vs. HIV-	No	Potential tissue donors, as reported by next of kin
	Smoking history	Sanchez et al.[103]	2006	NR	10	NR	56	NR	NS	Proportion in HIV+ vs. HIV	No	Potential tissue donors, as reported by next of kin
	Alcohol use	Sanchez et al.[103]	2006	NR	10	NR	56	NR	NS	Proportion in HIV+ vs. HIV	No	Potential tissue donors, as reported by next of kin
Tattoos and Piercing	Tattoos, body piercing, or acupuncture	Sanchez et al.[103]	2006	NR	10	NR	56	NR	NS	Proportion in HIV+ vs. HIV	No	Potential tissue donors, as reported by next of kin
Travel	Foreign travel	Sanchez et al.[103]	2006	NR	10	NR	56	NR	NS	Proportion in HIV+ vs. HIV	No	Potential tissue donors, as reported by next of kin

Category	Factor	Citation	Year	Percentage of Infected with Factor	Total Number Infected	Percentage of Uninfected with Factor	Total Number Uninfected	Effect Size*	p-Value**	Comparison Made	Associated in Study?	Population
General Population												
MSM	Male-to-male sex	McQuillan et al.[101]	2006	52%	21	4%	2,418	26.0 (10.8 to 62.7)†¶	<0.001	Proportion in HIV+ vs. HIV-	Yes	General population
	MSM, ever, men only	Nguyen et al.[110]	2008	53.8%	13	8.3%	577	15.11 (4.11 to 55.91)†	SS	Men who have had sex with women HIV+ vs. HIV-	Yes	General population of adults in New York City who have ever had sex
IDU	Injection drug use	Mehta et al.[109]	2008	9%	229	NR	16,467	1.17 (0.75 to 1.85)†	NR	Percent HIV+ vs. no injection drug use	No	Hospital inpatients and outpatients
	Ever injected drugs	McQuillan et al.[101]	2006	13%	30	2%	4,938	7.3 (2.5 to 21.6)†¶	0.001	Proportion in HIV+ vs. HIV-	Yes	General population
	Ever used a needle for drugs	Nguyen et al.[110]	2008	14.3%	21	1.2%	1,482	21.01 (3.99 to 110.64)†	SS	Never used needle	Yes	General population of adults in New York City
High-risk Sex Partners	Sex with HIV+ person	Mehta et al.[109]	2008	10%	229	NR	16,467	3.25 (2.11 to 5.01)†	NR	No sex with HIV+ person in HIV+	Yes	Hospital inpatients and outpatients

Category	Factor	Citation	Year	Percentage of Infected with Factor	Total Number Infected	Percentage of Uninfected with Factor	Total Number Uninfected	Effect Size*	p-Value**	Comparison Made	Associated in Study?	Population
Other Sex Practices	Number of sex partners 1	Mehta et al.[109]	2008	22%	229	NR	16,467	0.79 (0.41 to 1.53)†	NR	0 partners, HIV+	No	Hospital inpatients and outpatients
	Number of sex partners 2-4	Mehta et al.[109]	2008	34%	229	NR	16,467	1.03 (0.55 to 1.95)†	NR	0 partners, HIV+	No	Hospital inpatients and outpatients
	Number of sex partners 5-9	Mehta et al.[109]	2008	12%	229	NR	16,467	1.09 (0.54 to 2.20)†	NR	0 partners, HIV+	No	Hospital inpatients and outpatients
	Number of sex partners ≥10	Mehta et al.[109]	2008	10%	229	NR	16,467	1.14 (0.55 to 2.36)†	NR	0 partners, HIV+	No	Hospital inpatients and outpatients
	Number of sex partners – Data Missing	Mehta et al.[109]	2008	17%	229	NR	16,467	0.92 (0.47 to 1.80)†	NR	0 partners, HIV+	No	Hospital inpatients and outpatients
	Lifetime sex partners 0-1	McQuillan et al.[101]	2006	13%	31	26%	5,360	0.43 (0.15 to 1.2)†¶	0.11	Proportion HIV+ vs. HIV-	No	General population
	Lifetime sex partners 2-49	McQuillan et al.[101]	2006	55%	31	71%	5,360	0.50 (0.25 to 1.02)†¶	0.55	Proportion HIV+ vs. HIV	No	General population
	Lifetime sex partners 50+	McQuillan et al.[101]	2006	32%	31	4%	5,360	11.3 (5.5 to 24.3)†¶	<0.001	Proportion HIV+ vs. HIV	Yes	General population
	Multiple sex partners in past year	Nguyen et al.[110]	2008	30.0%	20	22.1%	1,346	1.41 (0.59 to 3.37)†	NS	Single sex partner past year	No	General population of adults in New York City who have ever had sex

Category	Factor	Citation	Year	Percentage of Infected with Factor	Total Number Infected	Percentage of Uninfected with Factor	Total Number Uninfected	Effect Size*	p-Value**	Comparison Made	Associated in Study?	Population
	Sex partner same gender or both	Mehta et al.[109]	2008	16%	229	NR	16,467	2.17 (1.49 to 3.15)†	NR	Prevalence of HIV+ with this factor vs. opposite gender only	Yes	Hospital inpatients and outpatients
	Age at first intercourse <18 years	McQuillan et al.[101]	2006	77%	31	58%	5,342	2.4 (1.0 to 5.6)†¶	0.038	Proportion in HIV+ vs. HIV-	Yes	General population
	Condom use, past month	Nguyen et al.[110]	2008	33.3	3	59.2	238	0.32 (0.03 to 3.83)†	NS	Sometimes or never used condoms	No	General population of adults in New York City who reported multiple sex partners during the past year and sexual activity during the past month
	Condom use with current partner – Sometimes	Mehta et al.[109]	2008	52%	229	NR	16,467	1.14 (0.76 to 1.70)†	NR	Prevalence of condom use always, HIV+	No	Hospital inpatients and outpatients
	Condom use with current partner – Never	Mehta et al.[109]	2008	20%	229	NR	16,467	0.75 (0.47 to 1.19)†	NR	Prevalence of condom use always, HIV+	No	Hospital inpatients and outpatients
	Condom use with current partner – Missing Data	Mehta et al.[109]	2008	14%	229	NR	16,467	1.54 (0.94 to 2.54)†	NR	Prevalence of condom use always, HIV+	No	Hospital inpatients and outpatients

Category	Factor	Citation	Year	Percentage of Infected with Factor	Total Number Infected	Percentage of Uninfected with Factor	Total Number Uninfected	Effect Size*	p-Value**	Comparison Made	Associated in Study?	Population
	Anal-insertive sex (men only) <6 weeks ago	Mehta et al.[109]	2008	7% of men	145 (men only)	NR	9,589	1.83 (0.94 to 3.57)†	NR	Did not have, HIV+	No	Hospital inpatients and outpatients
	Anal-insertive sex (men only) ≥6 weeks ago	Mehta et al.[109]	2008	14% of men	145 (men only)	NR	9,589	3.32 (2.01 to 5.48)†	NR	Did not have, HIV+	Yes	Hospital inpatients and outpatients
	Anal-insertive sex (men only) – Data missing	Mehta et al.[109]	2008	28% of men	145 (men only)	NR	9,589	1.43 (0.97 to 2.11)†	NR	Did not have, HIV+	No	Hospital inpatients and outpatients
	Anal-receptive sex <6 weeks ago	Mehta et al.[109]	2008	2%	229	NR	16,467	2.29 (0.93 to 5.65)†	NR	Did not have, HIV+	No	Hospital inpatients and outpatients
	Anal-receptive sex ≥6 weeks ago	Mehta et al.[109]	2008	6%	229	NR	16,467	6.56 (3.73 to 11.5)†	NR	Did not have, HIV+	Yes	Hospital inpatients and outpatients
	Anal receptive sex – Data Missing	Mehta et al.[109]	2008	21%	229	NR	16,467	1.70 (1.23 to 2.34)†	NR	Did not have, HIV+	Yes	Hospital inpatients and outpatients
	Vaginal sex <6 weeks ago	Mehta et al.[109]	2008	43%	229	NR	16,467	0.33 (0.22 to 0.50)†	NR	Did not have, HIV+	No (protective)	Hospital inpatients and outpatients

Category	Factor	Citation	Year	Percentage of Infected with Factor	Total Number Infected	Percentage of Uninfected with Factor	Total Number Uninfected	Effect Size*	p-Value**	Comparison Made	Associated in Study?	Population
	Vaginal sex ≥6 weeks ago	Mehta et al.[109]	2008	32%	229	NR	16,467	0.49 (0.32 to 0.74)†	NR	Did not have, HIV+	No (protective)	Hospital inpatients and outpatients
	Vaginal sex – Data Missing	Mehta et al.[109]	2008	21%	229	NR	16,467	0.56 (0.33 to 0.95)†	NR	Did not have, HIV+	No (protective)	Hospital inpatients and outpatients
Non-injection Drugs	Ever used cocaine/street drugs	McQuillan et al.[101]	2006	47%	30	21%	4,938	3.3 (1.6 to 6.9)†¶	<0.001	Proportion in HIV+ vs. HIV-	Yes	General population
	Crack cocaine use	Alpert et al.[115]	1996	NR	35	NR	840	NR‡	SS	Proportion in HCV+ vs. HCV-	Yes	Adults at emergency department room
	Alcohol and/or drug problem (as identified in health care database)	Fischer et al.[114]	2000	36%	11	12%	1,369	12.5 (2.3 to 69.0)†	0.004	Proportion in HCV+ vs. HCV-	Yes	Adults enrolled in HMO

* Odds ratios as reported in publication, unless otherwise specified

** As reported in publication, unless otherwise specified

† Univariate, unadjusted

‡ Multivariate, adjusted for other factors

¶ Calculated by ECRI Institute

Table 36. GRADE Table for Question 3 (Behavioral Risk Factors)

Factor	Virus	Quantity and Type of Evidence	Findings	Starting Grade	Decrease Grade					Increase Grade			GRADE of Evidence for Outcome
					Overall Quality	Consistency	Directness	Precision	Publication Bias	Large Magnitude	Dose Response	Associated Despite Confounders	
Factors Identified in Original Guideline													
Men who have Sex with Men (MSM)	HBV	2 OBS[29,124]	HBV was significantly associated with MSM in univariate analyses in two studies, one on the general population and one on college students. The college students study also performed an multivariate analysis and the association remained significant.[124]	Low	0	0	0	0	0	1	0	0	Moderate
	HCV	2 OBS[105,112]	One blood donor study found a significant association between HCV and MSM upon univariate but not multivariate analysis.[105] A general population study found no association at all in univariate analysis.[112]	Low	0	-1	0	0	0	0	0	0	Very Low
	HIV	2 OBS[101,110]	HIV infection was significantly associated with MSM in the general population in two univariate analyses.	Low	0	0	0	0	0	1	0	0	Moderate

Factor	Virus	Quantity and Type of Evidence	Findings	Starting Grade	Decrease Grade					Increase Grade			GRADE of Evidence for Outcome
					Overall Quality	Consistency	Directness	Precision	Publication Bias	Large Magnitude	Dose Response	Associated Despite Confounders	
Injection Drug Users (IDU)	HBV	5 OBS[116,121,124-126]	HBV was significantly associated with IDU in four studies, one of the general population[116] and three of special populations.[121,124,125] Three of these studies had large effect sizes, and the fourth came close.[124] The fifth study, another special population study, did not find any association. This may be a statistical anomaly due to the very low prevalence of HBV and IDU in this obstetric population.[126] The general population study and one of the special population studies[125] performed multivariate analyses, the rest were univariate. One of the special population studies also considered steroid injection but did not find a significant relationship.[124]	Low	0	0	0	0	0	0	0	0	Low
	HCV	7 OBS[30,104-106,112,114,116]	Three blood donor studies[104-106] and four general population studies[30,112,114,116] detected associations between IDU and HCV. All of these studies found large effect sizes. Two of the blood donor studies and three of general population studies[30,112,116] performed multivariate analyses and determined IDU is an independent risk factor (the other studies performed univariate assessments only). One of the blood donor studies also considered past steroid injection use and did not find a significant association with HCV.[104]	Low	0	0	0	0	0	1	0	0	Moderate

Factor	Virus	Quantity and Type of Evidence	Findings	Starting Grade	Decrease Grade					Increase Grade			GRADE of Evidence for Outcome
					Overall Quality	Consistency	Directness	Precision	Publication Bias	Large Magnitude	Dose Response	Associated Despite Confounders	
	HIV	3 OBS[101,109,110]	All three studies assessed IDU in the general population in univariate analyses. Two found a significant association with large effect sizes,[101,110] and the third did not find any association.[109]	Low	0	0	0	0	0	0	0	0	Low
Sex Work	HBV	3 OBS[103,121,125]	None of the studies found an association between sex work (including sex bartering or sex for drugs) and HBV; however, one was a very low-quality tissue donor study based upon next-of-kin interviews,[103] and the other two studied special populations.[121,125]	Low	0	0	-1	0	0	0	0	0	Very Low
	HCV	4 OBS[103,105,112,113]	The very low-quality tissue donor study based upon next-of-kin data did not detect any association between HCV and sex work. The remaining three studies did. One multivariate-analysis blood donor study[105] and two univariate-analysis general populations studies[112,113] did detect significant associations.	Low	0	0	0	0	0	0	0	0	Low
	HIV	1 OBS[103]	The very low-quality tissue donor study based upon next-of-kin data did not detect any association between HCV and sex work.	Low	-1	-1	0	-1	0	0	0	0	Very Low

Factor	Virus	Quantity and Type of Evidence	Findings	Starting Grade	Decrease Grade					Increase Grade			GRADE of Evidence for Outcome
					Overall Quality	Consistency	Directness	Precision	Publication Bias	Large Magnitude	Dose Response	Associated Despite Confounders	
High-risk Sex Partners: IDUs	HBV	4 OBS[116,117,121,124]	In a multivariate analysis in the general population, having a sex partner IDU was significantly associated with HBV.[116] In another general population study, recent sex *or* household contact with an IDU was associated with recent HBV infection.[117] In univariate analysis it was significantly associated with HBV in one special population study[124] but in not another.[121]	Low	0	-1	0	0	0	0	0	0	Very Low
	HCV	4 OBS[104,105,113,116]	A univariate investigation of blood donors,[105] a multivariate investigation of blood donors,[104] a univariate investigation of people in the general population,[113] and a multivariate investigation in a general population[116] all found a significant relationship between HCV and having sex with an IDU. In all four studies the effect size was large.	Low	0	0	0	0	0	1	0	0	Moderate
	HIV	No Studies Identified	-	-	-	-	-	-	-	-	-	-	NA
High-risk Sex Partners: Sex Worker	HBV	1 OBS[121]	Sex with a sex worker was not associated with HBV in a special population study.[121]	Low	0	-1	-1	-1	0	0	0	0	Very Low
	HCV	3 OBS[105,112,113]	Sex with a sex worker was associated with HCV in a multivariate analysis of blood donors[105] and in two univariate analyses of general populations.[112,113] However, one of those general population studies also performed a multivariate analyses and did not detect a relationship.[112]	Low	0	-1	0	0	0	0	0	0	Very Low

Factor	Virus	Quantity and Type of Evidence	Findings	Starting Grade	Decrease Grade					Increase Grade			GRADE of Evidence for Outcome
					Overall Quality	Consistency	Directness	Precision	Publication Bias	Large Magnitude	Dose Response	Associated Despite Confounders	
	HIV	No Studies Identified	-	-	-	-	-	-	-	-	-	-	NA
High-risk Sex Partners: People with Known Infection	HBV	2 OBS[124,126]	Of the two univariate analyses of special population studies, one study found a significant relationship between having a sexual partner with hepatitis and having HBV,[124] while the other did not.[126]	Low	-1	-1	-1	-1	0	0	0	0	Very Low
	HCV	2 OBS[104,105]	Two studies of blood donors, one with a multivariate analysis[105] and one with a univariate analysis,[104] found significant associations between having a sex partner with hepatitis and having HCV.	Low	0	0	0	0	0	0	0	0	Low
	HIV	1 OBS[109]	On general population study performed a univariate analysis and found that the relationship between having a sex partner with HIV and having HIV was significant and large.[109]	Low		-1	0	0	0	1	0	0	Low
Incarceration	HBV	4 OBS[103,117,121,124]	The tissue donor study based upon next-of-kin interview did not associate HBV with a history of incarceration.[103] Upon univariate analyses, one general population study[117] and two special population studies did find a significant association.[121,124] However, the general population study also performed a multivariate analysis and did not find an association.[117]	Low	0	-1	0	0	0	0	0	0	Very Low

Factor	Virus	Quantity and Type of Evidence	Findings	Starting Grade	Decrease Grade					Increase Grade			GRADE of Evidence for Outcome
					Overall Quality	Consistency	Directness	Precision	Publication Bias	Large Magnitude	Dose Response	Associated Despite Confounders	
	HCV	4 OBS[103-106,113]	The tissue donor study based upon next-of-kin interview did not associate HCV with a history of incarceration.[103] Three blood donor studies[104-106] found an association between HCV and history of incarceration, and of the two that performed multivariate analysis,[105,106] one found it was an independent risk factor.[105] Having ever been arrested was associated with HCV in the general population study.[113]	Low	0	0	0	0	0	0	0	0	Low
	HIV	1 OBS[103]	The tissue donor study based upon next-of-kin interview did not associate HIV with a history of incarceration.[103]	Low	-1	-1	0	-1	0	0	0	0	Very Low
Additional Potential Risk Factors Identified in the 2009 Literature Search													
Sex with Multiple Partners	HBV	5 OBS [29,116,117,124,125]	Various definitions of having multiple partners were associated with HBV in three general population studies[29,116,117] and two special population studies.[124,125] In all but one of these studies[124] multivariate analyses were performed.	Low	0	0	0	0	0	0	1	0	Moderate

Factor	Virus	Quantity and Type of Evidence	Findings	Starting Grade	Decrease Grade					Increase Grade			GRADE of Evidence for Outcome
					Overall Quality	Consistency	Directness	Precision	Publication Bias	Large Magnitude	Dose Response	Associated Despite Confounders	
	HCV	6 OBS [30,104,105,113,114,116]	As was the case for HBV, the studies testing the association of this factor with HCV defined "multiple" using different thresholds. A blood donor study found that having multiple partners was a risk factor for HCV among women but not men in a multivariate analysis.[105] The remaining 5 studies are all general population studies that performed univariate analyses and found associations between having multiple sex partners and having HCV.[30,104,113,114,116]	Low	0	0	0	0	0	0	1	0	Moderate
	HIV	3 OBS[101,109,110]	All 3 studies performed univariate analyses on general populations using different definitions for "multiple" partners. The study with the highest threshold for defining "multiple" (>50) found an association with HIV,[101] while the other two studies (one investigating having at least 10 lifetime[109] partners and other investigating having "multiple" partners in the past year) did not.[110]	Low	0	-1	0	0	0	0	1	0	Low
Same-Sex Partners, Not Restricted to MSM	HBV	No studies	-	-	-	-	-	-	-	-	-	-	NA
	HCV	2 OBS[105,113]	One blood donor study found a significant association between women who have sex with women and HCV infection, but in multivariate analysis this was only significant if the woman had had 2 or more same-sex partners. One general population study did not find an association between same-sex partners, not limited to MSM, in a univariate analysis.[113]	Low	0	-1	0	-1	0	0	0	0	Very Low

Factor	Virus	Quantity and Type of Evidence	Findings	Starting Grade	Decrease Grade					Increase Grade			GRADE of Evidence for Outcome
					Overall Quality	Consistency	Directness	Precision	Publication Bias	Large Magnitude	Dose Response	Associated Despite Confounders	
	HIV	1 OBS[109]	One general population study did detect an association between HIV and having a same-sex sex partner in a univariate analysis.[109]	Low	0	-1	0	0	0	1	0	0	Low
Age at First Sexual Intercourse	HBV	2 OBS[29,124]	Age of 18 years or younger was not associated with HBV in general population multivariate analysis.[29] Age at first intercourse of 15 years or younger was associated with HBV infection in a special population univariate analysis.[124]	Low	0	-1	0	0	0	0	1	0	Low
	HCV	1 OBS[30]	In the general population, age of 17 years or younger was associated with HCV in a univariate analysis.[30] In that study, the size of effect was larger for people who were younger than 11 or 12-15 than for those 16-17 years old.	Low	0	-1	0	0	0	0	1	0	Low
	HIV	1 OBS[101]	Age of 18 years or younger was associated with HIV in a univariate analysis of a general population.[101]	Low	0	-1	0	0	0	1	0	0	Low
Non-injection Illicit Drugs	HBV	5 OBS [29,103,121,124,125]	HBV was not associated with illicit non-injection drugs in the tissue donor study[103] or two special population studies.[121,125] A multivariate general population analysis[29] and univariate special population analysis[124] did find associations.	Low	0	-1	0	0	0	0	0	0	Very Low

Factor	Virus	Quantity and Type of Evidence	Findings	Starting Grade	Decrease Grade					Increase Grade			GRADE of Evidence for Outcome
					Overall Quality	Consistency	Directness	Precision	Publication Bias	Large Magnitude	Dose Response	Associated Despite Confounders	
	HCV	8 OBS[30,103-106,112-114]	The tissue donor study did not find an association between HCV and drug use as reported by next of kin.[103] Three blood donor studies did associate HCV with noninjection drug use,[104-106] including in multivariate analyses in two of them.[105,106] In a general population univariate analyses, use of snorting or inhaling nonprescription drugs,[113] inhaling cocaine,[114] using intranasal cocaine,[112] and use of non-injection drugs other than marijuana[30] were all associated with HCV. Two of these studies performed multivariate analyses,[30,112] and one did not find the factor to be an independent predictor of HCV.[112]	Low	0	0	0	0	0	0	0	0	Low
	HIV	2 OBS[101,115]	HIV was associated with ever using cocaine or street drugs in a univariate analysis[101] and in a multivariate analysis[115] among members of the general population.	Low	0	0	0	0	0	0	0	0	Low
Alcohol	HBV	2 OBS[103,125]	HBV was not associated with alcohol use in a univariate analysis of tissue donors[103] or alcohol use disorder in a multivariate analysis of a special population.[125]	Low	0	0	0	-1	0	0	0	0	Very Low
	HCV	5 OBS[102,103,112-114]	HCV was associated with “heavy” alcohol use in heart donors[102] and with having at least two units of alcohol per day in a general population.[112] HCV was not associated with alcohol use among tissue donors[103] or having at least 5 alcoholic drinks weekly[113] or alcoholism[114] in general populations. All of these analyses were univariate.	Low	0	-1	0	0	0	0	0	0	Very Low

Factor	Virus	Quantity and Type of Evidence	Findings	Starting Grade	Decrease Grade					Increase Grade			GRADE of Evidence for Outcome
					Overall Quality	Consistency	Directness	Precision	Publication Bias	Large Magnitude	Dose Response	Associated Despite Confounders	
	HIV	2 OBS[103,114]	HIV was associated with having an alcohol and/or (unspecified) drug problem in a general population[114], but not with alcohol use among potential tissue donors.[103] Both of these analyses were univariate.	Low	0	-1	0	-1	0	0	0	0	Very Low
Tobacco	HBV	1 OBS[103]	No association was found between cigarette smoking and HBV among tissue donors.[103]	Low	-1	-1	0	-1	0	0	0	0	Very Low
	HCV	2 OBS[102,103]	A history of tobacco use was associated with HCV in heart donors,[102] and cigarette smoking was associated with HCV in tissue donors.[103] Both of these associations were made using univariate analyses.	Low	-1	0	0	0	0	0	0	0	Very Low
	HIV	1 OBS[103]	No association was found between cigarette smoking and HIV among tissue donors.[103]	Low	-1	-1	0	-1	0	0	0	0	Very Low
Tattoos and Piercing	HBV	5 OBS [103,117,121,124,126]	Tattoos, piercing, and acupuncture (as collectively analyzed as one outcome and reported by next-of-kin) were not associated with HBV in tissue donors.[103] Tattoos were not associated with HBV in one general population study[117] or three special population studies.[121,124,126] Piercings were not associated with HBV in one general population study[117] or two special population studies.[121,124] All analyses were univariate.	Low	0	0	0	0	0	0	0	0	Low

Factor	Virus	Quantity and Type of Evidence	Findings	Starting Grade	Decrease Grade					Increase Grade			GRADE of Evidence for Outcome
					Overall Quality	Consistency	Directness	Precision	Publication Bias	Large Magnitude	Dose Response	Associated Despite Confounders	
	HCV	7 OBS[103-106,112-114]	Tattoos, piercing, and acupuncture (as collectively analyzed as one outcome and reported by next-of-kin) were not associated with HBV in tissue donors.[103] 3 blood donor studies[104-106] and three general population studies[112-114] detected significant associations between tattoos and HCV. Three performed multivariate analyses, and one found that tattoos were not an independent predictor[106] while the other two did.[105,112] Of 3 blood donor studies, HCV was associated with ear piercing among men in one study[106] and pierced ears or body parts in another[105]in multivariate analyses, but not recent body piercing in a third with univariate analysis.[104] In univariate analyses of general populations, HCV was not associated with body piercing in two studies[112,114] but was associated with ear piercing in a third study.[113]	Low	0	0	0	0	0	0	0	0	Low
	HIV	1 OBS[103]	Tattoos, piercing, and acupuncture (as collectively analyzed as one outcome and reported by next-of-kin) were not associated with HBV in tissue donors.[103]	Low	-1	-1	0	-1	0	0	0	0	Very Low

Factor	Virus	Quantity and Type of Evidence	Findings	Starting Grade	Decrease Grade					Increase Grade			GRADE of Evidence for Outcome
					Overall Quality	Consistency	Directness	Precision	Publication Bias	Large Magnitude	Dose Response	Associated Despite Confounders	
International Travel	HBV	2 OBS[103,117]	International travel was not associated with HBV among tissue donors[103] or with recent HBV infection in a general population.[117]	Low	0	0	0	-1	0	0	0	0	Very Low
	HCV	3 OBS[103-105]	International travel was not associated with HCV among tissue donors.[103] In blood donors neither recent travel outside the U.S.[104] nor ever having lived outside the U.S.[105] was associated with HCV.	Low	0	0	0	0	0	0	0	0	Low
	HIV	1 OBS[103]	International travel was not associated with HIV among tissue donors.[103]	Low	-1	-1	0	-1	0	0	0	0	Very Low

Table 37. Prevalence of Behavioral Risk Factors

Category	Risk Factor	Citation	Year	Prevalence	N = in population	Population
Potential and Actual Organ Donors						
Drug Abuse	Unspecified ongoing substance abuse	Hidalgo et al.[8]	2001	5.5%	55	Parental potential living donors to their children
Alcohol	Heavy alcohol use	Gasink et al.[102]	2006	20%	10,915	Actual organ (heart) donors
Tobacco	History of tobacco use	Gasink et al.[102]	2006	36%	10,915	Actual organ (heart) donors
General Population						
Men who have Sex with Men	Male-to-male sex	McQuillan et al.[101]	2006	3.7%	2,439 men	General population
	Men who have sex with men, history of	Nguyen et al.[110]	2008	9.3%	590 men	General population in N.Y.C.
Injection Drug Use	Ever used a needle for drugs	Nguyen et al.[110]	2008	1.4%	1,505	General population in N.Y.C.
	Lifetime injection drug use (participants aged 20-59)	Armstrong et al.[30]	2006	1.7%	5,368	General population, nationwide
	Injection drug use	Mehta et al.[109]	2008	7.9%	16,696	Patients in urban medical care center
	Injection drug use	Kaur et al.[116]	1996	3.5%	7,538	Volunteers from general population, mainly urban
	No use of needle exchange program among injection drug users	Mehta et al.[109]	2008	63.2%	1,258	Patients in medical care center
Sex Work	Exchanged sex for money or drugs	Mehta et al.[109]	2008	2.3%	16,696	Patients in an urban medical care center

Category	Risk Factor	Citation	Year	Prevalence	N = in population	Population
High-risk Sex Partners	Sexual partner with HIV	Mehta et al.[109]	2008	3.6%	16,696	Patients in urban medical care center
	Sex with IV drug user	Kaur et al.[116]	1996	5%	6,562	Volunteers from general population, mainly urban
	Sex with a commercial sex worker	Mehta et al.[109]	2008	7.4%	16,696	Patients in an urban medical care center
Additional Sex Practices	Sex with same or both genders (asked both men and women)	Mehta et al.[109]	2008	8.2%	15,586	Patients in urban medical care center
	Lifetime number of sexual partners 10+ (participants aged 18-59)	Armstrong et al.[30]	2006	29%	5,357	General population, nationwide
	Lifetime number of sexual partners 2+	McQuillan et al.[101]	2006	74%	5,391	General population, nationwide
	Lifetime number of sexual partners 2-49	Nguyen et al.[110]	2008	74%	1,469	General population in N.Y.C.
	Lifetime number of sexual partners 50+	McQuillan et al.[101]	2006	3.5%	5,391	General population, nationwide
	Lifetime number of sexual partners 50+	Nguyen et al.[110]	2008	6.6%	1,469	General population in N.Y.C.
	Sex with multiple partners	Kaur et al.[116]	1996	26%	7,325	Volunteers from general population, mainly urban
	Sex with multiple partners during previous year	Nguyen et al.[110]	2008	22%	1,368	General population in N.Y.C.
	Age at first intercourse younger than 18 years (participants aged 18-59)	Armstrong et al.[30]	2006	58%	5,054	General population, nationwide

Category	Risk Factor	Citation	Year	Prevalence	N = in population	Population
	Age at first intercourse younger than 18 years	McQuillan et al.[101]	2006	59%	5,373	General population, nationwide
Noninjection Substance Abuse	Lifetime drug use other than marijuana (participants aged 20-59)	Armstrong et al.[30]	2006	17%	5,683	General population, nationwide
	Ever used cocaine/ street drugs	McQuillan et al.[101]	2006	21%	4,969	General population, nationwide
	Ever used drugs, any	Nguyen et al.[110]	2008	18%	1,505	General population in N.Y.C.

Table 38. GRADE Table for Question 3: Prevalence of Behavioral Risk Factors

Factor	Quantity and Type of Evidence	Findings	Starting Grade	Decrease GRADE					Increase GRADE			GRADE of Evidence for Outcome
				Study Quality	Consistency	Directness	Precision	Publication Bias	Large Magnitude	Dose-response	Associated Despite Confounders	
Men who have sex with men	2 OBS*[101,110]	In two general population studies, one reported that 3.7% of men have sex with another man,[101] while the other reported that 9.3% have a history of having sex with another man.[128]	High	0	-1	-1	0	0	0	0	0	Low
Injection drug abuse	4 OBS[30,109,110,116]	All four studies assessed general populations. Reported prevalences of injection drug use were 1.4%,[110] 1.7%,[30] 3.5%,[116] and 7.9%.[109] The lower two estimates were derived from NHANES data, and the higher two were drawn from patients and volunteers in urban areas. (Of the injection drug users in one study, 63.2% reported they did not use needle exchange programs.[109])	High	0	-1	-1	0	0	0	0	0	Low
Sex Work	1 OBS[109]	One general population study reported 2.3% of participants reported exchanging sex for money or drugs.[109]	High	0	-1	-1	0	0	0	0	0	Low
High-Risk Sex Partners: Injection drug user	1 OBS[116]	Among general population volunteers from a mainly urban area, 5% reported having sex with an injection drug use.[116]	High	0	-1	-1	0	0	0	0	0	Low

Factor	Quantity and Type of Evidence	Findings	Starting Grade	Decrease GRADE					Increase GRADE			GRADE of Evidence for Outcome
				Study Quality	Consistency	Directness	Precision	Publication Bias	Large Magnitude	Dose-response	Associated Despite Confounders	
High-Risk Sex Partners: Sex workers	1 OBS[109]	In the same population, 7.4% reported sex with a commercial sex worker.[109]	High	0	-1	-1	0	0	0	0	0	Low
Multiple Sex Partners: Multiple undefined	2 OBS[110,116]	26% of volunteers in one study reported having sex with multiple partners,[116] while 22% of NHANES participants reported having multiple sex partners during the previous year.[110]	High	0	0	-1	0	0	0	0	0	Moderate
Multiple Sex Partners: At least 2 partners	2 OBS[101,129]	74% reported having sex with at least two partners,[101] 74% reported having sex with 2-49 partners.[110]	High	0	0	-1	0	0	0	0	0	Moderate
Multiple Sex Partners: At least 50 partners	2 OBS[101,110]	In one study, 3.5% reported having at least 50 sex partners,[101] while in another 6.6% did.[110]	High	0	-1	-1	0	0	0	0	0	Low
Age at first intercourse (<18 years)	2 OBS[30,101]	The proportion of adults who reported having sex at age 18 or younger were 58%[30] and 59%[101] in two general population studies.	High	0	0	-1	0	0	0	0	0	Moderate
Same-sex partner (not restricted to men)	1 OBS[109]	8.2% of men and women reported having sex with same or both genders.[109]	High	0	-1	-1	0	0	0	0	0	Low
Noninjection substance abuse: Ongoing	1 OBS[8]	Among potential living donors, 5.5% had unspecified ongoing drug abuse.[8]	High	0	-1	0	-1	0	0	0	0	Low

Factor	Quantity and Type of Evidence	Findings	Starting Grade	Decrease GRADE					Increase GRADE			GRADE of Evidence for Outcome
				Study Quality	Consistency	Directness	Precision	Publication Bias	Large Magnitude	Dose-response	Associated Despite Confounders	
Noninjection substance abuse: Lifetime	3 OBS[30,101,110]	In the general population, 17% reported lifetime use of drugs other than marijuana,[30] 18% reported ever having used any drugs,[110] and 21% reported ever using street drugs/cocaine.[101]	High	0	0	-1	0	0	0	0	0	Moderate
Alcohol	1 OBS[102]	Among heart donors, 20% reportedly drank alcohol heavily.[102]	High	-1	-1	0	0	0	0	0	0	Low
Tobacco	1 OBS[102]	Among heart donors, 36% reportedly used tobacco.[102]	High	-1	-1	0	0	0	0	0	0	Low

*Observational study

Question 4: Results

In this section, data on nonbehavioral potential risk factors including signs and symptoms indicative of infection, potential exposure, co-morbidities, and demographic factors are presented. Information regarding exclusionary factors listed in the 1994 guideline is presented first, and then information regarding additional factors for which at least two studies provided evidence regarding the same factor is presented. All of the data related to the identification of risk factors is provided in Table 39 (HBV), Table 40 (HCV), Table 41 (HIV), and Table 42 (GRADE tables). Prevalence information is provided in Table 43.

Exclusionary Criteria from 1994 Guideline

People with Hemophilia or Related Clotting Disorder who Received Clotting Factor Blood Products

The 1994 guideline excludes from donating "Persons with hemophilia or related clotting disorders who have received human-derived clotting factor concentrates." We identified zero studies that studied whether this factor was associated with an increased prevalence of infection. This may be due to the relative rarity of having hemophilia or a related blood clotting disorder in the populations included in the evidence base for these questions. However, we did identify a large number of studies that considered the association between blood transfusions and infection regardless of any underlying disease. For more information, see *Receipt of Blood Transfusion* under *Risk Factors Identified in the 2009 Literature Search.*

Exposure to Infected or Suspected Blood

The 1994 guideline excludes from donating "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."

Only one of the studies specifically inquired as to whether patients had been exposed to blood known or suspected to be infected. Among embalmers, Turner et al. did not find an association between needlestick injury with exposure to recognized HBV infection during embalming and HBV infection.[127]

GRADE Summary: This evidence is rated as "very low" because of indirectness, imprecision, and lack of consistency.

Many of the studies did, however, ask about exposure to blood in general, including by needlestick injuries and in other accidents. See *Nonspecific exposure* below for information on these factors.

Children

The nonbehavioral exclusion criteria for children are the same as listed in Question 3. We did not identify any information regarding the two (above) nonbehavioral exclusion criteria in children or in children of mothers with such factors, or any other clinical factors.

Additional Potential Risk Factors Identified in the 2009 Literature Search

In addition to the factors identified in the 1994 guideline, we extracted data on all other reported risk factors identified in the literature. The following sections describe the evidence regarding the various factors and infection reported by at least two studies.

Signs and Symptoms

An objective of this section was to identify nonbehavioral factors that could be predictive of infection, especially acute infection during the window period before diagnostic tests could recognize the infection. However, extremely little data on such signs and symptoms were identified.

The only signs identified were associated with HCV infection. In blood donors, alanine aminotransferase (ALT) reactivity was associated with infection by Orton et al.[104] In a general young adult population (aged 18 to 49), serum ALT of >40 U/L was associated with HCV by Armstrong et al.[30] "Elevated liver enzyme" was associated with HCV in adults comprising individuals at risk for HCV, and healthcare workers enrolled in a health maintenance organization (HMO) in Fischer et al.[114] In addition, jaundice was associated with HCV in adults in a general medical clinic by Nguyen et al.[113]

GRADE Summary: Although several signs were reported, they are all different and therefore must be considered in isolation. The association of HCV with jaundice, ALT reactivity, and elevated ALA were large effect sizes and therefore rated as low. The effect size for "elevated liver enzyme" was not large, and therefore rated as very low.

Prevalence: In a general population, 9% of survey respondents had ALT >40 U/L.[30]

GRADE Summary of Prevalence: The prevalence estimate was rated as low due to indirectness and lack of proof of consistency.

Receipt of Blood Transfusion

Although no studies reported on risk in people with clotting disorders or who have received clotting factor blood products, many did investigate risk of infection associated with blood transfusion. Two of three studies associated blood transfusion with HBV, and all eight studies associated it with HCV.

HBV: Blood transfusion was associated with HBV infection in a general population in Kaur et al.,[116] as was blood transfusion before 1991 among college students in Hwang et al.[124] Blood transfusion was not associated with HBV in the low prevalence obstetric patients study by Butterfield et al. (1990).[126]

HCV: All 8 studies that looked at this factor did find some association with transfusion and HCV infection. Receiving a blood transfusion was independently associated with HCV in three studies of blood donors, Conry-Cantilena et al.,[106] Murphy et al. (2000),[105] and Murphy et al. (1996).[107] In Murphy et al. (2000), the association was only significant among donors who had never injected drugs.[105]

In three studies of the general population, blood transfusion was associated with HCV by Nguyen et al.,[113] Hand and Vasquez,[112] and Kaur et al.,[116], and in the two studies that calculated multivariable models,[112,116] the association was independent. In the general population, Armstrong et al. found that the relationship between HCV and blood transfusion before 1992 was independent,[30] and Fischer et al. detected an association but did not test whether the risk factor was independent.[114] Sex with a blood transfusion recipient was also associated with HCV infection in Murphy et al. (2000).[105]

Some studies combined having received a blood transfusion with other outcomes. Being a blood transfusion recipient *or donor* (data not reported separately) as reported by next-of-kin was not associated with an increased risk of HBV, HCV, or HIV among potential tissue donors by Sanchez et al.[103] Either receiving a blood transfusion *or* having a household contact with a person who had was not associated with acute HBV by Alter et al.[117] We did not consider these outcomes sufficiently similar to group with receipt of blood transfusion only.

GRADE Summary: The evidence for HBV was mostly indirect, and downgraded to very low rating accordingly. For HCV, the evidence consistently pointed to an association with transfusion with large magnitude, and was rated as moderate.

Prevalence: Among general population survey respondents, 6% of those aged 20 to 59 years (in 2006) reported having a blood transfusion before 1992, and 16% of those aged at least 60 years did.[30] Among volunteers from an urban area, 20% reported having ever had a blood transfusion.[116]

GRADE Summary of Prevalence: The evidence of these prevalence estimates were rated as low due to indirectness and lack of proof of consistency.

Nonspecific Exposure

Although only one study asked participants whether they had ever been exposed to infected or potentially infected blood, many studies asked about exposure to blood without regard to any knowledge about the infection status of the blood. Besides hemodialysis, most of these factors were not found to be consistently associated with infection.

Accidental Needle Stick

According to data collected from next-of-kin, accidental needle sticks were not associated with HBV, HCV, or HIV among potential tissue donors in Sanchez et al.[103]

In a general population study by Kaur et al., needlestick injuries were actually associated with lower prevalence of HBV and HCV infection.[116] This may be because a substantial proportion of the enrollees were healthcare workers, and in that study healthcare workers had a lower prevalence of HBV than the group as a whole. Needlestick injuries among healthcare worker blood donors in Conry-Cantilena et al. were not associated with HCV either.[106] However, "bloody" needlestick injuries in a medical setting was associated with an increased prevalence of HCV in Murphy et al. (2000).[105]

GRADE Summary: For all three viruses this evidence was rated as "very low." For HBV this was due to lack of precision, for HCV it was due to inconsistency, and for HIV it was due to low quality, imprecision, and lack of consistency.

Hemodialysis

Most studies found an association between hemodialysis and HBV or HCV. Hemodialysis was associated with HBV among volunteers from the general population by Kaur et al.[116] and among college students by Hwang et al.[124] In studies that enrolled people from the general population, HCV infection was associated with hemodialysis in Kaur et al.,[116] and with "kidney dialysis" in Nguyen et al,[113] but not with hemodialysis in Hand and Vasquez.[112] The duration of administration of dialysis was not specified.

GRADE Summary: The evidence associating HBV with hemodialysis was rated as "moderate" because the size of the association in the special population was large. For HCV, strength of evidence was low.

Surgery

The relationship between surgery and infection was inconsistent. Based upon next-of-kin data for potential tissue donors, Sanchez et al. did not find any associations between HBV, HCV, or HIV and surgeries.[103] In the general population, surgery was associated with a lower HBV prevalence by Kaur et al.,[116] and surgery during the last six months was not associated with acute HBV in Alter et al.[117] Having surgery or a medical procedure in the six months before blood donation was not associated with HCV in Orton et al.,[104] and having a history of surgery was not associated with HCV in general population studies by Fischer et al.[114] or Kaur et al.[116] However, lifetime history of surgery or sutures was associated with elevated HCV prevalence in blood donors in Murphy et al. (2000).[105]

GRADE Summary: For all three viruses, the evidence was inconsistent and rated as "very low." For HIV the evidence base was also of very low quality and imprecise.

Organ and Corneal Transplantation Recipients

No organ transplantation studies were identified that met the inclusion critiera. Receipt of corneal transplantation was not associated with a greater risk of HBV, HCV, or HIV in the tissue donor study by Sanchez et al.[103], or with HBV among psychiatric inpatient veterans in the study by Tabibian et al.[121]

GRADE Summary: For all three viruses, the evidence was rated as very low due to imprecision. For HCV and HIV the evidence was also of very low quality with no proof of consistency.

Acupuncture

Acupuncture during the last six months was not associated with an increased incidence of acute HBV in Alter et al.[117] or increased prevalence of HBV among psychiatric inpatient veterans in Tabibian et al.,[121] or with HCV among blood donors in Conry-Cantilena et al.[106] or Murphy et al.,[107] or people in a general population in Hand and Vasquez et al.[112]

GRADE Summary: For both HBV and HCV, the GRADE was not decreased and the evidence was rated as low.

Dental Work

Dental work within the last six months was not associated with acute HBV in Alter et al.[117] Dental work was not associated with HCV among blood donors in Murphy et al.[105]; nor was having dental work in the six months before donation in Orton et al.[104]

GRADE Summary: For HBV, the evidence was downgraded due to imprecision and rated as very low. For HCV, the evidence was not downgraded and was rated as low.

Blood Draws

Blood draws should not expose patients to blood (and is probably a proxy for other risk factors). Sanchez et al. did not find an association between HIV testing and HIV, HBV, or HCV among tissue donors, based upon next-of-kin interviews.[103] However, Nguyen et al. (2005) did find an association between having had a blood test for HBV and having an HCV infection in a univariate analysis of adults in the general population.[113] Similarly, being a blood donor should not pose a direct infectious risk. In the

same study, Nguyen et al. found that being a blood donor was associated with reduced risk of HCV, and that having been rejected as a blood donor was associated with an increased risk of HCV.[113]

GRADE Summary: Because evidence was imprecise for each of the viruses and also inconsistent for HBV and HIV, the evidence regarding blood draws was rated as "very low."

Other Blood Exposure

Neither bloody object contact in Tabibian et al.[121] nor combat exposure in Butterfield et al. (2004)[125] were associated HBV among psychiatric inpatient veterans. Having been "stuck" or "cut" with a blood object was independently associated with HCV among blood donors in Murphy et al. (2000)[107] Among blood donors in Orton et al.[104] blood exposure during fighting, by biting, at an accident site, or during a manicure in the last six months was associated with HCV, but not during a haircut in the last six months. Contact with blood was not associated with HCV in members of a general population study by Hand and Vasquez.[112]

We report these factors here because of their relevance but did not rate the GRADE for these "other" outcomes due to lack of replication of the various factors.

Household Exposure

Whether hepatitis infection among other household members was a risk factor for exposure was investigated in several studies, with inconsistent findings. Having household contact with someone with hepatitis was associated with HBV among college students in Hwang et al.[124], as was a family history of HBV among Asian Americans in Lin et al.[123] Having a household member with hepatitis was not associated with HBV in an obstetric population in Butterfield et al.;[126] nor was being the wife of a man with HBV among Korean American church goers in Hann et al.[122] Among blood donors in Murphy et al., living with someone with hepatitis or having a relative with hepatitis was not associated with HCV infection, but living with a transfusion recipient was.[105] In general population studies, having at least one family member treated for viral hepatitis was not associated with an increased risk of HCV in Fischer et al.,[114] but having at least one family member with HCV was in Nguyen et al.[113]

Sharing a razor or toothbrush with another household member was not associated with HBV members of the general population in Alter et al.[117] However, sharing a toothbrush or razor with person(s) unspecified was associated with HCV among blood donors in Murphy et al.[105]

GRADE Summary: All of the evidence pertaining to household exposure and HBV and HCV infection was inconsistent, and therefore rated as very low. For HBV the evidence was also indirect: all of it came from special population studies.

Other Infections

Sexually transmitted infections were nearly universally associated with increased risk of HBV, HCV, or HIV. HBV surface antigen positivity was associated with HCV infection among heart donors in Gasink et al.[102] Among college students, HBV infection was associated with having had a sexually transmitted disease (STD) in Hwang et al.[124] Among blood donors, HCV was significantly associated with history of STD in Conry-Cantilena et al.[106] and Murphy et al. (2000),[105] and with having a STD within six months of donating in Orton et al.,[104] and with seropositivity for other reactive infectious diseases in Orton et al.[104] and Murphy et al. (1992).[107] Among people from general populations, having past treatment for

STDs was not associated with HCV in Nguyen et al.,[113] but having herpes simplex virus (HSV) infection was in Armstrong et al.[30] HIV infection was not associated with HCV infection upon univariate analysis of a general population in Hand and Vasquez.[112] Diagnosis of STD in Mehta et al.,[109] HSV-2 in McQuillan et al. (2006),[101] HSV-2 in Nguyen et al.,[110] and syphilis or other infection not apparently related to HIV in Alpert et al.,[115] were all associated with HIV in general populations. Rabies exposure was not associated with any of the viruses in the tissue donor study by Sanchez et al.[103]

GRADE Summary: For HBV and HIV, the evidence associating them with another infection was rated as low. For HCV the evidence was rated as very low due to inconsistency.

Prevalence: Antibodies to HSV-2 were detected in 19% of general nationwide population aged 18 to 49 years,[30] and 28% of New Yorkers.[110] STD diagnoses were reported by 18% of patients in an urban medical care center.[109]

GRADE Summary of Prevalence: The estimate of HSV-2 infection was rated as moderate due to indirectness. For unspecified STD it was rated as low due to indirectness and lack of proof of consistency.

Demographic Factors

Sex

Male sex was not consistently associated with an increased risk of infection. Males had higher rates of HBV than women in studies that considered the general population,[116] psychiatric inpatient veterans (of whom nearly all were male),[121] and Asian Americans,[123] but not Korean American church goers.[120] Among college students[124] females had higher rates of HBV, and among children who had received a blood transfusion, in Luban et al., rates were not significantly different.[118] Among heart transplant donors, being male was associated with an increased risk of HCV.[102] In one study of blood donors, being male was associated with an increased risk of HCV,[107] but among two others it was not.[104,106] In four general population studies, significantly higher proportions of males had HCV infection in four[30,108,113,116] out of five studies.[114] Male sex was not associated with HIV in three general population studies.[109-111]

GRADE Summary: For HBV and HCV, the evidence was rated as very low due to inconsistent findings. For HBV, the evidence was also indirect because it was drawn primarily from special population studies. For HIV, the evidence was rated as low because lack of association was consistently found.

Age

Studies assessed the relationship between age and infection in a variety of different ways. While some used mean age, others used various cutoffs (such as older or younger than 30 years) or categorization (such as age by decade). Older age was associated with a greater rate of HCV among heart transplant donors in Gasink et al.,[102] but inconsistently associated with HCV among blood donors, HCV or HIV in the general population, or HBV in special subpopulations.

GRADE Summary: Evidence on age was collected using inconsistent methods among studies, clouding any potential relationship between age and infection. For HBV the evidence was inconsistent and came primarily from special population studies, and was therefore rated as "very low." The evidence for HCV and HIV was also inconsistent and rated as very low.

Race or Ethnicity, and National Origin

HBV: Higher HBV prevalence in the general population was associated with non-Hispanic Black ethnicity compared with non-Hispanic White ethnicity in McQuillan et al.[29] In the same study, being Mexican-American was associated with no increase in prevalence compared with being non-Hispanic white. In another general population study, the prevalence of HBV was lower among white and Hispanic individuals than other races.[116] The rest of the studies examined subpopulations. Prevalence was higher for African Americans compared to white people among psychiatric inpatient veterans in Butterfield et al.[125] and among college students in Hwang et al.,[124] but not among inpatient veterans in Tabibian et al.[121] Hispanic or Latino ethnicity was not associated with HBV among psychiatric inpatient veterans in Tabibian et al.[121] or college students in Hwang et al.[124]Among college students in Hwang et al., Asian students had higher rates of HBV.[124]

HBV was associated with birth in a Southeast Asian or African country in a general population study by Kaur et al.[116] but not in a study of Asian Americans by Lin et al.[123] Acute HBV was not associated with birth in an area with a high endemic rate of HBV or having a household contact with someone who was born in an endemic area in Alter et al.[117] Among Asian Americans, being born in the U.S. was found to be protective in children in Hann et al.[122] and in Asian Americans of any age in Lin et al.[123] Any international birth was associated with increased prevalence of HBV in McQuillan et al.[29]

HCV: Among heart donors in Gasink et al., ethnicity was not associated with HCV.[102] Among blood donors, two studies associated increased prevalence with "black" race[106,107], and two studies found inconsistent relationships between Hispanic ethnicity and HCV.[104,107] However, black or Hispanic ethnicity was not associated with infection in general population studies,[30,108,113] Orton et al.[104] found that being born in a country other than the U.S. was associated with HCV among blood donors, but Murphy et al.[107] did not. McGinn et al. found an association between preferring to speak English or Spanish and HCV.[108]

HIV: HIV was not associated with Asian[109,110] or Hispanic ethnicity[110,111] but was associated with Black ethnicity in two[109,110] of three[111] studies. Being a Spanish speaker was not associated with prevalence of HIV among public emergency room patients in Zetola et al.[111]

GRADE Summary: All of the evidence regarding race or ethnicity was rated as very low. For HBV this was because most of the data came from special subpopulation studies and because some information was inconsistent. For HCV and HIV, most studies found no relationship between race or ethnicity and infection, but there were some inconsistencies. Very low evidence ratings for national origin/birthplace and preferred language were assigned for the same reasons.

Occupation

Unemployment was significantly associated with recent HBV infection in the general population in a multivariate analysis, in Alter et al.[117] Some of the studies investigated whether occupational exposure to blood was associated with hepatitis; however, findings were inconsistent. Being a healthcare worker with frequent blood exposure was associated with an increased prevalence of HBV in college students in Hwang et al.[124], but being a healthcare worker was not associated with HBV in a general population studies by Kaur et al.[116] or McQuillan et al.[29] or having been a healthcare worker in psychiatric inpatient veterans in Tabibian et al.[121] or a low-prevalence obstetric population in Butterfield et al.[126] Among blood donors, occupational blood exposure was associated with HCV infection in Murphy et al.,[105] but medical

or dental job or public safety job with frequent blood contact were not in Orton et al.[104] In the general population, work contact with blood was not associated with increased HCV in Fischer et al.[114], and being a healthcare worker was actually associated with a lower rate of HCV in Kaur et al.[116] Services in the armed forces was not associated with HBV in McQuillan et al.[29] or with HCV in either Fischer et al.[114] or Armstrong et al.[30] Having a job at a prison was associated with HCV in Nguyen et al.[113]

GRADE Summary: Most of the occupational information pertained to healthcare workers. Most evidence did not associate employment in healthcare with infection. For HBV this finding was consistent and rated as low. An additional study considered the association between HBV and military service and did not find a relationship and was rated very low for imprecision. For HCV associations with health care job or job with blood exposure was inconsistently related with HCV and was rated as very low due to inconsistency and imprecision. A lack of association between HCV and serving in the armed forces was found; this evidence was rated as very low due to imprecision. Findings associating HCV and working in public safety were inconsistent and therefore rated as very low.

Education

Inconsistent evidence suggests lower educational level attainment may be associated with infection. Less than a high school education was associated with a higher prevalence of HBV in the general population by McQuillan et al.[29], but total years of education was not associated with HBV among psychiatric inpatient veterans in Tabibian et al.[121] College students enrolled in 4-year colleges had lower rates of HBV than students enrolled in 2-year colleges in Hwang et al.[124] Lower educational attainment was associated with HCV in blood donors in Orton et al.[104] and Conry-Cantilena et al.[106] and in the general population in Armstrong et al.[30] However, this association was not found in the general population by McGinn et al.[108] or Nguyen et al.[113] An association between HIV and education was not detected in general population studies McQuillan et al.[101] or Mehta et al.[109]

GRADE Summary: The association between lower educational level and infection was inconsistent for HBV and HCV. For HBV the evidence was also indirect, and so it was rated as very low. For HCV, the evidence was rated as very low because there was a dose-response association. For HIV, information was consistent but imprecise and therefore rated as very low.

Economic Factors

Being homeless was not associated with an increased risk of HBV among psychiatric inpatient veterans in Tabibian et al.[121] Ever having been homeless was associated with an increased risk of HCV in adults attending general medicine or hepatology clinics in Nguyen et al.[113] and being homeless was associated with an increased prevalence of HIV in public hospital emergency room patients in Zetola et al.[111] Neither income or nor living in poverty was associated with HCV in Nguyen et al.[113] or Armstrong et al.[30] or with HIV in McQuillan et al.[101]

GRADE Summary: Economic factors were inconsistently associated with HCV and HIV, and imprecisely associated with HBV and HCV. For all three viruses, the evidence was rated as very low.

Health Insurance

Type of health insurance (Medicaid, Medicare, private, or self-pay) was significantly associated with HCV in McGinn et al., a general population study, with Medicaid patients having the highest rates of

HCV.[108] Patients with no health insurance had higher prevalence of HIV in one study of hospital patients, Mehta et al.,[109] but not in another such study, Zetola et al.[111]

GRADE Summary: The evidence relating health insurance and infection was inconsistent for HCV and HIV and imprecise for HIV and therefore rated as very low for both.

Marital Status

Being married may be associated with a lower risk of infection. Being divorced or separated was associated with a higher prevalence of HBV in McQuillan et al., a general population study, than any other status.[29] Being married was associated with a lower rate of HCV among blood donors in Murphy et al.[105] and a lower prevalence of HIV in the general population in McQuillan et al.[101] Marital status was not associated with HBV infection among psychiatric inpatient veterans in Butterfield et al.[125]

GRADE Summary: One study for each HCV and HIV found a relationship between being married and having a lower risk of infection and were rated as low. For HBV, infection was higher among divorced or single persons in a general population study. A special population study did not find any association between marital status and infection, but since it was a special population study we did not detract from the GRADE and rated it as low.

Evidence Tables for Question 4

Table 39. HBV Nonbehavioral Risk Factors

Category	Factor	Citation	Year	Percentage of Infected with Factor	Total Number Infected	Percentage of Uninfected with Factor	Total Number Uninfected	Effect Size*	p-Value**	Comparison Made	Associated in Study?	Population
Co-Morbidity												
Potential Tissue Donors												
Transfusion	Blood transfusion recipient or donor	Sanchez et al.[103]	2006	Not Reported (NR)	47	NR	56	NR	Not significant (NS)	Proportion in HBV+ vs. HBV	No	Potential tissue donors, as reported by next of kin
Nonspecific Exposure	Accidental needle stick	Sanchez et al.[103]	2006	NR	47	NR	56	NR	NS	Proportion in HBV+ vs. HBV	No	Potential tissue donors, as reported by next of kin
	History of transplant	Sanchez et al.[103]	2006	NR	47	NR	56	NR	NS	Proportion in HBV+ vs. HBV-	No	Potential tissue donors, as reported by next of kin
	Surgeries	Sanchez et al.[103]	2006	NR	47	NR	56	NR	NS	Proportion in HBV+ vs. HBV	No	Potential tissue donors, as reported by next of kin
	HIV testing	Sanchez et al.[103]	2006	NR	47	NR	56	NR	NS	Proportion in HBV+ vs. HBV	No	Potential tissue donors, as reported by next of kin

Category	Factor	Citation	Year	Percentage of Infected with Factor	Total Number Infected	Percentage of Uninfected with Factor	Total Number Uninfected	Effect Size*	p-Value**	Comparison Made	Associated in Study?	Population
Others	Liver disease	Sanchez et al.[103]	2006	NR	47	NR	56	NR	NS	Proportion in HBV+ vs. HBV	No	Potential tissue donors, as reported by next of kin
	Treatment by physician in last 2 years	Sanchez et al.[103]	2006	NR	47	NR	56	NR	NS	Proportion in HBV+ vs. HBV	No	Potential tissue donors, as reported by next of kin
	Medical hospitalizations	Sanchez et al.[103]	2006	NR	47	NR	56	NR	NS	Proportion in HBV+ vs. HBV	No	Potential tissue donors, as reported by next of kin
	Psychiatric hospitalizations	Sanchez et al.[103]	2006	NR	47	NR	56	NR	NS	Proportion in HBV+ vs. HBV	No	Potential tissue donors, as reported by next of kin
	Medical illnesses	Sanchez et al.[103]	2006	NR	47	NR	56	NR	NS	Proportion in HBV+ vs. HBV	No	Potential tissue donors, as reported by next of kin
	Medications	Sanchez et al.[103]	2006	NR	47	NR	56	NR	NS	Proportion in HBV+ vs. HBV	No	Potential tissue donors, as reported by next of kin
	Toxic exposure	Sanchez et al.[103]	2006	NR	47	NR	56	NR	NS	Proportion in HBV+ vs. HBV	No	Potential tissue donors, as reported by next of kin
	Malaria exposure or treatment	Sanchez et al.[103]	2006	NR	47	NR	56	NR	NS	Proportion in HBV+ vs. HBV	No	Potential tissue donors, as reported by next of kin

Category	Factor	Citation	Year	Percentage of Infected with Factor	Total Number Infected	Percentage of Uninfected with Factor	Total Number Uninfected	Effect Size*	p-Value**	Comparison Made	Associated in Study?	Population
	Chagas disease exposure or treatment	Sanchez et al.[103]	2006	NR	47	NR	56	NR	NS	Proportion in HBV+ vs. HBV	No	Potential tissue donors, as reported by next of kin
	Rabies exposure	Sanchez et al.[103]	2006	NR	47	NR	56	NR	NS	Proportion in HBV+ vs. HBV	No	Potential tissue donors, as reported by next of kin
	Heart disease	Sanchez et al.[103]	2006	NR	47	NR	56	NR	NS	Proportion in HBV+ vs. HBV	No	Potential tissue donors, as reported by next of kin
	Hypertension	Sanchez et al.[103]	2006	NR	47	NR	56	NR	NS	Proportion in HBV+ vs. HBV	No	Potential tissue donors, as reported by next of kin
	Kidney disease	Sanchez et al.[103]	2006	NR	47	NR	56	NR	NS	Proportion in HBV+ vs. HBV	No	Potential tissue donors, as reported by next of kin
	Gastro-intestinal disease	Sanchez et al.[103]	2006	NR	47	NR	56	NR	NS	Proportion in HBV+ vs. HBV	No	Potential tissue donors, as reported by next of kin
	Cancer history	Sanchez et al.[103]	2006	NR	47	NR	56	NR	NS	Proportion in HBV+ vs. HBV	No	Potential tissue donors, as reported by next of kin
	Diabetes history	Sanchez et al.[103]	2006	NR	47	NR	56	NR	NS	Proportion in HBV+ vs. HBV	No	Potential tissue donors, as reported by next of kin

Category	Factor	Citation	Year	Percentage of Infected with Factor	Total Number Infected	Percentage of Uninfected with Factor	Total Number Uninfected	Effect Size*	p-Value**	Comparison Made	Associated in Study?	Population
	Pulmonary disease	Sanchez et al.[103]	2006	NR	47	NR	56	NR	NS	Proportion in HBV+ vs. HBV	No	Potential tissue donors, as reported by next of kin
	Rheumatologic disease	Sanchez et al.[103]	2006	NR	47	NR	56	NR	NS	Proportion in HBV+ vs. HBV	No	Potential tissue donors, as reported by next of kin
	Connective tissue disease	Sanchez et al.[103]	2006	NR	47	NR	56	NR	NS	Proportion in HBV+ vs. HBV	No	Potential tissue donors, as reported by next of kin
	Dermatologic disease	Sanchez et al.[103]	2006	NR	47	NR	56	NR	NS	Proportion in HBV+ vs. HBV	No	Potential tissue donors, as reported by next of kin
	Neurologic disease	Sanchez et al.[103]	2006	NR	47	NR	56	NR	NS	Proportion in HBV+ vs. HBV	No	Potential tissue donors, as reported by next of kin
	Ocular disease	Sanchez et al.[103]	2006	NR	47	NR	56	NR	NS	Proportion in HBV+ vs. HBV	No	Potential tissue donors, as reported by next of kin

Category	Factor	Citation	Year	Percentage of Infected with Factor	Total Number Infected	Percentage of Uninfected with Factor	Total Number Uninfected	Effect Size*	p-Value**	Comparison Made	Associated in Study?	Population
General Population												
Transfusion	Blood transfusion	Kaur et al.[116]	1996	23%	1,432	18.2%	6,107	1.27 (1.04 to 1.57)‡	NR	Proportion in HBV+ vs. HBV-	Yes	Volunteers from general population
	Blood transfusion, history of, household contact	Alter et al.[117]	1989	5%	76	12%	152	NR	NS†	Proportion in HBV+ vs. HBV-	No	General population adults with no obvious cause of acute HBV and matched controls
Nonspecific Exposure	Needlestick injury	Kaur et al.[116]	1996	15.7%	1,406	19.9%	5,982	0.75 (0.64 to 0.87)†	NR	Proportion in HBV+ vs. HBV-	No (protec-tive)	Volunteers from general population (Note that a larger proportion of participants than would be expected in the general population were health care workers, and that in this population health care workers had significantly lower HBV prevalence)
	Hemodialysis	Kaur et al.[116]	1996	37.5%	1,396	18.7%	6,033	2.60 (1.14 to 5.96)†	NR	Proportion in HBV+ vs. HBV-	Yes	Volunteers from general population
	Surgery	Kaur et al.[116]	1996	17.9%	1,446	21.6%	6,147	0.79 (0.70 to 0.89)†	NR	Proportion in HBV+ vs. HBV-	No (protec-tive)	Volunteers from general population

Category	Factor	Citation	Year	Percentage of Infected with Factor	Total Number Infected	Percentage of Uninfected with Factor	Total Number Uninfected	Effect Size*	p-Value**	Comparison Made	Associated in Study?	Population
	Surgery, last six months	Alter et al.[117]	1989	4%	76	3%	152	NR	NS†	Proportion in HBV+ vs. HBV-	No	General population adults with no obvious cause of acute HBV and matched controls
	Hospitalization, last six months	Alter et al.[117]	1989	13%	76	8%	152	NR	NS†	Proportion in HBV+ vs. HBV-	No	General population adults with no obvious cause of acute HBV and matched controls
	Acupuncture, last six months	Alter et al.[117]	1989	1%	76	0%	152	NR	NS†	Proportion in HBV+ vs. HBV-	No	General population adults with no obvious cause of acute HBV and matched controls
	Medically-related injections, last six months	Alter et al.[117]	1989	16%	76	17%	152	NR	NS†	Proportion in HBV+ vs. HBV-	No	General population adults with no obvious cause of acute HBV and matched controls
	Dental work, any, last six months	Alter et al.[117]	1989	13%	76	22%	152	NR	NS†	Proportion in HBV+ vs. HBV-	No	General population adults with no obvious cause of acute HBV and matched controls
	Dental work, extensive, last six months	Alter et al.[117]	1989	5%	76	6%	152	NR	NS†	Proportion in HBV+ vs. HBV-	No	General population adults with no obvious cause of acute HBV and matched controls
Other	Vaccinated for hepatitis B	Kaur et al.[116]	1996	7.8%	1,356	22%	8,509	0.40 (0.31 to 0.52)‡	NR	Proportion in HBV+ vs. HBV-	No (pro-tective)	Volunteers from general population

Category	Factor	Citation	Year	Percentage of Infected with Factor	Total Number Infected	Percentage of Uninfected with Factor	Total Number Uninfected	Effect Size*	p-Value**	Comparison Made	Associated in Study?	Population
Special Population												
Exposure to Infected Blood	Needlestick injury with recognized HBV infection	Turner et al.[127]	1989	NR	14	NR	94	NR	NR†	Prevalence HBV+ vs. no injury	No	Embalmers in high-prevalence urban area
Transfusion	Blood transfusion before 1991	Hwang et al.[124]	2006	4%	269	2.4%	3,999	RR: 1.80 (1.04 to 3.11)†	<0.05	Prevalence HBV+ vs. HBV-	Yes	College students
	Blood transfusion	Butterfield et al.[126]	1990	0%	12	2.5%	1,454	1.54 (0.09 to 26.5)†¶	0.77¶	Prevalence HBV+ vs. HBV-	No	Obstetric population
Nonspecific Exposure	Organ transplantation	Tabibian et al.[121]	2008	0%	40	1%	89	NR	NS†	Prevalence in HBV+ vs. HBV-	No	Psychiatric inpatient veterans
	Hemodialysis	Hwang et al.[124]	2006	0.7%	270	0.05%	4,045	RR: 7.96 (2.97 to 21.35)†	<0.05	Prevalence HBV+ vs. HBV-	Yes	College students
	Acupuncture	Tabibian et al.[121]	2008	15%	40	17%	89	NR	NS†	Prevalence in HBV+ vs. HBV-	No	Psychiatric inpatient veterans
	Bloody object contact	Tabibian et al.[121]	2008	35%	40	20%	89	NR	NS†	Prevalence in HBV+ vs. HBV-	No	Psychiatric inpatient veterans
	Combat exposure	Butterfield et al.[125]	2004	NR	80	NR	276	1.30 (0.63 to 2.67)‡	NS	Prevalence HBV+ vs. HBV-	No	Psychiatric inpatient veterans

Category	Factor	Citation	Year	Percentage of Infected with Factor	Total Number Infected	Percentage of Uninfected with Factor	Total Number Uninfected	Effect Size*	p-Value**	Comparison Made	Associated in Study?	Population
	Household contact with hepatitis	Hwang et al.[124]	2006	12%	268	7%	3,987	RR: 1.70 (1.19 to 2.42)†	<0.05	Prevalence HBV+ vs. HBV-	Yes	College students
	Household member with hepatitis	Butterfield et al.[126]	1990	0	12	1.3%	1,454	2.96 (0.170 to 51.78)†¶	0.46¶	Prevalence HBV+ vs. HBV-	No	Obstetric population
	Wives of men surface antigen positive	Hann et al.[122]	2007	6.3 %HBsAg+, 57.1% anti-HBs+	NR	NR	NR	NR	0.23†	Married equivalent age group	No	Korean-American church-goers
	Family history of HBV (self-report)	Lin et al.[123]	2007	NR	283	NR	2,880	RR: 1.9 (1.4 to 2.6)‡	SS	Prevalence HBV+ vs. no history	Yes	Asian Americans
Other infection	Sexually transmitted disease	Hwang et al.[124]	2006	29%	256	13%	3,924	RR: 2.48 (1.92 to 3.58)†; OR: 1.61 (1.10 to 2.37)‡	<0.05	Prevalence HBV+ vs. HBV-	Yes	College students
Other	HBV Vaccination	Lee et al.[120]	2008	NR	NR	NR	NR	0.12 (0.05 to 0.29)†	SS	Prevalence of HBV vs. no vaccine	Yes, protec-tive	Korean-American church-goers
	HBV Vaccination (self-report)	Lin et al.[123]	2007	NR	283	NR	2,880	RR: 0.5 (0.3 to 0.8)‡	SS	Prevalence HBV+ vs. no vaccine	Yes, protec-tive	Asian Americans

Category	Factor	Citation	Year	Percentage of Infected with Factor	Total Number Infected	Percentage of Uninfected with Factor	Total Number Uninfected	Effect Size*	p-Value**	Comparison Made	Associated in Study?	Population
Demographics												
General Population												
Sex	Male	Kaur et al.[116]	1996	58%	1,416	35%	6,275	2.14 (1.82 to 2.51)‡	SS	Proportion in HBV+ vs. HBV-	Yes	Volunteers from general population
Age	Age >60	Kaur et al.[116]	1996	35%	1,356	19%	5,853	1.22 (1.21 to 1.23)‡	SS	Proportion in HBV+ vs. HBV- in age <60 years	Yes	Volunteers from general population
Race	Race White/Hispanic	Kaur et al.[116]	1996	65%	1,302	84%	5,764	0.32 (0.26 to 0.39)‡	SS	Proportion in HBV+ vs. HBV-	No (protec-tive)	Volunteers from general population
	Ethnicity Non-Hispanic Black	McQuillan et al.[29]	1999	NR	1,085	NR	20,180	3.9 (2.9 to 5.0)‡	SS	Proportion in HBV+ vs. HBV- vs. Non-Hispanic White	Yes	General population
	Ethnicity Mexican American	McQuillan et al.[29]	1999	NR	1,085	NR	20,180	0.7 (0.4 to 1.3)‡	NS	Proportion in HBV+ vs. HBV- vs. Non-Hispanic White	No	General population

Category	Factor	Citation	Year	Percentage of Infected with Factor	Total Number Infected	Percentage of Uninfected with Factor	Total Number Uninfected	Effect Size*	p-Value**	Comparison Made	Associated in Study?	Population
Birthplace	Born in S.E. Asia or Africa	Kaur et al.[116]	1996	52%	1,421	17.6%	6,069	3.87 (2.81 to 5.34)‡	SS	Proportion in HBV+ vs. HBV-	Yes	Volunteers from general population
	Birth in an area with high endemic rate of HBV, household contact with someone with	Alter et al.[117]	1989	3%	76	<1%	152	NR	NS†	Proportion in HBV+ vs. HBV-	No	General population adults with no obvious cause of acute HBV and matched controls
	Other than U.S.	McQuillan et al.[29]	1999	50%	1,236	16.5%	19,971	3.4 (2.0 to 5.8)‡	SS	Proportion in HBV+ vs. HBV-	Yes	General population
Occupation	Occupation Health Care Worker	Kaur et al.[116]	1996	11.6%	1,453	21.5%	6,185	0.48 (0.41 to 0.56)†	SS	Proportion in HBV+ vs. HBV-	No (protecti ve)	Volunteers from general population
	Medical occupation	McQuillan et al.[29]	1999	5%	955	4.7%	15,451	1.07 (0.79 to 1.44)†¶	0.67¶	Proportion in HBV+ vs. HBV-	No	General population aged at least 17 years
	Health care employment, household contact with	Alter et al.[117]	1989	0%	76	11%	152	NR	NS†	Proportion in HBV+ vs. HBV-	No	General population adults with no obvious cause of acute HBV and matched controls
	Military service, ever	McQuillan et al.[29]	1999	13.2%	961	14.6%	15,568	0.89 (0.73 to 1.08)‡	0.23	Proportion in HBV+ vs. HBV-	No	General population aged at least 17 years

Category	Factor	Citation	Year	Percentage of Infected with Factor	Total Number Infected	Percentage of Uninfected with Factor	Total Number Uninfected	Effect Size*	p-Value**	Comparison Made	Associated in Study?	Population
	Unemployed	Alter et al.[117]	1989	20%	76	6%	152	NR	0.01‡	Proportion in HBV+ vs. HBV-	Yes	General population adults with no obvious cause of acute HBV and matched controls
Education	Education: Less than high school	McQuillan et al.[29]	1999	56.4%	1,081	40.9%	15,431	1.5 (1.1 to 2.1)‡	SS	Proportion in HBV+ vs. HBV vs. some college	Yes	General population
	Education: High school	McQuillan et al.[29]	1999	24.3%	1,081	31.0%	15,431	1.1 (0.9 to 1.5)‡	SS	Proportion in HBV+ vs. HBV vs. some college	No	General population
Marital Status	Marital status: Divorced/ separated	McQuillan et al.[29]	1999	10.6%	1,301	10.7%	15,284	1.6 (1.1 to 2.2)‡	SS	Proportion in HBV+ vs. HBV vs. any other status	Yes	General population aged at least 17 years

Category	Factor	Citation	Year	Percentage of Infected with Factor	Total Number Infected	Percentage of Uninfected with Factor	Total Number Uninfected	Effect Size*	p-Value**	Comparison Made	Associated in Study?	Population
Children and Adolescents												
Birthplace	Korean-born children: Carrier rate	Hann et al.[122]	2007	NR	NR	NR	NR	NR	0.022†	U.S. born	Yes	Korean-American church-goers, children
	Korean-born children: antibody rate	Hann et al.[122]	2007	NR	NR	NR	NR	NR	<0.001†	U.S. born	Yes	Korean-American church-goers, children
Special Populations												
Sex	Male	Tabibian et al.[121]	2008	100%	40	96.6%	89	NR	NS†	Prevalence in HBV+ vs. HBV-	No	Psychiatric inpatient veterans
	Male	Hwang et al.[124]	2006	32%	274	39%	4,047	RR: 0.77 (0.61 to 0.99)†; OR: 0.69 (0.49 to 0.97)‡	<0.05 for both	Prevalence HBV+ vs. HBV-	No, protective	College students
	Male	Lin et al.[123]	2007	NR	NR	NR	NR	RR: 2.1 (1.6 to 2.7)‡	SS	Prevalence HBV+ in Females	Yes	Asian Americans
	Male	Lee et al.[120]	2008	NR	24	NR	609	1.69 (0.96 to 2.98)†	NS	Prevalence HBV+ vs. HBV-	No	Korean Americans

Category	Factor	Citation	Year	Percentage of Infected with Factor	Total Number Infected	Percentage of Uninfected with Factor	Total Number Uninfected	Effect Size*	p-Value**	Comparison Made	Associated in Study?	Population
Age	Age, mean	Tabibian et al.[121]	2008	48.9 mean	40	48.9 mean	89	NR	NS†	Mean age HBV+ vs. HBV-	No	Psychiatric inpatient veterans
	Age (continuous)	Hwang et al.[124]	2006	NR	269	NR	4,054	1.04 (1.03 to 1.06)‡	<0.05	Mean age in HBV+ vs. HBV-	Yes	College students
	Age ≤20 years	Hann et al.[122]	2007	NR	377	NR	5,753	NR	0.0051†	>20 years	Yes	Korean-American church-goers
	Age ≤30 years	Lee et al.[120]	2008	NR	NR	NR	NR	0.072 (0.02 to 0.21)	SS	HBV+ vs. HBV- in age >50 years	Yes, protective	Korean-American church-goers
	Age 30 to 49 years	Lee et al.[120]	2008	NR	NR	NR	NR	0.287 (0.15 to 0.55)†	<0.001	HBV+ vs. HBV- in age >50 years	Yes, protective	Korean-American church-goers
	Age over 35 years	Turner et al.[127]	1989	NR	14	NR	94	RR: 3.6 (1.2 to 11.2)†	NR	HBV+ in <35 years	Yes	Embalmers in high-prevalence urban area
	Age over 50 years	Butterfield et al.[125]	2004	NR	80	NR	276	1.27 (0.67 to 2.39)‡	NS	Prevalence HBV+ vs. HBV-	No	Psychiatric inpatient veterans
	Age 30-39	Lin et al.[123]	2007	NR	283	NR	2,880	RR: 1.4 (0.7 to 2.6)‡	NS	Prevalence HBV+ in age <30	No	Asian Americans

Category	Factor	Citation	Year	Percentage of Infected with Factor	Total Number Infected	Percentage of Uninfected with Factor	Total Number Uninfected	Effect Size*	p-Value**	Comparison Made	Associated in Study?	Population
	Age 40-49	Lin et al.[123]	2007	NR	283	NR	2,880	RR: 1.5 (0.9 to 2.7)‡	NS	Prevalence HBV+ in age <30	No	Asian Americans
	Age 50-59	Lin et al.[123]	2007	NR	283	NR	2,880	RR: 1.0 (0.6 to 1.5)‡	NS	Prevalence HBV+ in age <30	No	Asian Americans
	Age 60-69	Lin et al.[123]	2007	NR	283	NR	2,880	RR: 0.9 (0.5 to 1.7)‡	NS	Prevalence HBV+ in age <30	No	Asian Americans
	Age ≥70	Lin et al.[123]	2007	NR	283	NR	2,880	RR: 0.6 (0.3 to 1.2)‡	NS	Prevalence HBV+ in age <30	No	Asian Americans
Race/Ethnicity	Ethnicity, Caucasian	Tabibian et al.[121]	2008	40%	40	55%	89	NR	NS†	Prevalence in HBV+ vs. HBV-	No	Psychiatric inpatient veterans
	Ethnicity, African-American	Tabibian et al.[121]	2008	37.5%	40	31%	89	NR	NS†	Prevalence in HBV+ vs. HBV-	No	Psychiatric inpatient veterans

Category	Factor	Citation	Year	Percentage of Infected with Factor	Total Number Infected	Percentage of Uninfected with Factor	Total Number Uninfected	Effect Size*	p-Value**	Comparison Made	Associated in Study?	Population
	African-American Race	Butterfield et al.[125]	2004	NR	80	NR	276	2.79 (1.41 to 5.53)‡	<0.01	Prevalence HBV+ vs. HBV- vs. White	Yes	Psychiatric inpatient veterans
	Black non-Hispanic	Hwang et al.[124]	2006	36%	269	26%	4,001	RR: 1.92 (1.44 to 2.56)†; OR: 1.95 (1.34 to 2.84)‡	<0.05 for both	Prevalence HBV+ vs. HBV- vs. White non-Hispanic	Yes	College students
	Ethnicity, Hispanic	Tabibian et al.[121]	2008	12.5%	40	8%	89	NR	NS†	Prevalence in HBV+ vs. HBV-	No	Psychiatric inpatient veterans
	Hispanic or Latino	Hwang et al.[124]	2006	12%	269	23%	4,001	RR: 0.72 (0.48 to 1.08)†; OR: 0.81 (0.49 to 1.34)‡	NS	Prevalence HBV+ vs. HBV- vs. White non-Hispanic	No	College students

Category	Factor	Citation	Year	Percentage of Infected with Factor	Total Number Infected	Percentage of Uninfected with Factor	Total Number Uninfected	Effect Size*	p-Value**	Comparison Made	Associated in Study?	Population
	Asian	Hwang et al.[124]	2006	20%	269	5%	4,001	RR: 4.49 (3.26 to 6.19)†; OR: 9.98 (6.01 to 16.55)‡	<0.05 for both	Prevalence HBV+ vs. HBV- vs. White non-Hispanic	Yes	College students
Birth-country	Country of birth: East Asia, excluding China	Lin et al.[123]	2007	NR	283	NR	2,880	RR: 0.8 (0.6 to 1.1)‡	NS	Prevalence HBV+ vs. born in China	No	Asian Americans
	Country of birth: Southeast Asia/Pacific Islands	Lin et al.[123]	2007	NR	283	NR	2,880	RR: 1.2 (0.8 to 1.7)‡	NS	Prevalence HBV+ vs. born in China	No	Asian Americans
	Country of birth: United States	Lin et al.[123]	2007	NR	283	NR	2,880	RR: 0.05 (0.01 to 0.3)‡	SS	Prevalence HBV+ vs. born in China	Yes, protective	Asian Americans

Category	Factor	Citation	Year	Percentage of Infected with Factor	Total Number Infected	Percentage of Uninfected with Factor	Total Number Uninfected	Effect Size*	p-Value**	Comparison Made	Associated in Study?	Population
Occupation	Health care workers	Tabibian et al.[121]	2008	17.5%	40	12.0%	89	NR	NS†	Prevalence in HBV+ vs. HBV-	No	Psychiatric inpatient veterans
	Healthcare-related job with frequent blood exposure	Hwang et al.[124]	2006	7%	270	4%	3,987	RR: 1.83 (1.18 to 2.84)†	<0.05	HBV-	Yes	College students
	Healthcare worker or spouse of	Butterfield et al.[126]	1990	8%	12	7.5%	1,454	1.07 (0.13 to 8.7)†¶	0.947¶	Prevalence HBV+ vs. HBV-	No	Obstetric population
Education	Education, years	Tabibian et al.[121]	2008	13.5 mean	40	13.4 mean	129	NR	NS†	Mean years education in HBV+ vs. HBV-	No	Psychiatric inpatient veterans
	Enrolled in 2 year college	Hwang et al.[124]	2006	48%	274	33%	4,054	RR: 1.81 (1.44 to 2.27)†; OR: 1.64 (1.13 to 2.40)‡	p <0.05	HBV prevalence vs. 4 year college	Yes	College students

Category	Factor	Citation	Year	Percentage of Infected with Factor	Total Number Infected	Percentage of Uninfected with Factor	Total Number Uninfected	Effect Size*	p-Value**	Comparison Made	Associated in Study?	Population
Economic	Homeless	Tabibian et al.[121]	2008	77.5%	40	66%	89	NR	NS†	Prevalence in HBV+ vs. HBV-	No	Psychiatric inpatient veterans
	Independent or live with family (vs. homeless, institutionalized, or other)	Butterfield et al.[125]	2004	NR	80	NR	276	0.82 (0.39 to 1.72)‡	NS	Prevalence HBV+ vs. HBV-	No	Psychiatric inpatient veterans
Marital Status	Currently married	Butterfield et al.[125]	2004	NR	80	NR	276	1.67 (0.83 to 3.40)‡	NS	Prevalence HBV+ vs. HBV-	No	Psychiatric inpatient veterans

* Odds ratios as reported in publication, unless otherwise specified
** As reported in publication, unless otherwise specified

† Univariate, unadjusted
‡ Multivariate, adjusted for other factors
¶ Calculated by ECRI Institute

Table 40. HCV: Nonbehavioral Risk Factors

Category	Factor	Citation	Year	Percentage of Infected with Factor	Total Number Infected	Percentage of Uninfected with Factor	Total Number Uninfected	Effect Size*	p-Value**	Comparison made	Associated in Study?	Population
Signs and Symptoms												
Blood Donors												
Signs	ALT reactive	Orton et al.[104]	2004	20%	65	<1%	225	47 (6.7 to 2,004)†	<0.001	Proportion in HCV+ vs. HCV-	Yes	Blood donors
General Population												
Signs	Jaundice	Nguyen et al.[113]	2005	20.3%	225	5.4%	204	Not reported (NR)	<0.001	Proportion HCV+ vs. HCV-	Yes	Adults at general internal medicine clinic (controls) and hepatology clinic (cases)
	Serum alanine aminotransferase levels <40 U/L	Armstrong et al.[30]	2006	49%	220	92%	12,900	NR	Not significant (NS)†	0-39 U/L	No	General population aged 18 to 49 years
	Serum alanine aminotransferase levels 40-79 U/L	Armstrong et al.[30]	2006	35%	220	7%	12,900	NR	<0.005†	0-39 U/L	Yes	General population aged 18 to 49 years
	Serum alanine aminotransferase levels 80-119 U/L	Armstrong et al.[30]	2006	7%	220	1%	12,900	NR	>0.05†	0-39 U/L	Yes	General population aged 18 to 49 years

Category	Factor	Citation	Year	Percentage of Infected with Factor	Total Number Infected	Percentage of Uninfected with Factor	Total Number Uninfected	Effect Size*	p-Value**	Comparison made	Associated in Study?	Population
	Serum alanine aminotransferase levels ≥120 U/L	Armstrong et al.[30]	2006	8%	220	4%	12,900	NR	>0.05†	0-39 U/L	Yes	General population aged 18 to 49 years
	Elevated liver enzyme	Fischer et al.[114]	2000	27%	11	6%	1,369	NR	<0.05†	Proportion in HCV+ vs. HCV-	Yes	Adults comprising individuals at risk for HCV and healthcareworkers enrolled in HMO
	Hepatitis-related diagnoses (HAV, HBV, HIV, or elevated liver enzyme from health record)	Fischer et al.[114]	2000	NR	11	NR	1,369	13.9 (2.7 to 72.1)†	0.002	Proportion in HCV+ vs. HCV-	Yes	Adults comprising individuals at risk for HCV and healthcareworkers enrolled in HMO
Co-Morbidity												
Potential Tissue Donors												
Transfusion	Blood transfusion recipient or donor	Sanchez et al.[103]	2006	NR	18	NR	56	NR	NS	Proportion in HCV+ vs. HCV-	No	Potential tissue donors, as reported by next of kin

Category	Factor	Citation	Year	Percentage of Infected with Factor	Total Number Infected	Percentage of Uninfected with Factor	Total Number Uninfected	Effect Size*	p-Value**	Comparison made	Associated in Study?	Population
Nonspecific Exposure	History of transplant	Sanchez et al.[103]	2006	NR	18	NR	56	NR	NS	Proportion in HCV+ vs. HCV	No	Potential tissue donors, as reported by next of kin
	Accidental needle stick	Sanchez et al.[103]	2006	NR	18	NR	56	NR	NS	Proportion in HCV+ vs. HCV	No	Potential tissue donors, as reported by next of kin
	Surgeries	Sanchez et al.[103]	2006	NR	18	NR	56	NR	NS	Proportion in HCV+ vs. HCV	No	Potential tissue donors, as reported by next of kin
	HIV testing	Sanchez et al.[103]	2006	NR	18	NR	56	NR	NS†	Proportion in HCV+ vs. HCV	No	Potential tissue donors, as reported by next of kin
Other	Liver disease	Sanchez et al.[103]	2006	NR	18	NR	56	NR	NS	Proportion in HCV+ vs. HCV	No	Potential tissue donors, as reported by next of kin
	Chest pain	Sanchez et al.[103]	2006	NR	18	NR	56	2.66 (0.96 to 7.38)†	0.054	Proportion in HCV+ vs. HCV	Yes	Potential tissue donors, as reported by next of kin

Category	Factor	Citation	Year	Percentage of Infected with Factor	Total Number Infected	Percentage of Uninfected with Factor	Total Number Uninfected	Effect Size*	p-Value**	Comparison made	Associated in Study?	Population
	Cardiac medications	Sanchez et al.[103]	2006	NR	18	NR	56	2.84 (1.0 to 8.07)†	0.043	Proportion in HCV+ vs. HCV	Yes	Potential tissue donors, as reported by next of kin
	Kidney stones	Sanchez et al.[103]	2006	NR	18	NR	56	5.48 (1.38 to 21.80)†	0.008	Proportion in HCV+ vs. HCV	Yes	Potential tissue donors, as reported by next of kin
	Lung disease	Sanchez et al.[103]	2006	NR	18	NR	56	3.20 (0.98 to 10.41)†	0.044	Proportion in HCV+ vs. HCV	Yes	Potential tissue donors, as reported by next of kin
	Treatment by physician in last 2 years	Sanchez et al.[103]	2006	NR	18	NR	56	NR	NS†	Proportion in HCV+ vs. HCV	No	Potential tissue donors, as reported by next of kin
	Medical hospitalizations	Sanchez et al.[103]	2006	NR	18	NR	56	NR	NS†	Proportion in HCV+ vs. HCV	No	Potential tissue donors, as reported by next of kin
	Psychiatric hospitalizations	Sanchez et al.[103]	2006	NR	18	NR	56	NR	NS†	Proportion in HCV+ vs. HCV	No	Potential tissue donors, as reported by next of kin

Category	Factor	Citation	Year	Percentage of Infected with Factor	Total Number Infected	Percentage of Uninfected with Factor	Total Number Uninfected	Effect Size*	p-Value**	Comparison made	Associated in Study?	Population
	Medical illnesses	Sanchez et al.[103]	2006	NR	18	NR	56	NR	NS†	Proportion in HCV+ vs. HCV	No	Potential tissue donors, as reported by next of kin
	Medications	Sanchez et al.[103]	2006	NR	18	NR	56	NR	NS†	Proportion in HCV+ vs. HCV	No	Potential tissue donors, as reported by next of kin
	Toxic exposure	Sanchez et al.[103]	2006	NR	18	NR	56	NR	NS†	Proportion in HCV+ vs. HCV	No	Potential tissue donors, as reported by next of kin
	Malaria exposure or treatment	Sanchez et al.[103]	2006	NR	18	NR	56	NR	NS†	Proportion in HCV+ vs. HCV	No	Potential tissue donors, as reported by next of kin
	Chagas disease exposure or treatment	Sanchez et al.[103]	2006	NR	18	NR	56	NR	NS†	Proportion in HCV+ vs. HCV	No	Potential tissue donors, as reported by next of kin
	Rabies exposure	Sanchez et al.[103]	2006	NR	18	NR	56	NR	NS†	Proportion in HCV+ vs. HCV	No	Potential tissue donors, as reported by next of kin

Category	Factor	Citation	Year	Percentage of Infected with Factor	Total Number Infected	Percentage of Uninfected with Factor	Total Number Uninfected	Effect Size*	p-Value**	Comparison made	Associated in Study?	Population
	Heart disease	Sanchez et al.[103]	2006	NR	18	NR	56	NR	NS†	Proportion in HCV+ vs. HCV	No	Potential tissue donors, as reported by next of kin
	Hypertension	Sanchez et al.[103]	2006	NR	18	NR	56	NR	NS†	Proportion in HCV+ vs. HCV	No	Potential tissue donors, as reported by next of kin
	Kidney disease	Sanchez et al.[103]	2006	NR	18	NR	56	NR	NS†	Proportion in HCV+ vs. HCV	No	Potential tissue donors, as reported by next of kin
	Gastrointestinal disease	Sanchez et al.[103]	2006	NR	18	NR	56	NR	NS†	Proportion in HCV+ vs. HCV	No	Potential tissue donors, as reported by next of kin
	Cancer history	Sanchez et al.[103]	2006	NR	18	NR	56	NR	NS†	Proportion in HCV+ vs. HCV	No	Potential tissue donors, as reported by next of kin
	Diabetes history	Sanchez et al.[103]	2006	NR	18	NR	56	NR	NS†	Proportion in HCV+ vs. HCV	No	Potential tissue donors, as reported by next of kin

Category	Factor	Citation	Year	Percentage of Infected with Factor	Total Number Infected	Percentage of Uninfected with Factor	Total Number Uninfected	Effect Size*	p-Value**	Comparison made	Associated in Study?	Population
	Pulmonary disease	Sanchez et al.[103]	2006	NR	18	NR	56	NR	NS†	Proportion in HCV+ vs. HCV	No	Potential tissue donors, as reported by next of kin
	Rheumatologic disease	Sanchez et al.[103]	2006	NR	18	NR	56	NR	NS†	Proportion in HCV+ vs. HCV	No	Potential tissue donors, as reported by next of kin
	Connective tissue disease	Sanchez et al.[103]	2006	NR	18	NR	56	NR	NS†	Proportion in HCV+ vs. HCV	No	Potential tissue donors, as reported by next of kin
	Dermatologic disease	Sanchez et al.[103]	2006	NR	18	NR	56	NR	NS†	Proportion in HCV+ vs. HCV	No	Potential tissue donors, as reported by next of kin
	Neurologic disease	Sanchez et al.[103]	2006	NR	18	NR	56	NR	NS†	Proportion in HCV+ vs. HCV	No	Potential tissue donors, as reported by next of kin
	Ocular disease	Sanchez et al.[103]	2006	NR	18	NR	56	NR	NS†	Proportion in HCV+ vs. HCV	No	Potential tissue donors, as reported by next of kin

Category	Factor	Citation	Year	Percentage of Infected with Factor	Total Number Infected	Percentage of Uninfected with Factor	Total Number Uninfected	Effect Size*	p-Value**	Comparison made	Associated in Study?	Population
Potential and Actual Organ Donors												
Infection	HBV Surface Antigen Positive	Gasink et al.[102]	2006	0.4%	261	0.03%	10,654	NR	0.003†	Proportion in HCV+ vs. HCV-	Yes	Heart transplant donors
Other	Diabetes mellitus	Gasink et al.[102]	2006	1.6%	261	1.7%	10,654	NR	0.86†	Proportion in HCV+ vs. HCV	No	Heart transplant donors
	Previous myocardial infarction	Gasink et al.[102]	2006	0	261	0.68%	10,654	NR	0.18†	Proportion in HCV+ vs. HCV	No	Heart transplant donors
	Hypertension	Gasink et al.[102]	2006	15.2%	261	11.3%	10,654	NR	0.05†	Proportion in HCV+ vs. HCV	Yes	Heart transplant donors
	Creatinine >1.5 mg/dL	Gasink et al.[102]	2006	12.3%	261	13.4%	10,654	NR	0.60†	Proportion in HCV+ vs. HCV	No	Heart transplant donors

Category	Factor	Citation	Year	Percentage of Infected with Factor	Total Number Infected	Percentage of Uninfected with Factor	Total Number Uninfected	Effect Size*	p-Value**	Comparison made	Associated in Study?	Population
Blood Donors												
Transfusion	Transfusion	Conry-Cantilena et al.[106]	1996	27%	248	8%	131	4.68 (3.44 to 6.36)†¶	<0.001‡	Proportion in HCV+ vs. HCV-	Yes	Blood donors initially positive on enzyme-linked immunosorbent assay (EIA)
	Received blood transfusion	Murphy et al.[105]	2000	23%	758	6%	1,039	Non-IDU: 10.9 (6.5 to 18.2)†; IDU: 0.9 (0.1 to 9.1)†	Statistically significant (SS) for non-IDU, NS for IDU	Proportion in HCV+ vs. HCV- final multivariable logistic regression model	Yes, for non-IDU	Blood donors
	Previous blood transfusion	Murphy et al.[107]	1996	13%	3,126	5.9%	859,272	2.8 (2.5 to 3.1)‡	SS	Proportion in HCV+ vs. HCV-	Yes	Blood donors
Nonspecific Exposure	Needle stick among healthcare workers	Conry-Cantilena et al.[106]	1996	4%	248	2%	131	NR	>0.05†	Proportion in HCV+ vs. HCV-	No	Blood donors initially positive on EIA
	Bloody needle stick injury in medical context	Murphy et al.[105]	2000	11%	758	4%	1,039	3.2 (1.9 to 2.6)‡	SS	Proportion in HCV+ vs. HCV- adjusted for IDU	Yes	Blood donors

Category	Factor	Citation	Year	Percentage of Infected with Factor	Total Number Infected	Percentage of Uninfected with Factor	Total Number Uninfected	Effect Size*	p-Value**	Comparison made	Associated in Study?	Population
	Stuck/cut with bloody object	Murphy et al.[105]	2000	11%	758	4%	1,039	2.1 (1.1 to 4.1)‡	SS	Proportion in HCV+ vs. HCV-final multivariable logistic regression model	Yes	Blood donors
	Had same-day surgery in the 6 months before donation	Orton et al.[104]	2004	9.2%	65	6.3%	225	1.5 (0.5 to 4.5)†	0.41	Proportion in HCV+ vs. HCV-	No	Blood donors
	Had a medical and/or surgical procedure in the 6 months before donation	Orton et al.[104]	2004	21.5%	65	14.3%	225	1.6 (0.8 to 3.3)†	0.16	Proportion in HCV+ vs. HCV-	No	Blood donors
	Had surgery	Murphy et al.[105]	2000	74%	758	64%	1,039	1.7 (1.2 to 2.4)‡	SS	Proportion in HCV+ vs. HCV- adjusted for IDU	Yes	Blood donors
	Had sutures	Murphy et al.[105]	2000	77%	758	65%	1,039	1.7 (1.2 to 2.4)‡	SS	Proportion in HCV+ vs. HCV- adjusted for IDU	Yes	Blood donors

Category	Factor	Citation	Year	Percentage of Infected with Factor	Total Number Infected	Percentage of Uninfected with Factor	Total Number Uninfected	Effect Size*	p-Value**	Comparison made	Associated in Study?	Population
	Was hospitalized in the 6 months before donation	Orton et al.[104]	2004	7.7%	65	2.2%	225	3.7 (0.8 to 16)†	0.05	Proportion in HCV+ vs. HCV-	Yes	Blood donors
	Acupuncture treatment	Conry-Cantilena et al.[106]	1996	4%	248	1%	131	NR	>0.05†	Proportion in HCV+ vs. HCV-	No	Blood donors initially positive on EIA
	Acupuncture	Murphy et al.[105]	2000	9%	758	5%	1,039	1.4 (0.8 to 2.4)‡	NS	Proportion in HCV+ vs. HCV- adjusted for IDU	No	Blood donors
	Had dental work in the 6 months before donation	Orton et al.[104]	2004	35.4%	65	38.8%	225	0.9 (0.5 to 1.5)†	0.61	Proportion in HCV+ vs. HCV-	No	Blood donors
	Teeth cleaned 1-10 times	Murphy et al.[105]	2000	57%	758	46%	1,039	0.7 (0.3 to 1.4)‡	NS	Proportion in HCV+ vs. HCV- adjusted for IDU with reference to never had cleaning	No	Blood donors

Category	Factor	Citation	Year	Percentage of Infected with Factor	Total Number Infected	Percentage of Uninfected with Factor	Total Number Uninfected	Effect Size*	p-Value**	Comparison made	Associated in Study?	Population
	Teeth cleaned 11-20 times	Murphy et al.[105]	2000	23%	758	33%	1,039	0.5 (0.2 to 1.0)‡	NS	Proportion in HCV+ vs. HCV- adjusted for IDU with reference to never had cleaning	No	Blood donors
	Teeth cleaned >20 times	Murphy et al.[105]	2000	11%	758	12%	1,039	0.6 (0.2 to 1.3)‡	NS	Proportion in HCV+ vs. HCV- adjusted for IDU with reference to never had cleaning	No	Blood donors
	Tooth extraction	Murphy et al.[105]	2000	73%	758	68%	1,039	1.3 (0.9 to 1.8)‡	NS	Proportion in HCV+ vs. HCV- adjusted for IDU	No	Blood donors
	In a fight with blood exposure last 6 months	Orton et al.[104]	2004	7.7%	65	2.2%	225	3.7 (0.8 to 16†	0.05	Proportion in HCV+ vs. HCV-	Yes	Blood donors
	By a bite with blood exposure last 6 months	Orton et al.[104]	2004	4.6%	65	0%	225	Undefined (because zero in uninfected group)	0.01	Proportion in HCV+ vs. HCV-	Yes	Blood donors

Category	Factor	Citation	Year	Percentage of Infected with Factor	Total Number Infected	Percentage of Uninfected with Factor	Total Number Uninfected	Effect Size*	p-Value**	Comparison made	Associated in Study?	Population
	During a haircut with blood exposure last 6 months	Orton et al.[104]	2004	23.1%	65	13.8%	225	1.9 (0.9 to 3.9)†	0.11	Proportion in HCV+ vs. HCV-	No	Blood donors
	During a manicure with blood exposure last 6 months (women only)	Orton et al.[104]	2004	20.0%	30	3.8%	105	5.2 (1.1 to 27) †	0.02	Proportion in HCV+ vs. HCV-	Yes	Blood donors
	At accident site with blood exposure last 6 months	Orton et al.[104]	2004	6.2%	65	1.3%	225	4.9 (0.8 to 34) †	0.05	Proportion in HCV+ vs. HCV-	Yes	Blood donors
	Lived with hepatitis case	Murphy et al.[105]	2000	16%	758	6%	1,039	1.4 (0.9 to 1.5)‡	NS	Proportion in HCV+ vs. HCV- adjusted for IDU	No	Blood donors
	Relative with hepatitis	Murphy et al.[105]	2000	12%	758	8%	1,039	0.9 (0.6 to 1.5)‡	NS	Proportion in HCV+ vs. HCV- adjusted for IDU	No	Blood donors
	Lived with transfusion recipient	Murphy et al.[105]	2000	12%	758	7%	1,039	1.5 (1.0 to 2.3)‡	SS	Proportion in HCV+ vs. HCV- adjusted for IDU	Yes	Blood donors

Category	Factor	Citation	Year	Percentage of Infected with Factor	Total Number Infected	Percentage of Uninfected with Factor	Total Number Uninfected	Effect Size*	p-Value**	Comparison made	Associated in Study?	Population
Other infection	Had a sexually transmitted disease (STD) in last 6 months before donation	Orton et al.[104]	2004	6.2%	65	0%	225	Undefined (because zero in control group had factor)	0.002†	Proportion in HCV+ vs. HCV-	Yes	Blood donors
	History of STD	Conry-Cantilena et al.[106]	1996	28%	248	10%	131	NR	<0.001†	Proportion in HCV+ vs. HCV-	Yes	Blood donors initially positive on EIA
	STD	Murphy et al.[105]	2000	33%	758	15%	1,039	2.5 (1.8 to 3.5)‡	SS	Proportion in HCV+ vs. HCV- adjusted for IDU	Yes	Blood donors
	Other reactive infections disease markers (HIV, syphilis)	Orton et al.[104]	2004	8%	65	0%	225	Undefined (because zero in control group)	<0.001†	Proportion in HCV+ vs. HCV-	Yes	Blood donors
	Seropositive for other infectious diseases (HTLV I and II, HIV, HBV-core)	Murphy et al.[107]	1996	NR	3,126	NR	859,272	10.4 (9.6 to 11.4)‡	SS	Proportion in HCV+ vs. HCV-	Yes	Blood donors

Category	Factor	Citation	Year	Percentage of Infected with Factor	Total Number Infected	Percentage of Uninfected with Factor	Total Number Uninfected	Effect Size*	p-Value**	Comparison made	Associated in Study?	Population
Other	Received Hepatitis B Vaccine in last 6 months	Orton et al.[104]	2004	32.3%	65	24.6%	225	1.5 (0.8 to 2.7)†	0.21	Proportion in HCV+ vs. HCV-	No	Blood donors
	Gamma globulin injection	Murphy et al.[105]	2000	22%	758	16%	1,039	1.6 (1.0 to 2.6)‡	SS	Proportion in HCV+ vs. HCV-final multivariable logistic regression model	Yes	Blood donors
	History of hepatitis	Orton et al.[104]	2004	1.5%	65	1.8%	225	0.9 (0.02 to 10) †	1.00	Proportion in HCV+ vs. HCV-	No	Blood donors
	History of liver disease	Conry-Cantilena et al.[106]	1996	31%	248	5%	131	NR	<0.001†	Proportion in HCV+ vs. HCV-	Yes	Blood donors initially positive on EIA

Category	Factor	Citation	Year	Percentage of Infected with Factor	Total Number Infected	Percentage of Uninfected with Factor	Total Number Uninfected	Effect Size*	p-Value**	Comparison made	Associated in Study?	Population
General Population												
Transfusion	Blood transfusion	Nguyen et al.[113]	2005	43.2%	225	13.7%	204	8.62 (4.71 to 15.80)†	<0.001	HCV-	Yes	Adults at general internal medicine clinic (controls) and hepatology clinic (cases)
	Blood transfusion(s)	Hand and Vasquez[112]	2005	25%	320	19%	307	NR†; 3.2 (2.0 to 5.1)‡	0.051†; <0.001‡	Proportion in HCV+ vs. HCV-	Yes	Adults tested for HCV in health system because of clinical suspicion
	Blood transfusion	Kaur et al.[116]	1996	14.6%	559	7.1%	6,170	4.09 (2.97 to 5.62)‡	NR	Proportion in HCV+ vs. HCV-	Yes	Volunteers from general population
	Transfusion, blood, before 1992	Armstrong et al.[30]	2006	14%	128	5%	5,665	2.6 (0.9 to 7.3)‡	<0.005	Proportion in HCV+ vs. HCV-	Yes	General population aged 20 to 59 years
	Transfusion, blood, before 1992, self-reported	Fischer et al.[114]	2000	55%	11	25%	1,369	4.61 (3.42 to 6.21)†¶	<0.001	Proportion in HCV+ vs. HCV-	Yes	Adults comprising individuals at risk for HCV and healthcareworkers enrolled in HMO

Category	Factor	Citation	Year	Percentage of Infected with Factor	Total Number Infected	Percentage of Uninfected with Factor	Total Number Uninfected	Effect Size*	p-Value**	Comparison made	Associated in Study?	Population
	Transfusion, blood, before 1992, as recognized in HMO database	Fischer et al.[114]	2000	0%	11	<1%	1,369	NR	NS†	Proportion in HCV+ vs. HCV-	No	Adults comprising individuals at risk for HCV and healthcareworkers enrolled in HMO
Nonspecific Exposure	Needlestick injury	Kaur et al.[116]	1996	6.4%	543	8.9%	5,982	0.70 (0.55 to 0.89)†	NR	Proportion in HCV+ vs. HCV-	No (protective)	Volunteers from general population – Note this population had a large proportion of healthcare workers who had a lower infection prevalence
	Contact with blood	Hand and Vasquez[112]	2005	5%	320	4%	307	NR	0.798†	Proportion in HCV+ vs. HCV-	No	Adults tested for HCV in health system because of clinical suspicion
	Surgery, any	Fischer et al.[114]	2000	91%	11	78%	1,369	NR	NS†	Proportion in HCV+ vs. HCV-	No	Adults comprising individuals at risk for HCV and healthcareworkers enrolled in HMO

Category	Factor	Citation	Year	Percentage of Infected with Factor	Total Number Infected	Percentage of Uninfected with Factor	Total Number Uninfected	Effect Size*	p-Value**	Comparison made	Associated in Study?	Population
	Surgery	Kaur et al.[116]	1996	8.3%	565	8.6%	6,147	0.96 (0.80 to 1.16)†	NS	Proportion in HCV+ vs. HCV-	No	Volunteers from general population
	Surgery, exploratory	Fischer et al.[114]	2000	55%	11	41%	1,369	NR	NS†	Proportion in HCV+ vs. HCV-	No	Adults comprising individuals at risk for HCV and healthcareworkers enrolled in HMO
	Emergency department treatment	Nguyen et al.[113]	2005	88.3%	225	79.4%	204	NR	0.02†	Proportion HCV+ vs. HCV-	Yes	Adults at general internal medicine clinic (controls) and hepatology clinic (cases)
	Hospitalization	Nguyen et al.[113]	2005	87.8%	225	76.5%	204	NR	0.003†	Proportion HCV+ vs. HCV-	Yes	Adults at general internal medicine clinic (controls) and hepatology clinic (cases)
	Kidney dialysis	Nguyen et al.[113]	2005	5.4%	225	0.5%	204	11.36 (1.15 to 86.5)†¶	0.003†	Proportion HCV+ vs. HCV-	Yes	Adults at general internal medicine clinic (controls) and hepatology clinic (cases)

Category	Factor	Citation	Year	Percentage of Infected with Factor	Total Number Infected	Percentage of Uninfected with Factor	Total Number Uninfected	Effect Size*	p-Value**	Comparison made	Associated in Study?	Population
	Hemodialysis	Hand and Vasquez[112]	2005	1%	320	3%	307	NR	0.068†	Proportion in HCV+ vs. HCV-	No	Adults tested for HCV in health system because of clinical suspicion
	Hemodialysis	Kaur et al.[116]	1996	42.3%	544	8.1%	6,033	10.95 (3.85 to 31.13)‡	NR	Proportion in HCV+ vs. HCV-	Yes	Volunteers from general population
	Acupuncture	Hand and Vasquez[112]	2005	2%	320	0.7%	307	NR	0.106†	Proportion in HCV+ vs. HCV-	No	Adults tested for HCV in health system because of clinical suspicion
	Family member treated for viral hepatitis	Fischer et al.[114]	2000	9%	11	6%	1,369	NR	NS†	Proportion in HCV+ vs. HCV-	No	Adults comprising individuals at risk for HCV and healthcareworkers enrolled in HMO
	At least one family member with HCV	Nguyen et al.[113]	2005	21.2%	225	6.9%	204	NR	<0.001†	Proportion HCV+ vs. HCV-	Yes	Adults at general internal medicine clinic (controls) and hepatology clinic (cases)

Category	Factor	Citation	Year	Percentage of Infected with Factor	Total Number Infected	Percentage of Uninfected with Factor	Total Number Uninfected	Effect Size*	p-Value**	Comparison made	Associated in Study?	Population
	Had a blood test for HBV	Nguyen et al.[113]	2005	78.8%	225	24.5%	204	NR	<0.001†	Proportion HCV+ vs. HCV-	Yes	Adults at general internal medicine clinic (controls) and hepatology clinic (cases)
Other Infection	HIV positive	Nguyen et al.[113]	2005	1.8%	225	1.5%	204	NR	>0.99†	Proportion HCV+ vs. HCV-	No	Adults at general internal medicine clinic (controls) and hepatology clinic (cases)
	HIV positive	Armstrong et al.[30]	2006	3%	134	0.5%	5,549	NR	Incon-clusive due to small number positives	HCV-	Incon clus-ive	Adults in general population aged 18 to 49 years
	HIV positive	Hand and Vasquez[112]	2005	10%	320	8%	307	NR	0.351†	Proportion in HCV+ vs. HCV-	No	Adults tested for HCV in health system because of clinical suspicion
	HBV Positive, self-report	Nguyen et al.[113]	2005	21.2%	225	2.5%	204	4.71 (1.49 to 14.83)†	NR	Proportion HCV+ vs. HCV-	Yes	Adults at general internal medicine clinic (controls) and hepatology clinic (cases)

Category	Factor	Citation	Year	Percentage of Infected with Factor	Total Number Infected	Percentage of Uninfected with Factor	Total Number Uninfected	Effect Size*	p-Value**	Comparison made	Associated in Study?	Population
	Herpes Simplex Virus Type 2 (HSV-2) Positive	Armstrong et al.[30]	2006	43%	134	19%	5,476	NR	<0.005†	Proportion HCV+ vs. HCV-	Yes	General population age 18 to 49 years
	STD, past treatment for	Nguyen et al.[113]	2005	24.8%	225	18.1%	204	NR	0.10†	Proportion HCV+ vs. HCV-	No	Adults at general internal medicine clinic (controls) and hepatology clinic (cases)
Other	Blood donor	Nguyen et al.[113]	2005	38.7%	225	58.3%	204	NR	<0.001†	Proportion HCV+ vs. HCV-	No (protective)	Adults at general internal medicine clinic (controls) and hepatology clinic (cases)
	Blood donor, rejected as	Nguyen et al.[113]	2005	28.4%	225	16.2%	204	2.57 (1.49 to 4.43)†	0.002	Proportion HCV+ vs. HCV	Yes	Adults at general internal medicine clinic (controls) and hepatology clinic (cases)
	Vaccinated for hepatitis B	Kaur et al.[116]	1996	2.8%	528	10%	5,737	0.37 (0.22 to 0.62)‡	NR	Proportion in HCV+ vs. HCV-	No (protective)	Volunteers from general population

Category	Factor	Citation	Year	Percentage of Infected with Factor	Total Number Infected	Percentage of Uninfected with Factor	Total Number Uninfected	Effect Size*	p-Value**	Comparison made	Associated in Study?	Population
	Refused life insurance	Nguyen et al.[113]	2005	20.7%	225	3.9%	204	2.75 (1.05 to 7.25)†	<0.001	Proportion HCV+ vs. HCV-	Yes	Adults at general internal medicine clinic (controls) and hepatology clinic (cases)
	Hepatitis diagnosis	Fischer et al.[114]	2000	36%	11	4%	1,369	NR	<0.001†	Proportion in HCV+ vs. HCV-	Yes	Adults comprising individuals at risk for HCV and healthcareworkers enrolled in HMO
	Moving motor vehicle accident	Nguyen et al.[113]	2005	15.3%	225	5.4%	204	NR	<0.001†	Proportion HCV+ vs. HCV-	Yes	Adults at general internal medicine clinic (controls) and hepatology clinic (cases)
	Diabetes mellitus	Nguyen et al.[113]	2005	14.4%	225	9.8%	204	NR	0.18†	Proportion HCV+ vs. HCV-	No	Adults at general internal medicine clinic (controls) and hepatology clinic (cases)
	Heart disease	Nguyen et al.[113]	2005	5.4%	225	6.9%	204	NR	0.55†	Proportion HCV+ vs. HCV-	No	Adults at general internal medicine clinic (controls) and hepatology clinic (cases)

Category	Factor	Citation	Year	Percentage of Infected with Factor	Total Number Infected	Percentage of Uninfected with Factor	Total Number Uninfected	Effect Size*	p-Value**	Comparison made	Associated in Study?	Population
	"Blood problems"	Nguyen et al.[113]	2005	18.5%	225	5.4%	204	NR	<0.001†	Proportion HCV+ vs. HCV-	Yes	Adults at general internal medicine clinic (controls) and hepatology clinic (cases)
	Treated for chronic fatigue	Fischer et al.[114]	2000	18%	11	10%	1,369	NR	NS†	Proportion in HCV+ vs. HCV-	No	Adults comprising individuals at risk for HCV and healthcareworkers enrolled in HMO
	Injection of medication in Mexico	Hand and Vasquez[112]	2005	22%	320	27%	307	NR	0.164†	Proportion in HCV+ vs. HCV-	No	Adults tested for HCV in health system because of clinical suspicion
Demographics												
Potential Organ Donors												
Sex	Male Sex	Gasink et al.[102]	2006	80.1%	261	31%	10,654	NR	<0.001	HCV-	Yes	Heart transplant donors
Age	Age, median and interquartile range	Gasink et al.[102]	2006	Median: 38 (IQR: 32-43)	261	Median: 29 (IQR: 20-41)	10,654	NR	<0.001	HCV-	Yes	Heart transplant donors

Category	Factor	Citation	Year	Percentage of Infected with Factor	Total Number Infected	Percentage of Uninfected with Factor	Total Number Uninfected	Effect Size*	p-Value**	Comparison made	Associated in Study?	Population
Race/Ethnicity	Ethnicity: White	Gasink et al.[102]	2006	87.7%	261	85.5%	10,654	NR	0.55	Proportions in HCV+ vs. HCV-	No	Heart transplant donors
	Ethnicity: Black	Gasink et al.[102]	2006	10.7%	261	12.3%	1,304	NR				
	Ethnicity: Other	Gasink et al.[102]	2006	1.5%	261	2.2%	10,654	NR				
Blood Donors												
Sex	Male Sex	Orton et al.[104]	2004	54%	65	54%	225	1.0 (0.6 to 1.8)†	0.97	Proportion in HCV+ vs. HCV-	No	Blood donors
	Male Sex	Murphy et al.[107]	1996	66%	3,126	53%	859,272	1.9 (1.8 to 2.1)‡	SS	Proportion in HCV+ vs. HCV-	Yes	Blood donors
	Female sex	Conry-Cantilena et al.[106]	1996	44%	248	37%	131	NR	0.17†	Proportion in HCV+ vs. HCV-	No	Blood donors initially positive on EIA
Age	Mean age	Orton et al.[104]	2004	43 (mean age)	65	41 (mean age)	225	NR	<0.001	Mean in HCV+ vs. HCV-	No	Blood donors
	Mean age	Conry-Cantilena et al.[106]	1996	37 (mean age)	248	44 (mean age)	131	NR	<0.001†	Proportion in HCV+ vs. HCV-	Yes	Blood donors initially positive on EIA

Category	Factor	Citation	Year	Percentage of Infected with Factor	Total Number Infected	Percentage of Uninfected with Factor	Total Number Uninfected	Effect Size*	p-Value**	Comparison made	Associated in Study?	Population
Race/Ethnicity	White non-Hispanic	Orton et al.[104]	2004	84%	65	89%	225	1.6 (0.7 to 3.5)†	0.26	HCV+ race "other"	No	Blood donors
	Black race	Conry-Cantilena et al.[106]	1996	19%	248	7%	131	NR	0.002†	Proportion in HCV+ vs. HCV-	Yes	Blood donors initially positive on EIA
	Black race	Murphy et al.[107]	1996	17%	3,126	7%	859,272	1.7 (1.6 to 1.9)‡	SS	Proportion in HCV+ vs. HCV- with reference to white	Yes	Blood donors
	Asian	Murphy et al.[107]	1996	1.8%	3,126	3%	859,272	0.4 (0.3 to 0.6)‡	SS	Proportion in HCV+ vs. HCV- with reference to white	No (protective)	Blood donors
	Hispanic	Orton et al.[104]	2004	5%	65	7%	225	0.6 (0.1 to 2.1)†	0.58	Proportion in HCV+ vs. HCV-	No	Blood donors
	Hispanic	Murphy et al.[107]	1996	8.4%	3,126	6%	859,272	1.3 (1.1 to 1.5)‡	SS	Proportion in HCV+ vs. HCV- with reference to white	Yes	Blood donors
Birthplace	Foreign (not U.S.)	Orton et al.[104]	2004	1.5%	65	7.6%	225	0.2 (0.0 to 1.3)†	0.09	Proportion in HCV+ vs. HCV-	No	Blood donors

Category	Factor	Citation	Year	Percentage of Infected with Factor	Total Number Infected	Percentage of Uninfected with Factor	Total Number Uninfected	Effect Size*	p-Value**	Comparison made	Associated in Study?	Population
	Foreign (not U.S.)	Murphy et al.[107]	1996	6%	3,126	6%	859,272	2.8 (2.5 to 3.1)‡	SS	Proportion in HCV+ vs. HCV-	Yes	Blood donors
Occupation	Occupational blood exposure	Murphy et al.[105]	2000	24%	758	17%	1,039	1.7 (1.2 to 2.3)‡	SS	Proportion HCV+ vs. HCV-	Yes	Blood donors
	Medical or dental job (frequent blood contact)	Orton et al.[104]	2004	9.2%	65	3.6%	225	2.8 (0.8 to 9.4)†	0.09	Proportion in HCV+ vs. HCV-	No	Blood donors
	Public safety job (frequent blood contact)	Orton et al.[104]	2004	3.1%	65	3.6%	225	1.0 (0.1 to 5.4)†	1.00	Proportion in HCV+ vs. HCV-	No	Blood donors
Education	High School/ GED or less	Orton et al.[104]	2004	48%	65	28%	225	4.76 (confidence intervals not reported)	<0.001	Test for trend among the three educational strata	Yes – low level	Blood donor
	Associate/ vocational-technical	Orton et al.[104]	2004	40%	65	40%	225	2.8				
	At least Bachelor's degree	Orton et al.[104]	2004	12%	65	32%	225	1.0				
	No college education	Conry-Cantilena et al.[106]	1996	54%	248	16%	131	NR	<0.001	Proportion in HCV+ vs. HCV-	Yes	Blood donors initially positive on EIA

Category	Factor	Citation	Year	Percentage of Infected with Factor	Total Number Infected	Percentage of Uninfected with Factor	Total Number Uninfected	Effect Size*	p-Value**	Comparison made	Associated in Study?	Population
Marital Status	Married	Murphy et al.[105]	2000	60%	758	71%	1,039	0.61 (0.50 to 0.75)†¶	<0.001	Proportion in HCV+ vs. HCV-	Yes, pro-tec-tive	Blood donors
General Population												
Sex	Male	Nguyen et al.[113]	2005	55.0%	225	28.1%	204	NR	<0.001†	Proportion HCV+ vs. HCV-	Yes	Adults at general internal medicine clinic (controls) and hepatology clinic (cases)
	Male	McGinn et al.[108]	2009	40%	83	25%	917	NR	0.02†	Proportion in HCV+ vs. HCV-	Yes	In adult primary care clinic
	Male	Armstrong et al.[30]	2006	64%	238	48%	14,841	NR	<0.05†	Proportion with HCV+ vs. HCV-	Yes	General population
	Male	Fischer et al.[114]	2000	36%	11	43%	1,369	NR	NS †	Proportion with HCV+ vs. HCV-	No	Adults comprising individuals at risk for HCV and healthcareworkers enrolled in HMO
	Male	Kaur et al.[116]	1996	13.4%	544	4.7%	6,275	3.60 (2.66 to 4.87)‡	NR	Proportion in HCV+ vs. HCV-	Yes	Volunteers from general population

Category	Factor	Citation	Year	Percentage of Infected with Factor	Total Number Infected	Percentage of Uninfected with Factor	Total Number Uninfected	Effect Size*	p-Value**	Comparison made	Associated in Study?	Population
Age	Age, mean and standard deviation	McGinn et al.[108]	2009	Mean: 52.9 (SD: 9.7)	83	Mean: 49.8 (SD: 14.7)	917	NR	0.01†	Mean in HCV+ vs. HCV-	Yes	In adult primary care clinic
	Age, decade of Birth 1910-1919	Nguyen et al.[113]	2005	0%	225	0.5%	204	NR	<0.001†	Proportion HCV+ vs. HCV-	Yes	Adults at general internal medicine clinic (controls) and hepatology clinic (cases)
	Age, decade of Birth 1920-1929	Nguyen et al.[113]	2005	0.9%	225	5.4%	204					
	Age, decade of Birth 1930-1939	Nguyen et al.[113]	2005	7.7%	225	7.8%	204					
	Age, decade of Birth 1940-1949	Nguyen et al.[113]	2005	24.9%	225	14.7%	204					
	Age, decade of Birth 1950-1959	Nguyen et al.[113]	2005	51.4%	225	22.5%	204					
	Age, decade of Birth 1960-1969	Nguyen et al.[113]	2005	13.1%	225	24.0%	204					
	Age, decade of Birth 1970-1979	Nguyen et al.[113]	2005	2.3%	225	22.5%	204					
	Age, decade of Birth 1980-1989	Nguyen et al.[113]	2005	0%	225	2.5%	204					

Category	Factor	Citation	Year	Percentage of Infected with Factor	Total Number Infected	Percentage of Uninfected with Factor	Total Number Uninfected	Effect Size*	p-Value**	Comparison made	Associated in Study?	Population
	Age <50 years	Fischer et al.[114]	2000	55%	11	26%	1,369	NR	NS †	Proportion in HCV+ vs. HCV-	No	Adults comprising individuals at risk for HCV and healthcareworkers enrolled in HMO
	Age <60 years	Kaur et al.[116]	1996	12%	520	19%	5,853	0.53 (0.40 to 0.71)†	NR	Proportion in HCV+ vs. HCV- with references to age <60	No (protective)	Volunteers from general population
Race or Ethnicity	Ethnicity: White	Nguyen et al.[113]	2005	67.1%	225	57.9%	204	NR	0.15†	Proportion HCV+ vs. HCV-	No	Adults at general internal medicine clinic (controls) and hepatology clinic (cases)
	Ethnicity: Black	Nguyen et al.[113]	2005	23.9%	225	30.2%	204	NR				
	Ethnicity: Asian	Nguyen et al.[113]	2005	2.3%	225	5.9%	204	NR				
	Ethnicity: Latino	Nguyen et al.[113]	2005	3.6%	225	3.0%	204	NR				
	Ethnicity: Other	Nguyen et al.[113]	2005	3.2%	225	3.0%	204	NR				

Category	Factor	Citation	Year	Percentage of Infected with Factor	Total Number Infected	Percentage of Uninfected with Factor	Total Number Uninfected	Effect Size*	p-Value**	Comparison made	Associated in Study?	Population
	Ethnicity: White	McGinn et al.[108]	2008	11%	83	10%	917	NR	0.38†	Proportion in HCV+ vs. HCV-	No	In adult primary care clinic
	Ethnicity: Black	McGinn et al.[108]	2008	31%	83	32%	917	NR				
	Ethnicity: Other	McGinn et al.[108]	2008	0%	83	5%	917	NR				
	Ethnicity: Latino	McGinn et al.[108]	2008	58%	83	53%	917	NR				
	Ethnicity: non-Hispanic black	Armstrong et al.[30]	2006	42%	252	26%	13,691	1.9 (0.9 to 3.8)‡	NS	Proportion HCV+ vs. Non-Hispanic white	No	General population aged 20 to 59 years
	Ethnicity: Mexican-American	Armstrong et al.[30]	2006	23%	252	32%	13,691	2.6 (1.2 to 5.8)‡	SS	Proportion HCV+ vs. Non-Hispanic white	Yes	General population aged 20 to 59 years
	White/Hispanic	Kaur et al.[116]	1996	7.9%	507	9.2%	5,764	0.57 (0.39 to 0.83)‡	NR	Proportion HCV+ with reference to "other"	Yes, protective	Volunteers from general population

Category	Factor	Citation	Year	Percentage of Infected with Factor	Total Number Infected	Percentage of Uninfected with Factor	Total Number Uninfected	Effect Size*	p-Value**	Comparison made	Associated in Study?	Population
Nationality	U.S. Citizen	Nguyen et al.[113]	2005	97.7%	225	97.5%	204	NR	>0.99†	Proportion HCV+ vs. HCV-	No	Adults at general internal medicine clinic (controls) and hepatology clinic (cases)
	Born outside of U.S.	Armstrong et al.[30]	2006	6%	233	20%	14,787	0.2 (0.08-0.7)‡	SS	Born in U.S. HCV+	Yes	General population aged 20 to 59 years
	Born in Southeast Asia/Africa	Kaur et al.[116]	1996	7.7%	559	8.5%	6,069	0.90 (0.50 to 1.64)†	NS	Proportion in HCV+ vs. HCV-	No	Volunteers from general population
Language	Preferred language – English	McGinn et al.[108]	2008	89%	83	79%	917	NR	0.03†	Proportion in HCV+ vs. HCV-	Yes	In adult primary care clinic
	Preferred language – Spanish	McGinn et al.[108]	2008	11%	83	20%	917					
Occupation	Work contact with blood	Fischer et al.[114]	2000	27%	11	20%	1,369	NR	NS†	Proportion in HCV+ vs. HCV-	No	Adults comprising individuals at risk for HCV and healthcareworkers enrolled in HMO
	Healthcare worker	Kaur et al.[116]	1996	2.9%	568	10.3%	6, 185	0.26 (0.19 to 0.35)†	SS	Proportion in HCV+ vs. HCV-	Yes (protective)	Volunteers from general population

Category	Factor	Citation	Year	Percentage of Infected with Factor	Total Number Infected	Percentage of Uninfected with Factor	Total Number Uninfected	Effect Size*	p-Value**	Comparison made	Associated in Study?	Population
	Armed forces	Fischer et al.[114]	2000	36%	11	27%	1,369	NR	NS†	Proportion in HCV+ vs. HCV-	No	Adults comprising individuals at risk for HCV and healthcareworkers enrolled in HMO
	Services in U.S. armed forces	Armstrong et al.[30]	2006	32%	114	31%	4,063	NR	NS	Prevalence HCV+ vs. HCV-	No	Men aged at least 20 years in general population
	Job at prison	Nguyen et al.[113]	2005	7.7%	225	1.5%	204	NR	0.002†	Proportion HCV+ vs. HCV-	Yes	Adults at general internal medicine clinic (controls) and hepatology clinic (cases)
Education	Education – less than 12 years	Armstrong et al.[30]	2006	62%	172	43%	8,634	NR	<0.005†	Proportion HBV+ with >12 years	Yes	General population aged at least 20 years

Category	Factor	Citation	Year	Percentage of Infected with Factor	Total Number Infected	Percentage of Uninfected with Factor	Total Number Uninfected	Effect Size*	p-Value**	Comparison made	Associated in Study?	Population
	Education – 6th grade or less	McGinn et al.[108]	2008	10%	83	11%	917	NR	0.62†	Proportion with level in HCV+ vs. HCV-	No	In adult primary care clinic
	Education – 7-12th grade	McGinn et al.[108]	2008	38%	83	31%	917					
	Education – High school graduate	McGinn et al.[108]	2008	25%	83	25%	917					
	Education – Some college	McGinn et al.[108]	2008	19%	83	19%	917					
	Education – At least a college degree	McGinn et al.[108]	2008	7%	83	13%	917					
	Education – High school or less	Nguyen et al.[113]	2005	46.4%	225	22.7%	204	NR	0.15†	Proportion HCV+ vs. HCV-	No	Adults at general internal medicine clinic (controls) and hepatology clinic (cases)
	Education – Some college	Nguyen et al.[113]	2005	30.6%	225	25.1%	204					
	Education – At least a college graduate	Nguyen et al.[113]	2005	23.0%	225	52.2%	204					

Category	Factor	Citation	Year	Percentage of Infected with Factor	Total Number Infected	Percentage of Uninfected with Factor	Total Number Uninfected	Effect Size*	p-Value**	Comparison made	Associated in Study?	Population
Economic Factors	Homeless, ever	Nguyen et al.[113]	2005	9.2%	225	1.0%	204	NR	<0.001†	Proportion HCV+ vs. HCV-	Yes	Adults at general internal medicine clinic (controls) and hepatology clinic (cases)
	Annual Income <15,000	Nguyen et al.[113]	2005	13.1%	225	10.2%	204	NR	0.90†	Proportion HCV+ vs. HCV-	No	Adults at general internal medicine clinic (controls) and hepatology clinic (cases)
	Annual Income 15,000-25,000	Nguyen et al.[113]	2005	12.6%	225	11.7%	204					
	Annual Income 25,000-40,000	Nguyen et al.[113]	2005	15.9%	225	19.9%	204					
	Annual Income 40,000-75,000	Nguyen et al.[113]	2005	26.2%	225	29.1%	204					
	Annual Income 75,000-100,000	Nguyen et al.[113]	2005	18.7%	225	14.3%	204					
	Annual Income >100,000	Nguyen et al.[113]	2005	13.6%	225	14.8%	204					
	Family income ≥2 times poverty threshold	Armstrong et al.[30]	2006	31%	278	49%	13,362	NR	NS†	Proportion HCV+ vs. HCV-	No	General population

Category	Factor	Citation	Year	Percentage of Infected with Factor	Total Number Infected	Percentage of Uninfected with Factor	Total Number Uninfected	Effect Size*	p-Value**	Comparison made	Associated in Study?	Population
	Family income 1 to 1.9 times poverty threshold	Armstrong et al.[30]	2006	30%	278	27%	13,362	NR	NS†	Proportion HCV+ vs. HCV-	No	General population
Other	Community – Rural	Nguyen et al.[113]	2005	12.8%	225	10.9%	204	NR	<0.001†	Proportion HCV+ vs. HCV-	Yes	Adults at general internal medicine clinic (controls) and hepatology clinic (cases)
	Community – Suburban	Nguyen et al.[113]	2005	52.6%	225	30.6%	204					
	Community – Urban	Nguyen et al.[113]	2005	34.6%	225	58.6%	204					
	Insurance – Medicaid	McGinn et al.[108]	2008	77%	83	59%	917	NR	<0.001†	Proportion with insurance type in HCV+ vs. HCV-	Yes	In adult primary care clinic
	Insurance – Medicare	McGinn et al.[108]	2008	12%	83	19%	917					

Category	Factor	Citation	Year	Percentage of Infected with Factor	Total Number Infected	Percentage of Uninfected with Factor	Total Number Uninfected	Effect Size*	p-Value**	Comparison made	Associated in Study?	Population
	Insurance – Private	McGinn et al.[108]	2008	10%	83	21%	917					
	Insurance – Self Pay	McGinn et al.[108]	2008	1%	83	1%	917					
	Appointment type – Scheduled	McGinn et al.[108]	2008	76%	83	78%	917	NR	0.86†	Proportion with type in HCV+ vs. HCV-	No	In adult primary care clinic
	Appointment type – Urgent Care	McGinn et al.[108]	2008	17%	83	16%	917					
	Appointment type – Data Missing	McGinn et al.[108]	2008	7%	83	6%	917					
Children and Adolescents												
Sex	Male	Luban et al.[118]	2007	65%	43	58%	2,715	1.4 (0.7 to 2.5)†¶	0.36¶	Proportion HCV+ vs. HCV-	No	Children who have received blood transfusions
Race/ Ethnicity	African American	Luban et al.[118]	2007	42%	42	37%	2,474	1.2 (0.7 to 2.3)†¶	0.51¶	Proportion HCV+ vs. HCV	No	Children who have received blood transfusions
	Asian	Luban et al.[118]	2007	0%	42	1.5%	2,474	0.7 (0.05 to 12.6)†¶	0.85¶	Proportion HCV+ vs. HCV	No	Children who have received blood transfusions

Category	Factor	Citation	Year	Percentage of Infected with Factor	Total Number Infected	Percentage of Uninfected with Factor	Total Number Uninfected	Effect Size*	p-Value**	Comparison made	Associated in Study?	Population
	Caucasian	Luban et al.[118]	2007	57%	42	48%	2,474	1.4 (0.8 to 2.7)†¶	0.25¶	Proportion HCV+ vs. HCV	No	Children who have received blood transfusions
	Hispanic	Luban et al.[118]	2007	0%	42	3.4%	2,474	0.3 (0.02 to 5.4)†¶	0.44¶	Proportion HCV+ vs. HCV	No	Children who have received blood transfusions

* Odds ratios as reported in publication, unless otherwise specified
** As reported in publication, unless otherwise specified
† Univariate, unadjusted
‡ Multivariate, adjusted for other factors
¶ Calculated by ECRI Institute

Table 41. HIV: Nonbehavioral Risk Factors

Category	Factor	Citation	Year	Percentage of Infected with Factor	Total Number Infected	Percentage of Uninfected with Factor	Total Number Uninfected	Effect Size*	p-Value**	Comparison Made	Associated in Study?	Population
Tissue Donors												
Co-Morbidity												
Transfusion	Blood transfusion recipient or donor	Sanchez et al.[103]	2006	Not reported (NR)	10	NR	56	NR	Not significant (NS)	Proportion in HIV+ vs. HIV-	No	Potential tissue donors, as reported by next of kin
Nonspecific Exposure	Accidental needle stick	Sanchez et al.[103]	2006	NR	10	NR	56	NR	NS	Proportion in HIV+ vs. HIV-	No	Potential tissue donors, as reported by next of kin
	History of transplant	Sanchez et al.[103]	2006	NR	10	NR	56	NR	NS	Proportion in HIV+ vs. HIV-	No	Potential tissue donors, as reported by next of kin
	Surgeries	Sanchez et al.[103]	2006	NR	10	NR	56	NR	NS	Proportion in HIV+ vs. HIV-	No	Potential tissue donors, as reported by next of kin
Other	Treatment by physician in last 2 years	Sanchez et al.[103]	2006	NR	10	NR	56	NR	NS	Proportion in HIV+ vs. HIV-	No	Potential tissue donors, as reported by next of kin
	Liver disease	Sanchez et al.[103]	2006	NR	10	NR	56	NR	NS	Proportion in HIV+ vs. HIV-	No	Potential tissue donors, as reported by next of kin
	Medical hospitalizations	Sanchez et al.[103]	2006	NR	10	NR	56	NR	NS	Proportion in HIV+ vs. HIV-	No	Potential tissue donors, as reported by next of kin
	Psychiatric hospitalizations	Sanchez et al.[103]	2006	NR	10	NR	56	NR	NS	Proportion in HIV+ vs. HIV-	No	Potential tissue donors, as reported by next of kin

Category	Factor	Citation	Year	Percentage of Infected with Factor	Total Number Infected	Percentage of Uninfected with Factor	Total Number Uninfected	Effect Size*	p-Value**	Comparison Made	Associated in Study?	Population
	Medical illnesses	Sanchez et al.[103]	2006	NR	10	NR	56	NR	NS	Proportion in HIV+ vs. HIV-	No	Potential tissue donors, as reported by next of kin
	Medications	Sanchez et al.[103]	2006	NR	10	NR	56	NR	NS	Proportion in HIV+ vs. HIV-	No	Potential tissue donors, as reported by next of kin
	Toxic exposure	Sanchez et al.[103]	2006	NR	10	NR	56	NR	NS	Proportion in HIV+ vs. HIV-	No	Potential tissue donors, as reported by next of kin
	Malaria exposure or treatment	Sanchez et al.[103]	2006	NR	10	NR	56	NR	NS	Proportion in HIV+ vs. HIV-	No	Potential tissue donors, as reported by next of kin
	Chagas disease exposure or treatment	Sanchez et al.[103]	2006	NR	10	NR	56	NR	NS	Proportion in HIV+ vs. HIV-	No	Potential tissue donors, as reported by next of kin
	Rabies exposure	Sanchez et al.[103]	2006	NR	10	NR	56	NR	NS	Proportion in HIV+ vs. HIV-	No	Potential tissue donors, as reported by next of kin
	Heart disease	Sanchez et al.[103]	2006	NR	10	NR	56	NR	NS	Proportion in HIV+ vs. HIV-	No	Potential tissue donors, as reported by next of kin
	Hypertension	Sanchez et al.[103]	2006	NR	10	NR	56	NR	NS	Proportion in HIV+ vs. HIV-	No	Potential tissue donors, as reported by next of kin
	Kidney disease	Sanchez et al.[103]	2006	NR	10	NR	56	NR	NS	Proportion in HIV+ vs. HIV-	No	Potential tissue donors, as reported by next of kin
	Gastrointestinal disease	Sanchez et al.[103]	2006	NR	10	NR	56	NR	NS	Proportion in HIV+ vs. HIV-	No	Potential tissue donors, as reported by next of kin

Category	Factor	Citation	Year	Percentage of Infected with Factor	Total Number Infected	Percentage of Uninfected with Factor	Total Number Uninfected	Effect Size*	p-Value**	Comparison Made	Associated in Study?	Population
	Cancer history	Sanchez et al.[103]	2006	NR	10	NR	56	NR	NS	Proportion in HIV+ vs. HIV-	No	Potential tissue donors, as reported by next of kin
	Diabetes history	Sanchez et al.[103]	2006	NR	10	NR	56	NR	NS	Proportion in HIV+ vs. HIV-	No	Potential tissue donors, as reported by next of kin
	Pulmonary disease	Sanchez et al.[103]	2006	NR	10	NR	56	NR	NS	Proportion in HIV+ vs. HIV-	No	Potential tissue donors, as reported by next of kin
	Rheumatologic disease	Sanchez et al.[103]	2006	NR	10	NR	56	NR	NS	Proportion in HIV+ vs. HIV-	No	Potential tissue donors, as reported by next of kin
	Connective tissue disease	Sanchez et al.[103]	2006	NR	10	NR	56	NR	NS	Proportion in HIV+ vs. HIV-	No	Potential tissue donors, as reported by next of kin
	Dermatologic disease	Sanchez et al.[103]	2006	NR	10	NR	56	NR	NS	Proportion in HIV+ vs. HIV-	No	Potential tissue donors, as reported by next of kin
	Neurologic disease	Sanchez et al.[103]	2006	NR	10	NR	56	NR	NS	Proportion in HIV+ vs. HIV-	No	Potential tissue donors, as reported by next of kin
	HIV testing	Sanchez et al.[103]	2006	NR	10	NR	56	NR	NS	Proportion in HIV+ vs. HIV-	No	Potential tissue donors, as reported by next of kin
	Ocular disease	Sanchez et al.[103]	2006	NR	10	NR	56	NR	NS	Proportion in HIV+ vs. HIV-	No	Potential tissue donors, as reported by next of kin

Category	Factor	Citation	Year	Percentage of Infected with Factor	Total Number Infected	Percentage of Uninfected with Factor	Total Number Uninfected	Effect Size*	p-Value**	Comparison Made	Associated in Study?	Population
General Population												
Other Infection	STD, diagnosis of	Mehta et al.[109]	2008	25%	229	NR	16,467	1.56 (1.15 to 2.11)†	NR	No STD, HIV+	Yes	Hospital inpatients and outpatients
	Herpes simplex virus-2 (HSV-2) antibody	McQuillan et al.[101]	2006	81%	31	20%	5,570	17.1 (6.9 to 41.9)†¶	<0.001	Proportion in HCV+ vs. HCV-	Yes	General population
	HSV-2 serostatus	Nguyen et al.[110]	2008	71.2%	21	26.9%	1,589	6.46 (2.30 to 18.10)†	Statistically significant (SS)	Negative	Yes	General population of adults in New York City
	History of syphilis	Alpert et al.[115]	1996	NR	35	NR	840	NR‡	SS	Proportion in HCV+ vs. HCV-	Yes	Adults at emergency department room
	Infection not necessarily related to HIV	Alpert et al.[115]	1996	NR	35	NR	840	NR‡	SS	Proportion in HCV+ vs. HCV-	Yes	Adults at emergency department room
Demographics												
General Population												
Sex	Male	Mehta et al.[109]	2008	63%	229	NR	16,467	1.30 (0.98 to 1.71)†	NR	Female HIV+	No	Hospital inpatients and outpatients
	Male	Zetola et al.[111]	2008	NR	15	NR	1,632	7.68 (0.98 to 60.26)‡	0.053	Female HIV+	No	Public hospital emergency room patients
	Male	Nguyen et al.[110]	2008	57.1	21	42.4	1,602	2.01 (0.91 to 4.40)†	NS	Female HIV+	No	General population of adults in New York City

Category	Factor	Citation	Year	Percentage of Infected with Factor	Total Number Infected	Percentage of Uninfected with Factor	Total Number Uninfected	Effect Size*	p-Value**	Comparison Made	Associated in Study?	Population
Age	Age 18-30	Zetola et al.[111]	2008	NR	15	NR	1,632	3.15 (1.03 to 9.61)‡	0.044	Proportion HIV+ vs. HIV- >46 years	Yes	Public hospital emergency room patients
	Age 31-45	Zetola et al.[111]	2008	NR	15	NR	1,632	0.76 (0.15 to 2.76)†; NR‡	0.732†; NS‡	Proportion HIV+ vs. HIV- >46 years	No	Public hospital emergency room patients
	Age 25-39	Mehta et al.[109]	2008	48%	229	NR	16,467	3.22 (1.84 to 5.64)†	NR	Age 15-24, HIV+	Yes	Hospital inpatients and outpatients
	Age 40-54	Mehta et al.[109]	2008	42%	229	NR	16,467	3.39 (2.24 to 6.91)†	NR	Age 15-24 HIV+	Yes	Hospital inpatients and outpatients
	Age 55+	Mehta et al.[109]	2008	4%	229	NR	16,467	1.19 (0.50 to 2.85)†	NR	Age 15-24 HIV+	No	Hospital inpatients and outpatients
	Age 35 to 44 years	Alpert et al.[115]	1996	NR	35	NR	840	NR‡	SS	Proportion in HCV+ vs. HCV-	Yes	Adults at emergency department room
Race/Ethnicity	Ethnicity, Black	Mehta et al.[109]	2008	44%	229	NR	16,467	2.51 (1.61 to 3.93)†	NR	Proportion HIV+ vs. White	Yes	Hospital inpatients and outpatients
	Black	Zetola et al.[111]	2008	NR	15	NR	1,632	1.01 (0.24 to 4.22)†; NR‡	0.995†; NS‡	Proportion HIV+ vs. HIV- vs. White	No	Public hospital emergency room patients
	Black race/ethnicity	Nguyen et al.[110]	2008	55.0	20	20.9	1,578	5.53 (1.00 to 30.66)†	SS	White race/ethnicity HIV+	Yes	General population of adults in New York City

Category	Factor	Citation	Year	Percentage of Infected with Factor	Total Number Infected	Percentage of Uninfected with Factor	Total Number Uninfected	Effect Size*	p-Value**	Comparison Made	Associated in Study?	Population
	Ethnicity, Asian	Mehta et al.[109]	2008	0.4%	229	NR	16,467	0.50 (0.07 to 3.68)†	NR	Proportion HIV+ vs. HIV-	No	Hospital inpatients and outpatients
	Asian race/ethnicity	Nguyen et al.[110]	2008	5.0	20	13.0	1,578	1.12 (0.10 to 12.66)†	NS	White race/ethnicity HIV+	No	General population of adults in New York City
	Ethnicity, Cape Verdean	Mehta et al.[109]	2008	4%	229	NR	16,467	3.40 (1.16 to 7.15)†	NR	Proportion HIV+ vs. HIV-	Yes	Hospital inpatients and outpatients
	Ethnicity, Haitian	Mehta et al.[109]	2008	13%	229	NR	16,467	3.84 (2.24 to 6.60)†	NR	Proportion HIV+ vs. HIV	Yes	Hospital inpatients and outpatients
	Ethnicity, Other/ Not reported	Mehta et al.[109]	2008	11%	229	NR	16,467	3.43 (1.96 to 6.02)†	NR	Proportion HIV+ vs. HIV	Yes	Hospital inpatients and outpatients
	Hispanic	Zetola et al.[111]	2008	NR	15	NR	1,632	2.07 (0.83 to 8.99)†; NR‡	0.253†; NS‡	Proportion HIV+ vs. White	No	Public hospital emergency room patients
	Hispanic race/ethnicity	Nguyen et al.[110]	2008	30.0	20	36.0	1,578	2.07 (0.38 to 11.39)†	NS	White race/ethnicity HIV+	No	General population of adults in New York City
Language	Spanish speaker	Zetola et al.[111]	2008	NR	15	NR	1,632	0.58 (0.08 to 4.47)†; NR‡	0.559†; NS‡	English speakers HIV+	No	Public hospital emergency room patients

Category	Factor	Citation	Year	Percentage of Infected with Factor	Total Number Infected	Percentage of Uninfected with Factor	Total Number Uninfected	Effect Size*	p-Value**	Comparison Made	Associated in Study?	Population
Education	Less than high school	McQuillan et al.[101]	2006	39%	31	32%	5,889	1.4 (0.66 to 2.8)†¶	0.41	Proportion in HIV+ vs. HIV-	No	General population
	Less than high school	Mehta et al.[109]	2008	30%	229	NR	16,467	1.41 (0.96 to 2.07)†	NR	At least high school/ GED, HIV+	No	Hospital inpatients and outpatients
Economic Factors	Homeless	Zetola et al.[111]	2008	NR	15	NR	1,632	3.89 (1.32 to 11.45)‡	0.014	Non-homeless HIV+	Yes	Public hospital emergency room patients
	Poverty Index <1	McQuillan et al.[101]	2006	41%	27	33%	5,371	1.41 (0.65 to 3.0)†¶	0.38	Proportion HIV+ vs. HIV-	No	General population
Other	No health insurance	Mehta et al.[109]	2008	21%	212	NR	16,467	1.66 (1.19 to 2.32)†	NR	Insured HIV+	Yes	Hospital inpatients and outpatients
	No health insurance	Zetola et al.[111]	2008	NR	15	NR	1,632	1.09 (0.38 to 3.12)†; NS‡	0.875†; NS‡	Insured HIV+	No	Public hospital emergency room patients
Marital Status	Married/ living together	McQuillan et al.[101]	2006	24%	29	53%	5,631	0.28 (0.12 to 0.60)†¶	0.003¶	Proportion HIV+ vs. HIV- vs. Divorced, separated, never married	Yes (Protective)	General population adults

Category	Factor	Citation	Year	Percentage of Infected with Factor	Total Number Infected	Percentage of Uninfected with Factor	Total Number Uninfected	Effect Size*	p-Value**	Comparison Made	Associated in Study?	Population
Children and Adolescents												
Sex	Male	D'Angelo et al.[119]	1991	15%	13	33%	3,507	NR	<0.05†	Proportion HIV+ vs. HIV-	No (pro-tective)	Adolescents attending urban hospital
Age	Age >15 years	D'Angelo et al.[119]	1991	NR	13	NR	3,507	NR	<0.05†	Proportion HIV+ vs. Age <15	Yes	Adolescents attending urban hospital

* Odds ratios as reported in publication, unless otherwise specified
** As reported in publication, unless otherwise specified

† Univariate, unadjusted
‡ Multivariate, adjusted for other factors
¶ Calculated by ECRI Institute

Table 42. GRADE Table for Question 4 (Nonbehavioral Risk Factors)

Factor	Virus	Quantity and Type of Evidence	Findings	Starting Grade	Decrease Grade					Increase Grade			GRADE of Evidence for Outcome
					Overall Quality	Consistency	Directness	Precision	Publication Bias	Large Magnitude	Dose Response	Associated Despite Confounders	
Factors Identified in Original Guideline													
Exposure to Infected or Suspected Blood	HBV	1 OBS[127]	One study of embalmers who had a needle stick injury during embalming did not find an association between needlestick injuries with known or suspected HBV positive blood and HBV infection.[127]	Low	0	-1	-1	-1	0	0	0	0	Very Low
	HCV	No studies	-	-	-	-	-	-	-	-	-	-	Not Applicable (NA)
	HIV	-	-	-	-	-	-	-	-	-	-	-	NA
Signs and Symptoms	HBV	No studies	-	-	-	-	-	-	-	-	-	-	NA
	HCV	1 OBS[113]	Jaundice: Associated in one study[113]	Low	0	-1	0	0	0	1	0	0	Low
		1 OBS[104]	ALT Reactivity: Associated in one study.[104]	Low	0	-1	0	0	0	1	0	0	Low
		1 OBS[30]	ALT >40 U/L: Associated in one study[30]	Low	0	-1	0	0	0	1	0	0	Low
		1 OBS[114]	Elevated liver enzyme: Associated in one study[114]	Low	0	-1	0	0	0	0	0	0	Very Low
	HIV	No studies	-	-	-	-	-	-	-	-	-	-	NA

Factor	Virus	Quantity and Type of Evidence	Findings	Starting Grade	Decrease Grade					Increase Grade			GRADE of Evidence for Outcome
					Overall Quality	Consistency	Directness	Precision	Publication Bias	Large Magnitude	Dose Response	Associated Despite Confounders	
Receipt of Blood Transfusion	HBV	3 OBS[116,124,126]	Blood transfusion was associated with HBV infection in a general population,[116] as was blood transfusion before 1991 in a special population.[124] Blood transfusion was not associated with HBV in another special population study.[126]	Low	0	0	-1	0	0	0	0	0	Very Low
	HCV	8 OBS[30,105-107,112-114,116]	All 8 studies associated having had a blood transfusion with HCV, and in eight of them the effect size was large. It was independently associated with HCV with large effect sizes in three blood donor studies[105-107] and two general population studies.[112,116] Two additional general population study performed univariate analyses only and found large effect sizes.[113,114] The remaining general population study found an independent association between having a blood transfusion before 1992 and HCV, but the effect size was not large.[30]	Low	0	0	0	0	0	1	0	0	Moderate
	HIV	No studies	-	-	-	-	-	-	-	-	-	-	NA

Factor	Virus	Quantity and Type of Evidence	Findings	Starting Grade	Decrease Grade					Increase Grade			GRADE of Evidence for Outcome
					Overall Quality	Consistency	Directness	Precision	Publication Bias	Large Magnitude	Dose Response	Associated Despite Confounders	
Accidental Needlestick with Unknown Blood	HBV	2 OBS[103,116]	According to data collected from a low-quality next-of-kin, accidental needle sticks were not associated with HBV among potential tissue donors.[103] A general population study found a lower prevalence of HBV among people who reported a needlestick.[116]	Low	0	0	0	-1	0	0	0	0	Very Low
	HCV	4 OBS[103,105,106,116]	According to data collected from a low-quality next-of-kin, accidental needle sticks were not associated with HCV among potential tissue donors[103] A general population study found a lower prevalence of HCV among people who reported a needlestick.[116] Among blood donors who work in a healthcare setting, needlestick injuries were not associated with HCV in one study,[106] but "bloody" needlestick injuries were in another.[105]	Low	0	-1	0	0	0	0	0	0	Very Low
	HIV	1 OBS[103]	According to data collected from a low-quality next-of-kin, accidental needle sticks were not associated with HIV among potential tissue donors[103]	Low	-1	-1	0	-1	0	0	0	0	Very Low
Hemodialysis	HBV	2 OBS[116,124]	Hemodialysis was associated with HBV in one general population study[116] and one special population study.[124] Both analyses were univariate, and the special population study had a large effect size.	Low	0	0	0	0	0	1	0	0	Moderate
	HCV	3 OBS[112,113,116]	In general population studies, "kidney dialysis" was associated with HCV in a univariate analysis in one study,[113] and hemodialysis was associated with HCV with a large effect size in multivariate analysis in a second study.[116] A third study did not find an association between hemodialysis and HCV.[112]	Low	0	0	0	0	0	0	0	0	Low

Factor	Virus	Quantity and Type of Evidence	Findings	Starting Grade	Decrease Grade					Increase Grade			GRADE of Evidence for Outcome
					Overall Quality	Consistency	Directness	Precision	Publication Bias	Large Magnitude	Dose Response	Associated Despite Confounders	
	HIV	No studies	-	-	-	-	-	-	-	-	-	-	NA
Surgery	HBV	3 OBS[103,116,117]	The tissue donor study did not associate having had surgery with HBV.[103] One general population study found a lower prevalence of HBV among people who had surgery,[116] and another found no relationship.[117]	Low	0	-1	0	0	0	0	0	0	Very Low
	HCV	5 OBS[103-105,114,116]	The tissue donor study did not associate having had surgery with HCV.[103] One blood donor study did not find any association with recent surgery[104] and one general population study did not find any association with history of surgery.[114] However, one blood donor study did find an independent association between HCV and lifetime history of surgery (or sutures).[105] A general population study found no association.[116]	Low	0	-1	0	0	0	0	0	0	Very Low
	HIV	1 OBS[103]	The tissue donor study did not associate having had surgery with HIV.[103]	Low	-1	-1	0	-1	0	0	0	0	Very Low
Organ Transplant Recipients	HBV	2 OBS[103,121]	HBV was not associated with having an organ transplant in one very low-quality study[103] or a special population study.[121]	Low	0	0	0	-1	0	0	0	0	Very Low
	HCV	1 OBS[103]	HCV was not associated with having an organ transplant in one very low-quality study.[103]	Low	-1	-1	0	-1	0	0	0	0	Very Low
	HIV	1 OBS[103]	HCV was not associated with having an organ transplant in one very low-quality study.[103]	Low	-1	-1	0	-1	0	0	0	0	Very Low

Factor	Virus	Quantity and Type of Evidence	Findings	Starting Grade	Decrease Grade					Increase Grade			GRADE of Evidence for Outcome
					Overall Quality	Consistency	Directness	Precision	Publication Bias	Large Magnitude	Dose Response	Associated Despite Confounders	
Acupuncture	HBV	2 OBS[117,121]	Neither the general population study[117] nor the special population study[121] found an association between HBV and acupuncture.	Low	0	0	0	0	0	0	0	0	Low
	HCV	3 OBS[106,107,112]	Acupuncture was not associated with HCV infection in two studies of blood donors[106,107] or one study of a general population.[112]	Low	0	0	0	0	0	0	0	0	Low
	HIV	No studies	-	-	-	-	-	-	-	-	-	-	NA
Dental Work	HBV	1 OBS[117]	Dental work within the last six months was not associated with acute HBV in one general population study.[117]	Low	0	0	0	-1	0	0	0	0	Very Low
	HCV	2 OBS[104,105]	Dental work was not associated with HCV among blood donors in one study[105]; nor was having dental work in the six months before donation in another.[104]	Low	0	0	0	0	0	0	0	0	Low
	HIV	No Studies	-	-	-	-	-	-	-	-	-	-	NA
Blood Draws	HBV	1 OBS[103]	The tissue donor study did not find an association between HIV testing and HBV, based upon next-of-kin interviews.[103]	Low	-1	-1	0	-1	0	0	0	0	Very Low
	HCV	2 OBS[103,113]	The low-quality tissue donor study did not find an association between HIV testing and HCV, based upon next of-kin interviews.[103] One general population study did find an association between having had a blood test for HBV and having an HCV infection.[113] The same study also found that being a blood donor was associated with reduced risk of HCV.[113]	Low	0	0	0	-1	0	0	0	0	Very Low

Factor	Virus	Quantity and Type of Evidence	Findings	Starting Grade	Decrease Grade					Increase Grade			GRADE of Evidence for Outcome
					Overall Quality	Consistency	Directness	Precision	Publication Bias	Large Magnitude	Dose Response	Associated Despite Confounders	
	HIV	1 OBS[103]	The tissue donor study did not find an association between HIV testing and HIV, based upon next of-kin interviews.[103]	Low	-1	-1	0	-1	0	0	0	0	Very Low
Household Exposure	HBV	5 OBS[117,122-124,126]	Having household contact with someone with hepatitis was associated with HBV in a special population study[124], as was a family history of HBV in another special population study.[123] However, having a household member with hepatitis was not associated with HBV in a third special population study;[126] nor was being the wife of a man with HBV in a fourth special population study.[122] Sharing a razor or toothbrush with a household member was not associated with HBV in a general population study either.[117]	Low	0	-1	-1	0	0	0	0	0	Very Low
	HCV	3 OBS[105,113,114]	In one blood donor study, living with someone with hepatitis or having a relative with hepatitis was not associated with HCV , but living with a transfusion recipient and sharing a toothbrush or razor with person(s) unspecified was.[105] In general population studies, having at least one family member treated for viral hepatitis was not associated with an increased risk of HCV in one study,[114] but having at least one family member with HCV in another study was.[113]	Low	0	-1	0	0	0	0	0	0	Very Low
	HIV	No studies	-	-	-	-	-	-	-	-	-	-	NA

Factor	Virus	Quantity and Type of Evidence	Findings	Starting Grade	Decrease Grade					Increase Grade			GRADE of Evidence for Outcome
					Overall Quality	Consistency	Directness	Precision	Publication Bias	Large Magnitude	Dose Response	Associated Despite Confounders	
Other Infections	HBV	2 OBS[102,124]	HBV surface antigen positivity was associated with HCV infection among heart donors in one study.[102] HBV infection was associated with having had a sexually transmitted disease (STD) in a special population study.[124]	Low	0	0	0	0	0	0	0	0	Low
	HCV	6 OBS [30,104,106,107,112,113]	HCV was significantly associated with history of STD in two blood donor studies[106,107] but not a general population study.[113] HCV was associated with having a STD within six months of donating in another blood donor study.[104] Herpes infection was associated with HCV in a general population study[30] In addition, HCV was associated with seropositivity for other reactive infectious diseases in two blood donor studies.[104,107] HIV infection was not associated with HCV infection upon univariate analysis of a general population study.[112]	Low	0	-1	0	0	0	0	0	0	Very Low
	HIV	4 OBS[101,109,110,115]	In general population studies, HIV infection was associated with diagnosis of STD in one study,[109] HSV-2 in two studies,[101,110] and syphilis or other infection not apparently related to HIV in another study,[115]	Low	0	0	0	0	0	0	0	0	Low

Factor	Virus	Quantity and Type of Evidence	Findings	Starting Grade	Decrease Grade					Increase Grade			GRADE of Evidence for Outcome
					Overall Quality	Consistency	Directness	Precision	Publication Bias	Large Magnitude	Dose Response	Associated Despite Confounders	
Sex	HBV	6 OBS [116,118,120,121,123,124]	In one general population study[116] and 2 special population studies[121,123] males had higher prevalence of HBV. Two additional special populations studies found no difference[120] or a lower prevalence.[124] A study of children found no difference.[118]	Low	0	-1	-1	0	0	0	0	0	Very Low
	HCV	9 OBS[30,102,104,106-108,113,114,116]	One organ donor study found an increased prevalence of HCV in males.[102] Among blood donors it was in one study[107] but not in two others.[104,106] Four general population studies found an increased risk among males.[30,108,113,116] but one other did not.[114]	Low	0	-1	0	0	0	0	0	0	Very Low
	HIV	3 OBS[109-111]	None of three general population studies associated male sex with an increased prevalence of HIV.[109-111]	Low	0	0	0	0	0	0	0	0	Low
Age	HBV	8 OBS[116,120-125,127]	Every study tested the association of HBV and age in different ways, and the results are inconsistent and difficult to compare. One general population study found an increased risk of HBV when >60 years.[116] The rest of the studies were special population studies. One found an association with mean age (with older people having greater prevalence of HBV)[124] while another did not.[121] Increased prevalence was associated with age younger than 20 years,[122] age over 35 years,[127] and age over 50 years.[125] In another study lower prevalence was found in people under 49 years.[120] The remaining study did not find any association between age and HBV.[123]	Low	0	-1	-1	0	0	0	0	0	Very Low

Factor	Virus	Quantity and Type of Evidence	Findings	Starting Grade	Decrease Grade					Increase Grade			GRADE of Evidence for Outcome
					Overall Quality	Consistency	Directness	Precision	Publication Bias	Large Magnitude	Dose Response	Associated Despite Confounders	
	HCV	7 OBS [102,104,106,108,113,114,116]	Every study tested the association of HCV and age in different ways, and the results are inconsistent and difficult to compare. The organ donor study found that HCV infection was associated with older median age.[102] One of the blood donor studies associated HCV with older mean age,[104] the other did not.[106] In general population studies, HCV was associated with increased mean age[108] and decade of birth (with people born between 1940 and 1959 having the highest prevalence),[113] but not age less than 50 years[114] or age less than 60 years.[116]	Low	0	-1	0	0	0	0	0	0	Very Low
	HIV	3 OBS[109,111,115]	The HIV studies also measured age in different ways, complicating comparison. In general these studies found young adults to be at the highest risk. One study found younger adults (aged 18 to 30) had increased prevalence of HIV,[111] another found adults aged 25 to 40 had higher prevalence of HIV than younger people aged 15 to 24 years,[109] and the third found increased prevalence among adults aged 35 to 44 years.[115]	Low	0	-1	0	0	0	0	0	0	Low

Factor	Virus	Quantity and Type of Evidence	Findings	Starting Grade	Decrease Grade					Increase Grade			GRADE of Evidence for Outcome
					Overall Quality	Consistency	Directness	Precision	Publication Bias	Large Magnitude	Dose Response	Associated Despite Confounders	
Race or Ethnicity	HBV	2 OBS[116,121]	White or Hispanic race was associated with lower HBV prevalence in a general population study in a multivariate analysis[116] but not in a special population study.[121]	Low	0	-1	0	-1	0	0	0	0	Very Low
		4 OBS[29,121,124,125]	Non-Hispanic Black race was associated with a higher prevalence of HBV in a general population study multivariate analysis[29] and two special population studies[124,125] but not another special population study.[121]	Low	0	0	-1	0	0	0	0	0	Very Low
		3 OBS[29,121,124]	Being Mexican-American was not associated with a different prevalence of HBV than non-Hispanic White race in a multivariate analysis of a general population study.[29] In special population studies, Hispanic ethnicity[121] and Hispanic or Latino ethnicity[124] were not associated with HBV infection.	Low	0	0	-1	0	0	0	0	0	Very Low
		1 OBS[124]	A special population study found an increased prevalence of HBV among Asian Americans compared with non-Hispanic White Americans.[124]	Low	0	-1	-1	0	0	0	0	0	Very Low
		1 OBS[117]	Among African American, Caucasian, Asian, and Hispanic children who received blood transfusions, the prevalence was not significantly different.	Low	0	0	0	-1	0	0	0	0	Very Low

Factor	Virus	Quantity and Type of Evidence	Findings	Starting Grade	Decrease Grade					Increase Grade			GRADE of Evidence for Outcome
					Overall Quality	Consistency	Directness	Precision	Publication Bias	Large Magnitude	Dose Response	Associated Despite Confounders	
	HCV	7 OBS[30,102,104,106-108,113]	Because about half of the studies combined races in analyses (their results presented first), the different analyses are reported together here. The different analysis methods complicate side-by-side comparison, but the evidence rating would always be 'very low' for these studies. (These results are all presented in the same row because of overlap within the studies.) In organ donors, no relation between race and HCV infection was detected.[102] Three general population studies did not find any relation either.[30,108,113] White race was not associated with a difference in rate of HCV compared with other races.[104] Black race was associated with increased rates of HCV compared to Whites in two studies.[106,107] Being Asian was associated with having a lower prevalence of HCV compared to Whites among blood donors.[107] Among blood donors, one study found that Hispanics had a higher risk of HCV than Whites,[107] but another did not.[104]	Low	0	-1	0	0	0	0	0	0	Very Low
	HIV	3 OBS[109-111]	In univariate analyses, two general population studies found increased prevalence of HIV among people of Black race[109,110] but a third did not. [111]	Low	0	-1	0	0	0	0	0	0	Very Low
		2 OBS[109,110]	In univariate analyses, neither of two general population studies found a difference in HIV prevalence in Whites and Asians.[109,110]	Low	0	0	0	-1	0	0	0	0	Very Low

Factor	Virus	Quantity and Type of Evidence	Findings	Starting Grade	Decrease Grade					Increase Grade			GRADE of Evidence for Outcome
					Overall Quality	Consistency	Directness	Precision	Publication Bias	Large Magnitude	Dose Response	Associated Despite Confounders	
National Origin/Birthplace	HBV	5 OBS [29,116,117,122,123]	National origin and birthplace were reported differently among studies and most factors cannot be considered side-by-side. However, since the rating for any factor in this group will be 'very low' and there is some overlap among studies, we present the findings together. In multivariate analysis of general populations, HCV was associated with being born in Southeast Asia or Africa in one study.[116] A special population study found children born in Korea had higher prevalence of HBV than children born in the U.S.[122] Other special population studies did not find significantly different rates of Asian Americans born in East Asia (excluding China) or Southeast Asia or Pacific Islands compared to Asian Americans born in China.[123] Birth in an area with a high endemic rate *or* household exposure to someone born in a high endemic rate was not in another general population study.[117] In multivariate analyses, a general population study[29] and a special population study[123] found that being born in the U.S. was associated was lower prevalence of HBV.	Low	0	-1	-1	0	0	0	0	0	Very Low

Factor	Virus	Quantity and Type of Evidence	Findings	Starting Grade	Decrease Grade					Increase Grade			GRADE of Evidence for Outcome
					Overall Quality	Consistency	Directness	Precision	Publication Bias	Large Magnitude	Dose Response	Associated Despite Confounders	
	HCV	5 OBS [30,104,107,113,116]	One blood donor study did not associate foreign birth with HCV,[104] but another did in a multivariate analysis.[107] A general population study found people born outside of the U.S. had a lower prevalence of HCV.[30] Birth in Southeast Asia or Africa was not associated with an increased prevalence of HCV in another general population study.[116] A general population study found no association between HCV and U.S. citizenship.[113]	Low	0	-1	0	0	0	0	0	0	Very Low
	HIV	No studies	-	-	-	-	-	-	-	-	-	-	NA
Preferred Language	HBV	No studies	-	-	-	-	-	-	-	-	-	-	NA
	HCV	1 OBS[108]	One general population study found an association between preference of English or Spanish and HCV.[108]	Low	0	-1	0	0	0	0	0	0	Very Low
	HIV	1 OBS[111]	One general population study found no difference in prevalence of HIV among Spanish speakers.[111]	Low	0	-1	0	-1	0	0	0	0	Very Low

Factor	Virus	Quantity and Type of Evidence	Findings	Starting Grade	Decrease Grade					Increase Grade			GRADE of Evidence for Outcome
					Overall Quality	Consistency	Directness	Precision	Publication Bias	Large Magnitude	Dose Response	Associated Despite Confounders	
Occupation	HBV	6 OBS [29,116,117,121,124,126]	Occupation as a health care worker was protective against HBV in one general population study[116] and not associated with HBV in another general population study[29] or a special population study.[121] However, having a healthcare-related job with frequent blood exposure was associated with HBV in one special population study.[124] Another general population study did not associate healthcare employment or household contact with someone who is a health care worker with HBV,[117] and a special population study did not associate being a health care worker or the spouse of one with HBV.[126]	Low	0	0	0	0	0	0	0	0	Low
		1 OBS[29]	Ever being in the military was not associated with HBV in a general population study.[29]	Low	0	0	0	-1	0	0	0	0	Very Low
	HCV	2 OBS[105,114]	In any occupation, occupational blood exposure was associated with HCV among blood donors in one study,[105] but work contact with blood was not associated with HCV in a general population study.[114]	Low	0	-1	0	-1	0	0	0	0	Very Low
		2 OBS[104,116]	Medical or dental job with frequent blood contact was not associated with HCV in one blood donor study[104] and was associated with lower prevalence of HCV in a general population study.[116]	Low	0	-1	0	-1	0	0	0	0	Very Low
		2 OBS[30,114]	Neither of two general population studies associated ever having served in the armed forces with HCV.[30,114]	Low	0	0	0	-1	0	0	0	0	Very Low

Factor	Virus	Quantity and Type of Evidence	Findings	Starting Grade	Decrease Grade					Increase Grade			GRADE of Evidence for Outcome
					Overall Quality	Consistency	Directness	Precision	Publication Bias	Large Magnitude	Dose Response	Associated Despite Confounders	
		2 OBS[104,113]	Public safety job with frequent blood contact was not associated with HCV in one blood donor study.[104] Another study did associate having a job at a prison with having HCV.[113]	Low	0	-1	0	0	0	0	0	0	Very Low
	HIV	No studies	-	-	-	-	-	-	-	-	-	-	NA
Education	HBV	3 OBS[29,121,124]	Having less than a high school education was associated with HBV in one general population study, compared with some college.[29] In special population studies, one found a higher prevalence of HBV among students in 2-year colleges compared to those in 4-year colleges,[124] and the other study found no relationship between years of education and HBV.[121]	Low	0	-1	-1	0	0	0	0	0	Very Low
	HCV	5 OBS[30,104,106,108,113]	One blood donor study associated less education with HCV,[104] and another associated having no college education with having HCV.[106] One general population study associated having fewer than 12 years of education with having HCV,[30] but two others found no association between educational attainment and HCV.[108,113]	Low	0	-1	0	0	0	0	0	0	Very Low
	HIV	2 OBS[101,109]	Neither of two general population studies found an association between having less than a high school education and having HIV.[101,109]	Low	0	0	0	-1	0	0	0	0	Very Low

Factor	Virus	Quantity and Type of Evidence	Findings	Starting Grade	Decrease Grade					Increase Grade			GRADE of Evidence for Outcome
					Overall Quality	Consistency	Directness	Precision	Publication Bias	Large Magnitude	Dose Response	Associated Despite Confounders	
Economic Factors	HBV	2 OBS[121,125]	One special population study did not associate homelessness with HBV.[121] Another special population study did not associate homelessness, institutionalization, or other non-independent living arrangement with HBV.[125]	Low	0	0	-1	-1	0	0	0	0	Very Low
	HCV	2 OBS[30,113]	In a general population, ever having been homeless was associated with an increased risk of HCV.[113] In the same study, annual income was not associated with HCV. Another general population study did not find any association with family poverty level and HCV.[30]	Low	0	-1	0	-1	0	0	0	0	Very Low
	HIV	2 OBS[101,111]	Being homeless was associated with an increased prevalence of HIV in one general population study.[111] In another general population study, having a poverty index of less than one was not associated with HIV.[101]	Low	0	-1	0	0	0	0	0	0	Very Low
Health Insurance	HBV	No studies	-	-	-	-	-	-	-	-	-	-	NA
	HCV	1 OBS[108]	One general population study associated insurance with HCV infection, with people on Medicaid having the highest prevalence.[108]	Low	0	-1	0	0	0	0	0	0	Very Low
	HIV	2 OBS[109,111]	One general population study found a higher prevalence of HIV among people with no insurance[109] but a second did not.[111]	Low	0	-1	0	-1	0	0	0	0	Very Low

Factor	Virus	Quantity and Type of Evidence	Findings	Starting Grade	Decrease Grade					Increase Grade			GRADE of Evidence for Outcome
					Overall Quality	Consistency	Directness	Precision	Publication Bias	Large Magnitude	Dose Response	Associated Despite Confounders	
Marital Status	HBV	2 OBS[29,125]	Being divorced or separated was associated with a higher prevalence of HBV than any other status in one general population study.[29] Being currently married was not associated with any difference in HBV prevalence than any other status in one special population study.[125]	Low	0	0	0	0	0	0	0	0	Low
	HCV	1 OBS[105]	Being married was associated with a lower risk of HCV in one blood donor study.[105]	Low	0	0	0	0	0	0	0	0	Low
	HIV	1 OBS[101]	Being married or cohabitating was associated with a lower risk of HIV in one general population study.[101]	Low	0	0	0	0	0	0	0	0	Low

Table 43. Prevalence of Nonbehavioral Risk Factors among Potential Organ Donors

Category	Risk Factor	Citation	Year	Prevalence	Number of Participants	Population
General Population						
Serum alanine aminotransferase level	>40 U/L	Armstrong et al.[30]	2006	9%	13,113	General population, nationwide
Transfusion	Blood transfusion before 1992 (participants aged 20-59 years)	Armstrong et al.[30]	2006	6%	5,733	General population, nationwide
	Blood transfusion before 1992 (participants aged at least 60 years)	Armstrong et al.[30]	2006	16%	2,916	General population, nationwide
	Blood transfusion	Kaur et al.[116]	1996	20%	7,539	Volunteers from general population, mainly urban
Herpes simplex virus infection	Antibodies to herpes simplex type 2 (HSV-2) (ages 18-49)	Armstrong et al.[30]	2006	19%	5,610	General population, nationwide
	Seropositive for HSV-2	Nguyen et al.[110]	2008	28%	1,613	General population in N.Y.C.
STDs	STD diagnosis	Mehta et al.[109]	2008	18%	16,696	Patients in urban medical care center

Table 44. GRADE for Question 4: Prevalence of Nonbehavioral Risk Factors

Factor	Quantity and Type of Evidence	Findings	Starting Grade	Decrease GRADE					Increase GRADE			GRADE of Evidence for Outcome
				Study Quality	Consistency	Directness	Precision	Publication Bias	Large Magnitude	Dose-response	Associated Despite Confounders	
Serum alanine amino-transferase (ALA) level >40 U/L	1 OBS*[30]	In one general population study, 9% of participants had ALA >40 U/L.[30]	High	0	-1	-1	0	0	0	0	0	Low
Blood transfusion	2 OBS[30,116]	In one general population study, the prevalence of ever having received a blood transfusion was 20%.[116] In another, 6% of participants aged 20-59 years had received a blood transfusion before 1992, and 16% of participants aged at least 60 had.[30]	High	0	-1	-1	0	0	0	0	0	Low
Other infection: HSV-2	2 OBS[30,110]	Two studies assessed the prevalence of herpes simplex virus-2 (HSV-2) in general populations. In one, 19% of people aged 18-49 tested positive.[30] In the other, 28% of adults did.[110]	High	0	0	-1	0	0	0	0	0	Moderate
Other infection: Other STD	1 OBS[109]	Another study found that 18% of adults had had a STD diagnosis.[109]	High	0	-1	-1	0	0	0	0	0	Low

* Observational study

Question 5. What are the test characteristics of the screening methods available to detect HIV, HBV, and HCV in potential solid organ donors? Do test characteristics differ in particular populations and with donor clinical status (i.e., heart beating vs. non-heart beating donors OR adult vs. pediatric donors)?

The purpose of this question is to summarize information and evidence on 35 diagnostic tests of interest, as designated by CDC. A list of these tests of interest is presented in Table 4 of the introductory section. Tests of interest include immunoassay tests and nucleic acid tests (NAT) currently used in the U.S. by Organ Procurement Organizations (OPOs), as well as, fourth-generation HIV and HCV antibody/antigen tests currently in use outside of the U.S. The p24 antigen test for HIV was not included because it is no longer used by OPOs. Additionally, an HCV antigen assay used in Europe was not included because the assay was licensed after the literature search was conducted. In this question, the following information is addressed:

- U.S. FDA approval
- Test format: type of test
- Specimen collection: In particular, whether approved for use in non-heart-beating donors, which is primarily a consideration for testing tissue donors. Heart-beating potential organ donors are not deceased donors for the purposes of using these tests.
- Window period: The duration of time between infection and when the test can detect infection
- Turnaround time: The duration of time required for the test to be performed
- Diagnostic performance characteristics: In particular, sensitivity and specificity. Measures of diagnostic performance are described in greater detail under *Analysis Methods.*

To address this question, information will be provided in the following order: literature search methods and results; list of included peer-reviewed studies and gray literature; samples and study methods of peer-reviewed publications; analysis methods used in this question; study assessment; methods of risk of bias and GRADE assessment of peer-reviewed publications; results summary, followed by data extraction tables and GRADE tables.

Peer-reviewed publications and other types of information, as appropriate (see next paragraph), were only included if they presented information specific to the tests of interest as listed in Table 4. Information regarding any other tests was excluded unless the other test was used in reference to a test of interest. Information must have been reported for each test individually, not as part of a multiple-test algorithm, because the focus of this question is on the performance of individual tests. Highly selected data sets (such as seroconversion panels, or HIV-2 genetic diversity panels) were not included for the assessment of diagnostic performance due to both spectrum bias and lack of relevance to performance of the test in the U.S. in potential organ donors. Because they are influenced by disease prevalence, predictive values and likelihood ratios were only to be collected from studies that calculated them from data from reasonably relevant populations to the U.S. (such as clinical applications in a general population, or on

blood donors, not serial dilutions or other laboratory sets, or samples selected for being unusual or representative of an endemic area).

Initial searches of bibliographic databases were for diagnostic instruments for HBV, HCV, or HIV. Once the list of included tests was generated, additional searches were performed specifically by each test's name. The focus of these searches was to identify clinical literature regarding window period, turnaround time, and diagnostic performance characteristics. Because this strategy did not identify information for all of the listed tests, we also searched gray literature sources including FDA product labeling information, package inserts, manufacturer's Web sites, and additional sources including the World Health Organization (WHO). FDA approval information was searched for all tests as well. We used these sources for information on turnaround time and window period but not other diagnostic characteristics (e.g., sensitivity and specificity), because these sources of information generally do not report sufficient information to enable assessment of the study design, quality, and other factors that impact the outcomes and the strength of the evidence. This is a particular concern given the potential for inaccuracy in these various sources of literature. Where data from sources other than clinical literature were used for the other characteristics, the source is clearly noted in the extraction tables.

Three hundred and forty-eight potentially relevant articles were identified by the bibliographic searches. Most were excluded for not reporting on a test on the list of interest (including earlier generations of tests of interest). Most of the rest were excluded for not addressing an outcome of interest. Ultimately, 45 peer-reviewed publications, each presenting at least one outcome for at least one data set, were included. Included publications, including data sets from those publications, and the outcomes they address are listed alphabetically by author in Table 45. This table also includes information on what test(s) of interest the publications investigated and which data sets were included. Ninety nine pieces of gray literature were reviewed for potentially useful data. These included literature from manufacturers' Web sites (40), the internet (6), the Food and Drug Administration (FDA) (23), agencies in the United Kingdom (14), agencies from Australia (13), and items from the World Health Organization (3). Data from 26 pieces of gray literature reporting window period or turnaround time were included. These sources of information are listed in Table 46. Basic information on test format and approved uses were extracted from FDA approval documents and, for tests not approved in the U.S., manufacturers' Web sites.

Table 45. Included Data Sets from Peer-reviewed Publications

Citation	Year	Test Category	Index Test(s)	Data Set(s)	Outcomes Included					Reason Sample Set Excluded
					Diagnostic Performance			Window Period	Turn-around Time	
					Sensitivity & Specificity	Predictive Values	Likelihood Ratios			
Aboud et al.[130]	2006	HIV 4th generation	Vironostika HIV Uni-Form II Ag/AB	Blood donations and diagnostic test samples (clinical HIV submissions, antenatal syphilis submissions) combined (Tanzania)	✓					
Aghokeng et al.[131]	2004	HIV 4th generation	Genscreen plus HIV Ag/Ab	Blood donations (Cameroon)	✓					
Anderson et al.[132]	1995	HCV EIA	Abbott HCV EIA 2.0	Blood donations (U.S.)	✓					
Bamaga et al.[133]	2006	HCV NAT	COBAS AmpliScreen HCV 2.0	Blood donations (Saudi Arabia)	✓					
				Additional Information					✓	
		HIV NAT	COBAS AmpliScreen HIV 1.5	Blood donations (Saudi Arabia)	✓					
				Additional Information					✓	
Barbe et al.[134]	1994	HIV EIA, 3rd generation	Abbott recombinant HIV-1/HIV-2 3rd generation EIA	Prenatal screening test samples (France)	✓ Specificity					
				False-reactive EIA results						Over-selected
				HIV positive samples, archived (France)	✓ Sensitivity					
				Seroconversion samples (Commercial)				✓		

Citation	Year	Test Category	Index Test(s)	Data Set(s)	Outcomes Included					Reason Sample Set Excluded
					Diagnostic Performance			Window Period	Turn-around Time	
					Sensitivity & Specificity	Predictive Values	Likelihood Ratios			
Barrera et al.[135]	1995	HCV EIA, 3rd generation	Ortho HCV v3 ELISA	Seroconversion samples (U.S.)				✓		
Bourlet et al.[136]	2005	HIV 4th generation	AxSYM Ag/Ab Combo	Diagnostic samples (France)	✓					
				Seroconversion panels (commercial)				✓		
			VIDAS DUO ULTRA	Diagnostic samples (France)	✓					
				Seroconversion panels (commercial)				✓		
Busch et al.[137]	2005	HIV NAT	COBAS AmpliScreen HIV-1 v. 1.5	Seroconversion samples (U.S.)				✓		
		HCV NAT	COBAS AmpliScreen HCV v.2.0	Seroconversion samples (U.S.)				✓		
		HCV/HIV NAT	ProCleix HIV-1/HCV	Seroconversion samples (U.S.)				✓		

Citation	Year	Test Category	Index Test(s)	Data Set(s)	Outcomes Included					Reason Sample Set Excluded
					Diagnostic Performance			Window Period	Turn-around Time	
					Sensitivity & Specificity	Predictive Values	Likelihood Ratios			
Candotti et al.[138]	2003	HCV NAT, HIV NAT	ProCleix HIV-1/HCV	Blood donors (U.K.)						No reference standard
				Known positive samples with various subtypes						Overly selected/ specificity not appropriately reported (above)
				Additional information					✓	
				Seroconversion panels (commercial)				✓		
Denoyel et al.[139]	2004	HCV EIA	Advia Centaur HCV Assay	Blood donors and hospitalized patients (France, Germany)	✓ Specificity					
				Known positives (Commercial samples)	✓ Sensitivity					
				Seroconversion panels (Commercial)				✓		
				Interference samples						Overly selected
Diepersloot et al.[140]	2000	HBsAg	AxSYM HBsAg	Clinical submissions (U.S.)	✓					
Galel et al.[141]	2002	HCV EIA	Abbott HCV EIA 2.0	Blood donations (U.S.)				✓		
			Ortho HCV EIA 3.0	Blood donations (U.S.)				✓		

Citation	Year	Test Category	Index Test(s)	Data Set(s)	Outcomes Included					Reason Sample Set Excluded
					Diagnostic Performance			Window Period	Turn-around Time	
					Sensitivity & Specificity	Predictive Values	Likelihood Ratios			
Huzly et al.[142]	2008	anti-HBs	Advia Centaur anti-HBsAg	Patients and healthcare workers (Germany)	✓					
				Additional Information					✓	
Iqbal et al.[143]	2005	HIV 4th generation	Vironostika HIV Uni-Form II Ag/AB	Diagnostic samples (India)	✓					
				Commercial known-status samples	✓					
				Seroconversion panel (in-house)						Window period not reported
Jackson et al.[144]	2002	HCV NAT, HIV NAT	ProCleix HIV-1/HCV	High risk individuals (U.S.)	✓					
Katsoulidou et al.[145]	2004	HCV NAT, HIV NAT	ProCleix HIV/HCV	HCV and HIV patients (Greek)						Analytic sensitivity only
				Seronegative blood donors (Greek)						Sensitivity not reported; study must report both sensitivity and specificity to be included
				Seroconversion panels (Greek)				✓		
				HCV/HIV Co-infection (Greek)						Overly selected
				Various genotypes (Greek)						Overly selected

Citation	Year	Test Category	Index Test(s)	Data Set(s)	Outcomes Included					Reason Sample Set Excluded
					Diagnostic Performance			Window Period	Turn-around Time	
					Sensitivity & Specificity	Predictive Values	Likelihood Ratios			
Kita et al.[146]	2009	HCV EIA	Ortho EIA 3.0	Diagnostic samples (Japan)	✓					
				Seroconversion panel (Commercial)				✓		
			Advia Centaur HCV	Diagnostic samples (Japan)	✓					
				Seroconversion panels (Commercial)				✓		
Kleinman et al.[147]	2005	NAT HBV	COBAS AmpliScreen HBV test	Blood donations (U.S.)	✓					
Kolk et al.[148]	2002	HCV NAT, HIV NAT	ProCleix HIV-1/HCV	Seroconversion panels (Commercial)				✓		
Kwon et al.[149]	2006	HIV 4th generation	ARCHITECT HIV Ag/Ab Combo	Diagnostic samples with known status (Korea)	✓					
				p24 antigen subtype panel and p24 antigen sensitivity panel (Commercial)						Overly selected
				Seroconversion panels (Commercial)				✓		
				Low titer antibody panel (Commercial)						Overly selected

Citation	Year	Test Category	Index Test(s)	Data Set(s)	Outcomes Included					Reason Sample Set Excluded
					Diagnostic Performance			Window Period	Turn-around Time	
					Sensitivity & Specificity	Predictive Values	Likelihood Ratios			
				HIV antibody panel including various subtypes (Commercial)						Overly selected – diagnostic samples with known status used preferentially
			AxSYM HIV Ag/Ab Combo	Diagnostic samples with known status (Korea)	✓					
				p24 antigen subtype panel and p24 antigen sensitivity panel (Commercial)						Overly selected
				Seroconversion panels (Commercial)				✓		
				Low titer antibody panel (Commercial)						Overly selected
				HIV antibody panel including various subtypes (Commercial)						Overly selected – diagnostic samples with known status used preferentially
Laperche et al.[150]	2005	HCV NAT, HCV 4th generation	COBAS AmpliScreen HCV v. 2.0	Seroconversion panels (Commercial)				✓		
				Blood donations (France)						No reference standard
			Monolisa HCV Ag/Ab Ultra	Seroconversion panels (Commercial)				✓		
				Blood donations (France)						No reference standard

Citation	Year	Test Category	Index Test(s)	Data Set(s)	Outcomes Included					Reason Sample Set Excluded
					Diagnostic Performance			Window Period	Turn-around Time	
					Sensitivity & Specificity	Predictive Values	Likelihood Ratios			
Laperche et al.[151]	2005	HCV 4th generation	Monolisa HCV Ag/Ab Ultra	Seroconversion samples (France)				✓		
Laycock et al.[152]	1997	HCV EIA	Abbott HCV v. 2.0	Potential cornea donors, most of whom positive on previous test (U.S.)	✓					
Leon et al.[153]	1993	HCV EIA	Abbott HCV EIA 2.0	Unselected high-risk individuals plus known positives from archive (Spain)	✓					
Ly et al.[154]	2007	HIV 4th generation	ARCHITECT HIV Combo	Negative samples (French)	✓ Specificity					
				Positive samples from various HIV endemic areas of the world, including mosaics and subtypes	✓ Sensitivity					
				Seroconversion panels (Commercial)				✓		
			COBAS Core HIV Combi EIA	Negative samples (French)	✓ Specificity					
				Positive samples from various HIV endemic areas of the world, including mosaics and subtypes	✓ Sensitivity					
				Seroconversion panels (Commercial)				✓		

Citation	Year	Test Category	Index Test(s)	Data Set(s)	Outcomes Included					Reason Sample Set Excluded
					Diagnostic Performance			Window Period	Turn-around Time	
					Sensitivity & Specificity	Predictive Values	Likelihood Ratios			
			Genscreen Ag/Ab HIV Ultra	Negative samples (French)	✓ Specificity					
				Positive samples from various HIV endemic areas of the world, including mosaics and subtypes	✓ Sensitivity					
				Seroconversion panels (Commercial)				✓		
			VIDAS HIV DUO Quick	Seroconversion panels (Commercial)				✓		Sensitivity and specificity not assessed for this test in the publication
			VIDAS HIV DUO Ultra	Negative samples (French)	✓ Specificity					
				Positive samples from various HIV endemic areas of the world, including mosaics and subtypes	✓ Sensitivity					
				Seroconversion panels (Commercial)				✓		
Ly et al.[155]	2006	HBV EIA	Advia Centaur HBsAg	Reference HBsAg panel (France) and HBsAg mutants (commercial)					✓	No other outcomes of interest reported
Ly et al.[156]	2004	HIV 4th generation	AxSYM HIV Ag/Ab Combo	Positive samples from various HIV endemic areas of the world, including mosaics and subtypes	✓ Sensitivity					
				Negative samples	✓ Specificity					

Citation	Year	Test Category	Index Test(s)	Data Set(s)	Outcomes Included					Reason Sample Set Excluded
					Diagnostic Performance			Window Period	Turn-around Time	
					Sensitivity & Specificity	Predictive Values	Likelihood Ratios			
				Seroconversion panel (Commercial)				✓		
			Genscreen Plus Ag/Ab	Positive samples from various HIV endemic areas of the world, including mosaics and subtypes	✓ Sensitivity					
				Negative samples	✓ Specificity					
				Seroconversion panel (Commercial)				✓		
			Murex HIV Ag/Ab Combo	Positive samples from various HIV endemic areas of the world, including mosaics and subtypes	✓ Sensitivity					
				Negative samples	✓ Specificity					
				Seroconversion panel (Commercial)				✓		
			Vironostika Uni-Form II Ag/Ab	Positive samples from various HIV endemic areas of the world, including mosaics and subtypes	✓ Sensitivity					
				Negative samples	✓ Specificity					
				Seroconversion panel (Commercial)				✓		

Citation	Year	Test Category	Index Test(s)	Data Set(s)	Outcomes Included					Reason Sample Set Excluded
					Diagnostic Performance			Window Period	Turn-around Time	
					Sensitivity & Specificity	Predictive Values	Likelihood Ratios			
Ly et al.[157]	2001	HIV 4th generation	Vironostika HIV Uni-Form II Ag/AB	Seroconversion panels (Commercial)				✓		
				Additional information					✓	
				HIV-1 p24 antigen panel infected with HIV-1 M subtype B (Commercial)						Overly selected
Ly et al.[158]	2001	HIV 4th generation	AxSYM HIV Ag/Ab Combo	Panel with various HIV subtypes, including group M subtypes A, B, C, D, CRF A/e, F, G, group O (Commercial)						Sensitivity not reported; study must report both sensitivity and specificity to be included
				Seroconversion panel (Commercial)				✓		
			Murex HIV Ag/Ab Combo	Panel with various HIV subtypes, including group M subtypes A, B, C, D, CRF A/e, F, G, group O (Commercial)						Sensitivity not reported; study must report both sensitivity and specificity to be included
				Seroconversion panel (Commercial)				✓		
			VIDAS HIV DUO ULTRA	Panel with various HIV subtypes, including group M subtypes A, B, C, D, CRF A/e, F, G, group O (Commercial)						Sensitivity not reported; study must report both sensitivity and specificity to be included
				Seroconversion panel (Commercial)				✓		

Citation	Year	Test Category	Index Test(s)	Data Set(s)	Outcomes Included					Reason Sample Set Excluded
					Diagnostic Performance			Window Period	Turn-around Time	
					Sensitivity & Specificity	Predictive Values	Likelihood Ratios			
Owen et al.[159]	2008	HIV EIA, 3rd generation	Genetics System (GS) HIV-1/HIV-2 plus) EIA	Blood and plasma donors, including some international donors selected for being representative of non-subtype-B HIV-1 (78% U.S.)	✓					
				Seroconversion panels (Commercial)				✓		
			HIVAB HIV-1/HIV-2 (rDNA) EIA	Blood and plasma donors, including some international donors selected for being representative of non-subtype-B HIV-1 (78% U.S.)	✓					
				Seroconversion panels (Commercial)				✓		
		HIV NAT	COBAS AmpliScreen HIV-1 Test 1.5	Blood and plasma donors, including some international donors selected for being representative of non-subtype-B HIV-1 (78% U.S.)	✓					Seroconversion not reported for this test
Romano et al.[160]	2005	HBV NAT	COBAS AmpliScreen HBV v. 2.0	Blood donors (Probably Italian, unclear in publication)						No reference standard
				Blood donors with previous negative test results elevated ALT, chronic HCV						No reference standard

Citation	Year	Test Category	Index Test(s)	Data Set(s)	Outcomes Included					Reason Sample Set Excluded
					Diagnostic Performance			Window Period	Turn-around Time	
					Sensitivity & Specificity	Predictive Values	Likelihood Ratios			
				HBV DNA nucleic acid panel (Commercial)						Overly selected
				Seroconversion panels (Commercial)				✓		
Saville et al.[161]	2001	HIV 4th generation	VIDAS HIV DUO ULTRA	Mixed set comprised of U.S. blood donors (35%), U.S. clinical samples (18%), high-incidence population in Trinidad (40%), STD clinic attendees in Bahamas (3%), confirmed HIV-1 group 0 from Cameroon (0.4%), confirmed HIV-2 samples from Cote d'Ivoire (0.4%), p24 antigen-only (0.3%) Diagnostic performance reported for all samples together, and sample groups separately	✓					For U.S. sample, PPV & NPV only reported for patients seeking HIV tests (population may have different prevalence than potential organ donors).
				Seroconversion panel				✓		
Seyoum et al.[162]	2005	HIV 4th generation	Vironostika HIV Uni-Form II Ag/AB	Blood donors (Ethiopia)	✓					
Sickinger et al.[163]	2004	HIV 4th generation	AxSYM Ag/Ab Combo	Blood donors	✓ Specificity					
				Hospital patients	✓ Specificity					

Citation	Year	Test Category	Index Test(s)	Data Set(s)	Outcomes Included					Reason Sample Set Excluded
					Diagnostic Performance			Window Period	Turn-around Time	
					Sensitivity & Specificity	Predictive Values	Likelihood Ratios			
				Commercial panels tested together: Infected with HIV-2 group M subtypes; Non-staged individuals infected with unknown HIV-1 subtypes; Individuals with HIV-2 living in endemic areas; High-risk individuals; interference panel	✓ Sensitivity					
				Seroconversion panels				✓		
Sun et al.[164]	1999	HCV NAT	AmpliScreen HCV 2.0	Blood donors						No outcomes of interest reported
				Known positive, genotypes 1a, 1b, 2, 2b, 3a, 5a, 6a, from archives						No outcomes of interest reported
				Seroconversion panel (Commercial)				✓		
Van Binsbergen et al.[165]	1998	HIV 4th generation	Vironostika HIV Uni-Form II Ag/AB	HIV-1 sub-typed samples with A through F, and group O (Yaounde and Cameroon)						Overly selected (sub-types only)
				Samples with human anti-mouse antibody						Overly selected; not clinical samples
				Seroconversion panels (Commercial)				✓		

Citation	Year	Test Category	Index Test(s)	Data Set(s)	Outcomes Included					Reason Sample Set Excluded
					Diagnostic Performance			Window Period	Turn-around Time	
					Sensitivity & Specificity	Predictive Values	Likelihood Ratios			
Van Binsbergen et al.[166]	1999	HIV 4th generation	Vironostika HIV Uni-Form II Ag/AB	Worldwide HIV-1 Performance Panel, including various subgroups (group M subtypes A through F, and group O) (Commercial)						Specificity not reported; study must report both sensitivity and specificity to be included
				Seroconversion panels (Commercial)				✓		
Vargo et al.[128]	2002	HCV NAT, HIV NAT	ProCleix HIV/HCV	Known positive HIV-1 samples (Commercial)	✓ Sensitivity					
				Known positive HCV samples (Commercial)	✓ Sensitivity					
				Co-infected HIV-1/HCV samples	✓ Sensitivity					
				Negative samples	✓ Specificity					
				Seroconversion panels (Commercial)				✓		
Vrielink et al.[167]	1995	HCV EIA	Ortho 3.0 HCV EIA	Volunteer random blood donors (Dutch)	✓					
Vrielink et al.[168]	1995	HCV EIA	Ortho 3.0 HCV EIA	Blood donor samples submitted for characterization because of initial positive result, patients with non-A non-B hepatitis, multiply-transfused patients	✓ Sensitivity					

Citation	Year	Test Category	Index Test(s)	Data Set(s)	Outcomes Included					Reason Sample Set Excluded
					Diagnostic Performance			Window Period	Turn-around Time	
					Sensitivity & Specificity	Predictive Values	Likelihood Ratios			
				Positive blood donors' serial dilutions						No outcomes of interest
				First-time blood donors	✓ Specificity					
Weber et al,[169]	2002	HIV 4th generation	VIDAS DUO ULTRA	Seroconversion panels				✓		
				Dilutions of cell culture supernatants with different HIV-1 subtypes (incl. B, E, F, G, H, O)						Overly selected, not clinical samples
				Interference panel						Overly selected
				Additional Information					✓	
Weber et al.[170]	2002	HIV 4th generation	COBAS Core HIV Combo EIA	Seroconversion panels				✓		
				Acute infection panels						Overly selected
				Known positive samples from patients in different stages of HIV-1 and HIV-2						Overly selected
				Sub typed samples from different geographical locations						Overly selected
				Dilutions of cell culture supernatants from cells infected with different HIV-1 subtypes						Overly selected

Citation	Year	Test Category	Index Test(s)	Data Set(s)	Outcomes Included					Reason Sample Set Excluded
					Diagnostic Performance			Window Period	Turn-around Time	
					Sensitivity & Specificity	Predictive Values	Likelihood Ratios			
				Performance panels, low-titer or mixed titer (Commercial)						Overly selected
				Blood donor samples, unselected (European)	✓ Specificity					
				Diagnostic samples, unselected (European)	✓ Sensitivity					
				Interference panel						Overly selected
Willoughby et al.[171]	1989	HIV 4th generation	Coulter HIV-1 p24 Ag Assay	Blood donors, known seropositive samples, spinal cord fluid, interference samples						No other outcomes reported
				Additional Information					✓	
Yang et al.[172]	2001	HIV NAT	COBAS AmpliScreen HIV-1 v.1.5	Known negative blood donors						Specificity not reported; study must report both sensitivity and specificity to be included
				Seroconversion panel				✓		
				Group M subtype panel						Overly selected
				Interference panel						Overly selected

Citation	Year	Test Category	Index Test(s)	Data Set(s)	Outcomes Included					Reason Sample Set Excluded
					Diagnostic Performance			Window Period	Turn-around Time	
					Sensitivity & Specificity	Predictive Values	Likelihood Ratios			
Yang et al.[173]	1999	HIV NAT	AmpliScreen HIV-1 v.1.5	Genotype panel						Overly selected
				Blood donors, seronegative						Sensitivity not reported; study must report both sensitivity and specificity to be included
				Interference panels						Overly selected
				Seroconversion panels				✓		

Table 46. Included Data Sets from Gray Literature

Citation	Year	Test Category	Test(s) of Interest	Data Set(s) Included	Outcomes Included		Literature Type
					Window Period	Turn-around Time	
Abbott Laboratories[174]	Download 9/2009	4th generation HIV EIA	ARCHITECT HIV Ag/Ab Combo	(None)		✓	Manufacturer Web site product information (Seroconversion also reported but only for selected 3 or 31 panels, so not included)
BioMerieux Diagnostics[175]	Downloaded 9/2009	HIV 4th generation	VIDAS HIV DUO ULTRA	16 seroconversion panels	✓		Manufacturer Web site product information
BioMerieux Diagnostics[176]	Downloaded 9/2009	HIV 4th generation	VIDAS HIV DUO QUICK	25 seroconversion panels	✓		Manufacturer Web site product information
Burgess and Perry[177]	2008	4th generation HIV EIA	ARCHITECT HIV Ag/Ab Combo Assay AxSYM HIV Ag/Ab Combo GENSCREEN Ultra HIV Ag/Ab Murex HIV Ag/Ab Combination Vironostika HIV Uni-Form II Ag/Ab	20 seroconversion panels, with comparative data for 18 of them	✓	✓	Independent public health laboratory evaluation
Burgess et al.[178]	2001	4th generation HIV EIA	AxSYM HCV version 3.0	22 seroconversion panels		✓	Independent public health laboratory evaluation
Cooray et al.[179]	2003	4th generation HIV EIA	AxSYM HIV Ag/Ab Combo Murex HIV Ag/Ab Combination Genscreen PLUS HIV Ag/Ab Vironostika HIV Uni-Form Ag/Ab	35 seroconversion panels	✓	✓	Independent public health laboratory evaluation

Citation	Year	Test Category	Test(s) of Interest	Data Set(s) Included	Outcomes Included		Literature Type
					Window Period	Turn-around Time	
Coulter Corporation[180]	Downloaded 9/2009	HCV 4th generation	Coulter HIV-1 p24 Antigen Assay	5 seroconversion panels	✓		Manufacturer Web site product information
Curtis et al.[181]	2006	4th generation HIV EIA	Genscreen ULTRA HIV Ag/Ab Murex HIV Ag/Ab Combo Vironostika HIV Uni-Form Ag/Ab	21 seroconversion panels	✓	✓	Independent public health laboratory evaluation
Dean et al.[182]	2006	HCV 4th generation	MONOLISA HCV Ag/Ab ULTRA	19 seroconversion panels	✓		Independent public health laboratory evaluation
Delieu et al.[183]	2001	4th generation HIV EIA	Murex HIV Ag/AB Combination EIA	39 seroconversion panels	✓	✓	Independent public health laboratory evaluation
FDA approval documentation[184]	Package insert approved 5/2007	HCV NAT	COBAS AmpliScreen HCV Test	9 seroconversion panels	✓		FDA documentation including package insert
FDA approval documentation[185]	Package insert approval 8/2007	HBV NAT	COBAS AmpliScreen HBV Test Ortho HBsAg	40 seroconversion panels	✓		FDA documentation including package insert
FDA approval documentation[186]	Package insert approved 12/2004	HBV HBc	ADVIA Centaur HBc	7 seroconversion panels	✓		FDA documentation including package insert
FDA approval documentation[187]	Package insert approved 10/2005	HBV Core	PRISM HBcore	None reported	✓		FDA documentation including package insert

Citation	Year	Test Category	Test(s) of Interest	Data Set(s) Included	Outcomes Included		Literature Type
					Window Period	Turn-around Time	
FDA approval documentation[188]	Package insert approved 12/2004	HCV assay	ADVIA Centaur HCV Assay Ortho HCV v. 3	23 seroconversion panels	✓		FDA documentation including package insert
FDA approval documentation[189]	Package insert approved 5/2005	HBV HBsAg	ADVIA Centaur HBsAg	6 seroconversion panels	✓		FDA documentation including package insert
FDA approval documentation[190]	Package insert approved 7/2004	3rd generation HIV EIA	HIVAB HIV-1/HIV-2 (rDNA) EIA	9 seroconversion panels	✓		FDA documentation including package insert
FDA approval information[191]	Package insert approved 2/2002	HIV/HCV NAT	ProCleix HIV-1/HCV Assay	10 HIV seroconversion panels 10 HCV seroconversion panels	✓		FDA documentation including package insert
FDA approval information[192]	Current package insert approved 5/2007	HIV NAT	COBAS AmpliScreen HIV-1 Test Coulter HVI-1 p24 Ag test	41 seroconversion panels	✓		FDA documentation including package insert
FDA approval information[193]	Package insert approved 1/2003	HBsAg EIA	Genetic Systems HBsAg EIA 3.0	21 seroconversion panels	✓		FDA documentation including package insert
FDA approval information[194]	Package insert approved 2006	HBsAg Assay	AxSYM HBsAg Assay	15 seroconversion panels	✓		FDA documentation including package insert

Citation	Year	Test Category	Test(s) of Interest	Data Set(s) Included	Outcomes Included		Literature Type
					Window Period	Turn-around Time	
FDA approval information[195]	Package insert approved 8/2003	3rd generation HIV EIA	Genetic Systems HIV-1/HIV-2 Plus O EIA	50 seroconversion panels	✓		FDA documentation including package insert
Innogenetics[196]	Downloaded 9/2009	HCV 4th generation	Innotest HCV Ab IV Ortho HCV 3.0	30 seroconversion panels	✓		Manufacturer Web site product information
Ortho-Clinical Diagnostics[197]	Downloaded 9/2009	HBV HBsAg	Genetic Systems HBsAg EIA 3.0	21 seroconversion panels	✓		Manufacturer Web site product information
White and Perry[198]	2003	HBc	Ortho HBc ELISA Test System	4 seroconversion panels	✓		Independent public health laboratory evaluation
World Health Organization[199]	2004	4th generation EIA	Enzygnost HIV Integral II Genscreen Plus HIV Ag/Ab Murex HIV Ag/Ab Combination Vironostika HIV Uni-Form II Ag/Ab	8 seroconversion panels	✓	✓	Independent public health laboratory evaluation

Samples and Study Methods in Peer-reviewed Publications

Table 47 shows a summary of the general study and sample characteristics for each of the included peer-reviewed publications. We sometimes refer to the tested blood sets as samples because not all came from clinical populations (most were purchased from laboratory supply companies). Publications were first categorized by whether or not the test(s) of interest are currently in use by U.S. O.P.Os. Tests were further categorized as immunoassays (e.g., EIA) or nucleic acid tests (NAT). All were further subdivided by which virus(es) they are intended to detect. (Where studies addressed tests of interest from more than one category, the study information is repeated for each category. The test pertinent to the category is bolded.)

For each of the publications, information regarding the national origin of the samples, the sources(s) of the samples, how the samples were selected, references standard(s) employed, and source(s) funding (if reported) is listed. Many of these studies were conducted internationally, and some conducted domestically used international samples. Although most of the commercial samples were purchased from U.S. companies, many of those U.S.-purchased panels had samples from all over the world. None of the sources of samples were potential organ donors. Publications used samples from a variety of sources (and often, multiple sources within the same publication), including clinical samples from routine screening or diagnosis, blood donor samples, and commercially purchased or archived known-status samples and seroconversion panels. Correspondingly, the prevalence of infection ranged widely, from a very small fraction of 1% to over 60% (not including seroconversion panels or all known-positive sets). Some sample sets were unselected (i.e., part of a consecutive or randomly selected sample), while others were selected for known characteristics (e.g., known infection or known non-infection, known seroconversion). All samples appear to have been drawn from living individuals, with the exception of one publication. None appear to have specifically studied pediatric populations. Everything from previous-generation EIA to NAT to exhaustive algorithms were employed as reference standards. Well-defined commercially purchased samples did not always have the reference standard explicitly described in the study, but those that did typically used multiple confirmatory analyses and quantitative analyses to determine the sample status. Some studies report funding from the manufacturer and some appear to have been publicly funded through federal health organizations, but for most the funding source was not reported.

In gray literature, window periods were always determined relative to other tests using seroconversion panels. Methods used to determine turnaround time were not reported.

Table 47. General Study and Sample Characteristics of Peer-reviewed Studies

Virus/ Test Type	Index Test(s)	Citation	Year	National Origin of Included Samples	Source(s) of Included Samples	How Selected (Enrollment)	Reference Standard(s)	Blinding (Masking) Clearly Stated	Funding Source
Tests currently in use in U.S. Organ Procurement Organization (OPO): Immunoassays									
HIV EIA 3rd generation	**Abbott recombinant HIV-1/HIV-2 3rd generation EIA**	Barbe et al.[134]	1994	France	Obstetric samples (n = 1,546) (for specificity) Prevalence 0.05% HIV positive samples (n = 7) (for sensitivity) Seroconversion samples (8 samples)	Unselected prenatal screening at an OB/GYN office Seroconversion and infected samples selected for known properties	Known status for seroconversion panel For clinical samples, bioMerieux Vidas test with Western blot (WB) confirmation	No	None reported
	Genetics System (GS) HIV-1/HIV-2 plus EIA; **HIVAB HIV-1/HIV-2 (rDNA) EIA (Abbott);** COBAS AmpliScreen HIV-1 Test 1.5	Owen et al.[159]	2008	Mostly U.S., also Cameroon and unspecified international samples with non-subtype-B HIV-1	Tested together: U.S. blood donors (n = 997), international donors (n = 97). samples from Cameroon (n = 114) HIV-2 specimens from Ivory Coast (n = 32) and commercial HIV-2 specimens (n = 2) Prevalence 56% (53% HIV-1, 2% HIV-2) Seroconversion panels (15 panels, 183 specimens)	For defined properties (at left); all commercially purchased	Known status for seroconversion and purchased panels For negatives, consensus negative with other screening tests Confirmation of positives with Western blot	No	Not reported, but all authors affiliated with Centers for Disease Control (CDC)

Virus/ Test Type	Index Test(s)	Citation	Year	National Origin of Included Samples	Source(s) of Included Samples	How Selected (Enrollment)	Reference Standard(s)	Blinding (Masking) Clearly Stated	Funding Source
HBsAg	**AxSYM HBsAg**	Diepersloot et al.[140]	2000	U.S.	Clinical submissions for HBV tests (n = 200) Prevalence: 6%	Not reported, but study states selection was prospective	Abbott Imx and DPC IMMULITE assays AxSYM total anti-HBV core assay for discrepancies	No	None reported
anti-HBs	**Advia Centaur anti-HBsAG**	Huzly et al.[142]	2008	Germany	Patients and healthcare workers (n = 200) Prevalence of surface antigen (including vaccinated individuals 73%); Core antigen 12%	Unselected	Bitros anti-HBs Roche Elecsys anti-HBs Liasion anti-HBs Abbott Architect anti-HBs ETI-AB-AUK-3 Enzygnost anti-HBs Monolisa anti-HBS AxSYM AUSAB	No	None reported

Virus/ Test Type	Index Test(s)	Citation	Year	National Origin of Included Samples	Source(s) of Included Samples	How Selected (Enrollment)	Reference Standard(s)	Blinding (Masking) Clearly Stated	Funding Source
HCV EIA	**Abbott HCV EIA 2.0**	Anderson et al.[132]	1995	U.S.	Blood donors (n = 21,431) Prevalence 0.6%	Unselected	Ortho Anti-HCV 2.0 For confirmation of positives, Matrix HCV anti-HCV RIBA-II PCR	No	None reported
		Laycock et al.[152]	1997	U.S.	Potential cornea donors (n = 101) Prevalence: 62%	Selected from archives, but apparently not for any particular characteristics	Matrix-HCV RIBA	No	Grants from Mid-America Transplant Association and Research to Prevent Blindness Inc.
		Leon et al.[153]	1993	Spain	High-risk individuals (n = 398) Prevalence 2% Known positive blood donations from archive (n = 102) Overall prevalence 22%	High-risk individuals unselected (men who have sex with men, inmates, "mentally retarded") Blood donors who were known to have tested positive on first generation HCV ELISA test	All samples tested by 11 methods, Negatives by consensus Those reactive in at least one also tested with supplemental assays to confirm positives	No	Not reported, but performed at a national microbiology center

Virus/ Test Type	Index Test(s)	Citation	Year	National Origin of Included Samples	Source(s) of Included Samples	How Selected (Enrollment)	Reference Standard(s)	Blinding (Masking) Clearly Stated	Funding Source
	Abbott HCV EIA 2.0 **Ortho HCV EIA 3.0**	Galel et al.[141]	2002	U.S.	Blood donors (n = 5.5 ×10^6)	Previously negative	COBAS AmpliScreen HCV test 2.0	No	Not reported. Abbott performed PRISM testing, Roche Molecular provided RNA testing and equipment
	Advia Centaur HCV Assay	Denoyel et al.[139]	2004	Noncommercial samples from Europe or U.S. Seroconversion samples commercial	Seroconversion panels (20 panels) For specificity, blood donors (n = 5,015) and people (n = 213) Prevalence 0.4% For sensitivity, samples presumed infected (n = 472)	Commercial panels and positives selected for known properties. Blood donors and hospitalized patients unselected	Commercial panels: Known samples Blood donors and hospitalized patients: Abbott AxSYM 3.0 and verification of positives with RIBA immunoblot testing	No	None reported

Virus/ Test Type	Index Test(s)	Citation	Year	National Origin of Included Samples	Source(s) of Included Samples	How Selected (Enrollment)	Reference Standard(s)	Blinding (Masking) Clearly Stated	Funding Source
	Advia Centaur HCV **Ortho 3.0 EIA**	Kita et al.[146]	2009	Clinical samples from Japan. Seroconversion panels purchased from U.S. companies.	Clinical submissions for HCV tests (n = 500) Prevalence: 2.6% Commercially purchased seroconversion panels (2 series)	Clinical samples appear to be unselected. Seroconversion panels selected seroconversion	Panels: known status. Clinical samples compared among other tests to define negativity (Ortho Quick Chaser HCV Ab, VITROS HCV, Ortho HCV Ab PA Test II, Imx HCV Dainapak-II, Architect HCV, Lumipulse IT Ortho HCV, Lumipulse Presto HCV) and confirmatory analyses to define positivity (RIBA III, or RNA PCR)	No	None reported
	Ortho 3.0 HCV EIA	Barrera et al.[135]	1995	U.S.	Serial specimens from individuals who developed post-transfusion HCV (n = 21)	For seroconversion	Known status	No	None reported, but most of the authors employed at Ortho Diagnostic Systems

Virus/ Test Type	Index Test(s)	Citation	Year	National Origin of Included Samples	Source(s) of Included Samples	How Selected (Enrollment)	Reference Standard(s)	Blinding (Masking) Clearly Stated	Funding Source
		Vrielink et al.[167]	1995	The Netherlands	Blood bank archives (n = 2,153) Prevalence <1%	Unselected blood donors	For specificity, Ortho 2.0 HCV EIA For sensitivity, Ortho 2.0 HCV EIA, PCR, RIBA-2	No	None reported
		Vrielink et al.[168]	1995	The Netherlands	Tested together: Repeatedly positive blood donors (403 samples), non-A non-B hepatitis patients (212 samples), multiply-transfused patients (253 samples), unselected first-time donors (1,055 samples) Prevalence 21%	For properties at left	PCR, RIBA-2	No	None reported
Tests currently in use in U.S. Organ Procurement Organizations (OPO): NAT									
HIV NAT	COBAS AmpliScreen HCV 2.0; **COBAS AmpliScreen HIV 1.5**	Bamaga et al.[133]	2006	Saudi Arabia	Blood donors (n = 3,288) Prevalence: 0.2%	Unselected blood donors	Abbott AxSYM HCV 3.0, Enzygnost HIV	No	None reported

Virus/ Test Type	Index Test(s)	Citation	Year	National Origin of Included Samples	Source(s) of Included Samples	How Selected (Enrollment)	Reference Standard(s)	Blinding (Masking) Clearly Stated	Funding Source
	COBAS AmpliScreen HIV-1, COBAS AmpliScreen HCV, ProCleix HIV-1/HCV	Busch et al.[137]	2005	U.S.	Archived plasma donations with confirmed viremia and/or seroconversion (12 HIV seroconversion panels, 12 HCV seroconversion panels)	Serial samples available at least two weeks before samples became quantifiable, with short collection intervals (less than one week)	Known-status seroconversion panels (no negative samples)	No	Funded in part by National Heart, Lung, and Blood Institute contracts.
	Genetics System (GS) HIV-1/HIV-2 plus) EIA; HIVAB HIV-1/HIV-2 (rDNA) EIA (Abbott); **COBAS AmpliScreen HIV-1 Test 1.5**	Owen et al.[159]	2008	Mostly U.S., also Cameroon and unspecified international samples with non-subtype-B HIV-1	Tested together: U.S. blood donors (n = 997), international donors (n = 97). samples from Cameroon (n = 114) HIV-2 specimens from Ivory Coast (n = 32) and commercial HIV-2 specimens (n = 2) Prevalence 56% (53% HIV-1, 2% HIV-2) Seroconversion panels(5 panels, 183 specimens)	For defined properties (at left); all commercially purchased	Known status for seroconversion and purchased panels For negatives, consensus negative with other screening tests Confirmation of positives with Western blot	No	Not reported, but all authors affiliated with Centers for Disease Control (CDC)
	COBAS AmpliScreen HIV-1 v.1.5	Yang et al.[173]	1999	Commercial panels	Seroconversion panels (10 panels)	For seroconversion	Known status	No	None reported, but all authors affiliated with Roche Molecular Systems, Inc.

Virus/ Test Type	Index Test(s)	Citation	Year	National Origin of Included Samples	Source(s) of Included Samples	How Selected (Enrollment)	Reference Standard(s)	Blinding (Masking) Clearly Stated	Funding Source
		Yang et al.[172]	2001	Commercial panels	Seroconversion panels (10 panels)	For seroconversion	Known status	No	None reported, but all authors affiliated with Roche Molecular Systems, Inc.
HCV NAT	**COBAS AmpliScreen HCV 2.0;** COBAS AmpliScreen HIV 1.5	Bamaga et al.[133]	2006	Saudi Arabia	Blood donors (n = 3,288) Prevalence: 0.2%	Unselected blood donors	Abbott AxSYM HCV 3.0, Enzygnost HIV	No	None reported
	COBAS AmpliScreen HIV-1, **COBAS AmpliScreen HCV,** ProCleix HIV-1/HCV	Busch et al.[137]	2005	U.S.	Archived plasma donations with confirmed viremia and/or seroconversion (12 HIV seroconversion panels, 12 HCV seroconversion panels)	Serial samples available at least two weeks before samples became quantifiable, with short collection intervals (less than one week)	Known-status seroconversion panels (no negative samples)	No	Funded in part by National Heart, Lung, and Blood Institute contracts.
	COBAS AmpliScreen HCV v. 2.0 Monolisa HCV Ag/Ab Ultra	Laperche et al.[150]	2005	Commercial seroconversion panels from U.S. companies	Commercial seroconversion panels (10 panels, 107 samples)	Seroconversion panels for defined properties (seroconversion)	For seroconversion	No	Not reported, appears to be French public source

Virus/ Test Type	Index Test(s)	Citation	Year	National Origin of Included Samples	Source(s) of Included Samples	How Selected (Enrollment)	Reference Standard(s)	Blinding (Masking) Clearly Stated	Funding Source
	COBAS AmpliScreen HCV 2.0	Sun et al.[164]	1999	Commercial panels	Commercial seroconversion panels (5 panels)	For seroconversion	Known status	No	None reported, but all authors affiliated with Roche Molecular Systems, Inc.
HBV NAT	**COBAS AmpliScreen HBV**	Kleinman et al.[147]	2005	U.S.	Blood donors (n = 581,790) Prevalence: 0.02%	All donors meeting standard criteria included	HBsAg Auszyme and anti-HBc EIA (Abbott Laboratories) *or* HBsAg test system 2 and anti-HBc total (Ortho Clinical Diagnostics). Discordant results: ID NAT with the AmpliScreen HBV test, alternative NAT, and DNA quantification.	No	Roche Molecular Systems
		Romano et al.[160]	2005	Commercial	Seroconversion panels (5 panels) (commercial)	For seroconversion	Known status	No	None reported

Virus/ Test Type	Index Test(s)	Citation	Year	National Origin of Included Samples	Source(s) of Included Samples	How Selected (Enrollment)	Reference Standard(s)	Blinding (Masking) Clearly Stated	Funding Source
HIV-1 and HCV NAT	COBAS AmpliScreen HIV-1, COBAS AmpliScreen HCV, **ProCleix HIV-1/HCV**	Busch et al.[137]	2005	U.S.	Archived plasma donations with confirmed viremia and/or seroconversion (12 HIV seroconversion panels, 12 HCV seroconversion panels)	Serial samples available at least two weeks before samples became quantifiable, with short collection intervals (less than one week)	Known-status seroconversion panels (no negative samples)	No	Funded in part by National Heart, Lung, and Blood Institute contracts.
	ProCleix HIV-1 /HCV	Candotti et al.[138]	2003	Commercial	Commercial seroconversion panels (2 panels)	For seroconversion	Known status	No	National Blood Service NAT steering committee and Chiron Corporation
		Jackson et al.[144]	2002	U.S.	High-risk individuals' archived samples (n = 539) Prevalence: 2.2% HIV only, 48% HCV only, 2% co-infected	At high risk for HIV and HCV	"Standard" serological test, p24 antigen test, alternative NAT, follow up if needed	No	Not reported, but 3 co-authors employed at Gen-Probe Inc.
		Katsoulidou et al.[145]	2004	Greece	Seroconversion panels from dialysis patients (25 panels)	For seroconversion	Known status	No	None reported, but Chiron Corp. provided reagents.
		Kolk et al.[148]	2002	Commercial	Commercial seroconversion panels (26 panels HIV, 24 panels HCV)	For seroconversion	Known status	No	In part by National Heart, Lung, and Blood Institute. Authors employed at Gen-Probe Inc.

Virus/ Test Type	Index Test(s)	Citation	Year	National Origin of Included Samples	Source(s) of Included Samples	How Selected (Enrollment)	Reference Standard(s)	Blinding (Masking) Clearly Stated	Funding Source
		Vargo et al.[128]	2002	U.S. Commercial	Blood donors (n = 191,200) for specificity Commercial: Positive samples (n = 2,015: 1,040 HIV infected, 1,015 HCV infected)) for sensitivity Seroconversion panels (10 panels HIV-1 and 10 HCV)	Blood donors appear to be unselected Panels for seroconversion	Serology, with WB and/or immunofluorescence and/or p24 Ag test for HIV and RIBA for HCV to confirm positives Panels and infected samples: Known status	Yes	Not reported but some authors affiliated with Chiron Corp.
Tests currently not in use in U.S. Organ Procurement Organization (OPO): Fourth Generation Immunoassays									
HIV 4th generation EIA	**ARCHITECT HIV Ag/Ab Combo,** **AxSYM HIV Ag/Ab Combo**	Kwon et al.[149]	2006	Korea Commercial	Korean samples in collection at university laboratory (143 infected, 412 uninfected) Three commercial seroconversion panels (n = 21)	Panels selected for defined properties (positive, negative, seroconversion)	Known status for commercial panels Negatives by other Ab/Ag test consensus Clinical samples Western blot confirmed.	No	None reported

Virus/ Test Type	Index Test(s)	Citation	Year	National Origin of Included Samples	Source(s) of Included Samples	How Selected (Enrollment)	Reference Standard(s)	Blinding (Masking) Clearly Stated	Funding Source
	ARCHITECT HIV Combo **Cobas Core HIV Combi** **Genscreen Ag/Ab HIV Ultra** **VIDAS HIV DUO Quick** **VIDAS HIV DUO Ultra**	Ly et al.[154]	2007	France Commercial	Lab archives: For specificity: HIV negative samples (1,005) For sensitivity: known positive samples from endemic areas (669) Seroconversion panels (24 panels), commercial	For known characteristics (positive, negative, seroconversion)	Known status for commercial panels and positives Samples were considered negative if all samples run were negative	No	None reported
	AxSYM Ag/Ab Combo **VIDAS DUO ULTRA**	Bourlet et al.[136]	2005	Serum samples from France Commercial panels	Serum samples submitted to university hospital microbiology department (n = 1,443) Prevalence: 0.8% Commercial panel: Seroconversion panels (14 panels, n = 112)	Serum samples consecutive. Seroconversion panels selected for defined properties (seroconversion).	Panels known status. Serum sample positives confirmed by Western blot or HIV-1 antigen assay or HIV-1 RNA assay Negative if all three 4th generation tests of interest negative.	No	None reported

Virus/ Test Type	Index Test(s)	Citation	Year	National Origin of Included Samples	Source(s) of Included Samples	How Selected (Enrollment)	Reference Standard(s)	Blinding (Masking) Clearly Stated	Funding Source
	AxSYM HIV Ag/Ab Combo, **Genscreen Plus Ag/Ab** **Murex HIV Ag/Ab Combo,** **Vironostika Uni-Form II Ag/Ab**	Ly et al.[156]	2004	Including U.S., France, Cameroon, Ghana, Uganda, U.K., Brazil, South Africa, Thailand, Argentina	25 seroconversion panels (176 samples) Antibody positive samples (669 samples) for sensitivity Unselected negatives (1,005 samples) (for specificity)	For defined properties (positive, negative, seroconversion)	Known status	No	None reported
	AxSYM Ag/Ab Combo	Sickinger et al.[163]	2004	Various panels purchased from U.S., Germany. Blood donations and diagnostic samples possibly German because diagnosis confirmation held to German standards.	Commercial panels tested together for sensitivity: HIV-1+ (n = 453), HIV-2 from endemic area (n = 108), HIV+ not staged or genotyped (n = 107) HIV-1 group O (n = 19) HIV-1 with p24 Ag (n = 50) Blood donors (n = 7,900) (specificity) Diagnostic submissions (n = 1,939) (specificity)	Known properties (positive, negative, or seroconversion)	Panels known status. Blood donors and diagnostic population RNA test, with AmpliCore HIV-1 Monitor RNA test, Lav Blot I or Lav Blot II for confirmation	No	Not reported, but all authors affiliated with Abbott

Virus/ Test Type	Index Test(s)	Citation	Year	National Origin of Included Samples	Source(s) of Included Samples	How Selected (Enrollment)	Reference Standard(s)	Blinding (Masking) Clearly Stated	Funding Source
	COBAS Core HIV Combo EIA	Weber et al.[170]	2002	>10 countries, including Cameroon, Germany, Luxembourg, Belgium, Portugal, Switzerland, South Africa, Thailand, and Zimbabwe	Commercial seroconversion panels (94 panels, 709 sera) Assessed together for specificity: blood donor samples (n = 7,579), daily routine samples (n = 303), samples from hospitalized patients (n=997), potentially interfering samples (n = 1,222) Assessed together for sensitivity: acute positives (n = 32), HIV-1 positive (n = 620), HIV-1 subtyped (n = 462), HIV-2 positive (n = 462), HIV p24 Ag/Ab positive (n = 120), commercial performance panel (n = 102)	For known status (positive, negative, seroconversion) or variations of positive types (at left)	Seroconversion panels known status Negative with respect to alternate screening assays or negative WB, or WB indeterminate and p24 Ag negative Positives confirmed by WB	No	Roche Diagnostics provided reagents, analyzers, and financial support for testing WB and confirmation assays
	Coulter HIV-1 p24 Ag Assay	Willoughby et al.[171]	1989	U.S.	Seropositive samples (from 34 individuals)	For seroconversion	Known status	No	National Institutes of Health

Virus/ Test Type	Index Test(s)	Citation	Year	National Origin of Included Samples	Source(s) of Included Samples	How Selected (Enrollment)	Reference Standard(s)	Blinding (Masking) Clearly Stated	Funding Source
	Genscreen plus HIV Ag/Ab	Aghokeng et al.[131]	2004	Cameroon	Blood donors (n = 503) Prevalence: 56% confirmed positive	Unclear whether samples were selected for any particular characteristic but HIV prevalence was high (56% confirmed) Intended to represent group M genetic diversity	Specificity determined with reference to 8 other tests: 4 rapid assays, Enzygnost HIV Integral, Wellcozyme HIV Recombinant, HIV Blot 2.2, INNO-LIA. Positives confirmed with Inno-Lia HIV Confirmation or HIV Blot 2.2	No	National French agency for AIDS research

Virus/ Test Type	Index Test(s)	Citation	Year	National Origin of Included Samples	Source(s) of Included Samples	How Selected (Enrollment)	Reference Standard(s)	Blinding (Masking) Clearly Stated	Funding Source
		Saville et al.[161]	2001	US, Trinidad, the Bahamas, Cote d'Ivorie, Cameroon	Mixed set comprised of U.S. diagnostic samples (n = 503) U.S. blood donors (n = 1,010) High-incidence population in Trinidad (n = 1,141) STD clinic attendees in Bahamas (N = 83) Confirmed HIV-1 group 0 from Cameroon (n = 10) Confirmed HIV-2 (n = 16) Commercial panels: 1 panel HIV-1 group M antigen reactive (n = 9) Prevalence (without seroconversion panel): 4.5% Seroconversion panel (10 panels with n = 74)	Mostly unselected donors or patients Archived positives Commercially available seroconversion panel	Known status (for panel and known samples) Genetic Systems HIV-1 and HIV-2 ELISA, or rDNA EIA and HIV AG-1 monoclonal p24 assay by Abbott, with additional reference tests WB and/or RT-PCR to investigate discrepancies and confirm positives	Yes	Funded by bioMerieux
	VIDAS HIV DUO ULTRA	Weber et al.[169]	2002	Commercial panels	Commercial seroconversion panels (16 panels)	For seroconversion	Known status	No	Roche Diagnostics provided test kits and financial support

Virus/ Test Type	Index Test(s)	Citation	Year	National Origin of Included Samples	Source(s) of Included Samples	How Selected (Enrollment)	Reference Standard(s)	Blinding (Masking) Clearly Stated	Funding Source
	Murex HIV Ag/Ab Combo, **VIDAS HIV DUO ULTRA,** **prototype AxSYM HIV Ag/Ab combo**	Ly et al.[158]	2001	Commercial panels	Seroconversion panels (19 panels)	For seroconversion	Known samples	No	Not reported, but most co-authors employed at Abbot Laboratories
	Vironostika HIV Uni-Form II Ag/AB	Aboud et al.[130]	2006	Tanzania	Submitted for diagnostic HIV testing (n = 361) or antenatal testing (n = 511) in hospital lab, or by blood donors (n = 508) Prevalence: 22% overall confirmed	Not reported, appears to be all samples from sources	For negative, other tests: Enzygnost anti-HIV 1/2 Plus Vironostika HIV Uni-Form II plus O Murex HIV antigen/antibody. To confirm positives Inno-Lia antibody assay. For discrepancies, Innotest p24 Ag assay.	No	Financial support from Swedish International Development Agency (SIDA), Department of Research Cooperation Some materials provided by tests manufacturers
		Iqbal et al.[143]	2005	India	Clinical samples from AIDS counseling center (n = 264) Prevalence: 48%	Clinical samples unselected	Western Blot	Blinded to patient infection status	None reported

Virus/ Test Type	Index Test(s)	Citation	Year	National Origin of Included Samples	Source(s) of Included Samples	How Selected (Enrollment)	Reference Standard(s)	Blinding (Masking) Clearly Stated	Funding Source
		Ly et al.[157]	2001	Commercial panels	Seroconversion panels, commercial (30 panels, 175 samples)	Selected for defined properties (seroconversion)	Known status	No	None reported, but manufacturers supplied panels and kits
		Seyoum et al.[162]	2005	Ethiopia (n = 408)	Blood donors Prevalence: 3.4%	Unselected	Amplicor DNA PCR ExaVir Load Test for HIV reverse transcriptase (v.2) Amplicor HIV-1 RNA test for discrepancies, or other antibody tests	No	Collaboration of several public health services, Red Cross, and a University department
		Van Binsbergen et al.[165]	1998	Commercial panels	Commercial seroconversion panels (7 panels, 41 samples)	Selected for defined properties (seroconversion)	Known status	No	None reported. All but one author affiliated with Organon-Teknika (manufacturer at time of publication)
		Van Binsbergen et al.[166]	1999	Commercial	Seroconversion panels (10 panels)	For seroconversion	Known samples	No	Not reported, but all authors affiliated with Organon-Teknika (manufacturer at time of publication)

Virus/ Test Type	Index Test(s)	Citation	Year	National Origin of Included Samples	Source(s) of Included Samples	How Selected (Enrollment)	Reference Standard(s)	Blinding (Masking) Clearly Stated	Funding Source
HCV 4th generation EIA	**Monolisa HCV Ag/Ab Ultra**	Laperche et al.[151]	2005	France	Blood donors (n = 12), Hemodialysis patients (n = 23)	Selected for defined properties (all in seroconversion)	Known status (Based upon tests and follow-up)	No	Not reported. All authors appear to be affiliated with public sources in France.
	COBAS AmpliScreen HCV v. 2.0 **Monolisa HCV Ag/Ab Ultra**	Laperche et al.[150]	2005	Commercial seroconversion panels from U.S. companies	Commercial seroconversion panels (10 panels, 107 samples)	For seroconversion	Known status	No	Not reported, appears to be French public source

Analysis Methods

The characteristics of interest for this question are turnaround time, window period, and diagnostic performance. The methods used to assess each of these outcomes differ. The following paragraphs define those characteristics and explain the procedures used to collect information regarding them. In data extraction tables, data are presented separately for each test because results may vary by test, even within the same generation.

Turnaround Time

Turnaround time is the duration of time required for a sample to be fully assessed. As this information was sparsely reported in clinical literature, we also extracted relevant data from other sources, particularly review articles and grey literature including primary technology assessments and package insert information. Where no other data were available we also extracted similar information such as "run time." Note that "run time" is only the analytic component of turnaround time and does not include time needed for specimen preparation and ost-analytic reporting time. These instances are clearly noted in the data tables.

Window Period

Window period refers to the duration of time between infection and test positivity. The information regarding window periods comes from using the test of interest on seroconversion panels. Seroconversion panels are series of blood draws from patients who eventually become seropositive. They are typically collected from people at high risk for infection. Although a few investigators studied their own in-house seroconversion panels, most such panels were purchased from laboratory supply companies. These tests enable estimation of time to positive test result from first blood collection. However, the first day of blood collection may not coincide with the day of infection. Also, these samples are typically collected at irregular intervals, not daily. These limitations cloud the estimation of the period of time between infection and when the test detects infection. Studies generally reported the difference in window period between two tests (e.g., Test 2 detected infection an average of 5 days later than Test 1). This type of information comprises the information in the results section on window period. No information was identified that captured absolute window periods using actual samples.

Diagnostic Performance

The most commonly used study design to evaluate the accuracy of a diagnostic test is the diagnostic cohort study, in which all enrolled patients are examined with both the diagnostic test of interest and the accepted reference standard test. "Accuracy" is defined as the proportion of times the test of interest correctly categorizes an individual as having disease or not. The accepted reference standard test accurately categorizes the patient as having infection or not. (A reference standard capable of determining the true infection status of the patient is sometimes referred to as the "gold standard.") The accuracy of the test of interest is determined with reference to the infection status of the patient, as determined by the reference standard, as shown in Table 48. The information in this table can be used to calculate sensitivity and specificity of the test of interest, and where the prevalence of disease in the tested data set is similar to the prevalence in the target population, can be used to determine predictive values and likelihood ratios (these terms are defined in the text following the table).

Table 48. Determining Diagnostic Performance

		True Status (Reference Standard)	
		Infected	Not Infected
Test of interest	Positive	True Positive	False Positive
	Negative	False Negative	True Negative

However, because there are no perfect tests for the diagnosis of HBV, HCV, or HIV, no true single gold standard test currently exists. True disease state would be most accurately determined using information from more than one source (e.g., confirmatory tests, clinical assessment), possibly with repeat testing at a follow-up time to confirm negatives (after a window period has passed). However, for the purposes of identifying as much information as possible for inclusion in this report, data were collected without regard to the accuracy of the reference standard (although studies that employ poor reference standards will be downgraded for study design and quality). It is important to bear this in mind when assessing the extracted data because the reference standard influences diagnostic performance data. This is particularly true when a more sensitive test is compared to a less sensitive test. For instance, if the test of interest is more sensitive than the reference standard and no additional discriminatory tests are performed, positives that the test of interest catches but the reference standard misses will be misclassified as false positives and specificity will be underestimated. (For this reason we refer to these outcomes as measures of "Diagnostic Performance" rather than "Diagnostic Accuracy.") In the data extraction tables, the reference standard used is always presented alongside the diagnostic performance data. Where more than one set of information is reported for a particular test of interest, greatest heed should be paid to the statistic determined using the most accurate reference standard(s).

Commonly used diagnostic performance measures are calculated from the type of information provided in Table 48 and include sensitivity and specificity, predictive values, and likelihood ratios. Sensitivity is the proportion of people with the infection (as determined by the reference standard) that the test of interest correctly recognizes as positive. A test with high sensitivity will rarely misclassify people with the disease as not having the disease (the test has a low rate of false-negatives). Specificity is the proportion of people without infection (as determined by the reference standard) that the test of interest correctly recognizes as negative. A test with high specificity will rarely misclassify people without the disease as diseased (it has a low rate of false-positives). Sensitivity and specificity are both expressed on a scale of 0% to 100%, with greater values showing more agreement between the test of interest and the reference standard, and a value of 50% being correct as frequently as random guessing. However, knowing the sensitivity and specificity of a test does not tell you whether a particular patient with a positive or negative test is infected or not.

Other measures of diagnostic performance are more clinically applicable. The positive predictive value (PPV) of a test is the probability of a patient having the disease following a positive test result. The negative predictive value (NPV) is the probability of a patient not having the disease following a negative test result. Likelihood ratios indicate how much more likely patients with the disease are to have that particular result than patients without the disease. Positive likelihood ratios (PLR) indicate how much more likely people with infection are to have a positive test result, and negative likelihood ratios (NLR)

indicate how much more people with infection are to have a negative result. Values of greater than one suggest infection, and values of less than one suggest not having infection. Unlike sensitivity and specificity, predictive values and likelihood ratios are influenced by the prevalence of the disease in the population of patients being tested. For this reason, we did not report (or calculate) predictive values or likelihood ratios from data not applicable to potential organ donors.

Diagnostic performance measures typically involve a trade-off between counterpart metrics. For instance, increasing sensitivity (catching more of the true positives) may be at the expense of decreasing specificity (more false positives too). Acceptable thresholds for diagnostic performance and trade-off between sensitivity and specificity will vary by intended use of the test.

Assessment of Peer-reviewed Studies

We assessed the design and risk of bias (quality) of the peer-reviewed studies and rated the strength of the evidence using guidelines proposed by the GRADE working group (Schunemann et al. (2008)[2]; also available online through links found at the GRADE Web site.) We assessed studies reporting diagnostic characteristics using these protocols. It is likely that there is an interaction between study design and study limitations/risk of bias, with the lower-rated studies providing less reliable results. Where multiple studies report data on the same test, the study or studies with the fewest detractions on quality should be considered more reliable.

We did not assess turnaround time because most of that information was not evidence-based. We did not assess window period in this manner either, because much of the information came from sources other than peer-reviewed publications and insufficient information was reported to assess them in full, and because there was no information directly pertinent to absolute window period.

Study Design

According to the GRADE diagnostics rating guidance, study design should initially be considered "high" quality if the study assesses patients with diagnostic uncertainty (e.g., unknown infection status) and comparison of results of test of interest with an appropriate reference standard.[2] The following paragraphs describe the standards we used to determine appropriateness of reference standard and diagnostic uncertainty. Studies that fulfilled both of these criteria were initially rated as "high." Studies that fulfilled only one were initially rated as "moderate." For evidence bases comprised of more than one study, we used the median number of items to determine the overall initial GRADE rating. Individual study design factors are itemized in Table 49.

Reference Standard

As described in the Methods section, the correctness of the reference standard in deeming whether or not the sample is infected influences the diagnostic characteristics reported in that study, because all characteristics are calculated with reference to that standard. When a reference standard mis-categorizes the true status of samples, correct identification of samples by the test of interest will be considered wrong. An example of a test that is not reasonable could be an earlier generation of the test of interest. Because a first-generation EIA should be less sensitive than a third generation test, it is an inappropriate reference standard and will lead to positive samples identified by the more sensitive 3rd generation that were not recognized by the older test being misclassified as false positives rather than true positives. If the older test has more frequent false positives, the sensitivity of the newer test will be underestimated.

Although another EIA may be an appropriate reference standard for specificity (to confirm negatives), a NAT or Western blot (WB) would have been more appropriate reference standards for sensitivity (to confirm positives) or to resolve discrepancies between the EIAs. However, because no single test is always correct, the most accurate way to determine the true status of the sample is to use multiple testing methods, including using additional tests to resolve discrepant findings between the test of interest and the reference test, and to confirm positives. Clinical information could also contribute to the definitive status. In addition, to determine whether either the reference test or the test of interest may have both misclassified an infected sample as negative, samples should be drawn again after completion of a window period. Such practices could provide a very convincing and definitive reference standard by which to judge the characteristics of the test of interest. Well-characterized commercially purchased samples (such as from a laboratory supply company) should also provide a very accurate reference standards. Commercial samples are typically characterized using a variety of tests, including confirmatory tests and quantitative tests for positive samples.

Diagnostic Uncertainty

Diagnostic uncertainty pertains to whether the infection status of a sample is known before study enrollment. Selecting individuals based upon their infection status is likely to cause spectrum bias. Spectrum bias is mostly an issue of external validity; however, it may also bias diagnostic performance characteristics. If only patients who are either infected or uninfected are selected for inclusion, the study results generally suggest the test is more accurate than it really is. Spectrum bias would be best controlled for by enrolling an unselected (preferably consecutive or random) group of potential organ donors. Other unselected populations, such as general populations or blood donors, may provide reasonable substitutes, although these populations may differ in unknown way from potential organ donors (the characteristics of whom have been poorly described), including prevalence of infection and severity of disease. When test performance is measured within a cohort of individuals with unknown disease status representative of the target population, the study is assessing "clinical" performance. Such studies minimize the potential influence of spectrum bias and provide the best approximation of real-world use.

Studies that only assessed sensitivity *or* specificity (or only positive *or* negative likelihood ratios or predictive values) were excluded from the evidence base. We included studies that reported both sensitivity and specificity with the intent of assessing both counterpart statistics derived from testing the same set of samples, to assess "clinical" diagnostic performance. However, some studies assessed sensitivity in known infected samples only and specificity in known uninfected samples only. Characterized infected and uninfected samples were purchased from laboratory supply companies or retrieved from laboratory archives. This type of a study is assessing "analytic" performance. Such studies may not accurately represent the performance of the test in real-world use (typically, overestimation can be expected) and are ripe for spectrum bias. They may also be susceptible to further potential bias if no blinding occurs, especially if investigators have a vested interest in any particular test(s). Because the true status of the samples is already known, these analytic studies have some of the same limitations as other retrospective studies.

Table 49. Study Design Items for Diagnostic Performance

Virus/ Test Type	Test Trade Name	Manufacturer	Cite	Study Design Factor Satisfied		Individual Study Design Rating	GRADE Study Design Starting Point for Test
				Reference Standard	Diagnostic Uncertainty		
Tests currently in use in U.S. Organ Procurement Organization (OPO): Immunoassays							
HIV 3rd generation EIA	Genetics System (GS) HIV-1/HIV-2 Plus 0 EIA	Bio-Rad Laboratories	Owen et al. 2008[159]	✓	-	Moderate	Moderate
	HIVAB HIV-1/HIV-2 (rDNA) EIA	Abbott Laboratories	Barbe et al. 1994[134]	✓	-	Moderate	Moderate
			Owen et al. 2008[159]	✓	-	Moderate	
HBV (HBsAg; the surface antigen)	Abbott AxSYM HBsAg Assay	Abbott Laboratories	Diepersloot et al. 2000[140]	✓	✓	High	High
	Abbott PRISM HBsAg	Abbott Laboratories	No studies	-	-	-	-
	ADVIA Centaur HBsAg Assay	Siemens Healthcare Diagnostics	Huzly et al. 2008[142]	✓	-	Moderate	Moderate
	Genetic Systems (GS) HBsAg EIA 3.0	Bio-Rad Laboratories	No studies	-	-	-	-
HBV (anti-HBs; antibodies to the surface antigen)	Ortho Antibody to HBsAg ELISA Test System 3	Ortho Clinical Diagnostics	No studies	-	-	-	-
HBV (anti-HBc; antibodies to the core antigen)	Abbott PRISM HBcore	Abbott Laboratories	No studies	-	-	-	-
	ADVIA Centaur HBc Total Assay	Siemens Healthcare Diagnostics	No studies	-	-	-	-

Virus/ Test Type	Test Trade Name	Manufacturer	Cite	Study Design Factor Satisfied		Individual Study Design Rating	GRADE Study Design Starting Point for Test
				Reference Standard	Diagnostic Uncertainty		
	AxSYM Core 2.0	Abbott Laboratories	No studies	-	-	-	-
	CORZYME	Abbott Laboratories	No studies	-	-	-	-
	Ortho HBc ELISA Test System	Ortho Clinical Diagnostics	No studies	-	-	-	-
HCV	Abbott HCV EIA 2.0	Abbott Laboratories	Anderson et al. 1995[132]	-	✓	Moderate	High
			Laycock et al. 1997[152]	✓	✓	High	
			Leon et al. 1993[153]	✓	✓	High	
	ADVIA Centaur HCV assay	Siemens Healthcare Diagnostics	Denoyel et al. 2004[139]	✓	-	Moderate	High
			Kita et al. 2009[146]	✓	✓	High	
	AxSYM Anti-HCV	Abbott Laboratories	No studies	-	-	-	-
	Ortho HCV Version 3.0 ELISA Test System	Ortho Clinical Diagnostics	Kita et al. 2009[146]	✓	✓	High	High
			Vrielink et al. 1995[167]	✓	✓	High	
			Vrielink et al. 1995[168]	✓	-	Moderate	

Virus/ Test Type	Test Trade Name	Manufacturer	Cite	Study Design Factor Satisfied		Individual Study Design Rating	GRADE Study Design Starting Point for Test
				Reference Standard	Diagnostic Uncertainty		
Tests currently in use in U.S. Organ Procurement Organization (OPO): NAT							
HIV NAT	COBAS AmpliScreen HIV-1 Test v. 1.5	Roche Diagnostics	Bamaga et al. 2006[133]	-	✓	Moderate	Moderate
			Owen et al. 2008[159]	✓	-	Moderate	
HCV NAT	COBAS AmpliScreen HCV Test version. 2.0	Roche Diagnostics	Bamaga et al. 2006[133]	-	✓	Moderate	Moderate
HBV NAT	COBAS AmpliScreen HBV Test	Roche Diagnostics	Kleinman et al. 2005[147]	✓	✓	High	High
HCV and HIV-1 NAT	ProCleix HIV-1/HCV Assay	Gen-Probe Incorporated	Jackson et al. 2002[144] – HIV	✓	✓	High	Moderate
			Vargo et al. 2002[128] – HIV	✓	-	Moderate	
			Jackson et al. 2002[144] – HCV	✓	✓	High	
			Vargo et al. 2002[128] – HCV	✓	-	Moderate	
			Vargo et al. 2002[128] – Co-infected	✓	-	Moderate	

Virus/ Test Type	Test Trade Name	Manufacturer	Cite	Study Design Factor Satisfied		Individual Study Design Rating	GRADE Study Design Starting Point for Test
				Reference Standard	Diagnostic Uncertainty		
Tests not in use in U.S. Organ Procurement Organization (OPO): 4th generation Ag/Ab Immunoassays							
HIV 4th generation	ARCHITECT HIV Combo	Abbott Laboratories	Kwon et al. 2006[149]	✓	-	Moderate	Moderate
			Ly et al. 2007[154]	✓	-	Moderate	
	AxSYM HIV Ag/Ab Combo	Abbott Laboratories	Bourlet et al. 2005[136]	✓	✓	High	Moderate
			Kwon et al. 2006[149]	✓	-	Moderate	
			Ly et al. 2007[156]	✓	-	Moderate	
			Sickinger et al. 2007[163]	✓	-	Moderate	
	COBAS Core HIV Combi	Roche Diagnostics	Ly et al. 2007[154]	✓	-	Moderate	Moderate
			Weber et al. 2002[170]	✓	-	Moderate	
	Coulter HIV-1 p24 Antigen Assay	Coulter Corporation	No studies	-	-	-	-
	Enzygnost HIV Integral II	Siemens Healthcare Diagnostics	No studies	-	-	-	-
	Genscreen Plus HIV Ag/Ab Combo	Bio-Rad Laboratories	Aghokeng et al. 2004[131]	✓	✓	High	High
			Ly et al. 2007[156]	✓	-	Moderate	
	Genscreen HIV Ultra Ag-Ab Assay	Bio-Rad Laboratories	Ly et al. 2007[154]	✓	-	Moderate	Moderate

Virus/ Test Type	Test Trade Name	Manufacturer	Cite	Study Design Factor Satisfied		Individual Study Design Rating	GRADE Study Design Starting Point for Test
				Reference Standard	Diagnostic Uncertainty		
	Modular HIV Combi	Roche Diagnostics	No studies	-	-	-	-
	Murex HIV Ag/Ab Combo	Abbott Laboratories	Ly et al. 2007[156]	✓	-	Moderate	Moderate
	VIDAS DUO QUICK	bioMerieux Clinical Diagnostics	No studies	-	-	-	-
	VIDAS DUO ULTRA	bioMerieux Clinical Diagnostics	Bourlet et al. 2005[136]	✓	✓	High	High
			Ly et al. 2007[154]	✓	-	Moderate	
			Saville et al. 2001[161]	✓	✓	High	
	Vironostika HIV Uni-Form II Ag/Ab	bioMerieux Clinical Diagnostics	Aboud et al. 2006[130]	✓	✓	High	High
			Iqbal et al. 2005[143]*	✓	✓	High	
			Ly et al. 2007[156]	✓	-	Moderate	
			Seyoum et al. 2005[162]	✓	✓	High	
HCV 4th generation	INNOTEST HCV Ab IV	Innogenetics NV	No studies	-	-	-	-
	Monolisa HCV Ag/Ab Ultra	Bio-Rad Laboratories	No studies	-	-	-	-
	Murex 4.0	Abbott Laboratories	No studies	-	-	-	-

* Iqbal et al. reported outcomes for two data sets, which are both shown in Table 56. However, for the purposes of assessment of the evidence base (to eliminate double-influence of one study on the overall rating), the diagnostic data set is represented here.

Limitations (Risk of Bias/Quality)

In addition to study design, we assessed the limitations of each study using three more items. To assess the limitations of the included studies that report diagnostic performance outcomes, we asked the following three questions:

- Enrollment: Was there enrollment of consecutive/all, or random sample, of eligible patients?
- Data loss: Is data loss minimal?
- Blinding: Was blinding performed for both the test of interest and the reference standard?

Failure to apply a reference standard to all samples was basis for exclusion (e.g., if all negatives were assumed to be true negatives), so we did not assess that factor.

The following paragraphs describe the criteria used to determine whether a particular study had a limitation. Itemized limitation assessment for all included studies is provided in Table 50. Studies with one or more limitations are detracted one point in GRADE. If the majority of studies in a multiple-study evidence base have one or more limitations, the strength is likewise detracted one point in GRADE. Following these paragraphs, itemized assessment for each study is provided in Table 50.

Enrollment

Enrollment of all eligible patients, a consecutive series of patients, or a random selection of patients or blood samples minimizes the threat of sampling bias. Samples that are "unselected" with unknown status also satisfy this criterion. Selecting panels for a particular characteristic (i.e., known infected or known uninfected) does not satisfy this item regardless of the method used to select them because such sample sets are highly selected and prone to selection bias.

Data Loss

Although there may be no attrition in diagnostic cohort studies, data may be excluded from the evidence base when the true status of the sample is inconclusive. Ideally, researchers would deal with conflicting or inconclusive test results by performing additional tests on the sample. Samples that remain inconclusive may have low antibody titers or amounts of nucleic acid and were possibly collected during a window period. Re-testing at a later date (to allow for a window period to pass) could help to establish definitive status. Rather than perform these additional tests to reconcile conflicting results with true status, some studies simply exclude the inconclusive samples from the data set. Data may also be excluded if there are errors in collecting the samples or performing the test. If enough data sets are excluded to impact the outcome statistics, diagnostic performance is likely to be overestimated. We considered this criterion not satisfied if more than 5% of data are lost due to any cause.

Blinding

Blinding is a commonly recognized way to protect against diagnostic bias when interpreting results. Although qualitative assessment of a sample should require little interpretation, lack of blinding could lead to miscategorization. Knowing the sample status could lead to misclassification of incorrect results as inconclusive (possibly resulting in the exclusion of that sample), especially if the result is close to the threshold or if it leads the researcher to recognize an error was made. This could be a particular problem if the investigator has a potential conflict of interest with the study findings.

Table 50. Quality Assessment of Question 5: Diagnostic Characteristics

Virus/ Test Type	Test Trade Name	Manufacturer	Cite	Limitation Item Met			Number of Items Satisfied	Starting Grade Adjustment for Quality
				Enrollment	Data Loss (Excessive Exclusions)	Blinding		
Tests currently in use in U.S. Organ Procurement Organization (OPO): Immunoassays								
HIV 3rd generation EIA	Genetics System (GS) HIV-1/HIV-2 Plus 0 EIA	Bio-Rad Laboratories	Owen et al. 2008[159]	✓	✓	-	2	-1
	HIVAB HIV-1/HIV-2 (rDNA) EIA	Abbott Laboratories	Barbe et al. 1994[134]	✓	✓	-	2	-1
			Owen et al. 2008[159]	✓	✓	-	2	
HBV (HBsAg; the surface antigen)	Abbott AxSYM HBsAg Assay	Abbott Laboratories	Diepersloot et al. 2000[140]	✓	✓	-	2	-1
	Abbott PRISM HBsAg	Abbott Laboratories	No studies	-	-	-	-	-
	ADVIA Centaur HBsAg Assay	Siemens Healthcare Diagnostics	Huzly et al. 2008[142]	✓	✓	-	2	-1
	Genetic Systems (GS) HBsAg EIA 3.0	Bio-Rad Laboratories	No studies	-	-	-	-	-
HBV (anti-HBs; antibodies to the surface antigen)	Ortho Antibody to HBsAg ELISA Test System 3	Ortho Clinical Diagnostics	No studies	-	-	-	-	-
HBV (anti-HBc; antibodies to the core antigen)	Abbott PRISM HBcore	Abbott Laboratories	No studies	-	-	-	-	-
	ADVIA Centaur HBc Total Assay	Siemens Healthcare Diagnostics	No studies	-	-	-	-	-

Virus/ Test Type	Test Trade Name	Manufacturer	Cite	Limitation Item Met			Number of Items Satisfied	Starting Grade Adjustment for Quality
				Enrollment	Data Loss (Excessive Exclusions)	Blinding		
	AxSYM Core 2.0	Abbott Laboratories	No studies	-	-	-	-	-
	CORZYME	Abbott Laboratories	No studies	-	-	-	-	-
	Ortho HBc ELISA Test System	Ortho Clinical Diagnostics	No studies	-	-	-	-	-
HCV	Abbott HCV EIA 2.0	Abbott Laboratories	Anderson et al. 1995[132]	✓	✓	-	2	-1
			Laycock et al. 1997[152]	✓	✓	-	2	
			Leon et al. 1993[153]	✓	✓	-	2	
	ADVIA Centaur HCV assay	Siemens Healthcare Diagnostics	Denoyel et al. 2004[139]	-	✓	-	1	-1
			Kita et al. 2009[146]	✓	✓	-	2	
	AxSYM Anti-HCV	Abbott Laboratories	No studies	-	-	-	-	-
	Ortho HCV Version 3.0 ELISA Test System	Ortho Clinical Diagnostics	Kita et al. 2009[146]	✓	✓	-	2	-1
			Vrielink et al. 1995[167]	✓	✓	-	2	
			Vrielink et al. 1995[168]	-	✓	-	1	

Virus/ Test Type	Test Trade Name	Manufacturer	Cite	Limitation Item Met			Number of Items Satisfied	Starting Grade Adjustment for Quality
				Enrollment	Data Loss (Excessive Exclusions)	Blinding		
Tests currently in use in U.S. Organ Procurement Organization (OPO): NAT								
HIV NAT	COBAS AmpliScreen HIV-1 Test v. 1.5	Roche Diagnostics	Bamaga et al. 2006[133]	✓	✓	-	2	-1
			Owen et al. 2008[159]	✓	✓	-	2	
HCV NAT	COBAS AmpliScreen HCV Test version. 2.0	Roche Diagnostics	Bamaga et al. 2006[133]	✓	✓	-	2	-1
HBV NAT	COBAS AmpliScreen HBV Test	Roche Diagnostics	Kleinman et al. 2005[147]	✓	✓	-	2	-1
HCV and HIV-1 NAT	ProCleix HIV-1/HCV Assay	Gen-Probe Incorporated	Jackson et al. 2002[144] – HIV	✓	✓	-	2	0
			Vargo et al. 2002[128] – HIV	✓	✓	✓	3	
			Jackson et al. 2002[144] – HCV	✓	✓	-	2	
			Vargo et al. 2002[128] – HCV	✓	✓	✓	3	
			Vargo et al. 2002[128] – Co-infected	✓	✓	✓	3	

Virus/ Test Type	Test Trade Name	Manufacturer	Cite	Limitation Item Met			Number of Items Satisfied	Starting Grade Adjustment for Quality
				Enrollment	Data Loss (Excessive Exclusions)	Blinding		
Tests not in use in U.S. Organ Procurement Organization (OPO): 4th generation Ag/Ab Immunoassays								
HIV 4th generation	ARCHITECT HIV Combo	Abbott Laboratories	Kwon et al. 2006[149]	-	✓	-	1	-1
			Ly et al. 2007[154]	-	✓	-	1	
	AxSYM HIV Ag/Ab Combo	Abbott Laboratories	Bourlet et al. 2005[136]	✓	✓	-	2	-1
			Kwon et al. 2006[149]	-	✓	-	1	
			Ly et al. 2007[156]	-	✓	-	1	
			Sickinger et al. 2007[163]	-	✓	-	1	
	COBAS Core HIV Combi	Roche Diagnostics	Ly et al. 2007[154]	-	✓	-	1	-1
			Weber et al. 2002[170]	-	✓	-	1	
	Coulter HIV-1 p24 Antigen Assay	Coulter Corporation	No studies	-	-	-	-	-
	Enzygnost HIV Integral II	Siemens Healthcare Diagnostics	No studies	-	-	-	-	-

Virus/ Test Type	Test Trade Name	Manufacturer	Cite	Limitation Item Met			Number of Items Satisfied	Starting Grade Adjustment for Quality
				Enrollment	Data Loss (Excessive Exclusions)	Blinding		
	Genscreen Plus HIV Ag/Ab Combo	Bio-Rad Laboratories	Aghokeng et al. 2004[131]	✓	✓	-	2	-1
			Ly et al. 2007[156]	-	✓	-	1	
	Genscreen HIV Ultra Ag-Ab Assay	Bio-Rad Laboratories	Ly et al. 2007[154]	-	✓	-	1	-1
	Modular HIV Combi	Roche Diagnostics	No studies	-	-	-	-	-
	Murex HIV Ag/Ab Combo	Abbott Laboratories	Ly et al. 2007[156]	-	✓	-	1	-1
	VIDAS DUO QUICK	bioMerieux Clinical Diagnostics	No studies	-	-	-	-	-
	VIDAS DUO ULTRA	bioMerieux Clinical Diagnostics	Bourlet et al. 2005[136]	✓	✓	-	2	-1
			Ly et al. 2007[154]	-	✓	-	1	
			Saville et al. 2001[161]	✓	✓	✓	3	
	Vironostika HIV Uni-Form II Ag/Ab	bioMerieux Clinical Diagnostics	Aboud et al. 2006[130]	✓	✓	-	2	-1
			Iqbal et al. 2005[143]*	✓	✓	-	2	
			Ly et al. 2007[156]	-	✓	-	1	

Virus/ Test Type	Test Trade Name	Manufacturer	Cite	Limitation Item Met			Number of Items Satisfied	Starting Grade Adjustment for Quality
				Enrollment	Data Loss (Excessive Exclusions)	Blinding		
			Seyoum et al. 2005[162]	✓	✓	-	2	
HCV 4th generation	INNOTEST HCV Ab IV	Innogenetics NV	No studies	-	-	-	-	-
	Monolisa HCV Ag/Ab Ultra	Bio-Rad Laboratories	No studies	-	-	-	-	-
	Murex 4.0	Abbott Laboratories	No studies	-	-	-	-	-

* Iqbal et al. reported outcomes for two data sets, which are both shown in Table 55. However, for the purposes of assessment of the evidence base (to eliminate double-influence of one study on the overall rating), the diagnostic data set is represented here.

Additional Considerations

Consistency

Although in some instances several studies addressed the same test of interest, different reference standards and samples were used. Differences in these two fundamental study design factors can be expected to lead to differences in outcomes and to dictate generalizability. In this respect, each study should probably best be considered in isolation. For this reason we did not downgrade for inconsistency, although we do summarize multiple studies to provide an overall picture of the tests' performances.

Directness

In the assessment of diagnostic technologies, GRADE assessment of directness pertains to whether direct measures of diagnostic performance (e.g., patient-oriented clinical outcome) or indirect measures of diagnostic performance (e.g., intermediate or surrogate outcomes such as sensitivity and specificity) are reported. In this assessment, all data were indirect. However, the purpose of the question was to assess "test characteristics," specifically including sensitivity and specificity. Detracting points because the study addresses the question of interest is inappropriate; therefore, we did not.

Precision

Lack of precision is typically measured by 95% confidence intervals (CI) of outcome statistics. Because not all studies reported CI or data necessary to calculate CI, we considered the factor that influences precision instead, number of samples assessed. As most of the sample sets assessed were large (only four had 200 or fewer samples) and the smaller evidence bases had an over-representation of infection compared with real-world prevalence, we did not detract for precision.

Publication Bias

Because traditional methods of publication bias assessment are not useful for small evidence bases and evidence bases for which quantitative assessment is inappropriate, such as those addressing each test of interest, we assessed the potential for publication bias by considering whether at least half of the studies for a particular test were funded by the test's manufacturer. If studies with significant findings are more likely to be published, and if only manufacturers funded the published studies, it is possible that independently funded studies with non-significant findings were never published. The main limitation of this method is that most of the studies did not report a funding source.

Full GRADE assessments are shown in Table 56, after the *Results* section and tables.

Results

Although a large number of peer-reviewed publications and pieces of gray literature were included, little (or no) data addressed each of the individual studies of interest. Only one study may have collected samples from deceased individuals (corneal donors). None of the studies appear to have focused on pediatric use. Due to this, it was not possible to determine differential test performance among populations or by donor clinical status.

The following sections provide summaries of results. Full results data are provided in the tables following these sections.

Turnaround Time

Information on the time required to fully administer diagnostic tests was sparse. For most of the test categories, no data were identified, despite consulting multiple sources for data. Available turnaround times are summarized by test type in Table 51. Full data extraction on turnaround time on a per-test basis is shown in Table 4.

Table 51. Summary of Turnaround Times

Test Category	Turnaround Time
Tests currently in use in U.S. Organ Procurement Organizations (OPO): Immunoassays	
HIV, 3rd generation EIA	No data
HBsAg EIA	29 minutes for Advia Centaur (not reported for any of the others)
Anti-HBs EIA	No data
Anti-HBc EIA	No data
HCV, 2nd or 3rd generation EIA	No data
Tests currently in use in U.S. Organ Procurement Organizations (OPO): NAT	
HIV NAT	2 hours
HCV NAT	2 hours
HBV NAT	No data
HCV and HIV-1 NAT Combined	6 hours
Tests not in use by U.S. Organ Procurement Organizations (OPO): 4th generation Ag/Ab Immunoassays	
HIV 4th generation Ag/Ab EIA	26 minutes to 4 hours, depending on test brand
HCV 4th generation Ag/Ab EIA	190 minutes for one test brand

Window Period

Due to the limitations of using seroconversion panels to attempt to determine absolute window periods (previously defined as the duration between being infected and testing positive), we summarized the window periods relative to other tests. We report mean differences in time to detection among tests, and where reported, the range of time to detection. "Mean range" refers to the range of means when more than one study reported this data. These data were extracted from peer-reviewed publications and gray literature including independent laboratory assessments and product labeling information.
This information is presented in Table 52. Full data extraction on window periods and additional related information on a per-test basis is shown in Table 4.

Table 52. Summary of Window Periods and Related Data

Test Category	Window Period
Tests currently in use in U.S. Organ Procurement Organizations (OPO): Immunoassays	
HIV, 3rd generation EIA	Positive mean 12-14 days before Western blot, but in one panel at the same time as Western blot
HBsAg EIA	Positive range of 0-7 days before other unnamed licensed test
Anti-HBs EIA	Positive range of 14-18 days after NAT Positive later than HBsAg EIA on some samples
Anti-HBc EIA	Positive 1-4 weeks after HBsAg, coincident with symptom onset
HCV, 2nd or 3rd generation EIA	Positive mean of 30-35 days after RNA test, and overall range of time to detect infection 4-118 days
Tests currently in use in U.S. Organ Procurement Organizations (OPO): NAT	
HIV NAT*	Positive range of 2-15 days before Ab test Positive range 7-10 days before p24 Ag test Positive range of 0-28 days before Ag test alone
HCV NAT*	Positive mean range of 25-85 days (and where reported absolute range 5-186 days) before confirmed 3rd generation Ab test (and a mean of 113 days before 2nd generation Ab test) Positive mean 5 days (range: 0-24 days) before 4th generation test
HBV NAT	Positive mean range 10 to 15 days (overall range where reported 4-18 days) before HBsAg (single-sample procedure)
Tests not in use by U.S. Organ Procurement Organizations (OPO): 4th generation Ag/Ab Immunoassays	
HIV 4th generation Ag/Ab EIA	Positive means of 1.4 to 2 days after PCR Positive means of 1.5 to several days before 3rd generation
HCV 4th generation Ag/Ab EIA	Positive mean of 5 days (range: 0-24 days) after NAT, a mean of 4.8 days (range: 0-32 days) after PCR, and a mean of 30 days after RNA assay Positive mean of 26 days (range: 0-72 days) before 3rd generation

*Includes data from combined HIV/HCV NAT

Diagnostic Performance

All of the extracted diagnostic performance data were sensitivity and specificity, drawn from clinical and analytic performance studies. Predictive values and likelihood ratios from potentially generalizable populations were not reported. We did not calculate these values because the prevalence of infection among potential solid organ donors has not been clearly defined. A summary of sensitivity and specificity data by test category are shown in Table 53. The summarized data are point estimates. Where multiple estimates were reported, the lowest and highest (range of) values are reported. Full data extraction per test by name is shown in Table 55.

The last column of Table 53 shows the median GRADE assessment for the evidence base for the test category; full GRADE assessments for each test are shown in Table 56. In brief, reasons for GRADE detraction most commonly included lack of blinding and lack of diagnostic uncertainty. Inappropriate reference standard was encountered less frequently, but could have strong effects on the outcomes (see HIV NAT and HCV NAT summary statistics in the table below). No studies had substantial data loss. Table 56 also notes whether each statistic was calculated from an analytic study or a clinical study.

Table 53. Summary of Sensitivity and Specificity Data (Range of Reported Point Estimates)

Test Category	Sensitivity	Specificity	GRADE (Table 56)
Tests currently in use in U.S. Organ Procurement Organizations (OPO): Immunoassays			
HIV, 3rd generation EIA	99.4% to 100%	97.7% to 99.7%	Low
HBsAg EIA	100%	97.9% to 99.4%	Low to Moderate
Anti-HBs EIA	No data	No data	-
Anti-HBc EIA	No data	No data	-
HCV, 2nd or 3rd generation EIA	73.2% to 100%	92.7% to 99.9%	Moderate
Tests currently in use in U.S. Organ Procurement Organizations (OPO): NAT*			
HIV NAT**	92.6% to 100%	96.9% to 100%	Low
HCV NAT**	99.3% to 99.6%	97.4% to 99.6%	Low
HBV NAT	84.8%	100%	Very Low
Tests not in use by U.S. Organ Procurement Organizations (OPO): 4th generation Ag/Ab Immunoassays			
HIV 4th generation Ag/Ab EIA	100% (all)	82.5% to 100% (Most >99%)	Low to Moderate
HCV 4th generation Ag/Ab EIA	No data	No data	-

*Includes data from combined HIV/HCV test

**Summary table does not include data from Bamaga et al. due to lack of sufficiently accurate reference standard for determining sensitivity and specificity. Data from that study are shown in the evidence tables.

Table 54. Overview of Diagnostic Tests

Virus	Test Trade Name	Manufacturer	FDA Approval	Format*	Specimen Collection	Window Period	Turnaround Time
Tests Currently in Use by U.S. Organ Procurement Organizations (OPOs): Immunoassays							
HIV 3rd generation EIA	Genetics System (GS) HIV-1/HIV-2 Plus 0 EIA	Bio-Rad Laboratories	8/5/2003	EIA	Living (serum, plasma), Deceased donor (serum)	From 15 seroconversion panels, at least half of the results were positive about 14 days before Western blot.[159] In the package labeling in the FDA approval document, data are reported on use in 50 seroconversion panels, compared with FDA licensed HIV-1/HIV-2 EIAs and a licensed HIV-1 Western blot. Compared with (unnamed) kit 1, it detected infection sooner 74% of the time and at the same time in the remainder. Compared with (unnamed) kit 2 (in only 46 of the panels), it detected HIV sooner 18% of the time, at the same time 70% of the time, and later 12% of the time. Compared with the Western blot it became positive sooner in 74% and at the same time in 26%.[195]	-
	HIVAB HIV-1/HIV-2 (rDNA) EIA	Abbott Laboratories	7/22/2004	EIA	Living (serum, plasma), Deceased donor (serum)	In 7 of 8 seroconversion panels, positive responses were obtained 4 to >9 days sooner than Western blot, and at the same time in the eighth.[134] From 15 seroconversion panels, at least half of the test results were positive about 12 days before Western blot.[159] In the package insert, on 9 seroconversion panels this test detected antibody at the same time or sooner than the Abbott HIVAB HIV-1 EIA (three times positive when Abbott was inconclusive, and one time inconclusive when Abbott was negative). In one of the panels it detected HIV two bleeds (8 days) before Western blot.[190]	-
HBV (HBsAg; the surface antigen)	Abbott AxSYM HBsAg Assay	Abbott Laboratories	6/1/2006 original approval; 2/5/2007 manufac-turing change; 12/19/2007 labeling change	Micro-particle EIA	Living (serum, plasma)	In its FDA Summary of Safety and Effectiveness Data and Product Label, AxSYM HBsAg detected infection 3 to 7 days earlier than a (unnamed) FDA-licensed reference in 5 out of 15 seroconversion panels, and on the same day in the remaining 10.[194]	-

Virus	Test Trade Name	Manufacturer	FDA Approval	Format*	Specimen Collection	Window Period	Turnaround Time
	Abbott PRISM HBsAg	Abbott Laboratories	7/18/2006	ChLIA	Living (serum, plasma), Deceased donor (serum)	-	-
	ADVIA Centaur HBsAg Assay	Siemens Healthcare Diagnostics	5/26/2005 original approval; 3/4/2009 process change	EIA	Living (serum, plasma)	In the product label, in 6 seroconversion panels this test was positive at the same time as the (unnamed) reference assay in 5 serials, and two bleeds sooner in the remaining serial.[189]	29[155] to 30[142] minutes
	Genetic Systems (GS) HBsAg EIA 3.0	Bio-Rad Laboratories	1/23/2003	EIA	Living (serum, plasma) Deceased donor (serum)	As reported on its package insert, on 21 seroconversion panels, the GS HBsAg EIA 3.0 detected infection at the same time or earlier than the two unnamed licensed EIA comparison tests.[193]	-
HBV (anti-HBs; antibodies to the surface antigen)	Ortho Antibody to HBsAg ELISA Test System 3†	Ortho Clinical Diagnostics	4/23/2003	EIA	Serum, plasma	In the FDA product label for Cobas AmpliScreen HBV test, on 40 seroconversion panels Ortho HBsAg System 3 detected HBV a median of 14 to 18 days later than the NAT, depending on preparation method.[185] In company marketing materials for Genetic Systems HBsAg EIA, the window period for the GS test and this Ortho test was the same for 10 of 21 commercial seroconversion panels. For the remaining 11, GS detected reactive results sooner.[197]	-

Virus	Test Trade Name	Manufacturer	FDA Approval	Format*	Specimen Collection	Window Period	Turnaround Time
HBV (anti-HBc; antibodies to the core antigen)	Abbott AxSYM Core 2.0	Abbott Laboratories	9/8/2006 original approval; 2/5/2007 manufacturing and packaging change	Micro-particle EIA	Living (serum, plasma)	-	-
	Abbott PRISM HBcore	Abbott Laboratories	10/13/2005	ChLIA	Living (serum, plasma)	The product label states, "Anti-HBc appears in the serum of patients infected with HBV one to four weeks after the appearance of HBsAg, at the onset of symptoms."[187]	-
	ADVIA Centaur HBc Total Assay	Siemens Healthcare Diagnostics	12/22/2004	ChLIA	Living (serum, plasma)	The product labeling reports that, in a study of 7 seroconversion panels, the Advia Centaur detected infection at the same time as the (unnamed) reference in 6 panels and one day sooner in the seventh.[186]	-
	CORZYME†	Abbott Laboratories	3/19/1991 initial approval	EIA	Living (serum, plasma)	-	-
	Ortho HBc ELISA Test System†	Ortho Clinical Diagnostics	4/18/1991	EIA	Living (serum, plasma)	In a U.K. Health Protection Agency-sponsored evaluation of the ORTHO HBc ELISA Test System, the test was evaluated in four seroconversion panels. All evaluated HBc tests detected the same number of samples.[198]	-

Virus	Test Trade Name	Manufacturer	FDA Approval	Format*	Specimen Collection	Window Period	Turnaround Time
HCV	Abbott AxSYM Anti-HCV	Abbott Laboratories	2/5/2004 initial; 6/30/2004; 12/3/2004, 12/14/2004, 1/31/2005, 2/5/2007 manu-facturing changes; 2/22/2008 labeling changes	Micro-particle EIA	Living (serum)	In an independent laboratory evaluation sponsored by the U.K. Medical Devices Agency, AxSYM HCV v.3 and six other HCV tests were evaluated. On 22 seroconversion panels and 2 performance panels AxSYM detected HCV a mean of 1.6 days after the most sensitive assay for a given panel (ranking #2 out of all the tests), compared with 1.1 for Vitros ECi anti-HCV (which ranked first).[178] In an evaluation sponsored by the U.K. Health Protection Agency on 19 seroconversion panels, the Monolisa HCV Ab/Ab Ultra detected infection a mean of 4.8 days after PCR at a 0.5 threshold, and 7.5 days after PCR at a 1.0 threshold. For either threshold the range of days to detection was 0-32. By comparison, *AxSYM HCV v. 3.0* detected HCV a mean of 19.7 days (range: 0-38) after PCR.[182]	-
	Abbott HCV EIA 2.0	Abbott Laboratories	7/22/2004	EIA	Living (serum, plasma), Deceased donor (serum)	Of 19 blood donors who were RNA-positive but initially EIA-2 antibody negative, EIA-2 was positive at follow-up a median of 63 days later, but 4 of the samples were still not EIA-2 reactive on the last follow-up sample available (at 23 days, 93 days, 317 days, and 190 days, respectively). For comparison, 8 of the donors were EIA-3 positive at initial test, 9 more were reactive at first follow-up, and all were reactive by second follow-up. So, by the last follow-up time EIA-3 was positive for all donors, but for 4 of them EIA-2 was never reactive within the duration of the study. Intervals between blood draws were long, the authors noted.[141]	-

Virus	Test Trade Name	Manufacturer	FDA Approval	Format*	Specimen Collection	Window Period	Turnaround Time
	ADVIA Centaur HCV assay	Siemens Healthcare Diagnostics	12/22/2004 initial; 3/4/2009 manu-facturing process change; 4/9/2009 trade name labeling change	ChLIA	Living (serum, plasma)	Advia detected infection a mean of 34.6 days (range: 6 to 182 days) from the initial draw date on 20 panels.[139] In a study with two panels, Advia detected infection on bleed day 11 on one and day 28 on the other.[146] In its FDA submission of Summary of Safety and Effectiveness data, on 23 seroconversion panels, Advia Centaur was "at least as sensitive in the detection of seroconversion for HCV as commercially available assays," compared with published data. In the same document, on 20 seroconversion panels Centaur detected HCV on the same day as Ortho HCV v. 3.0 in 14 series, three days later in one, and a mean of 3.25 days sooner on the remaining 4.[188]	-

Virus	Test Trade Name	Manufacturer	FDA Approval	Format*	Specimen Collection	Window Period	Turnaround Time
	Ortho HCV Version 3.0 ELISA Test System	Ortho Clinical Diagnostics	5/20/1996; changes to package insert and indications 2/9/2009	EIA	Living (serum, plasma), Deceased donor (serum, EDTA)	8 of 19 blood donors who were RNA-positive but initially EIA-2 antibody negative were EIA-3 reactive. 17 of the 19 were reactive when recalled for additional testing a median of 34 (range: 5 to 70) days later, and all were reactive by the next follow-up. This includes 4 who were EIA-2 negative for the entire duration of the study, with blood last tested at 23 days, 93 days, 190 days, and 317 days, respectively.. Intervals between blood draws were long, the authors noted.[141] The mean time to detect infection in transfusion recipients was 74 days post-transfusion(range: 26 to 118 days). 15/21 cases were detected in the same bleed by Ortho 3.0 and the second generation version. In the other 5, this test detected infection a mean of 26 days (range: 20 to 34 days) earlier than the second generation version.[135] In a study with two panels, this test detected infection on bleed day 11 day on one and day 14 on the other.[146] In the FDA product label for COBAS AmpliScreen HCV Test 2.0, on 9 seroconversion panels it detected HCV a mean of 32 days before seroconversion, defined as positive results on both *Ortho 3.0 EIA* and Chiron RIBA 3.0.[184] In its FDA submission of Summary of Safety and Effectiveness data and product label, on 20 seroconversion panels Centaur detected HCV on the same day as *Ortho HCV v. 3.0* in 14 series, three days later in one, and a mean of 3.25 days sooner on the remaining 4.[188]	-

Virus	Test Trade Name	Manufacturer	FDA Approval	Format*	Specimen Collection	Window Period	Turnaround Time
Tests Currently in Use by U.S. Organ Procurement Organizations (OPOs): Nucleic Acid Tests (NAT)							
HIV NAT	COBAS AmpliScreen HIV-1 Test v. 1.5	Roche Diagnostics	12/20/2002 initial approval; 12/19/2003 expanded indications; 3/9/2005 expanded indications; 5/23/2007 changes in labeling and directions	PCR	Living (plasma); Deceased donor (serum, plasma)	Based upon modeling, the window period was about 12 hours (95% CI: 5 to 19 hours) less than the Gen-Probe TMA HIV-NAT test.[137] In 10 seroconversion panels, this test was positive 2 to 14 days (range) days before antibody seroconversion and 0 to 28 days (range) before p24 antigen test.[172] In 10 seroconversion panels, this test was positive 7 to 17 days before antibody seroconversion tested with anti-HIV-1 Ortho Anti-HIV1/2 Test.[173] According to its FDA product label, AmpliScreen HIV Test v.1.5 detected HIV a mean of 12 days before Abbott HIV-1-2 antibody test on 41 seroconversion panels, 6.8 days before the Abbott p24 antigen test on 40 panels, and 4.4 days before the Coulter p24 antigen test on 38 panels, using the multiprep procedure. As reported in its FDA product label, this test detected HIV a mean of 14.2 days before Abbott HIV-1-2 antibody test on 41 panels, 8.3 days before the Abbott p24 antigen test on 40 panels, and 5.8 days before the Coulter p24 antigen test on 38 panels using the standard processing procedures.[192] Also reported in its FDA product label, COBAS HIV-1 Test v. 1.5 was evaluated on 10 plasma seroconversion panels. COBAS v.1.5 recognized HIV a mean of 12 days before Abbott HIV-1/2, 7.5 days before Abbott HIV-1 p24 Antigen, and 4.3 days before Coulter HIV-1 Antigen test.[192]	One study reported the turnaround time of two hours.[133]

Virus	Test Trade Name	Manufacturer	FDA Approval	Format*	Specimen Collection	Window Period	Turnaround Time
HCV NAT	COBAS AmpliScreen HCV Test version. 2.0	Roche Diagnostics	12/3/2002 original approval; 5/13/2004 expanded indications; 3/9/2005 expanded indications; 5/22/2007 labeling	PCR	Living (plasma), Deceased donor (serum, plasma)	Based upon modeling, the window period was about 14 hours (95% CI: 10 to 9 hours) less than the Gen-Probe TMA HCV-NAT test.[137] In 4 of 5 seroconversion panels, the AmpliScreen test returned positive results 23 to 32 days before seroconversion panels. In the other panel, it detected infection later[164] On 44 blood donor samples in the window period, this test returned positive results a mean of 5.1 days (range: 0 to 24 days) before Monolisa HCV Ag-Ab testing.[150] In the FDA product label for COBAS AmpliScreen HCV Test 2.0, on 9 seroconversion panels it detected HCV a mean of 32 days before seroconversion, defined as positive results on both Ortho 3.0 EIA and Chiron RIBA 3.0.[184]	One study reported the turnaround time as two hours.[133]
HBV NAT	COBAS AmpliScreen HBV Test	Roche Diagnostics	4/21/2005 original approval; 8/2/2005 additional indications; 8/16/2007 labeling changes	PCR	Living (plasma), Deceased donor (serum, plasma)	Using 5 seroconversion panels this test was positive a mean of 10 days (range: 4 to 18 days) before HBsAg in single-sample procedure; mean 3.7 days (0 to 11) with minipool.[160] In the FDA product label, in 40 seroconversion panels this test had a window period of 15 (SD: 17) days fewer than Ortho 3 for HBsAg using multiprep procedure and 20 (SD: 17) days fewer using the standard preparation.[185]	-

Virus	Test Trade Name	Manufacturer	FDA Approval	Format*	Specimen Collection	Window Period	Turnaround Time
HIV-1 and HCV NAT	ProCleix HIV-1/HCV Assay	Gen-Probe Incorporated	2/27/2002 initial approval; 6/4/2004 expanded indications	TMA	Living (plasma), Deceased donor (serum, plasma)	Based upon modeled data and compared with AmpliScreen, the window period with ProCleix for HIV is an estimated 12 hours (95% CI: 5 to 19 hours) less, and for HCV it was an estimated 14 hours (95% CI: 5 to 19 hours).[137] *HIV:* In two seroconversion panels, ProCleix was positive 7 to 10 days before p24 antigen and 12 to 14 days before an antibody test for HIV.[138] In 26 seroconversion panels, ProCleix was positive for HIV at a mean of 10.2 bleed days (range: 0 to 61), compared with 12.3 (range: 1 to 61) for PCR, 16.9 (range: 1 to 67) for HIV-1 antigen, and 24.5 (range: 9 to 74) for HIV-1 antibody. The window period was reduced by a mean of 14.6 (SD: 6.2) days compared with antibody testing and a mean of 6.6 (SD: 4.4) days compared with antigen testing.[148] In 10 HIV seroconversion panels, ProCleix tested neat was positive a median of 12 days (neat) or 10 days (diluted 1:16) before antibody test (HIV 1/2 antibody assay by Abbott). It was positive a median of 7 days (neat) or 3 days (diluted) before p24 antigen test (Abbott or Coulter). The discriminatory assay was positive a median of 12 days before the antibody test and 6 days before the antigen test.[128] In its product label, on 10 HIV seroconversion panels ProCleix detected infection a median of 10 days before Abbott HIV-1/2 and 3 days before the Abbott or Coulter p24 antigen test in a 1:16 dilution. The discriminatory assay tested neat detected infection a median of 12 days before the antibody test and 6 days before the antigen tests. ProCleix recognized HIV before the comparators in 8 panels and at the same time as the other two.[191]	One study reported an "experienced operator" required 6 hours to perform two HIV/HCV tests, and 6.5 hours to perform three.[138]

Virus	Test Trade Name	Manufacturer	FDA Approval	Format*	Specimen Collection	Window Period	Turnaround Time
						HCV: In 2 seroconversion panels, one of the HCV panels had "similar" findings; the other had an 85 day difference between detection of HCV RNA and confirmed 3rd generation antibody test.[138] In 25 seroconversion panels, ProCleix detected HCV a mean of 113.2 (Standard Deviation [SD]: 98.7) days before a 2nd generation anti-HCV assay and 80.5 (SD: 55.9) days before a 3rd-generation assay.[145] (The window period for HIV was not reported in the article.) In 24 seroconversion panels, ProCleix detected HCV at a mean of 12 days (range: 0 to 140) compared with 13.35 for PCR (of the 20 panels tested, range: 0 to 140) and 37.9 (range: 5 to 186) for antibody test. Compared with an antibody test, this test had a mean reduction of 25.8 (SD: 15.5) day reduction in detection.[148] In 10 HCV seroconversion panels, ProCleix (including the discriminatory assay) was positive a median of 25 days before the antibody test (Ortho 3.0).[128] In its product label, on 10 HCV seroconversion panels, ProCleix detected HCV sooner than the Ortho HCV 3.0 ELISA or the Abbott Anti-HCV 2.0 for every series, and a median of 25 earlier whether diluted or not.[191]	
Tests not currently in use in U.S. Organ Procurement Organization (OPO): 4th generation Immunoassays							
HIV 4th generation	ARCHITECT HIV Combo	Abbott Laboratories	Not FDA Approved	Micropart icle ChLIA (CMIA)	Serum or plasma	In 24 seroconversion panels, ARCHITECT HIV Combo was positive at mean of 13.1 days (range: 1 to 37).[154] In 3 panels, it was positive on day 8 in two and day 23 on the third.[149] In an evaluation funded by the U.K. Health Protection Agency on 18 seroconversion panels, the mean delay (range) in days of the Architect HIV Ag/Ab Combo was 0.9 (0-6) compared with the most sensitive assay. (For AxSYM HIV Ag/Ab Combo this was 0.6 (0-7); Genscreen Ultra HIV Ag-Ab 1.5 (0-7); Murex HIV Ag/Ab Combo 4.8 (0-53); Vironostika HIV Uni-Form II Ag/Ab 8.6 (0-57)).[177]	Run time 26 minutes[154] Or, 29 minutes per company marketing materials[174] Or, 30 minutes in an independent evaluation[177]

Virus	Test Trade Name	Manufacturer	FDA Approval	Format*	Specimen Collection	Window Period	Turnaround Time
	AxSYM HIV Ag/Ab Combo	Abbott Laboratories	Not FDA Approved	Micro-particle EIA	Serum or plasma	In 24 seroconversion panels, AxSYM HIV Ag/Ab Combo was positive at mean of 14.8 days (range: 1 to 37).[156] In 19 seroconversion panels, it was positive at a mean of 13.2 days (range: 1 to 35).[158] In 14 seroconversion panels it detected HIV at a mean of 24.6 days (range: 7 to 50).[136] In 3 seroconversion panels it detected HIV at 15, 23, and 34 days.[149] In 25 seroconversion panels, it detected HIV a mean of 0.44 days (range: 0-5 days) after the first assay (which varied by panel).[156] This was 2-3 days before the 3rd-generation assays. In 22 panels, compared with a 3rd generation test (AxSYM gO), the window period was reduced by a mean of 6.15 days.[163] It was positive first by 1 to 2 bleeds in 18 of the panels, and equal in the other 4. In an evaluation funded by the U.K. Health Protection Agency on 18 seroconversion panels, the mean delay (range) in days of the Architect HIV Ag/Ab Combo was 0.9 (0-6) compared with the most sensitive assay. (For *AxSYM HIV Ag/Ab Combo* this was 0.6 (0-7); Genscreen Ultra HIV Ag-Ab 1.5 (0-7); Murex HIV Ag/Ab Combo 4.8 (0-53); Vironostika HIV Uni-Form II Ag/Ab 8.6 (0-57)).[177] In an evaluation by the U.K. Medicines and Healthcare products Regulation Agency of 35 seroconversion panels, AxSYM Ag/Ab combo was always the first positive test out of the other tested 4th and 3rd generation assays. By comparison, the mean (range) of days longer for positivity by Murex HIV Ag/Ab Combination were 2.4 (0-53), Genscreen PLUS HIV Ag-Ab were 3.6 (0-53), and Vironostika HIV Uni-Form II Ag/Ab 5.9 (0-57).[179] In an evaluation of the Genscreen ULTRA HIV Ag-Ab funded by the U.K. Health Protection Agency, in 21 seroconversion panels, this test detected HIV a mean of 1 day (range: 0-6) after AxSYM (the earliest test). By comparison, Murex HIV Ag/Ab Combination detected HIV a mean of 3.8 days (range: 0-53) days later, and Vironostika HIV Uni-Form II Ag/Ab detected HIV a mean of 7.3 (range: 0-57) days later.[181]	Run time 40 minutes[154] Time to completion about 2 hours for 90 specimens in a Health Protection Agency evaluation.[179]

Virus	Test Trade Name	Manufacturer	FDA Approval	Format*	Specimen Collection	Window Period	Turnaround Time
	COBAS Core HIV Combi	Roche Diagnostics	Not FDA Approved	EIA		Of 24 seroconversion panels, COBAS Core Combi only recognized HIV in 23 of the sample sets. Of those 23, the mean time to positive test result was 16.8 days (overall range 1 to never within panel set).[154] In 94 seroconversion panels, compared with 3rd generation tests the window period was reduced by 3.6 to 5.7 days.[170] In 87 panels in the same study, it detected HIV a mean of 2.75 days after RT-PCR.[170]	Run time 75 minutes[154]
	Coulter HIV-1 p24 Antigen Assay	Coulter Corporation	Not FDA Approved	EIA	Plasma, serum, or tissue culture super-natants	In the package insert, on 5 seroconversion panels the Coulter test detected HIV antigen prior to antibodies (tested by Abbott HIVAB HIV-1 antibody EIA test) on 4 tests, by 21 days, 23 days, 42 days, and 28 days. In the other panel, antigen was not detected.[180] The package insert also reported on findings on 31 seroconversion panels by "independent investigators." Window period was compared with Abbott HIVAB HIV-1/HIV-2 (rDNA) EIA and GS HIV-1/HIV-2 EIA, and several investigational tests. The Coulter test detected antigen prior to seroconversion in 80.6% of panels, and at the same time in 9.7%. Of the three remaining panels, one was not RNA-positive either. The Coulter test reportedly detect antigen at the same time as the investigational tests detected RNA in the rest.[180] As reported in its FDA product label, this test detected HIV a mean of 14.2 days before Abbott HIV-1-2 antibody test on 41 panels, 8.3 days before the Abbott p24 antigen test on 40 panels, and 5.8 days before the *Coulter p24 antigen test* on 38 panels using the standard processing procedures.[192] Also reported in its FDA product label, COBAS HIV-1 Test v. 1.5 was evaluated on 10 plasma seroconversion panels. COBAS v.1.5 recognized HIV a mean of 12 days before Abbott HIV-1/2, 7.5 days before Abbott HIV-1 p24 Antigen, and 4.3 days before *Coulter HIV-1 Antigen test*.[192]	Total test time 4 hours.[171]

Virus	Test Trade Name	Manufacturer	FDA Approval	Format*	Specimen Collection	Window Period	Turnaround Time
	Enzygnost HIV Integral II	Siemens Healthcare Diagnostics	Not FDA Approved	EIA	Serum, plasma	In a WHO/UNAIDS evaluation, Enzygnost HIV Integral II detected HIV a mean of 1 day (range: 0 to 2) earlier than Enzygnost HIV 1/2 Plus, using 8 seroconversion series. By comparison, means were 0.9 for Genscreen Plus HIV Ag/Ab, - 0.9 for Murex HIV Ag/Ab Combination, and -0.7 for Vironostika HIV Uni-Form II Ag/Ab.[199]	Total time 2 hours 50 minutes for 96 sera, according to WHO/UNAIDS report 15.[199]
	Genscreen Plus HIV Ag/Ab Combo	Bio-Rad Laboratories	Not FDA Approved	EIA	Serum, plasma	In an evaluation by the U.K. Health Protection Agency on 18 seroconversion panels, the mean delay (range) in days of the Architect HIV Ag/Ab Combo was 0.9 (0-6) compared with the most sensitive assay. (For AxSYM HIV Ag/Ab Combo this was 0.6 (0-7); *Genscreen Ultra HIV Ag-Ab 1.5 (0-7)*; Murex HIV Ag/Ab Combo 4.8 (0-53); Vironostika HIV Uni-Form II Ag/Ab 8.6 (0-57)).[177] In an evaluation funded by the U.K. Medical Devices Agency of 38 seroconversion panels, the Murex Combo test detected HIV a mean of 3.9 days (range: 0 to 20) before the most sensitive antibody test. By comparison, the mean (range) was 2.76 (0 to 20) for *Genscreen PLUS HIV Ag-Ab and 0.34 (-9 to 20)* for Vironostika Uni-Form II Ag/Ab.[183] In an evaluation funded by the U.K. Medicines and Healthcare products Regulation Agency of 35 seroconversion panels, AxSYM Ag/Ab combo was always the first positive test out of the other tested 4th and 3rd generation assays. By comparison, the mean (range) of days longer for positivity by Murex HIV Ag/Ab Combination were 2.4 (0-53), *Genscreen PLUS HIV Ag-Ab* were 3.6 (0-53), and Vironostika HIV Uni-Form II Ag/Ab 5.9 (0-57).[179] In a WHO/UNAIDS evaluation on 8 seroconversion panels, Genscreen Plus HIV Ag/Ab was positive a mean of 0.9 days (range: -0.1 to 1.75 days) earlier than the reference assay, Enzygnost HIV1/2 Plus. By comparison, means were -1 for Enzygnost HIV Integral II, -0.9 for Genscreen Plus, -0.9 for Murex HIV Ag/Ab Combination, and -0.7 for Vironostika HIV Uni-Form II Ag/Ab.[199]	Total time 3 hours for 96 tests, according to WHO/UNAIDS report 15[199] Or 152 minutes in an independent laboratory evaluation.[181]

Virus	Test Trade Name	Manufacturer	FDA Approval	Format*	Specimen Collection	Window Period	Turnaround Time
	Genscreen HIV Ultra Ag-Ab Assay	Bio-Rad Laboratories	Not FDA Approved	EIA		In 24 seroconversion panels, Genscreen HIV Ultra Ag-Ab was positive at mean of 18.3 days (range: 1 to 37).[154] In an evaluation of the Genscreen ULTRA HIV Ag-Ab funded by the U.K. Health Protection Agency, in 21 seroconversion panels, this test detected HIV a mean of 1 day (range: 0-6) after AxSYM (the earliest test). By comparison, Murex HIV Ag/Ab Combination detected HIV a mean of 3.8 days (range: 0-53) days later, and Vironostika HIV Uni-Form II Ag/Ab detected HIV a mean of 7.3 (range: 0-57) days later.[181]	Approximate time to completion 152 minutes, according to the U.K. Health Protection Agency.[181]
	Modular HIV Combi	Roche Diagnostics	Not FDA Approved	EIA		Of 24 seroconversion panels, Modular Combi only recognized HIV in 23 of the sample sets. Of those 23, the mean time to positive test result was 15.4 days (overall range 1 to never within panel set).[154]	

Virus	Test Trade Name	Manufacturer	FDA Approval	Format*	Specimen Collection	Window Period	Turnaround Time
	Murex HIV Ag/Ab Combo	Abbott Laboratories	Not FDA Approved	EIA	Serum, plasma	Of 24 seroconversion panels, Murex Combo only recognized HIV in 23 of the sample sets. Of those 23, the mean time to positive test result was 14.6 days (overall range 1 to never within panel set).[154] In 19 seroconversion panels, it recognized HIV in 16 of the sample sets. Of those 16, the mean time to positive test was 15 days (overall range 1 to never within panel set).[158] In 25 seroconversion panels it recognized HIV a mean of 0.92 days (range: 0-15 days) after the first assay (which varied by panel).[156] This was about 1.5 days before the 3rd generation assays. In an evaluation funded by the U.K. Health Protection Agency on 18 seroconversion panels, the mean delay (range) in days of the Architect HIV Ag/Ab Combo was 0.9 (0-6) compared with the most sensitive assay. (For AxSYM HIV Ag/Ab Combo this was 0.6 (0-7); Genscreen Ultra HIV Ag-Ab 1.5 (0-7); *Murex HIV Ag/Ab Combo 4.8 (0-53)*; Vironostika HIV Uni-Form II Ag/Ab 8.6 (0-57)).[177] In an evaluation by the U.K. Medical Devices Agency of 38 seroconversion panels, the Murex Combo test detected HIV a mean of 3.9 days (range: 0 to 20) before the most sensitive antibody test. By comparison, the mean (range) was 2.76 (0 to 20) for Genscreen PLUS HIV Ag-Ab and 0.34 (-9 to 20) for Vironostika Uni-Form II Ag/Ab.[183] In an evaluation funded by the U.K. Medicines and Healthcare products Regulation Agency of 35 seroconversion panels, AxSYM Ag/Ab combo was always the first positive test out of the other tested 4th and 3rd generation assays. By comparison, the mean (range) of days longer for positivity by *Murex HIV Ag/Ab Combination were 2.4 (0-53),* Genscreen PLUS HIV Ag-Ab were 3.6 (0-53), and Vironostika HIV Uni-Form II Ag/Ab 5.9 (0-57).[179] In an evaluation of the Genscreen ULTRA HIV Ag-Ab funded by the U.K. Health Protection Agency, in 21 seroconversion panels, this test detected HIV a mean of 1 day (range: 0-6) after AxSYM (the earliest test). By comparison, *Murex HIV Ag/Ab Combination* detected HIV a mean of 3.8 days (range: 0-53) days later, and Vironostika HIV Uni-Form II Ag/Ab detected HIV a mean of 7.3 (range: 0-57) days later. By comparison, means were -1 for Enzygnost HIV Integral II, -0.9 for Genscreen Plus HIV Ag/Ab, -0.7 for Vironostika HIV Uni-Form II Ag/Ab.[181]	Total time to run assay 2 hours 55 minutes according to WHO/UNAIDS report 15.[199] Run time 120 minutes[183] Time to completion 140 minutes, as reported in a U.K. Medical Devices Agency report

Virus	Test Trade Name	Manufacturer	FDA Approval	Format*	Specimen Collection	Window Period	Turnaround Time
	VIDAS DUO QUICK	bioMerieux Clinical Diagnostics	Not FDA Approved	EIA		In 24 seroconversion panels, VIDAS DUO QUICK was positive at mean of 13.2 bleeding days (range: 1 to 37).[154] On the manufacturer Web site, on 25 seroconversion panels there was a mean delay of 1.44 days in HIV detection compared to an RNA test.[176]	Run time 80 minutes[154]
	VIDAS DUO ULTRA	bioMerieux Clinical Diagnostics	Not FDA Approved	EIA		In 14 seroconversion panels, VIDAS DUO ULTRA was positive at a mean of 23.5 days (range: 2 to 47)[136] In 24 seroconversion panels, it was positive at mean of 13.5 days (range: 1 to 30).[154] In 19 seroconversion panels, it was positive a mean of 16.2 days (range: 1 to 35).[158] In 16 seroconversion panels, it was positive at a mean of 2.31 days (range: 0 to 20) after RT-PCR.[169] Compared with the most sensitive antibody test in the test's information enclosure, on 10 seroconversion panels it detected HIV one bleed earlier in 2 cases, 2 bleeds earlier in 3, 3 bleeds earlier in 4, and 5 bleeds earlier in 1.[161] On the same panels compared with the most sensitive antigen test, it tested infection at the same time in 7 panels, 4 bleeds earlier in 1, 1 bleed earlier in 1, and 1 bleed later in the other.[161] On the company Web site, in 16 seroconversion panels this test detected infection at a mean of 2.13 bleeding days (range: 0-20) compared with 2.38 (range: 0-22) for an antigen test.[175]	Run time 120 minutes[154,169]
	Vironostika HIV Uni-Form II Ag/Ab	bioMerieux Clinical Diagnostics	Not FDA Approved	EIA	Serum, plasma	Of 24 seroconversion panels, Vironostika Uni-Form II Ag/Ab only recognized infection in 21. Of those 21, the mean time to positivity was 19.3 days (range 1 to never within panel set).[156] Of 19 seroconversion panels, it only recognized HIV in 16. Of those 16, the mean time to positivity was 15.6 days (overall range 1 to never within panel set).[158] Of 7 seroconversion panels, it was positive on day bleed 7, 15, 47, 26, 9, 18, and 27, respectively. It was always positive before Western blot and was positive from 0 to 37 days before the	Total time to perform assay 2 hours 15 minutes, according to WHO/UNAIDS report 15.[199] Run time 90 minutes[154,157]

Virus	Test Trade Name	Manufacturer	FDA Approval	Format*	Specimen Collection	Window Period	Turnaround Time
						3rd generation Vironostika test.[165] In 10 seroconversion panels this test was found to have a window period shortened by 6.2 days compared with the 3rd generation Vironostika test. This is 2.2 days longer than a HIV-1 p24 antigen assay.[166] Modeling from the same study suggests a total window period of 18 days.[166] In 30 seroconversion panels, it missed 3 positives. Of the rest, it detected HIV at a mean of 17.1 days (overall range 0 to never).[157] On the same panels three 3rd generation tests all missed either 3 or 4 positives, and had means detection at 17.6 days, 20.3 days, and 23.3 days. In 25 seroconversion panels, it detected HIV a mean of 2.6 days (range: 0 to 19 days) after the most sensitive assay (which varied by panel).[156] This was about the same as one 3rd generation assay and a day sooner than another 3rd generation assay. In an evaluation by the U.K. Health Protection Agency on 18 seroconversion panels, the mean delay (range) in days of the Architect HIV Ag/Ab Combo was 0.9 (0-6) compared with the most sensitive assay. (For AxSYM HIV Ag/Ab Combo this was 0.6 (0-7); Genscreen Ultra HIV Ag-Ab 1.5 (0-7); Murex HIV Ag/Ab Combo 4.8 (0-53); *Vironostika HIV Uni-Form II Ag/Ab 8.6 (0-57)).*[177] In an evaluation funded by the U.K. Medical Devices Agency of 38 seroconversion panels, the Murex Combo test detected HIV a mean of 3.9 days (range: 0 to 20) before the most sensitive antibody test. By comparison, the mean (range) was 2.76 (0 to 20) for Genscreen PLUS HIV Ag-Ab and *0.34 (-9 to 20) for Vironostika Uni-Form II Ag/Ab.*[183] In an evaluation by the U.K. Medicines and Healthcare products Regulation Agency of 35 seroconversion panels, AxSYM Ag/Ab combo was always the first positive test out of the other tested 4th and 3rd generation assays. By comparison, the mean (range) of days longer for positivity by Murex HIV Ag/Ab Combination were 2.4 (0-53), Genscreen PLUS HIV Ag-Ab were 3.6 (0-53), and	

Virus	Test Trade Name	Manufacturer	FDA Approval	Format*	Specimen Collection	Window Period	Turnaround Time
						Vironostika HIV Uni-Form II Ag/Ab 5.9 (0-57).[179] In an evaluation of the Genscreen ULTRA HIV Ag-Ab by the U.K. Health Protection Agency, in 21 seroconversion panels, this test detected HIV a mean of 1 day (range: 0-6) after AxSYM (the earliest test). By comparison, Murex HIV Ag/Ab Combination detected HIV a mean of 3.8 days (range: 0-53) days later, and *Vironostika HIV Uni-Form II Ag/Ab detected HIV a mean of 7.3 (range: 0-57) days later*.[181] In a WHO/UNAIDS evaluation on 8 seroconversion panels, Vironostika HIV Uni-Form II Ag/Ab was positive a mean of 0.6 days (range: -0.2 to 1.5 days) earlier than the reference assay, Enzygnost HIV1/2 Plus. By comparison, means were -1 for Enzygnost HIV Integral II, -0.9 for Genscreen Plus HIV Ag/Ab, - 0.9 for Murex HIV Ag/Ab Combination.[199]	
HCV	INNOTEST HCV Ab IV	Innogenetics NV	Not FDA Approved	EIA	Serum, plasma	In company marketing materials, on 30 seroconversion panels the Innotest HCV Ab IV had a total delay of 22 days for the detection of HCV, compared with 122 days for Ortho 3.0 test (a 3rd generation assay).[196]	-

Virus	Test Trade Name	Manufacturer	FDA Approval	Format*	Specimen Collection	Window Period	Turnaround Time
	Monolisa HCV Ag/Ab Ultra	Bio-Rad Laboratories	Not FDA Approved	EIA		In 10 seroconversion panels, there was a mean delay in positivity between the Monolisa HCV Ag/Ab Ultra and MP-NAT of 5.1 days (range: 0 to 24 days).[150] Compared with Prism HCV EIA (Abbott) (3rd generation EIA), this was a reduction of 26.8 days (range: 0 to 72 days).[150] In non-commercial conversion panels of 23 hemodialysis patients, there Monolisa Ultra detected HCV a mean of 21.6 days before the most sensitive antibody test (which varied by panel).[151] The mean delay of the Monolisa after RNA assay was 30.3 days. The mean delay after the trak-C antigen assay was 27.9 days compared with the HCV core Ag quantification assay and 16.3 days compared with the HCV Ag blood screening assay.[151] In an evaluation funded by the U.K. Health Protection Agency on 19 seroconversion panels, the Monolisa HCV Ab/Ab Ultra detected infection a mean of 4.8 days after PCR at a 0.5 threshold, and 7.5 days after PCR at a 1.0 threshold. For either threshold the range of days to detection was 0-32. By comparison, AxSYM HCV v. 3.0 detected HCV a mean of 19.7 days (range: 0-38) after PCR.[182]	Approximate time to completion 190 minutes, as reported by study funded by U.K. Health Protection Agency.[182]
	Murex 4.0	Abbott Laboratories	Not FDA Approved	EIA		-	-

* ChLIA: Chemiluminescent immunoassay; EIA: Enzyme Immunoassay; PCR: Polymerase chain reaction; TMA: Transcription-mediated amplification

† No FDA approval documentation found

Table 55. Diagnostic Characteristics

Virus/ Type	Test Trade Name	Manufacturer	Cite	Study Type	Sensitivity			Specificity			Data Loss	Comments
					Samples	Reference	Sensitivity	Samples	Reference	Specificity		
Tests currently in use in U.S. Organ Procurement Organization (OPO): Immunoassays												
HIV 3rd generation EIA	Genetics System (GS) HIV-1/HIV-2 Plus 0 EIA	Bio-Rad Laboratories	Owen et al. 2008[159]	Analytic	621 infected	Other serological tests, nucleic acid tests (NAT), Western blot (WB) for confirmation	99.8%	513 un-infected	Other serological tests, NAT, WB	99.4%	None	Positives not tested in duplicate
	HIVAB HIV-1/HIV-2 (rDNA) EIA	Abbott Laboratories	Barbe et al. 1994[134]	Analytic	7 infected	Archived samples	100%	1,546 negative	Repeat testing, BioMerieux Assay, WB	99.74%	None	
			Owen et al. 2008[159]	Analytic	621 infected	Other serological tests, NAT, WB for confirmation	99.4%	513 un-infected	Other serological tests, NAT, WB	97.7%	None	Positives not tested in duplicate
HBV (HBsAg; the surface antigen)	Abbott AxSYM HBsAg Assay	Abbott Laboratories	Diepersloot et al. 2000[140]	Clinical	200	Abbott IMx and DPC IMMULITE assays. Discrepancies by confirmatory assay	100%	200	Abbott IMx and DPC IMMULITE assays	99.4%	None	
	Abbott PRISM HBsAg	Abbott Laboratories	None identified	-	-	-	-	-	-	-	-	-

Virus/ Type	Test Trade Name	Manufacturer	Cite	Study Type	Sensitivity			Specificity			Data Loss	Comments
					Samples	Reference	Sensitivity	Samples	Reference	Specificity		
	ADVIA Centaur HBsAg Assay	Siemens Healthcare Diagnostics	Huzly et al. 2008[142]	Analytic	139	Consensus by >6 of 9 assays	100%	47 (exclude vacci-nated)	Consensus by >6 of 9 assays	97.9%	Not all patients included for calculation of sensitivity and specificity due to vaccination history.	Patients unselected at enrollment but included for sensitivity or specificity retrospec-tively based upon vaccination history
	Genetic Systems (GS) HBsAg EIA 3.0	Bio-Rad Laboratories	None identified	-	-	-	-	-	-	-	-	-
HBV (anti-HBs; antibodies to the surface antigen)	Ortho Antibody to HBsAg ELISA Test System 3	Ortho Clinical Diagnostics	None identified	-	-	-	-	-	-	-	-	-
HBV (anti-HBc; antibodies to the core antigen)	Abbott PRISM HBcore	Abbott Laboratories	None identified	-	-	-	-	-	-	-	-	-
	ADVIA Centaur HBc Total Assay	Siemens Healthcare Diagnostics	None identified	-	-	-	-	-	-	-	-	-
	AxSYM Core 2.0	Abbott Laboratories	None identified	-	-	-	-	-	-	-	-	-
	CORZYME	Abbott Laboratories	None identified	-	-	-	-	-	-	-	-	-
	Ortho HBc ELISA Test System	Ortho Clinical Diagnostics	None identified	-	-	-	-	-	-	-	-	-

Virus/ Type	Test Trade Name	Manufacturer	Cite	Study Type	Sensitivity			Specificity			Data Loss	Comments
					Samples	Reference	Sensitivity	Samples	Reference	Specificity		
HCV	Abbott HCV EIA 2.0	Abbott Laboratories	Anderson et al. 1995[132]	Clinical	21,432	Ortho Anti-HCV 2.0	73.2% (64.6% to 80.7%)*	21,432	Ortho Anti-HCV 2.0	99.9% (99.9% to 100%*	None	Positives tested in duplicate Additional tests were used but results reported with respect to the 2.0 EIA reported
			Laycock et al. 1997[152]	Clinical	101	Matrix HCV RIBA	100%	101	Matrix HCV RIBA	92.7%	None	
			Leon et al. 1993[153]	Clinical	496	Consensus by 11 tests plus supple-mental confirmatory assays	85.7% (80.5% to 89.9%)*	496	Consensus by 11 tests	99.8% (99.7% 99.9%)*	4 indeterminate (0.8%)	
	ADVIA Centaur HCV assay	Siemens Healthcare Diagnostics	Denoyel et al. 2004[139]	Analytic	472 presumed infected	Abbott AxSYM 3.0, verification of positives with Chiron RIBA 3.0	100% (99.18% to 100%)	5,228	Abbott AxSYM 3.0	99.9% (99.78% to 99.97%)	For sensitivity, 3.4% (16 samples) excluded. For specificity, 0.08% (4 samples) excluded.	Based upon repeated testing
			Kita et al. 2009[146]	Clinical	500	Consensus of 9 screening assays and PCR	100% (85.8% to 100%)*	500	Consensus of 9 screening assays and PCR	94.4% (91.1% to 96.3%)*	None	PCR used as reference standard instead of RIBA here to avoid data loss

Virus/ Type	Test Trade Name	Manufacturer	Cite	Study Type	Sensitivity			Specificity			Data Loss	Comments
					Samples	Reference	Sensitivity	Samples	Reference	Specificity		
	AxSYM Anti-HCV	Abbott Laboratories	No studies	-	-	-	-	-	-	-	-	-
	Ortho HCV Version 3.0 ELISA Test System	Ortho Clinical Diagnostics	Kita et al. 2009[146]	Clinical	500	Consensus of 9 screening assays and PCR	100% (89.7% to 100%)*	500	Consensus of 9 screening assays and PCR	95.5% (93.2% to 97.2%)	None	PCR used as reference standard instead of RIBA here to avoid data loss
			Vrielink et al. 1995[167]	Clinical	2,153	Ortho 2.0, PCR, and RIBA-2	100%	2,153	Ortho 2.0	99.7% (99.4% to 99.9%)	No data loss (because PCR used as reference standard instead of RIBA)	
			Vrielink et al. 1995[168]	Analytic	868 high probability infected	Murex 3.0 EIA and Abbott 3.0 EIA, PCR confirmation	100%	1,055 un-selected	Murex 3.0 EIA and Abbott 3.0 EIA	99.9%	No data loss (because PCR used as reference standard instead of RIBA)	
Tests currently in use in U.S. Organ Procurement Organization (OPO): NAT												
HIV NAT	COBAS AmpliScreen HIV-1 Test v. 1.5	Roche Diagnostics	Bamaga et al. 2006[133]	Clinical	3,288	Enzygnost HCV (EIA)	7.7% (0% to 52.8%) (Note: EIA used as reference standard)	3,288	Enzygnost HCV (EIA)	100% (99.9% to 100%)	None	0.5 was added to TP and FP (which were zero) to enable calculation.
			Owen et al. 2008[159]	Analytic	621 infected	Other assays, NAT, WB	92.6%	513 un-infected	Other assays, NAT, WB	96.9%	None	

Virus/ Type	Test Trade Name	Manufacturer	Cite	Study Type	Sensitivity			Specificity			Data Loss	Comments
					Samples	Reference	Sensitivity	Samples	Reference	Specificity		
HCV NAT	COBAS AmpliScreen HCV Test version. 2.0	Roche Diagnostics	Bamaga et al. 2006[133]	Clinical	3,288	AxSYM 3.0 HCV EIA	20% (8.4% to 36.9%) (Note: EIA used as reference standard)	3,288	AxSYM 3.0 HCV EIA	99.4% (99% to 99.6%)	None	
HBV NAT	COBAS AmpliScreen HBV Test	Roche Diagnostics	Kleinman et al. 2005[147]	Clinical	581,790	HBsAg, anti-HBc, and follow-up if discordant	84.8% (79.2% to 100%)*	581,790	HBsAg, anti-HBc, and follow-up if discordant	100% (100% to 100%)*	None	
HCV and HIV-1 NAT	ProCleix HIV-1/HCV Assay	Gen-Probe Incorporated	Jackson et al. 2002[144] – HIV	Clinical	530	Serology, p24 antigen (Ag), alternate NAT, re-test at follow up if inconclusive	100% (85.2% to 100%)*	530	Serology, p24 Ag, alternate NAT, re-test at follow up if inconclusive	100% (99.3% to 100%)*	1.7% data loss due to 9 inconclusive samples	Tested neat
			Vargo et al. 2002[128] – HIV	Analytic	1,040 infected	Clinical status	99.9% (99.4% to 100%)	192,288	Serology, with WB and/or immunofluorescence (IFA), if needed	99.67% (99.55% to 99.77%) overall	44 (2%) of all samples used in sensitivity in this study (for both viruses) were excluded	Positives tested neat
			Jackson et al. 2002[144] – HCV	Clinical	520	Serology, alternate NAT, re-test at follow-up if inconclusive	99.3% (97.3% to 99.9%)	520	Serology, alternate NAT, re-test at follow-up if inconclusive	97.4% (94.4% to 99.0%)	3.5% data loss due to 19 inconclusive samples	

Virus/ Type	Test Trade Name	Manufacturer	Cite	Study Type	Sensitivity			Specificity			Data Loss	Comments
					Samples	Reference	Sensitivity	Samples	Reference	Specificity		
			Vargo et al. 2002[128] – HCV	Analytic	1,015 infected	Clinical status	99.6% (98.9% to 99.9%)	192,288	Serology, RIBA, follow-up if needed	99.6%	44 (2%) of all samples used in sensitivity in this study (for both viruses) were excluded	Tested neat
			Vargo et al. 2002[128] – Co-infected	Analytic	180 co-infected	Clinical status	100% (98% to 100%)	192,288	Serology (as above for HIV and HCV separately)	100%	44 (2%) of all samples used in sensitivity in this study (for both viruses) were excluded	Tested neat
Tests currently not in use in U.S. Organ Procurement Organization (OPO): 4th generation Immunoassays												
HIV 4th generation EIA	ARCHITECT HIV Combo	Abbott Laboratories	Kwon et al. 2006[149]	Analytic	149 infected	Known samples	100%	412 un-infected	Known samples	99.6%	None	
			Ly et al. 2007[154]	Analytic	553 infected	10 other 4th generation assays and 2 3rd generation assays, WB, p24 Ag, and PCR confirmation	100%	1,005 un-infected	10 other 4th genera-tion assays and 2 3rd genera-tion assays	99.9% initially reactive, 100% repeatedly reactive	None	
	AxSYM HIV Ag/Ab Combo	Abbott Laboratories	Bourlet et al. 2005[136]	Clinical	1,443	2 other assays plus confirmation	100%	1,443	2 other assays	99.65%	None	
			Kwon et al. 2006[149]	Analytic	149 infected	Known samples	100%	412 un-infected	Known samples	98.0%	None	

Virus/ Type	Test Trade Name	Manufacturer	Cite	Study Type	Sensitivity			Specificity			Data Loss	Comments
					Samples	Reference	Sensitivity	Samples	Reference	Specificity		
			Ly et al. 2007[156]	Analytic	669 infected	Known samples characterized genetically or by p24 Ag or WB	100%	1,005 un-infected	8 screening assays, or WB negative or indeterminate and p24 Ag negative	99.8% initially reactive, same for repeatedly reactive	None	
			Sickinger et al. 2007[163]	Analytic	453 infected	Known samples	100%	1,938 (hospitalized patients)	RNA and "marker" negative	99.90%	None	
								7,900 (blood donors)	RNA and "marker" negative	99.87%	None	
	COBAS Core HIV Combi	Roche Diagnostics	Ly et al. 2007[154]	Analytic	669 infected	10 other 4th generation assays and 2 3rd generation assays, WB, p24 Ag, and PCR confirmation	100%	1,005 un-infected	10 other 4th generation assays and 2 3rd generation assays	99.3% initially reactive, 99.4% repeatedly reactive	None	
			Weber et al. 2002[170]	Analytic	1,641 infected	WB, p24 Ag, RNA assay	100% (99.82% to 100%)	10,031 negative (including interference)	Other screening assays all negative, or WB negative, or WB indeterminate and p24 Ag negative	99.73% (99.61% to 99.82%)	None	
	Coulter HIV-1 p24 Antigen Assay	Coulter Corporation	-	-	-	-	-	-	-	-	-	

Virus/ Type	Test Trade Name	Manufacturer	Cite	Study Type	Sensitivity			Specificity			Data Loss	Comments
					Samples	Reference	Sensitivity	Samples	Reference	Specificity		
	Enzygnost HIV Integral II	Siemens Healthcare Diagnostics	-	-	-	-	-	-	-	-	-	
	Genscreen Plus HIV Ag/Ab Combo	Bio-Rad Laboratories	Aghokeng et al. 2004[131]	Clinical	503	Another EIA, 1 discriminatory assay, 2 confirmatory assays	100% (99.6% to 100%)	503	Another EIA, 1 discriminatory assay, 2 confirmatory assays	95%, or 82.5% (79.2% to 85.8%) with indeterminate samples included	None when indeterminate samples included. 8.4% (42) of the samples were indeterminate.	
			Ly et al. 2007[156]	Analytic	669 infected	Known samples characterized genetically or by p24 Ag or WB	100%	1,005 uninfected	8 screening assays, or WB negative or indeterminate and p24 Ag negative	99.9% initial, 99.9% repeat	None	
	Genscreen HIV Ultra Ag-Ab Assay	Bio-Rad Laboratories	Ly et al. 2007[154]	Analytic	669 infected	10 other 4th generation assays and 2 3rd generation assays and PCR	100%	1,005 uninfected	10 other 4th generation assays and 2 3rd generation assays	99.7% initially reactive, 99.8% repeatedly reactive	None	
	Modular HIV Combi	Roche Diagnostics	-	-	-	-	-	-	-	-	-	
	Murex HIV Ag/Ab Combo	Abbott Laboratories	Ly et al. 2007[156]	Analytic	669 infected	Known samples characterized genetically or by p24 Ag or WB	100%	1,005 uninfected	8 screening assays, or WB negative or indeterminate and p24 Ag negative	99.5% initially reactive, 99.6% for repeatedly reactive	None	

Virus/ Type	Test Trade Name	Manufacturer	Cite	Study Type	Sensitivity			Specificity			Data Loss	Comments
					Samples	Reference	Sensitivity	Samples	Reference	Specificity		
	VIDAS DUO QUICK	bioMerieux Clinical Diagnostics	-	-	-	-	-	-	-	-	-	
	VIDAS DUO ULTRA	bioMerieux Clinical Diagnostics	Bourlet et al. 2005[136]	Clinical	1,443	2 other assays plus confirmation tests	100%	1,443	2 other assays	99.86%	None	
			Ly et al. 2007[154]	Analytic	669 infected	10 other 4th generation assays and 2 3rd generation assays and PCR	100%	1,005 un-infected	10 other 4th genera-tion assays and 2 3rd genera-tion assays	98.8% initial, 99.5% repeatedly reactive	None	
			Saville et al. 2001[161]	Clinical	2,773	Antibody screening, p24 Ag, confirmatory assays, NAT	100%	2,773	Antibody screening, p24 Ag, confirmatory assays, NAT	99.5%	0.1% (3 samples) excluded be because not "fully resolved."	
	Vironostika HIV Uni-Form II Ag/Ab	bioMerieux Clinical Diagnostics	Aboud et al. 2006[130]	Clinical	1,380	Another EIA and confirmation	100% (98.8% to 100%)	1,380	Another EIA	99.4% (98.8% to 99.8%)	None	
			Iqbal et al. 2005[143]	Clinical	264	WB	100% (100% to 100%)	264	WB	99.3% (97.8% to 100%)	0.4% (1 sample) excluded for being indeterminate	
			Iqbal et al. 2005[143]	Analytic	104 infected	WB	100%	100 un-infected	WB	100%	None	This set not included in GRADE assessment (clinical set above included instead)

Virus/ Type	Test Trade Name	Manufacturer	Cite	Study Type	Sensitivity			Specificity			Data Loss	Comments
					Samples	Reference	Sensitivity	Samples	Reference	Specificity		
			Ly et al. 2007[156]	Analytic	669 infected	Known samples characterized genetically or by p24 Ag or WB	100%	1,005 un-infected	8 screening assays, or WB negative or indeterminate and p24 Ag negative	97.21% initially reactive, 99.6% for repeatedly reactive	None	
			Seyoum et al. 2005[162]	Clinical	408	NAT and ExaVir Load test	100%	408	NAT and ExaVir Load test	99.2%	None	
HCV 4th generation EIA	INNOTEST HCV Ab IV	Innogenetics NV	-	-	-	-	-	-	-	-	-	
	Monolisa HCV Ag/Ab Ultra	Bio-Rad Laboratories	-	-	-	-	-	-	-	-	-	
	Murex 4.0	Abbott Laboratories	-	-	-	-	-	-	-	-	-	

Table 56. GRADE Table for Question 5: Diagnostic Performance (Sensitivity/Specificity)

Virus	Test Trade Name	Manufacturer	Quantity and Type of Evidence	Findings (Point Estimates)	Starting GRADE (Study Design Table 49)	Decrease GRADE					GRADE for Evidence for Outcome
						Quality (Table 49)	Consistency	Directness	Precision	Publication Bias	
Tests currently in use in U.S. Organ Procurement Organization (OPO): Immunoassays											
HIV 3rd generation EIA	Genetics System (GS) HIV-1/HIV-2 Plus 0 EIA	Bio-Rad Laboratories	1 A*[159]	Sensitivity: 99.8%A** Specificity: 99.4%A Main limitations: lack of diagnostic uncertainty, no blinding	Moderate	-1	0	0	0	0	Low
	HIVAB HIV-1/HIV-2 (rDNA) EIA	Abbott Laboratories	2 A[134,159]	Sensitivity: 99.4%A[159] and 100%A[134] Specificity: 97.7%A[159] and 99.74%A[134] Main limitations: lack of diagnostic uncertainty, no blinding. Study design and quality assessment equal for the two studies.	Moderate	-1	0	0	0	0	Low
HBV (HBsAg; the surface antigen)	Abbott AxSYM HBsAg Assay	Abbott Laboratories	1 CDx†[140]	Sensitivity: 100%C‡ Specificity: 99.4%C Main limitation: no blinding	High	-1	0	0	0	0	Moderate
	Abbott PRISM HBsAg	Abbott Laboratories	No studies	-	-	-	-	-	-	-	-

Virus	Test Trade Name	Manufacturer	Quantity and Type of Evidence	Findings (Point Estimates)	Starting GRADE (Study Design Table 49)	Decrease GRADE					GRADE for Evidence for Outcome
						Quality (Table 49)	Consistency	Directness	Precision	Publication Bias	
	ADVIA Centaur HBsAg Assay	Siemens Healthcare Diagnostics	1 A[142]	Sensitivity: 100%A Specificity: 97.9%A Main limitations: lack of diagnostic uncertainty, no blinding	Moderate	-1	0	0	0	0	Low
	Genetic Systems (GS) HBsAg EIA 3.0	Bio-Rad Laboratories	No studies	-	-	-	-	-	-	-	-
HBV (anti-HBs; antibodies to the surface antigen)	Ortho Antibody to HBsAg ELISA Test System 3	Ortho Clinical Diagnostics	No studies	-	-	-	-	-	-	-	-
HBV (anti-HBc; antibodies to the core antigen)	Abbott PRISM HBcore	Abbott Laboratories	No studies	-	-	-	-	-	-	-	-
	ADVIA Centaur HBc Total Assay	Siemens Healthcare Diagnostics	No studies	-	-	-	-	-	-	-	-
	AxSYM Core 2.0	Abbott Laboratories	No studies	-	-	-	-	-	-	-	-
	CORZYME	Abbott Laboratories	No studies	-	-	-	-	-	-	-	-
	Ortho HBc ELISA Test System	Ortho Clinical Diagnostics	No studies	-	-	-	-	-	-	-	-

Virus	Test Trade Name	Manufacturer	Quantity and Type of Evidence	Findings (Point Estimates)	Starting GRADE (Study Design Table 49)	Decrease GRADE					GRADE for Evidence for Outcome
						Quality (Table 49)	Consistency	Directness	Precision	Publication Bias	
HCV	Abbott HCV EIA 2.0	Abbott Laboratories	3 CDx[132,152,153]	Sensitivity: 73.2%C[132], 85.7%C[153], 100%C[152] Specificity: 92.7%C[152], 99.8%C[153], 99.9%C[132] Main limitations: one study less appropriate reference standard, no blinding in any. Anderson et al.[132] used a less reliable reference standard. All other factors in study design and limitations assessment the same for all three studies.	High	-1	0	0	0	0	Moderate
	ADVIA Centaur HCV assay	Siemens Healthcare Diagnostics	1 A[139] 1 DxC[146]	Sensitivity: Both 100% Specificity: 94.4%C[146], 99.9%A[139] Main limitations: one study suboptimal enrollment methods, no blinding in either. Denoyel et al.[139] did not report appropriate enrollment methods. All other study design and limitations assessments were the same.	High	-1	0	0	0	0	Moderate
	AxSYM Anti-HCV	Abbott Laboratories	No studies	-	-	-	-	-	-	-	-

Virus	Test Trade Name	Manufacturer	Quantity and Type of Evidence	Findings (Point Estimates)	Starting GRADE (Study Design Table 49)	Decrease GRADE					GRADE for Evidence for Outcome
						Quality (Table 49)	Consistency	Directness	Precision	Publication Bias	
	Ortho HCV Version 3.0 ELISA Test System	Ortho Clinical Diagnostics	2 CDx[146,167] 1 A[168]	Sensitivity: All three 100%C Specificity: 95.5%C[146], 99.7%C[167], 99.9%A[168] Main limitations: one study lack of diagnostic uncertainty, one study suboptimal enrollment methods, no blinding. Vrielink et al.[168] did not use samples with diagnostic uncertainty or report adequate enrollment methods. The rest of the study design and limitations assessment factors were the same for all three studies.	High	-1	0	0	0	0	Moderate

Virus	Test Trade Name	Manufacturer	Quantity and Type of Evidence	Findings (Point Estimates)	Starting GRADE (Study Design Table 49)	Decrease GRADE					GRADE for Evidence for Outcome
						Quality (Table 49)	Consistency	Directness	Precision	Publication Bias	
Tests currently in use in U.S. Organ Procurement Organization (OPO): NAT											
HIV NAT	COBAS AmpliScreen HIV-1 Test v. 1.5	Roche Diagnostics	1 DxC[133] 1 A[159]	Sensitivity: 7.7%C[133] and 92.6%A[159] Specificity: 96.9%A[159] and 100%C[133] Main limitations: one study inappropriate reference standard, other lack of diagnostic uncertainty, neither blinded The main difference in findings appears to be due to the use of a reference standard inappropriate to calculate sensitivity in Bamaga et al.[133]	Moderate	-1	0	0	0	0	Low
HCV NAT	COBAS AmpliScreen HCV Test version. 2.0	Roche Diagnostics	1 CDx[133]	Sensitivity: 20%C Specificity: 99.4%C Main limitations: inappropriate reference standards, no blinding	Moderate	-1	0	0	0	0	Low
HBV NAT	COBAS AmpliScreen HBV Test	Roche Diagnostics	1 CDx[147]	Sensitivity: 84.8%C Specificity: 100%C Main limitations: no blinding, potential for publication bias	Moderate	-1	0	0	0	-1	Very Low

Virus	Test Trade Name	Manufacturer	Quantity and Type of Evidence	Findings (Point Estimates)	Starting GRADE (Study Design Table 49)	Decrease GRADE					GRADE for Evidence for Outcome
						Quality (Table 49)	Consistency	Directness	Precision	Publication Bias	
HCV and HIV-1 NAT	ProCleix HIV-1/ HCV Assay	Gen-Probe Incorporated	1 CDx[144] 1 A[128]	HIV Sensitivity: 99.9%A[128] and 100%C[144] Specificity: 99.67%A[128] and 100%C[144] HCV Sensitivity: 99.3%C[144] and 99.6%A[128] Specificity: 97.4%C[144] and 99.6%A[128] Main limitations: one study lack of diagnostic uncertainty, one study no blinding, potential for publication bias. Vargo et al.[128] did not have diagnostic uncertainty, and Jackson et al. did not have blinding. The studies were on the same for the rest of the study design and limitations assessment factors.	Moderate	0	0	0	0	-1	Low

Virus	Test Trade Name	Manufacturer	Quantity and Type of Evidence	Findings (Point Estimates)	Starting GRADE (Study Design Table 49)	Decrease GRADE					GRADE for Evidence for Outcome
						Quality (Table 49)	Consistency	Directness	Precision	Publication Bias	
Tests currently not in use in U.S. Organ Procurement Organization (OPO): 4th generation Immunoassays											
HIV 4th generation	ARCHITECT HIV Combo	Abbott Laboratories	2 A[149,154]	Sensitivity: Both 100%A Specificity: 99.6%A[149] and 100%A[154] Main limitations: lack of diagnostic uncertainty, suboptimal enrollment methods, no blinding. The study design and limitations assessments were the same for both studies.	Moderate	-1	0	0	0	0	Low

Virus	Test Trade Name	Manufacturer	Quantity and Type of Evidence	Findings (Point Estimates)	Starting GRADE (Study Design Table 49)	Decrease GRADE					GRADE for Evidence for Outcome
						Quality (Table 49)	Consistency	Directness	Precision	Publication Bias	
	AxSYM HIV Ag/Ab Combo	Abbott Laboratories	1 CDx[136] 3 A[149,156,163]	Sensitivity: All 100% Specificity: 98%A,[149] 99.65%C,[136] 99.8%A,[156] 99.9%/99.87%A[163] (last two from same study, different data sets) Main limitations: two studies lack of diagnostic uncertainty and/or suboptimal enrollment methods, all studies no blinding. Bourlet et al.[136] had diagnostic uncertainty and appropriate enrollment methods while the rest did not. The studies were the same on all other study design and limitations assessment factors.	Moderate	-1	0	0	0	0	Low

Virus	Test Trade Name	Manufacturer	Quantity and Type of Evidence	Findings (Point Estimates)	Starting GRADE (Study Design Table 49)	Decrease GRADE					GRADE for Evidence for Outcome
						Quality (Table 49)	Consistency	Directness	Precision	Publication Bias	
	COBAS Core HIV Combi	Roche Diagnostics	2 A[154,170]	Sensitivity: Both 100%A Specificity: 99.3%A[154] and 99.73%A[170] Main limitations: lack of diagnostic uncertainty, one study suboptimal enrollment methods, both no blinding. The two studies were the same for study design and limitations assessment.	Moderate	-1	0	0	0	0	Low
	Coulter HIV-1 p24 Antigen Assay	Coulter Corporation	No studies	-	-	-	-	-	-	-	-
	Enzygnost HIV Integral II	Siemens Healthcare Diagnostics	No studies	-	-	-	-	-	-	-	-

Virus	Test Trade Name	Manufacturer	Quantity and Type of Evidence	Findings (Point Estimates)	Starting GRADE (Study Design Table 49)	Decrease GRADE					GRADE for Evidence for Outcome
						Quality (Table 49)	Consistency	Directness	Precision	Publication Bias	
	Genscreen Plus HIV Ag/Ab Combo	Bio-Rad Laboratories	1 DxC[131] 1A[156]	Sensitivity: Both 100% Specificity: 82.5%C,[131] 99.9%A[156] Main limitations: One study lack of diagnostic uncertainty, one suboptimal enrollment methods, neither blinded. Ly et al.[156] did not have diagnostic uncertainty or report appropriate enrollment methods. All other study design and limitation assessment factors were the same.	High	-1	0	0	0	0	Moderate
	Genscreen HIV Ultra Ag-Ab Assay	Bio-Rad Laboratories	1 A[154]	Sensitivity:100%A Specificity: 99.8%A Main limitations: lack of diagnostic uncertainty, suboptimal enrollment methods, blinding	Moderate	-1	0	0	0	0	Low
	Modular HIV Combi	Roche Diagnostics	No studies	-	-	-	-	-	-	-	-

Virus	Test Trade Name	Manufacturer	Quantity and Type of Evidence	Findings (Point Estimates)	Starting GRADE (Study Design Table 49)	Decrease GRADE					GRADE for Evidence for Outcome
						Quality (Table 49)	Consistency	Directness	Precision	Publication Bias	
	Murex HIV Ag/Ab Combo	Abbott Laboratories	1 A[154]	Sensitivity: 100%A Specificity: 99.6%A Main limitations: lack of diagnostic uncertainty, suboptimal enrollment methods, blinding	Moderate	-1	0	0	0	0	Low
	VIDAS DUO QUICK	bioMerieux Clinical Diagnostics	No studies	-	-	-	-	-	-	-	-
	VIDAS DUO ULTRA	bioMerieux Clinical Diagnostics	2 DxC[136,161] 1 A[154]	Sensitivity: All 100% Specificity:99.5%C,[154] 99.5%A,[161] 99.86%C[136] Main limitations: one study lack of diagnostic uncertainty, one study suboptimal enrollment methods, two studies lack of blinding Ly et al.[154] did not have diagnostic uncertainty or report appropriate enrollment methods. None of the studies besides Saville et al.[161] used blinding. All other study design and limitation assessment factors were the same.	High	-1	0	0	0	0	Moderate

Virus	Test Trade Name	Manufacturer	Quantity and Type of Evidence	Findings (Point Estimates)	Starting GRADE (Study Design Table 49)	Decrease GRADE					GRADE for Evidence for Outcome
						Quality (Table 49)	Consistency	Directness	Precision	Publication Bias	
	Vironostika HIV Uni-Form II Ag/Ab	bioMerieux Clinical Diagnostics	3 CDx[130,143,162] 1 A[156]	Sensitivity: All 100% Specificity: 99.2%C,[162] 99.3%C,[143] 99.4%C,[130] 99.6%A[156] Main limitations: one study lack of diagnostic uncertainty, no blinding Ly et al.[156] did not have diagnostic uncertainty or report appropriate enrollment methods. All other study design and limitation assessment factors were the same.	High	-1	0	0	0	0	Moderate
HCV 4th generation	INNOTEST HCV Ab IV	Innogenetics NV	No studies	-	-	-	-	-	-	-	-
	Monolisa HCV Ag/Ab Ultra	Bio-Rad Laboratories	No studies	-	-	-	-	-	-	-	-
	Murex 4.0	Abbott Laboratories	No studies	-	-	-	-	-	-	-	-

* A: Analytic study
** A: Analytic sensitivity/specificity
† CDx: Clinical diagnostic cohort
‡ C: Clinical sensitivity/specificity

Evidence Reviews: III. Donor interventions to decrease transmission of HIV, HBV,or HCV from infected donors

Question 6. Which donor interventions reduce the probability of pathogen transmission from an organ donor infected with HIV, HBV, or HCV to a previously uninfected recipient?

Two publications of the same study of virus inactivation in organs met the inclusion criteria.[200,201] The study described kidney perfusion techniques that may potentially inactivate hepatitis C. The study methods and results are shown in Table 57 and Table 58, respectively. The study procured kidneys from HCV positive deceased donors, and investigated the virus-reducing capacity of four inactivation protocols:

- The first (called "standard" by the authors) involved initial flushing with 1.0L of University of Wisconsin (U/W) solution, 20 hours of pulsatile perfusion, and another U/W flushing. U/W solution is "a normokalemic, intracellular colloid injected into vital organs during harvesting to preserve function before transplantation".[202]
- The second (called "enhanced") involved a second pulsatile perfusion and additional flushings.
- The third involved 24 hours of pulsatile perfusion at a lower flow rate
- The fourth ("ultrafiltered") involved the filtration of used perfusate during the perfusion process.

The results (Table 58) showed that all four methods substantially reduced the viral load. The best results were found with the enhanced pulsatile perfusion, for which 99.7% of the HCV viral particles had been removed within 15 minutes after the start of the second perfusion.

Regarding study quality (Table 59), there was no control group that did not receive inactivation; no "patients" were actually enrolled. Applying the GRADE system (Table 60) resulted in a grade of Low. This was based on the fact that it was only a single study, and there was no non-inactivated control group, but it did find a large magnitude of effect as well as a dose response association.

Table 57. Inactivation Methods in Zucker et al. (1994)

Kidney Donor	Inactivation Procedure	Procedural Steps
Donor 1, Deceased HCV positive	Standard pulsatile perfusion	1) Flushed with 1.0 L of U/W solution 2) 20 hours of perfusion on a Waters MOX-9 pulsatile perfusion apparatus using 1.0 L of silica gel-treated plasma at between 4-6 degrees Celsius at a flow rate of approximately 400mL/minute 3) Again flushed with 1.0 L of U/W solution
Donor 2, Deceased HCV positive	Enhanced pulsatile perfusion	Steps 1-2 of the standard procedure, and then: 3) Three additional flushes with 1.0 L of U/W solution 4) Another 20 hours of perfusion using 1.0 L of silica gel-treated plasma at between 4-6 degrees Celsius at a flow rate of approximately 400mL/minute 5) Again flushed with 1.0 L of U/W solution
Donor 3, Deceased HCV positive, Kidney 1	Pulsatile perfusion, **without** ultrafiltration of perfusate	1) Flushed with 1.0 L of U/W solution 2) 24 hours of perfusion on a Waters MOX-9 pulsatile perfusion apparatus using 1.0 L of silica gel-treated plasma at between 6 degrees Celsius at a flow rate of 200mL/minute
Donor 3, Deceased HCV positive, Kidney 2	Pulsatile perfusion, **with** ultrafiltration of perfusate	1) Flushed with 1.0 L of U/W solution 2) 24 hours of perfusion on a Waters MOX-9 pulsatile perfusion apparatus using 1.0 L of silica gel-treated plasma at between 6 degrees Celsius at a flow rate of 200mL/minute, with ultrafiltration of perfusate using a high-flow hollow-fiber filter with a molecular weight cut-off of 300k daltons

Table 58. Inactivation Results in Zucker et al. (1994)

Total Viral Burden BEFORE Inactivation	When the Viral Load was Measured	Total Viral Burden AFTER Inactivation	% of Viral Copies that had been Removed
Standard Pulsatile Renal Preservation Procedure			
4.78×10^5	After the first 4 hours of pulsatile perfusion	1.28×10^5	**73%**
Enhanced Pulsatile Renal Preservation Procedure			
247×10^5	After the full 20 hours of the first pulsatile perfusion	60.5×10^5	**76%**
247×10^5	After the 3 additional U/W flushes and 15 minutes after the start of the second pulsatile perfusion	0.74×10^5	**99.7%**
Pulsatile Renal Preservation Procedure, without Ultrafiltration of Perfusate			
160×10^5	After the first 1 hour of pulsatile perfusion	120×10^5	**25%**
160×10^5	After the full 24 hours of pulsatile perfusion	50×10^5	**69%**
Pulsatile Renal Preservation Procedure, with Ultrafiltration of Perfusate			
160×10^5	After the first 1 hour of ultrafiltered pulsatile perfusion	60×10^5	**63%**
160×10^5	After the full 24 hours of ultrafiltered pulsatile perfusion	15×10^5	**91%**

Table 59. Question 6: Quality Assessment

Study	6a	6b	6c	6d	6e	6f	6g	6h
Zucker et al. (1994)[200,201]		✓					✓	

A checkmark (✓) means that the study met the quality criterion for this Question; the lack of a checkmark means that the study either did not meet the criterion, or it was unclear whether the study met the criterion. The criteria specific to this Question were:

6a. Were the patients randomly assigned to treatments?
6b. Was the study planned prospectively (i.e., before any data were collected)
6c. Were all consecutive patients enrolled (or a random sample of eligible patients)?
6d. Were the two groups comparable at baseline? (age, sex, comorbidities, indication for transplant, previous duration on waitlist)
6e. If not, were statistical adjustments performed to control for baseline differences?
6f. Were the two groups treated concurrently?
6g. Did at least 85% of the study enrollees provide data?
6h. Was the between-group difference in study completion rates less than 15%?

Table 60. GRADE Table for Question 6 (Inactivation)

Comparison	Outcome	Quantity and Type of Evidence	Findings	Starting Grade	Decrease GRADE					Increase GRADE			GRADE of Evidence for Outcome
					Study Quality	Consistency	Directness	Precision	Publication Bias	Large Magnitude	Dose Response	Confounders would reduce the effect	
Inactivating vs. not inactivating pathogens in solid organs	Viral burden	One study[200,201]	The four inactivation procedures reduced viral burden 69%% to 99.7%	Low	-1	-1	0	0	0	+1	+1	0	Low

Evidence Reviews: IV. Potential risks and benefits of transplanting, or not transplanting, solid organs from donors positive for HIV, HBV, or HCV

Question 7. How do the clinical outcomes of recipients of organs from donors infected with HIV, HBV, or HCV compare to those who remain on the transplant list?

This question involves whether the long-term health of a recipient will be better if 1) an organ from a known infected donor is transplanted, or 2) the patient remains on the waiting list for an organ from an uninfected donor. Transplanting an organ from an infected donor incurs the chance of a new infection, in addition to the usual risks of organ transplantation (e.g., graft failure, graft-vs. host disease). However, remaining on the waiting list also entails risks, primarily the risk of death before an organ becomes available. Even if an organ from an uninfected donor become available, transplantation procedural risks will still apply, and these risks would be slightly higher at that time because the recipient would be older.

This question should not be confused with Question 8, which considers clinical outcomes after the transplantation of organs from *at-risk* donors with unknown infection status.

Our original inclusion criteria for this question (Table 2) required a waitlist control group; only one study met those original criteria: Abbott et al. (2004).[82] This study involved the transplantation of kidneys from deceased donors known to have been infected with HCV; its methods and results are detailed in the next section. Due to the paucity of evidence, we relaxed the initial inclusion criteria to include:

- Studies of recipients who were **negative** before transplant that compared the clinical outcomes after *receiving an organ from a positive donor* vs. *receiving an organ from a negative donor*
- Studies of recipients who were **positive** before transplant that compared clinical outcomes after *receiving an organ from a positive donor* vs. *receiving an organ from a negative donor*

This expansion yielded 7 and 22 additional publications, respectively; they are listed in Table 64. Although these comparisons do not involve the waitlist, they are still relevant. When a potential organ recipient does not receive an organ because it is from a known positive donor, the recipient remains on the waitlist for an organ from a negative donor. This hoped-for organ may or may not become available before the patient dies. The comparison group "receiving an organ from a negative donor" represents the realization of this hope, so it estimates a relatively good waitlist outcome.

The use of organs from infected donors may be more acceptable for recipients who are already positive before transplant, because disease transmission is less important (although dual infection with a different genotpye is possible). Their outcomes may be quite different from the outcomes of recipients who were negative before transplant, which is why we considered the two types of recipients separately.

Some centers may reserve organs from infected donors only for the most ill recipients. For example, Haji et al. (2004)[77] stated that "at our institution, an HCV-seropositive donor was used when, in the judgment of the transplant team, the recipient was critically ill and not a candidate for mechanical

ventricular assist device or had a significant complication while on the ventricular assist device."[77] (page 278) Based on this practice, a simple comparison of survival times between those who received organs from infected donors and those who received organs from uninfected donors would be biased against the former group. Thus, a better analysis would attempt to control for pre-transplant differences so that the comparison is more balanced.

Organs from Positive Donors Compared to Remaining on the Waitlist

Abbott et al. (2004)[82] considered the clinical scenario of a patient with end-stage renal disease (ESRD) on dialysis, and a kidney from a deceased HCV+ donor becomes available to this patient. Authors used retrospective data on Medicare beneficiaries in the United States Renal Data System who had been on the kidney transplant waiting list between 4/1/1995 and 7/31/2000. Of the 38,270 potential recipients:

- 389 patients (1%) were transplanted with kidneys from **deceased HCV+ donors** (abbreviated DHCV+). Of these 389 recipients, 201 of them (52%) were HCV+ before the transplant.
- 16,106 patients (42%) were transplanted with kidneys from **deceased HCV- donors**. Of these recipients, 508 of them (3%) were HCV+ before the transplant.
- 17,044 patients (45%) were **not transplanted** during the study period. The pre-transplant HCV status of these recipients was not reported.
- 4,731 patients (12%) were transplanted prior to dialysis, or transplanted with an organ other than a kidney, or transplanted with any kidney from a living donor (neither separate counts not outcome data were reported for these patients). The pre-transplant HCV status of these recipients was not reported.

A critical question is whether these groups of patients were similar before the transplantations occurred. If they were not, then pre-transplant factors (e.g., age, or amount of time already on waitlist) could explain subsequent differences in mortality rates. In this study, there were some differences between the 389 patients who received kidneys from DHCV+ and the full group of patients (all reported characteristics are listed in Table 61 below). The only characteristic with a particularly large difference at baseline involved race: 58% of recipients of organs from DHCV+ donors were African-American, as compared to only 30.4% of the full group of enrolled patients. Several of the other differences were statistically significant (due to the extremely large number of enrolled patients), but the actual size of the baseline differences were not generally large.

The authors performed adjusted analyses to control for pre-transplant differences. Any variable that was statistically significantly associated with mortality (defined as $p < 0.10$) was adjusted for: recipient age, recipient race, cause of end-stage renal disease (ESRD), year of first dialysis, presence of congestive heart failure, ischemic heart disease, peripheral vascular disease, serum albumin level, Medicare claims for access-related complications, and Medicare HCV claims at the time of listing.

The mortality analyses contained an important limitation: if an organ from any donor other than a deceased HCV+ donor was transplanted, all subsequent survival times were excluded from the analysis. Therefore, the mortality from remaining on the waitlist was only up to the point of receiving an alternate kidney. A more comprehensive approach would have included post-transplant survival times for those who did eventually receive kidneys from alternate donors.

Authors compared the adjusted mortality rates of kidney recipients from a DHCV+ donor to waitlist patients. The reported results are shown in Figure 11. The adjusted hazard ratio of 0.76 (95% confidence interval 0.60 to 0.96) indicated reduced mortality after receiving a kidney from a deceased HCV+ donor as compared to being on the waitlist.

Authors did not directly compare the mortality rates of recipients of kidneys from HCV+ donors to recipients of kidneys from HCV- donors. However, they did report a comparison between receiving a kidney from *any* deceased donor (regardless of donor HCV status) and being on the waitlist. This comparison favored transplantation substantially (adjusted hazard ratio of 0.47; 95% CI: 0.43 to 0.50). Thus, the mortality advantage of receiving a kidney more than doubled when recipients of HCV- donor kidneys were included in the analysis (i.e., the 24% mortality advantage in the primary analysis increased to a 53% advantage).

The GRADE evidence profile appears in Table 63. The grade was Very Low, which was due to three factors: 1) the study did not randomly assign recipients to groups; 2) the study excluded survival data after the transplantation of any kidney that was not a kidney from a deceased HCV+ donor; and 3) that there was only one study. If either of the latter two factors were removed, the rating would still be "Very Low".

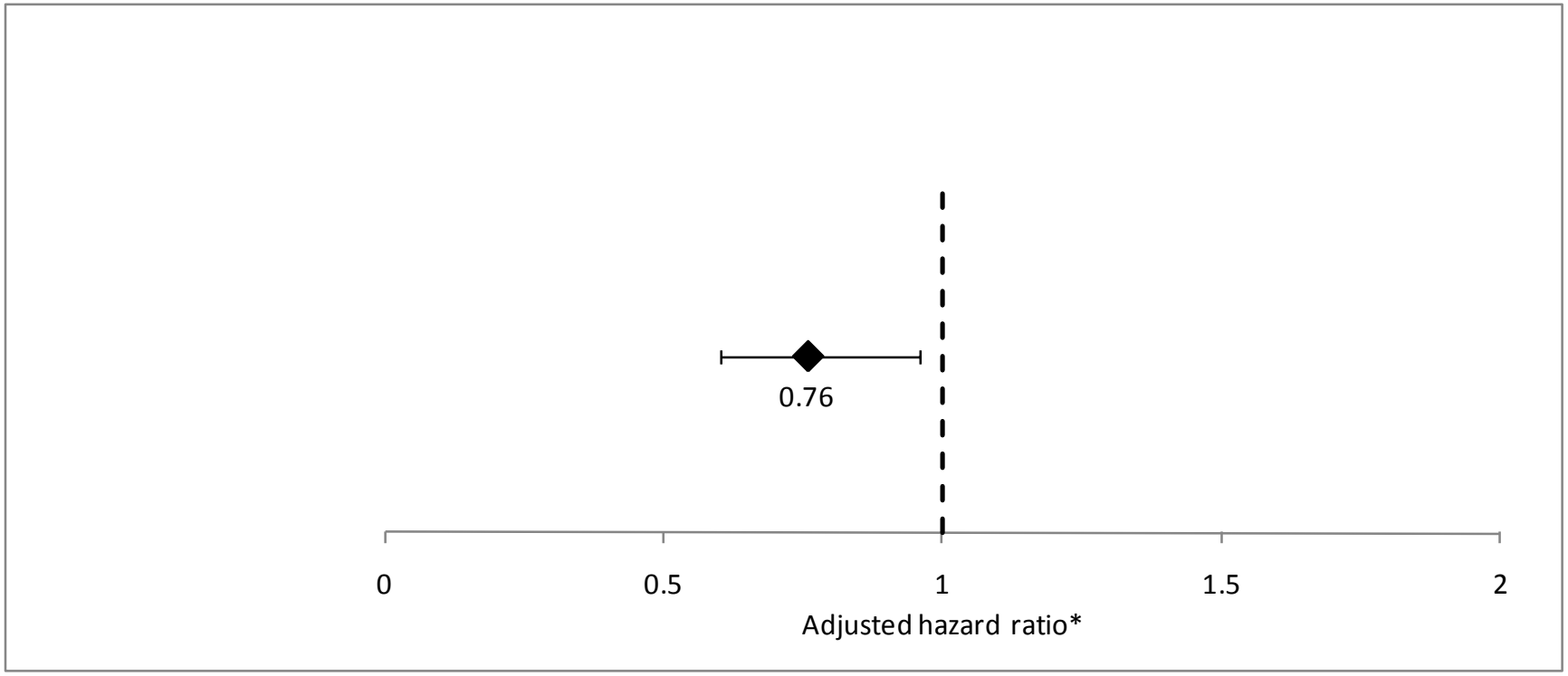
Table 61. Baseline Characteristics in the Abbott et al. (2004) Study

Characteristic	DHCV+ (N = 389)	Full Group of Enrolled Patients (N = 38,270)	Between-group Difference in Percentage Points (p.p.), or Hedges' g
% male	75.3%	61.3%	14 p.p.
% African-American	58.4%	30.4%	28 p.p.; Large difference at baseline
% with diabetes as the cause of end-stage renal disease	29.8%	35.3%	5 p.p.
% with hypertension	77%	73.9%	4 p.p.
% with congestive heart failure	15.9%	13.8%	2 p.p.
% ischemic heart disease	9.7%	8.9%	1 p.p.
% with smoking history	8.4%	5.3%	3 p.p.
% with hemodialysis (not peritoneal)	86.1%	80.5%	6 p.p.
% with peripheral vascular disease	4.4%	5.3%	1 p.p.
% with Medicare claims for HCV at the time of listing	5.4%	0.5%	5 p.p.
% with positive HCV serology by UNOS	51.7%	Not reported	Not calculable
% with Medicare claims for access	17.7%	14.2%	3.5 p.p.
Mean Age	51.2 (SD: 11.3)	47.6 (SD: 13.8)	g = 0.26
Mean Body Mass Index	26.0 (SD: 5.5)	26.7 (SD: 6.2)	g = 0.11
Mean Serum albumin (gm/dL)	3.2 (SD: 0.7)	3.4 (SD: 0.7)	g = 0.29
Mean Hematocrit	28.2 (SD: 5.8)	27.9 (SD: 5.7)	g = 0.05

Note: Shaded cells represent baseline characteristics that differed by 15+ percentage points, or differed by 0.4+ on the scale of Hedges' g. Hedges' g is the difference between means divided by the pooled standard deviation. The difference in percentage points, and values for Hedges' g, were calculated by ECRI Institute

SD – Standard deviation

Figure 11. Adjusted Mortality Results of Transplanting Kidneys from DHCV+ Donors Compared to the Waitlist



Note: The horizontal bars represent the reported 95% confidence interval around the adjusted hazard ratio. The fact that the confidence intervals was fully below 1.0 indicates that the adjusted hazard ratio was statistically significantly in favor of receiving a kidney from a DHCV+ donor over being on the waitlist.

*Variables adjusted for included recipient age, recipient race, cause of end-stage renal disease, year of first dialysis, presence of congestive heart failure, ischemic heart disease, peripheral vascular disease, serum albumin level, and Medicare claims for access-related complications and Medicare claims for access-related complications HCV

Organs from Positive Donors Compared to Organs from Negative Donors *When the Recipients were Negative Before Transplant*

We included seven publications (five unique studies) that made this comparison. One study involved HBV, and four involved HCV. General study characteristics are listed in the upper portion of Table 64, and details of methods appear in the upper portion of Table 65.

Regarding quality (the upper portion of Table 67), none of the studies were randomized or prospective, but all five treated the groups concurrently, and three studies enrolled patients consecutively. Two studies reported data on at least 85% of the enrolled patients and also had less than a 15% difference in completion rates between groups. For baseline comparability of groups (upper portion of Table 66), only two of the five studies reported any specific characteristics to enable a comparison (the Fong et al. [2002][55] study of HBV, and the Haji et al. [2004][77,79] study of HCV). Our analyses of between-group comparability identified three large differences at baseline (identified as gray cells in the upper portions of Table 66). For Fong et al. (2002)[55], the rate of donor death due to stroke was substantially higher in the D+ group (51% than the D- group (36%). For Haji et al. (2004)[77,79], the percentage of donors who were male was greater in the D+ group (74%) than in the D- group (57%), and also the mean recipient age was greater in the D+ group (age 57) than in the D- group (age 52).

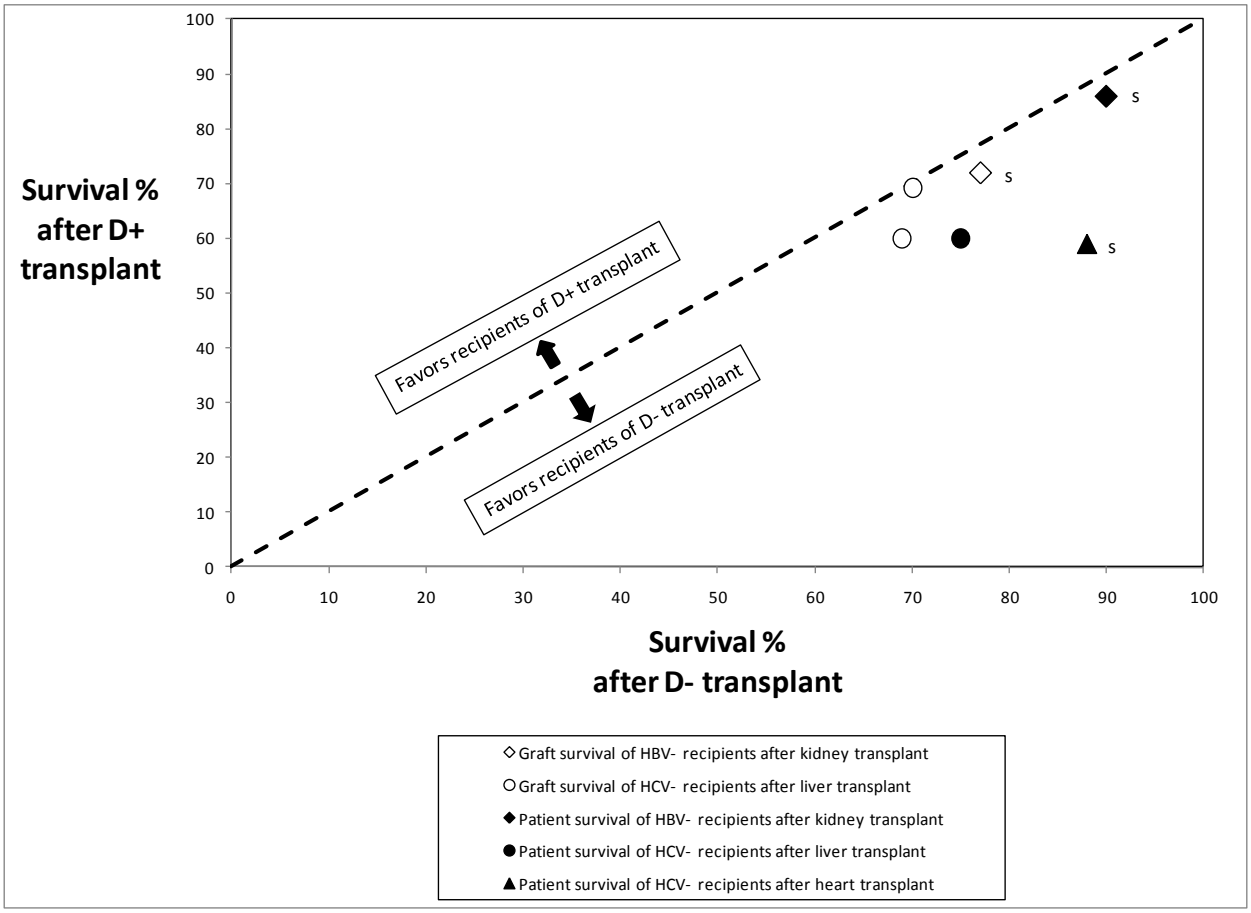
One way to address the problem of differing pre-transplant characteristics is to perform statistical adjustments of the results. Only one of the five studies (Abbott et al. 2003)[83,84] clearly performed such adjustments. The methods section of the Haji et al. (2004)[77,79] study reported some use of Cox regression "to adjust for significant covariates", but authors did not report whether the reported hazard ratio of 2.8 was adjusted or unadjusted.

All study results appear in the upper portion of Table 68, and pertinent plots are in Figure 12. The points appear without confidence intervals because studies did not report enough information to permit such calculation, which is also why no meta-analyses of these results were possible. Note that in the figure, the data generally fall below the 45 degree line, suggesting shorter survival among those who received D+ organs than those who received D- organs. However, the lack of demonstrated group comparability, and the possibility that in some studies the pre-transplant prognosis was poorer for recipients of D+ organs, make it difficult to interpret these raw results. The one study that controlled for baseline differences (Abbott et al. 2003)[83,84]) found a significantly shorter survival of those who received D+ organs (adjusted hazard ratio of 2.25; see footnote to the figure). The Haji et al. (2004)[77,79] study, which may have controlled for baseline differences, also reported shorter survival for recipients of D+ organs (see Table 68).

Regarding different genotypes of HBV and HCV, none of the five studies reported donors' genotypes, or stated whether recipient survival was different by donor genotype.

The GRADE evidence profiles appear in Table 63. We graded the evidence as Very Low for all of these evidence bases, except for the comparison of recipient survival of HCV+ and HCV- organs, which we graded as Low. None of these studies had randomized recipients to groups, and several had pre-transplant differences between groups that were not statistically adjusted for. The single "Low" GRADE (for recipient survival comparing HCV+ and HCV- donors) was due to the large effect magnitudes found in those three studies.

Figure 12. Clinical Outcomes of Negative Recipients: Positive vs. Negative Donors, any Pathogen, any Organ



Note: The diagonal line represents no difference in survival between those who received an organ from a positive donor and those who received an organ from a negative donor. Points above the diagonal line favor recipients of organs from positive donors, whereas points below the diagonal line favor recipients of organs from negative donors. This figure only includes studies that reported graft or survival data as percentages, and it only includes the longest followup timepoint from each study. The full data are provided in Table 68. None of the plotted studies reported confidence intervals. Studies with a lower case 's' next to the point reported that the comparison of full survival curves was statistically significant; all other studies either did not report whether the difference was statistically significant, or reported that the difference was not statistically significant. One of the studies did not report results on a percentage scale, and so its results do not appear in the plot. This was the Abbott et al. (2003)[83,84] study, which found an adjusted hazard ratio of death of 2.25 (95% CI: 1.56 to 3.24) in favor of recipients of organs from HCV- donors.

Organs from Positive Donors Compared to Organs from Negative Donors *When the Recipients were Positive Before Transplant*

We included 22 publications (17 unique studies) that made this comparison. Three studies involved HBV only, 13 studies involved HCV only, and one study provided separate data on both HBV and HCV. General study characteristics are listed in the lower portion of Table 64, and details of methods appears in the lower portion of Table 65.

Regarding quality (the lower portion of Table 67), none of the studies were randomized or prospective, but all 17 treated the groups concurrently, and 13 studies enrolled patients consecutively. Ten studies reported data on at least 85% of the enrolled patients and also had less than a 15% difference in completion rates between groups.

For baseline comparability of groups, 10 of the 17 studies (two of HBV and eight of HCV) reported specific characteristics to enable a comparison. These 10 studies reported 128 characteristics that could be compared (listed in the lower portions of Table 66), and we classified 27 of these 128 were as large differences (reproduced below in Table 62). In the HBV studies, the differences involved rates of donor HCV (HBV+ donors were more likely to also be HCV+), donor and recipient age (both were higher in D+ groups), and race (D+ donors were more likely to be African-American and less likely to be Caucasian-American). In the HCV studies, we noticed two types of consistent differences: donor/recipient ages (which were higher in D+ groups) and the recipient's amount of time on the waitlist (which was much shorter in the D+ groups: 9.9 months vs. 17.7 months in Woodside et al. (2003)[85], and 9 months vs. 29 months in Mandal et al. (2000).[86]

Table 62. Large Pre-transplant Differences between Recipients of D+ and D- Organs in Studies of Pre-transplant Positive Recipients

Study	Characteristic	Mean (SD) or % for Recipients of D+ Organs	Mean (SD) or % for Recipients of D- Organs	Difference in Percentage Points, or Hedges' g
Recipients Infected Before Transplant; Comparison of Clinical Outcomes after HBV+ Donor vs. HBV- Donor				
Fong et al. (2002)[55]	Donor % HCV+	22% (31/140)	5% (105/2093)	17 p.p.
	Recipient % African-American	56% (78/140)	39% (816/2093)	17 p.p.
	Donor age	42.7 (SD: 13.9)	34.9 (SD: 18.2)	g = 0.43
Madayag et al. (1997)[56]	Recipient % Caucasian-American	26% (12/45)	49% (22/45)	23 p.p.
	Recipient age	49.1 (SD: 11.8)	43.6 (SD: 11.8)	g = 0.47
Recipients Infected Before Transplant; Comparison of Clinical Outcomes after HCV+ Donor vs. HCV- Donor				
Woodside et al. (2003)[85]	CMV % donor/recipient pairs with both CMV+	70% (14/20)	55% (11/20)	15 p.p.
	Recipient % anti-HBc+	20% (4/20)	35% (7/20)	15 p.p.
	Recipient % Caucasian-American	15% (3/20)	35% (7/20)	20 p.p.
	Recipient % Hispanic-American	35% (7/20)	5% (1/20)	30 p.p.
	Recipient % male	80% (16/20)	65% (13/20)	15 p.p.
	Recipient Triple drug therapy %	100% (20/20)	80% (16/20)	20 p.p.
	Recipient time on waitlist (months)	9.9 (SD: 8)	17.7 (SD: 14.8)	g = 0.66

Study	Characteristic	Mean (SD) or % for Recipients of D+ Organs	Mean (SD) or % for Recipients of D- Organs	Difference in Percentage Points, or Hedges' g
Mandal et al. (2000)[86]	Donor % CMV+	87% (16/18)	50% (5/10)	37 p.p.
	Recipient % with diabetes	28% (5/18)	10% (1/10)	18 p.p.
	Recipient % being retransplanted	28% (5/18)	60% (6/10)	32 p.p.
	AB mismatch	3.2 (SD: 0.8)	2.3 (SD: 0.9)	g = 1.08
	Cold ischemia time (hrs)	28 (SD: 8.5)	22 (SD: 9.5)	g = 0.68
	Donor age	46 (SD: 8.5)	35 (SD: 19)	g = 0.84
	DR mismatch	1.6 (SD: 0.8)	1.3 (SD: 0.3)	g = 0.45
	Recipient age	48 (SD: 8.5)	44 (SD: 6.3)	g = 0.51
	Recipient time on waitlist (months)	9 (SD: 12.7)	29 (SD: 9.5)	g = 1.71
Morales et al. (1995)[87]	Recipient % abnormal liver histology	31% (7/24)	50% (20/40)	19 p.p.
	Recipient % anti-HBc+	50% (12/24)	23% (9/40)	27 p.p.
	Recipient % renal disease: chronic glomerulonephritis	55% (13/24)	35% (14/40)	20 p.p.
	Recipient pre-transplant number of transfusions	7 (SD: 8)	21 (SD: 39)	g = 0.45
Salizzoni et al. (2001)[88]	Donor age	62.6 (SD: NR)	53.7 (SD: NR)	g = 0.49
Testa et al. (1998)[89]	Recipient % male	50% (11/22)	73% (84/115)	23 p.p.

Note: This table only includes pre-transplant differences that met our criteria for "large", which was a Hedges' g of 0.4 or more for continuous data, or a difference in percentage points of 15 or more. These differences were calculated by ECRI Institute. The full list of reported baseline characteristics is in Table 66.

One way to address the problem of differing pre-transplant characteristics is to perform statistical adjustments of the results. Only four of the 17 studies did this (Fong et al. [2002][55], Madayag et al. [1997][56], Abbott et al. [2003][83,84], and Marroquin et al. [2001]).[90]

All study results appear in the lower portion of Table 68, and pertinent plots are in Figure 13, Figure 14, and Figure 15. The points appear without confidence intervals because studies did not report enough information to permit such calculation; this also explains why no meta-analyses of these results were possible. The HBV plot (Figure 13) shows no consistent trend: two data points favored the D+ group, three data points favored the D- group, and four data points suggested equivalence. Restricting the analysis to the two HBV studies that used statistical adjustments to control for baseline prognosis, one study (Madayag et al. [1997][56]) found poorer graft survival in the D+ group, and the other study (Fong et al. [2002][55]) found no large differences in either graft survival or patient survival.

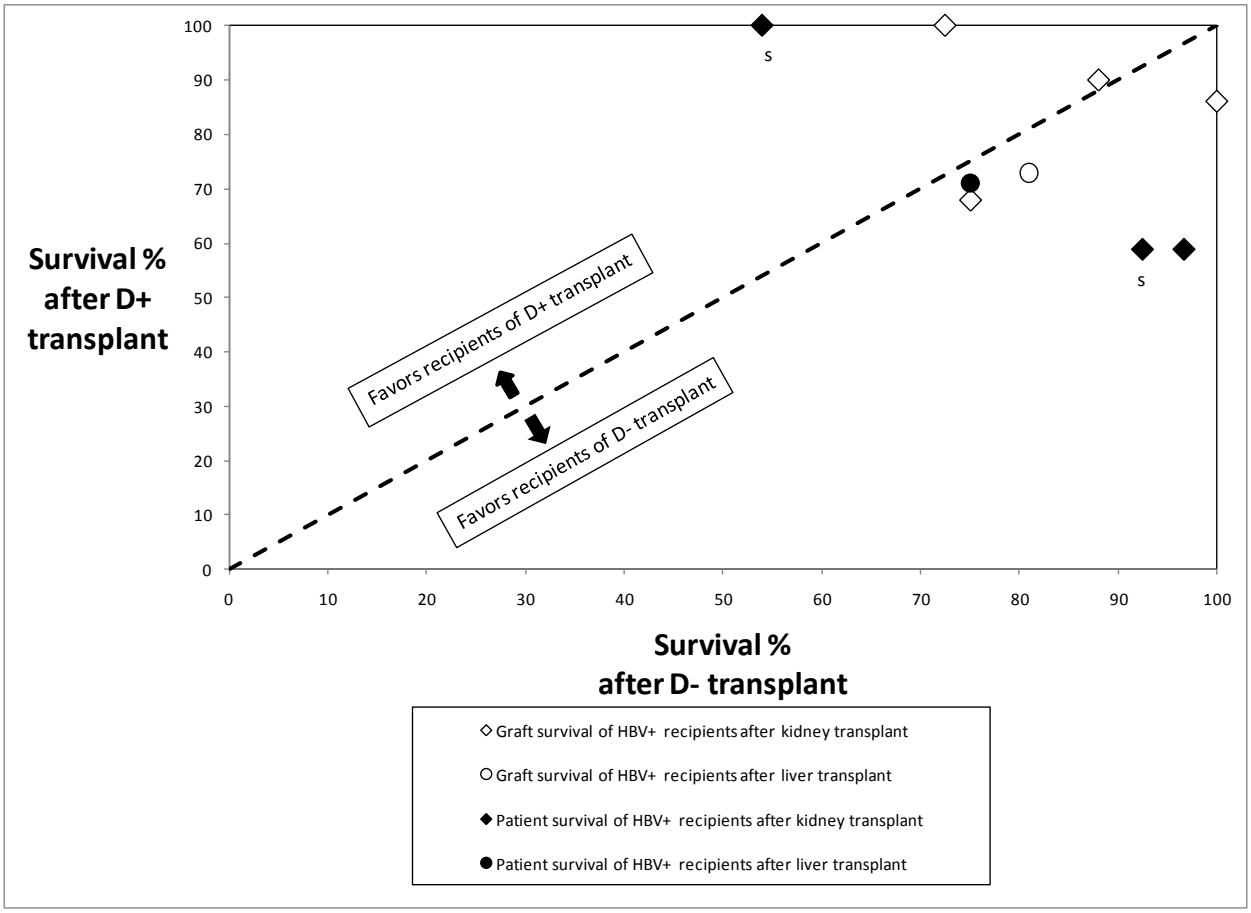
The two HCV plots (Figure 14 for kidney transplants, and Figure 15 for liver transplants) each suggest a small but consistently better survival for recipients of D+ organs than recipients of D- organs; one cannot determine the statistical significance of this effect due to insufficient reporting. Restricting the analysis to the two HCV studies that used statistical adjustments to control for baseline prognosis, they found conflicting results. Whereas Abbott et al. (2003)[83,84] found *shorter* survival in the D+ group (adjusted hazard ratio 2.04), Marroquin et al. (2001)[90] found *longer* survival in the D+ group (adjusted odds of patient survival at two years was 0.51) (results of these two studies are not plotted because the results were not reported as percentages; see the footnote to the figure).

Regarding different genotypes of HBV, none of the four studies reported donors' genotypes, or stated whether recipient survival different by donor genotype. For HCV genotypes, two studies[88,91] attempted to investigate the impact of genotype, but they did not draw conclusions due to the paucity of data. A third study[92] provided pre-tranpslant genotypes for all donors and recipients, as well which which genotype predominated for each donor-recipient pair. Recipient survival was unaffected by whether the predominant genotype was from the donor or was already present in the recipient. None of the other studies attempted analyses by HCV genotype.

GRADE Assessment of Clinical Outcomes After Receiving Organs from Infected Donors

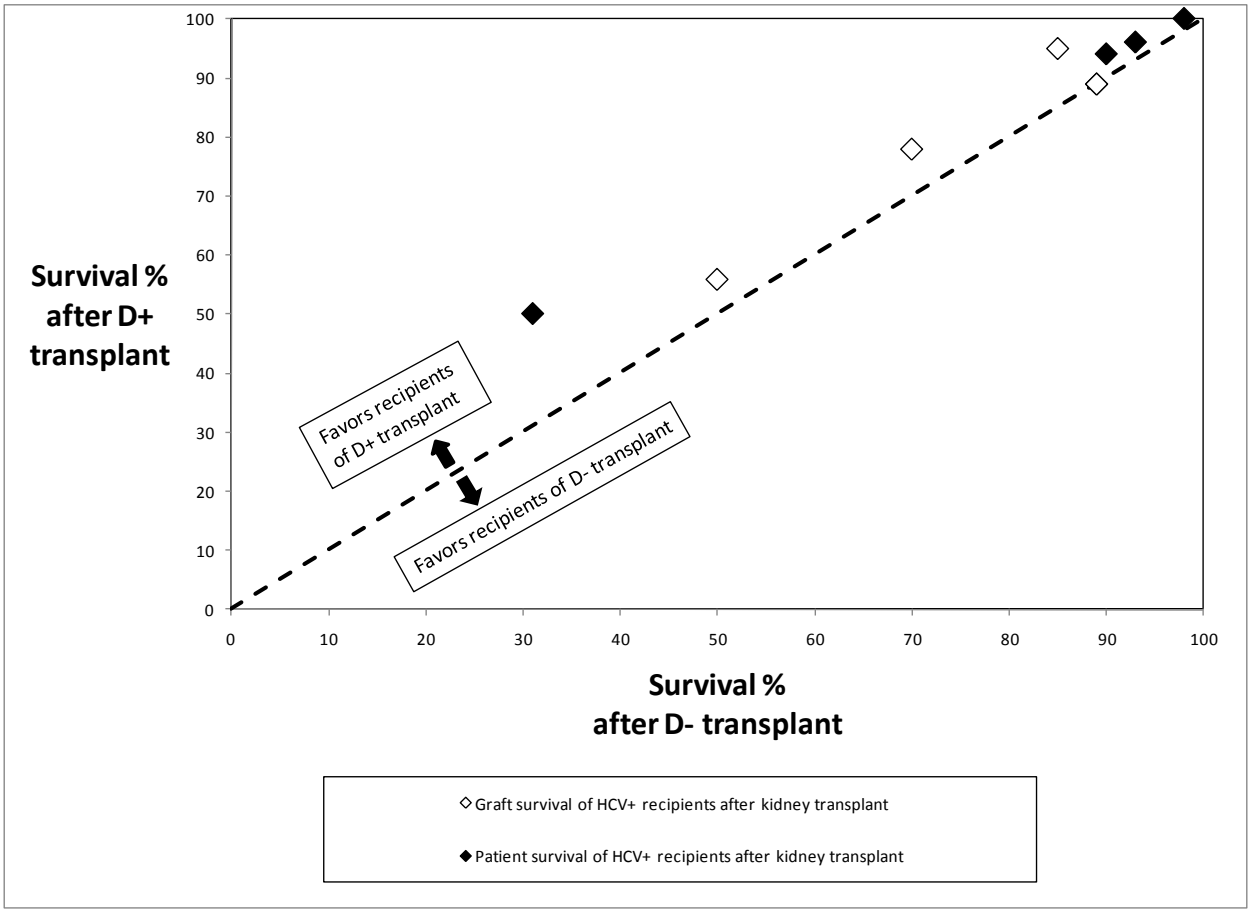
The GRADE evidence profiles (HBV graft survival; HBV patient survival; HCV graft survival; and HCV patient survival) appear in Table 63. We graded the evidence as Very Low for all four pathogen/outcome combinations, due to the lack of randomization to groups and the pre-transplant differences between groups.

Figure 13. Clinical Outcomes of Positive Recipients: Positive vs. Negative Donors, HBV, Kidney or Liver



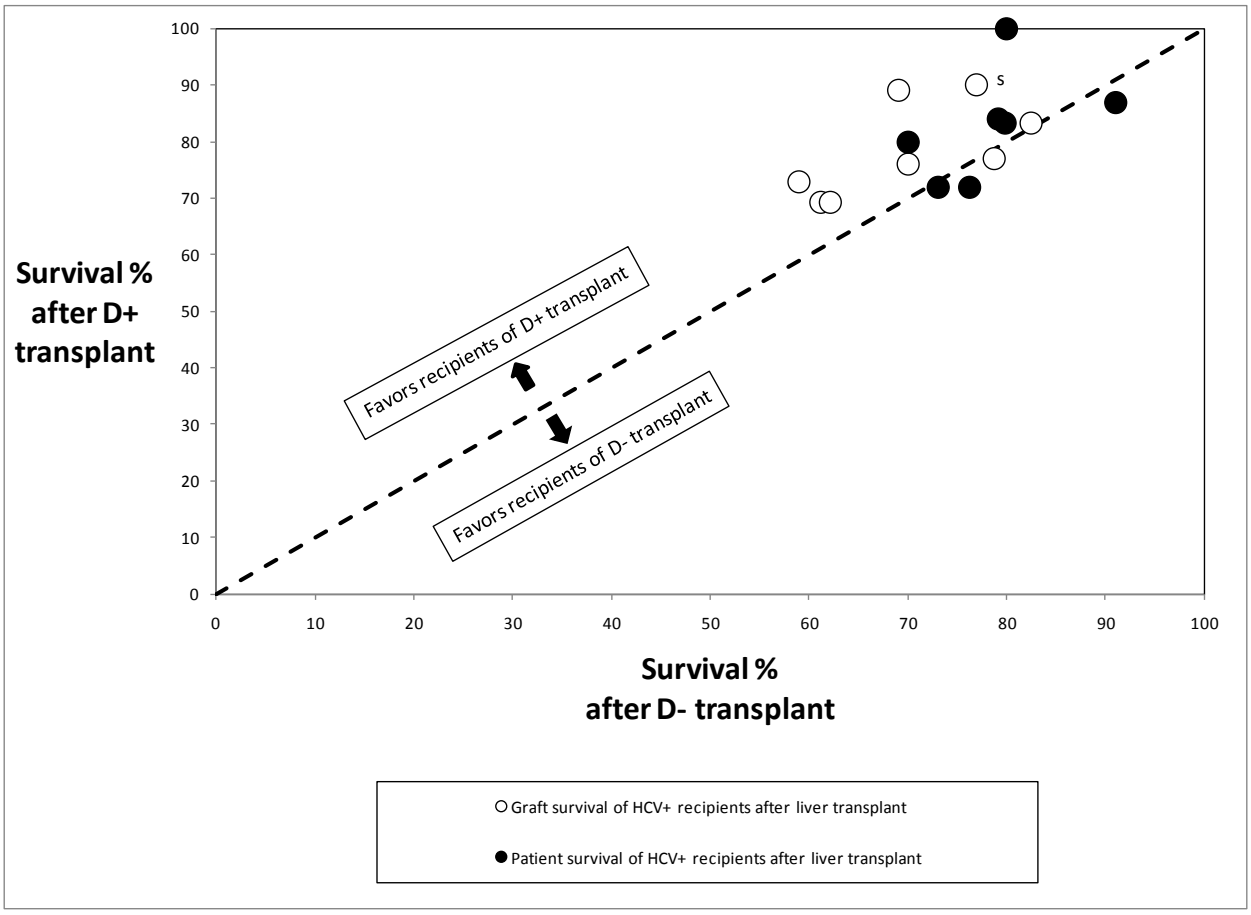
Note: The diagonal line represents no difference in survival between those who received an organ from a positive donor and those who received an organ from a negative donor. Points above the diagonal line favor recipients of organs from positive donors, whereas points below the diagonal line favor recipients of organs from negative donors. This figure only includes studies that reported graft or survival data as percentages, and it only includes the longest followup timepoint from each study. The full data are provided in Table 68. None of the plotted studies reported confidence intervals. Studies with a lower case 's' next to the point reported that the comparison of full survival curves was statistically significant; all other studies either did not report whether the difference was statistically significant, or reported that the difference was not statistically significant.

Figure 14. Clinical Outcomes of Positive Recipients: Positive vs. Negative Donors, HCV, Kidney



Note: The diagonal line represents no difference in survival between those who received an organ from a positive donor and those who received an organ from a negative donor. Points above the diagonal line favor recipients of organs from positive donors, whereas points below the diagonal line favor recipients of organs from negative donors. This figure only includes studies that reported graft or survival data as percentages, and it only includes the longest followup timepoint from each study. The full data are provided in Table 68. None of the plotted studies reported confidence intervals. Studies with a lower case 's' next to the point reported that the comparison of full survival curves was statistically significant; all other studies either did not report whether the difference was statistically significant, or reported that the difference was not statistically significant. One of the studies did not report results on a percentage scale, and so its results do not appear in the plot. This was the Abbott et al. (2003)[83,84] study, which found an adjusted hazard ratio of death of 2.04 (95% CI: 1.20 to 3.45) in favor of recipients of negative organs.

Figure 15. Clinical Outcomes of Positive Recipients: Positive vs. Negative Donors, HCV, Liver



Note: The diagonal line represents no difference in survival between those who received an organ from a positive donor and those who received an organ from a negative donor. Points above the diagonal line favor recipients of organs from positive donors, whereas points below the diagonal line favor recipients of organs from negative donors. This figure only includes studies that reported graft or survival data as percentages, and it only includes the longest followup timepoint from each study. The full data are provided in Table 68. None of the plotted studies reported confidence intervals around the data. Studies with a lower case 's' next to the point reported that the comparison of full survival curves was statistically significant; all other studies either did not report whether the difference was statistically significant, or reported that the difference was not statistically significant. One of the studies did not report results on a percentage scale, and so its results do not appear in the plot. These was the Marroquin et al. (2001)[90] study, which found an adjusted two-year odds of graft failure of 0.88, in favor of recipients of positive organs, and an adjusted two-year odds of patient death of 0.51, also in favor of recipients of positive organs.

Table 63. GRADE Table for Question 7 (Clinical Outcomes of Known Positive Organs vs. Waitlist or Known Negative Organs)

Comparison	Outcome	Quantity and Type of Evidence	Findings	Starting Grade	Decrease GRADE					Increase GRADE			GRADE of Evidence for Outcome	Overall GRADE of Evidence Base
					Study Quality	Consistency	Directness	Precision	Publication Bias	Large Magnitude	Dose Response	Confounders would reduce the effect		
Receiving an HCV+ organ compared to remaining on the waitlist	Recipient survival	One observational study[82]	Adjusted hazard ratio 0.76 (95% CI: 0.6 to 0.96) (in favor of transplantation over the waitlist)	Low	-1	-1	0	0	0	0	0	0	Very Low	Very Low
Receiving an HBV+ organ compared to receiving a negative organ for recipients who were NEGATIVE before transplant	Graft survival	One observational study[55]	Results favored receiving an organ from a negative donor: 1 year: D+ 87%, D- 88% 2 yrs.: D+ 78%, D- 83% 3 yrs: D+ 72%, D- 77%	Low	-1	-1	0	0	0	0	0	0	Very Low	Very Low
	Recipient survival	One observational study[55]	Results favored receiving an organ from a negative donor: 1 year: D+ 94%, D- 94% 2 yrs.: D+ 90%, D- 92% 3 yrs: D+ 86%, D- 90%	Low	-1	-1	0	0	0	0	0	0	Very Low	

Comparison	Outcome	Quantity and Type of Evidence	Findings	Starting Grade	Decrease GRADE					Increase GRADE			GRADE of Evidence for Outcome	Overall GRADE of Evidence Base
					Study Quality	Consistency	Directness	Precision	Publication Bias	Large Magnitude	Dose Response	Confounders would reduce the effect		
Receiving a HCV+ organ compared to receiving a negative organ for recipients who were NEGATIVE before transplant	Graft survival	Three observational studies [16,83,84,93,94]	No statistically significant difference was reported by any of the three studies.	Low	-1	0	0	0	0	0	0	0	Very Low	Low
	Recipient survival	Three observational studies [16,77,79,83,84]	Two of the three studies reported results in favor of receiving an organ from a negative donor. The third study found a statistically nonsignificant result.	Low	-1	0	0	0	0	+1	0	0	Low	

Comparison	Outcome	Quantity and Type of Evidence	Findings	Starting Grade	Decrease GRADE					Increase GRADE			GRADE of Evidence for Outcome	Overall GRADE of Evidence Base
					Study Quality	Consistency	Directness	Precision	Publication Bias	Large Magnitude	Dose Response	Confounders would reduce the effect		
Receiving an HBV+ organ compared to receiving a negative organ for recipients who were POSITIVE before transplant	Graft survival	Four observational studies[55,56,91,95-97]	Only one of the four studies reported any statistically significant difference. This study found that if the kidney donor was living, results slightly favored receiving an organ from an HBsAg+ donor, whereas if the kidney donor was deceased, results favored receiving an organ from an HBsAg- donor.	Low	-1	-1	0	0	0	0	0	0	Very Low	Very Low
	Recipient survival	Three observational studies[55,91,95-97]	Only one of the three studies reported any statistically significant difference. This study found that if the kidney donor was living, there was no statistically significant difference, whereas if the kidney donor was deceased, results favored receiving an organ from an HBsAg- donor.	Low	-1	-1	0	0	0	0	0	0	Very Low	

Comparison	Outcome	Quantity and Type of Evidence	Findings	Starting Grade	Decrease GRADE					Increase GRADE			GRADE of Evidence for Outcome	Overall GRADE of Evidence Base
					Study Quality	Consistency	Directness	Precision	Publication Bias	Large Magnitude	Dose Response	Confounders would reduce the effect		
Receiving a HCV+ organ compared to receiving a negative organ for recipients who were POSITIVE before transplant	Graft survival	13 observational studies[12,16,83-94,98,99]	No statistically significant difference was reported by any of the 13 studies.	Low	-1	0	0	0	0	0	0	0	Very Low	Very Low
	Recipient survival	11 observational studies[12,16,83-92,98]	Only 2 of the 11 studies found any statistically significant difference. One of the two favored recipients of organs of positive donors, and the other favored recipients of organs of negative donors.	Low	-1	0	0	0	0	0	0	0	Very Low	

Note: The shaded rows denote recipient survival, which was considered a "critical" outcome. Graft survival is unshaded because it was not considered "critical" for the purpose of evidence grading.

Additional Evidence Tables for Question 7

Table 64. Question 7: General Information about Included Studies

Study	Country	Center(s) or Program(s)	Organ	Number of Centers	Transplantation Dates	Funding
Recipients Negative Before Transplant; Comparison of Clinical Outcomes After HBV+ Donor vs. HBV- Donor						
Fong et al. (2002)[55]	USA	UNOS Scientific Renal Transplant Registry	Kidney	UNOS	1994 to 1999	NR
Recipients Negative Before Transplant; Comparison of Clinical Outcomes After HCV+ Donor vs. HCV- Donor						
Abbott et al. (2003)[83,84]	USA	United States Renal Data System (USRDS)	Kidney	USRDS	Jan-96 to May-01	NR
Velidedeoglu et al. (2002)[93,94]	USA	University of Pennsylvania (Penn), Philadelphia, PA, and UNOS	Liver	1	Jan-95 to Dec-99	NR
Shah et al. (1993)[12,16]	USA	University of Pittsburgh School of Medicine, Pittsburgh, PA	Liver	1	Mar-86 to Mar-90	NR
Haji et al. (2004)[77,79]	USA	Cleveland Clinic, Cleveland, OH	Heart	1	Jul-93 to Dec-98	NR
Recipients Positive Before Transplant; Comparison of Clinical Outcomes After HBV+ Donor vs. HBV- Donor						
Fong et al. (2002)[55]	USA	UNOS Scientific Renal Transplant Registry	Kidney	UNOS	1994 to 1999	NR
Madayag et al. (1997)[56]	USA	University of Maryland, Baltimore, MD	Kidney	1	Jan-92 to Jul-96	NR
Lai et al. (1996)[95-97]	Taiwan	National Taiwan University, Taipei, Taiwan	Kidney	NR	Jul-81 to Jan-94	NR
Saab et al. (2003)[91]	USA	Dumont-UCLA Liver Transplant Center, Los Angeles, CA	Liver	1	Jan-90 to Apr-01	NR

Study	Country	Center(s) or Program(s)	Organ	Number of Centers	Transplantation Dates	Funding
Recipients Positive Before Transplant; Comparison of Clinical Outcomes After HCV+ Donor vs. HCV- Donor						
Kasprzyk et al. (2007)[98]	Poland	Medical University of Wroclas, Wroclas, Poland	Kidney	NR	Jul-94 to Jul-06	NR
Abbott et al. (2003)[83,84]	USA	USRDS	Kidney	USRDS	Jan-96 to May-01	NR
Woodside et al. (2003)[85]	USA	University of Texas Medical Branch, Galveston, TX	Kidney	1	Jul-92 to Jul-00	NR
Mandal et al. (2000)[86]	USA	Johns Hopkins Hospital, Baltimore, MD	Kidney	1	Jan-97 to Jun-99	NR
Ali et al. (1998)[99]	USA	Washington Hospital Center, Washington, DC	Kidney	1	Feb-91 to Sep-96	NR
Morales et al. (1995)[87]	Spain	Hospital 12 de Octubre, Madrid, and Hospital Clinic, Barcelona	Kidney	2	Mar-90 to Dec-92	Partially supported by FIS grant No. 94/1002
Saab et al. (2003)[91]	USA	Dumont-UCLA Liver Transplant Center, Los Angeles, CA	Liver	1	Jan-90 to Apr-01	NR
Velidedeoglu et al. (2002)[93,94]	USA	University of Pennsylvania, Philadelphia, PA, and UNOS	Liver	1 for Penn data, many for UNOS data	Jan-95 to Dec-99	NR
Marroquin et al. (2001)[90]	USA	UNOS Scientific Renal Transplant Registry	Liver	UNOS	Apr-94 to Jun-97	NR
Salizzoni et al. (2001)[88]	Italy	S. Giovanni Battista Hospital, Torino, Italy	Liver	1	Jul-98 to Dec-99	NR
Vargas et al. (1999)[92]	USA	Thomas E. Starzl Transplantation Institute, Pittsburgh, PA	Liver	1	Feb-92 to May-05	NR
Testa et al. (1998)[89]	USA	Baylor University Medical Center, Dallas, Texas	Liver	1	Jul-85 to Jul-95	NR

Study	Country	Center(s) or Program(s)	Organ	Number of Centers	Transplantation Dates	Funding
Shah et al. (1993)[12,16]	USA	University of Pittsburgh School of Medicine, Pittsburgh, PA	Liver	1	Mar-86 to Mar-90	NR

NR – Not reported

Table 65. Question 7: Details of Study Methods

Study	Prospective	Consecutive	Duration of Follow-up	N Enrolled for D+	N Enrolled for D-	Definition of Positivity	Specific Test Used
Recipients Negative Before Transplant; Comparison of Clinical Outcomes after HBV+ Donor vs. HBV- Donor							
Fong et al. (2002)[55]	No	Yes	NR	763	24,661	anti-HBc+	NR
Recipients Negative Before Transplant; Comparison of Clinical Outcomes after HCV+ Donor vs. HCV- Donor							
Abbott et al. (2003)[83,84]	No	Yes	Mean: 33 (SD: 20)	280	34,151	anti-HCV	"Presumably ELISA"
Velidedeoglu et al. (2002)[93,94]	No	Yes	For Pennsylvania data, the mean followup was 23.4 months. For UNOS data, the mean followup was 22.4 months.	29	7,811	"HCV+"	NR
Shah et al. (1993)[12,16]	No	No	NR	25	375	anti-HCV	ELISA2
Haji et al. (2004)[77,79]	No	No	Mean: 50 months (SD: 23)	34	183	anti-HCV	ELISA2
Recipients Positive Before Transplant; Comparison of Clinical Outcomes after HBV+ Donor vs. HBV- Donor							
Fong et al. (2002)[55]	No	Yes	NR	140	2,093	anti-HBc+	NR
Madayag et al. (1997)[56]	No	Yes	Mean: 24 (Range: 2-64)	45	45	Donor anti-HBc+ and HBsAg-; Recipient had prior HBV infection or had been vaccinated	Abbott tests
Lai et al. (1996)[95-97]	No	Yes	NR	25	42	HBsAg	Austria II and Ausab (Abbott)

Study	Prospective	Consecutive	Duration of Follow-up	N Enrolled for D+	N Enrolled for D-	Definition of Positivity	Specific Test Used
Saab et al. (2003)[91]	No	NR	For HBV+ recipients, mean follow-up for patient survival data was 2.3 years (Range: 0-8.7), and for graft survival data was 2.0 years (Range: 0-8.7). For HCV+ recipients, mean follow-up for patient survival data was 2.6 years (Range: 0-5.8), and for graft survival data was 1.8 years (Range: 0-5.8).	74	42	anti-HBc+	NR
Recipients Positive Before Transplant; Comparison of Clinical Outcomes after HCV+ Donor vs. HCV- Donor							
Kasprzyk et al. (2007)[98]	No	Yes	Range: 12-156	60	199	anti-HCV	NR
Abbott et al. (2003)[83,84]	No	Yes	Mean: 33 (SD: 20)	593	1,932	anti-HCV	"Presumably ELISA"
Woodside et al. (2003)[85]	No	Yes	Mean: 26 months (Range: 0.4-119) for those who received a positive organ, and 34 months (Range: 0.2-66) for those who received a negative organ	20	20	"seropositive"	NR
Mandal et al. (2000)[86]	No	Yes	Median: 16, Mean: 15 (standard error of the mean: 2), Range: 3-33	18	10	anti-HCV and HCV-RNA+	HCV RNA measured by PCR
Ali et al. (1998)[99]	No	Yes	Mean: 36, Range: 12-60	28	16	anti-HCV	NR

Study	Prospective	Consecutive	Duration of Follow-up	N Enrolled for D+	N Enrolled for D-	Definition of Positivity	Specific Test Used
Morales et al. (1995)[87]	NR	Yes	Mean: 26 months (SD: 8) for those who received a positive organ, and 30 months (SD: 10) for those who received a negative organ	24	40	anti-HCV	ELISA2 (Ortho) and RIBA (Chiron)
Saab et al. (2003)[91]	No	NR	For HBV+ recipients, mean follow-up for patient survival data was 2.3 years (Range: 0-8.7), and for graft survival data was 2.0 years (Range: 0-8.7). For HCV+ recipients, mean follow-up for patient survival data was 2.6 years (Range: 0-5.8), and for graft survival data was 1.8 years (Range: 0-5.8)	27	212	anti-HCV	NR
Velidedeoglu et al. (2002)[93,94]	No	Yes	For Penn data, the mean followup was 23.4 months. For UNOS data, the mean followup was 22.4 months.	Penn: 13; UNOS: 190	Penn: 103; UNOS: 5,053	Penn: "HCV+"; UNOS: Donors were anti-HCV+, and of recipients, 96% were anti-HCV+ and 4% were RIBA+ and/or HCV-RNA+	NR
Marroquin et al. (2001)[90]	No	Yes	Median was 34 months for those who received a positive organ, and 37 months for those who received a negative organ	96	2,827	"HCV+"	NR

Study	Prospective	Consecutive	Duration of Follow-up	N Enrolled for D+	N Enrolled for D-	Definition of Positivity	Specific Test Used
Salizzoni et al. (2001)[88]	No	NR	Mean: 12, Range: 1-25	12	103	anti-HCV	NR
Vargas et al. (1999)[92]	No	Yes	NR	23	169	anti-HCV	ELISA3 (Abbott)
Testa et al. (1998)[89]	No	Yes	Mean: 40 months (Range: 12-58) for those who received a positive organ, and 36 months (Range: 17-135) for those who received a negative organ	22	115	anti-HCV	ELISA1 until 1990, then ELISA2
Shah et al. (1993)[12,16]	No	No	NR	5	111	anti-HCV	ELISA2

NR – Not reported

Table 66. Question 7: Pre-transplant Patient Characteristics

Study	Characteristic	Mean (SD) or % for Recipients of D+ Organs	Mean (SD) or % for Recipients of D- Organs	Difference in percentage points (p.p.), or Hedges' g	Comments
Recipients Negative Before Transplant; Comparison of Clinical Outcomes After HBV+ Donor vs. HBV- Donor					
Fong et al. (2002)[55]	Donor % African-American	17% (130/763)	10% (2,466/24,661)	7 p.p.	
	Donor % death due to stroke	51% (389/763)	36% (8,878/24,661)	15 p.p.	Large difference at baseline.
	Donor % HCV+	11% (84/763)	2% (493/24,661)	9 p.p.	
	Donor % male	42% (320/763)	41% (10,111/24,661)	1 p.p.	
	Recipient % African-American	34% (259/763)	25% (6,165/24,661)	9 p.p.	
	Recipient % Asian-American	5% (38/763)	3% (740/24,661)	2 p.p.	
	Recipient % HCV+	11% (84/763)	5% (1,233/24,661)	6 p.p.	
	Recipient % male	63% (481/763)	61% (15,043/24,661)	2 p.p.	
	Recipient % being retransplanted	12% (92/763)	13% (3,206/24,661)	1 p.p.	
	Mean Cold ischemia time (hours)	22.1 (SD: 8.5)	20.6 (SD: 8.2)	g = 0.18	
	Mean Donor age	40.5 (SD: 16)	33.7 (SD: 18.1)	g = 0.38	

Study	Characteristic	Mean (SD) or % for Recipients of D+ Organs	Mean (SD) or % for Recipients of D- Organs	Difference in percentage points (p.p.), or Hedges' g	Comments
	Number of HLA mismatches	3.7 (SD: 1.6)	3.4 (SD: 1.8)	g = 0.17	
	Mean Recipient age	47.8 (SD: 13.1)	45.5 (SD: 14.2)	g = 0.16	
	Recipient duration of dialysis (months)	38.1 (SD: 34.6)	36.6 (SD: 36.9)	g = 0.04	
	Recipient Peak Panel Reactive Antibody	13.2 (SD: 24.3)	14 (SD: 25.8)	g = 0.03	
Recipients Negative Before Transplant; Comparison of Clinical Outcomes After HCV+ Donor vs. HCV- Donor					
Abbott et al. (2003)[83,84], Velidedeoglu et al. (2002)[93,94]	These studies did not report pre-transplant characteristics comparing those who received organs from infected donors vs. those who received organs from uninfected donors				
Shah et al. (1993)[12,16]	Study only reported that "No statistical difference in disease indication for OLTx was evident between the 4 study groups"				
Haji et al. (2004)[77,79]	% "Cause" was dilated cardiomyopathy	32% (11/34)	34% (62/183)	2 p.p.	
	% "Cause" was ischemic cardiomyopathy	62% (21/34)	56% (102/183)	6 p.p.	
	% "Cause" was something else	5% (2/34)	9% (16/183)	4 p.p.	
	Donor % male	74% (25/34)	57% (104/183)	17 p.p.	Large difference at baseline.
	Recipient % male	76% (26/34)	79% (145/183)	3 p.p.	
	Mean Donor age	39 (SD: 9)	35 (SD: 14)	g = 0.3	

Study	Characteristic	Mean (SD) or % for Recipients of D+ Organs	Mean (SD) or % for Recipients of D- Organs	Difference in percentage points (p.p.), or Hedges' g	Comments
	Mean Recipient age	57 (SD: 10)	52 (SD: 11)	g = 0.46	Large difference at baseline.
	Mean Recipient average biopsy score	1.31 (SD: 0.65)	1.51 (SD: 0.66)	g = 0.3	
	Mean number of recipient episodes of acute rejection before this transplant	1.7 (SD: 1.5)	1.8 (SD: 1.6)	g = 0.06	
Recipients Positive Before Transplant; Comparison of Clinical Outcomes After HBV+ Donor vs. HBV- Donor					
Lai et al. (1996)[95-97], Saab et al. (2003)[91]	These studies did not report pre-transplant characteristics comparing those who received organs from infected donors vs. those who received organs from uninfected donors				
Fong et al. (2002)[55]	Donor % African-American	26% (36/140)	13% (272/2,093)	13 p.p.	
	Donor % death due to stroke	47% (66/140)	37% (774/2,093)	10 p.p.	
	Donor % HCV+	22% (31/140)	5% (105/2,093)	17 p.p.	Large difference at baseline.
	Donor % male	34% (48/140)	42% (879/2,093)	8 p.p.	
	Recipient % African-American	56% (78/140)	39% (816/2,093)	17 p.p.	Large difference at baseline.
	Recipient % Asian-American	16% (22/140)	10% (209/2,093)	6 p.p.	
	Recipient % being retransplanted	8% (11/140)	10% (290/2,093)	2 p.p.	
	Recipient % HCV+	35% (49/140)	21% (440/2,093)	14 p.p.	

Study	Characteristic	Mean (SD) or % for Recipients of D+ Organs	Mean (SD) or % for Recipients of D- Organs	Difference in percentage points (p.p.), or Hedges' g	Comments
	Recipient % male	73% (102/140)	64% (1,340/2,093)	9 p.p.	
	Mean Cold ischemia time (hours)	20.6 (SD: 8.2)	20.7 (SD: 8.7)	g = 0.01	
	Mean Donor age	42.7 (SD: 13.9)	34.9 (SD: 18.2)	g = 0.43	Large difference at baseline.
	Mean number of HLA mismatches	4.3 (SD: 1.4)	3.7 (SD: 1.7)	g = 0.36	
	Mean Recipient age	49.7 (SD: 10.7)	46.5 (SD: 14)	g = 0.23	
	Mean Recipient duration of dialysis (months)	42.1 (SD: 31.3)	44.2 (SD: 40.2)	g = 0.05	
	Mean Recipient Peak Panel Reactive Antibody	14.3 (SD: 23.6)	14.3 (SD: 25.6)	g = 0	
Madayag et al. (1997)[56]	Donor % deceased	69% (31/45)	58% (26/45)	11 p.p.	
	Donor % living related	29% (13/45)	40% (18/45)	11 p.p.	
	Recipient % anti-lymphocyte therapy	40% (18/45)	33% (15/45)	7 p.p.	
	Recipient % Asian-American	60% (27/45)	49% (22/45)	11 p.p.	
	Recipient % Caucasian-American	26% (12/45)	49% (22/45)	23 p.p.	Large difference at baseline.
	Recipient % other race	13% (6/45)	2% (1/45)	11 p.p.	

Study	Characteristic	Mean (SD) or % for Recipients of D+ Organs	Mean (SD) or % for Recipients of D- Organs	Difference in percentage points (p.p.), or Hedges' g	Comments
	Recipient % HCV+	31% (14/45)	31% (14/45)	0 p.p.	
	Recipient % high-risk behavior	13% (6/45)	18% (8/45)	5 p.p.	
	Recipient % history of alcohol abuse	13% (6/45)	7% (3/45)	6 p.p.	
	Recipient % intraoperative or postoperative transfusion	85% (38/45)	81% (36/45)	4 p.p.	
	Recipient % male	68% (31/45)	62% (28/45)	6 p.p.	
	Recipient % Simultaneous kidney-pancreas transplant	2% (1/45)	2% (1/45)	0 p.p.	
	Recipient % with pre-transplant transfusion	60% (27/45)	47% (21/45)	13 p.p.	
	Mean Recipient age	49.1 (SD: 11.8)	43.6 (SD: 11.8)	g = 0.47	Large difference at baseline. Dispersion reported as "+/-" but authors did not specify what this was; ECRI Institute estimated the SD for each group to be 11.8 based on the reported p = 0.03 for ANOVA
	Recipient date of transplant	The study intentionally matched patients on this characteristic			

Study	Characteristic	Mean (SD) or % for Recipients of D+ Organs	Mean (SD) or % for Recipients of D- Organs	Difference in percentage points (p.p.), or Hedges' g	Comments
	Recipient Pre-transplant HBV serology	The study intentionally matched patients on this characteristic			
	Type of organ transplanted	The study intentionally matched patients on this characteristic			
Recipients Positive Before Transplant; Comparison of Clinical Outcomes After HCV+ Donor vs. HCV- Donor					
Kasprzyk et al. (2007)[98], Abbott et al. (2003)[83,84], Ali et al. (1998)[99], Saab et al. (2003)[91]	These studies did not report pre-transplant characteristics comparing those who received organs from infected donors vs. those who received organs from uninfected donors				
Woodside et al. (2003)[85]	% Immunosuppressive induction therapy	90% (18/20)	80% (16/20)	10 p.p.	
	CMV % donor/recipient pairs with both CMV-	5% (1/20)	5% (1/20)	0 p.p.	
	CMV % donor/recipient pairs with both CMV+	70% (14/20)	55% (11/20)	15 p.p.	Large difference at baseline.
	CMV % donor/recipient pairs with only donor+	0% (0/20)	10% (2/20)	10 p.p.	
	CMV % donor/recipient pairs with only recipient+	20% (4/20)	20% (4/20)	0 p.p.	
	CMV % donor/recipient pairs with unknown recipient status	5% (1/20)	0% (0/20)	5 p.p.	
	Donor % anti-HBc+	20% (4/20)	20% (4/20)	0 p.p.	
	Donor % HBsAg+	0% (0/20)	0% (0/20)	0 p.p.	

Study	Characteristic	Mean (SD) or % for Recipients of D+ Organs	Mean (SD) or % for Recipients of D- Organs	Difference in percentage points (p.p.), or Hedges' g	Comments
	Recipient % anti-HBc+	20% (4/20)	35% (7/20)	15 p.p.	Large difference at baseline.
	Recipient % African-American	50% (10/20)	45% (9/20)	5 p.p.	
	Recipient % Asian-American	0% (0/20)	10% (2/20)	10 p.p.	
	Recipient % Caucasian-American	15% (3/20)	35% (7/20)	20 p.p.	Large difference at baseline.
	Recipient % Hispanic-American	35% (7/20)	5% (1/20)	30 p.p.	Large difference at baseline.
	Recipient % HBsAg+	0% (0/20)	0% (0/20)	0 p.p.	
	Recipient % male	80% (16/20)	65% (13/20)	15 p.p.	Large difference at baseline.
	Recipient % being retransplanted	15% (3/20)	15% (3/20)	0 p.p.	
	Recipient % with 1 prior transplant	5% (1/20)	10% (2/20)	5 p.p.	
	Recipient % with 2 prior transplants	5% (1/20)	5% (1/20)	0 p.p.	
	Recipient % with 3 prior transplants	5% (1/20)	0% (0/20)	5 p.p.	
	Recipient Triple drug therapy %	100% (20/20)	80% (16/20)	20 p.p.	Large difference at baseline.

Study	Characteristic	Mean (SD) or % for Recipients of D+ Organs	Mean (SD) or % for Recipients of D- Organs	Difference in percentage points (p.p.), or Hedges' g	Comments
	Mean Cold ischemia time (hours)	24.3 (SD: 9.8)	21.5 (SD: 2.7)	g = 0.39	ECRI Institute estimated the SDs using the reported SEMs and Ns
	Mean Recipient age	44 (SD: 13.4)	45 (SD: 44.7)	g = 0.03	ECRI Institute estimated the SDs using the reported SEMs and Ns
	Mean Recipient time on waitlist (months)	9.9 (SD: 8)	17.7 (SD: 14.8)	g = 0.66	Large difference at baseline. ECRI Institute estimated the SDs using the reported SEMs and Ns
Mandal et al. (2000)[86]	Donor % CMV+	87% (16/18)	50% (5/10)	37 p.p.	Large difference at baseline.
	Donor % history of alcohol abuse	5% (1/18)	10% (1/10)	5 p.p.	
	Donor % prior cocaine snorting or selling of drugs	NR	NR	NC	
	Recipient % African-American	66% (12/18)	60% (6/10)	6 p.p.	
	Recipient % CMV+	83% (15/18)	70% (7/10)	13 p.p.	
	Recipient % male	66% (12/18)	80% (8/10)	14 p.p.	
	Recipient % with diabetes	28% (5/18)	10% (1/10)	18 p.p.	Large difference at baseline.

Study	Characteristic	Mean (SD) or % for Recipients of D+ Organs	Mean (SD) or % for Recipients of D- Organs	Difference in percentage points (p.p.), or Hedges' g	Comments
	Recipient % with hypertension	33% (6/18)	40% (4/10)	7 p.p.	
	Recipient % being retransplanted	28% (5/18)	60% (6/10)	32 p.p.	Large difference at baseline.
	Mean AB mismatch	3.2 (SD: 0.8)	2.3 (SD: 0.9)	g = 1.08	Large difference at baseline. ECRI Institute estimated the SDs using the reported SEMs and Ns
	Mean Cold ischemia time (hours)	28 (SD: 8.5)	22 (SD: 9.5)	g = 0.68	Large difference at baseline. ECRI Institute estimated the SDs using the reported SEMs and Ns
	Mean Donor age	46 (SD: 8.5)	35 (SD: 19)	g = 0.84	Large difference at baseline. ECRI Institute estimated the SDs using the reported SEMs and Ns
	Mean DR mismatch	1.6 (SD: 0.8)	1.3 (SD: 0.3)	g = 0.45	Large difference at baseline. ECRI Institute estimated the SDs using the reported SEMs and Ns

Study	Characteristic	Mean (SD) or % for Recipients of D+ Organs	Mean (SD) or % for Recipients of D- Organs	Difference in percentage points (p.p.), or Hedges' g	Comments
	Mean Recipient age	48 (SD: 8.5)	44 (SD: 6.3)	g = 0.51	Large difference at baseline. ECRI Institute estimated the SDs using the reported SEMs and Ns
	Mean Recipient duration of dialysis (months)	88 (SD: 152.7)	79 (SD: 66.4)	g = 0.07	ECRI Institute estimated the SDs using the reported SEMs and Ns
	Mean Recipient Terminal creatinine (mg/dL)	0.9 (SD: 0.8)	0.9 (SD: 0.6)	g = 0	ECRI Institute estimated the SDs using the reported SEMs and Ns. One of the reported SDs was 0, which is not reasonable, therefore we used the SD from the other group
	Mean Recipient time on waitlist (months)	9 (SD: 12.7)	29 (SD: 9.5)	g = 1.71	Large difference at baseline. ECRI Institute estimated the SDs using the reported SEMs and Ns
Morales et al. (1995)[87]	Recipient % abnormal liver histology	31% (7/24)	50% (20/40)	19 p.p.	Large difference at baseline.
	Recipient % anti-HBc+	50% (12/24)	23% (9/40)	27 p.p.	Large difference at baseline.

Study	Characteristic	Mean (SD) or % for Recipients of D+ Organs	Mean (SD) or % for Recipients of D- Organs	Difference in percentage points (p.p.), or Hedges' g	Comments
	Recipient % chronic active hepatitis	0% (0/24)	10% (4/40)	10 p.p.	
	Recipient % chronic liver disease	4% (1/24)	5% (2/40)	1 p.p.	
	Recipient % chronic persistent hepatitis	17% (4/24)	8% (3/40)	9 p.p.	
	Recipient % elevated ALT	54% (13/24)	50% (20/40)	4 p.p.	
	Recipient % HBsAg+	8% (2/24)	3% (1/40)	5 p.p.	
	Recipient % hemosiderosis	0% (0/24)	5% (2/40)	5 p.p.	
	Recipient % history of drug abuse	0% (0/24)	0% (0/40)	0 p.p.	
	Recipient % HIV+	0% (0/24)	0% (0/40)	0 p.p.	
	Recipient % male	67% (16/24)	60% (24/40)	7 p.p.	
	Recipient % mild elevated ALT	50% (12/24)	45% (18/40)	5 p.p.	
	Recipient % PCR+	71% (17/24)	79% (32/40)	8 p.p.	
	Recipient % renal disease: arterial hypertension	8% (2/24)	7% (3/40)	1 p.p.	
	Recipient % renal disease: chronic glomerulonephritis	55% (13/24)	35% (14/40)	20 p.p.	Large difference at baseline.

Study	Characteristic	Mean (SD) or % for Recipients of D+ Organs	Mean (SD) or % for Recipients of D- Organs	Difference in percentage points (p.p.), or Hedges' g	Comments
	Recipient % renal disease: chronic interstitial nephritis	29% (7/24)	33% (13/40)	4 p.p.	
	Recipient % renal disease: cystic disease	0% (0/24)	5% (2/40)	5 p.p.	
	Recipient % renal disease: other	8% (2/24)	20% (8/40)	12 p.p.	
	Recipient % RIBA+	100% (24/24)	100% (40/40)	0 p.p.	
	Recipient % being retransplanted	8% (2/24)	20% (8/40)	12 p.p.	
	Mean Recipient age	47 (SD: 12)	44 (SD: 14)	g = 0.23	
	Mean Recipient duration of dialysis (months)	72 (SD: 53)	75 (SD: 49)	g = 0.06	
	Mean Recipient pre-transplant number of transfusions	7 (SD: 8)	21 (SD: 39)	g = 0.45	Large difference at baseline.
Velidedeoglu et al. (2002)[93,94]	Recipient % UNOS status 1	23.1% (3/13)	15.4% (16/103)	7.7 p.p.	Only reported comparative characteristics for the Penn data, not for the UNOS data
	Recipient % UNOS status 2A	15.4% (2/13)	24.2% (25/103)	8.8 p.p.	Only reported comparative characteristics for the Penn data, not for the UNOS data

Study	Characteristic	Mean (SD) or % for Recipients of D+ Organs	Mean (SD) or % for Recipients of D- Organs	Difference in percentage points (p.p.), or Hedges' g	Comments
	Recipient % UNOS status 2B	61.5% (8/13)	60.4% (62/103)	1.1 p.p.	
	Mean Cold ischemia time (hours)	8.5 (SD: 3.2)	8.5 (SD: 3)	g = 0	ECRI Institute estimated the SDs using the reported SEMs and Ns. Only reported comparative characteristics for the Penn data, not for the UNOS data
	Mean Donor age	36.5 (SD: 8.7)	36.9 (SD: 16.2)	g = 0.03	ECRI Institute estimated the SDs using the reported SEMs and Ns. Only reported comparative characteristics for the Penn data, not for the UNOS data
	Mean Recipient age	52.6 (SD: 8.3)	50.2 (SD: 8.1)	g = 0.3	ECRI Institute estimated the SDs using the reported SEMs and Ns. Only reported comparative characteristics for the Penn data, not for the UNOS data

Study	Characteristic	Mean (SD) or % for Recipients of D+ Organs	Mean (SD) or % for Recipients of D- Organs	Difference in percentage points (p.p.), or Hedges' g	Comments
	Mean Warm ischemia time (hours)	51 (SD: 15.1)	50.6 (SD: 42.6)	g = 0.01	ECRI Institute estimated the SDs using the reported SEMs and Ns. One of the reported SDs was 0, which is not reasonable, therefore we used the SD from the other group. Only reported comparative characteristics for the Penn data, not for the UNOS data
Marroquin et al. (2001)[90]	ABO % incompatibility	4.2% (4/96)	1.3% (37/2,827)	2.9 p.p.	
	Donor % cause of death: cardiovascular event	1% (1/96)	3.2% (90/2,827)	2.2 p.p.	
	Donor % cause of death: cerebrovascular accident	46.9% (45/96)	39.8% (1,125/2,827)	7.1 p.p.	
	Donor % cause of death: head trauma	45.8% (44/96)	50.6% (1,430/2,827)	4.8 p.p.	
	Donor % cause of death: other	6.3% (6/96)	6.4% (181/2,827)	0.1 p.p.	
	Donor % male	68.8% (66/96)	63.3% (1,789/2,827)	5.5 p.p.	
	Recipient % hepatocellular carcinoma	8.3% (8/96)	3.1% (88/2,827)	5.2 p.p.	

Study	Characteristic	Mean (SD) or % for Recipients of D+ Organs	Mean (SD) or % for Recipients of D- Organs	Difference in percentage points (p.p.), or Hedges' g	Comments
	Recipient % male	67.6% (65/96)	68.5% (1,936/2,827)	0.9 p.p.	
	Recipient % use of vasopressor	68.7% (66/96)	67% (1,894/2,827)	1.7 p.p.	
	Recipient % being retransplanted	4% (4/96)	10% (277/2,827)	6 p.p.	
	Recipient % year of transplant 1997 (the last year of study enrollment)	21% (20/96)	15% (424/2,827)	6 p.p.	
	Mean Cold ischemia time (hours)	9.4 (SD: NR)	8.8 (SD: NR)	g = 0.07	Dispersion not reported, but p >0.05 reported. ECRI Institute estimated Hedges' g using an estimated SD of 8.2 for both groups, which was based on pooling on other studies' reported SDs for this characteristic.

Study	Characteristic	Mean (SD) or % for Recipients of D+ Organs	Mean (SD) or % for Recipients of D- Organs	Difference in percentage points (p.p.), or Hedges' g	Comments
	Mean Donor age	38.5 (SD: NR)	35.8 (SD: NR)	g = 0.15	Dispersion not reported, but p >0.05 reported. ECRI Institute estimated Hedges' g using an estimated SD of 18 for both groups, which was based on pooling on other studies' reported SDs for this characteristic.
	Mean Recipient age	49.5 (SD: NR)	48.6 (SD: NR)	g = 0.06	Dispersion not reported, but p >0.05 reported. ECRI Institute estimated Hedges' g using an estimated SD of 14.1 for both groups, which was based on pooling on other studies' reported SDs for this characteristic.
	Mean Recipient creatinine mg/dL	1.2 (SD: NR)	1.2 (SD: NR)	NC	Dispersion not reported, but p >0.05 reported
	Mean Recipient hospital stay (days)	18.7 (SD: NR)	27.1 (SD: NR)	NC	Dispersion not reported, but p >0.05 reported

Study	Characteristic	Mean (SD) or % for Recipients of D+ Organs	Mean (SD) or % for Recipients of D- Organs	Difference in percentage points (p.p.), or Hedges' g	Comments
	Mean Recipient ICU stay (days)	11.5 (SD: NR)	15.1 (SD: NR)	NC	Dispersion not reported, but p >0.05 reported
	Mean Recipient weight (kg)	73.6 (SD: NR)	72.9 (SD: NR)	NC	Dispersion not reported, but p >0.05 reported
	Mean Warm ischemia time (hours)	45.9 (SD: NR)	46.8 (SD: NR)	NC	Dispersion not reported, but p >0.05 reported
Salizzoni et al. (2001)[88]	Mean Donor age	62.6 (SD: NR)	53.7 (SD: NR)	g = 0.49	Large difference at baseline. These are medians. Dispersion not reported, but authors stated there was "no significant difference". ECRI Institute estimated Hedges' g using an estimated SD of 18 for both groups, which was based on pooling on other studies' reported SDs for this characteristic.

Study	Characteristic	Mean (SD) or % for Recipients of D+ Organs	Mean (SD) or % for Recipients of D- Organs	Difference in percentage points (p.p.), or Hedges' g	Comments
	Mean Recipient coagulation time (INR)	1.2 (SD: NR)	1.2 (SD: NR)	NC	These are medians. Dispersion not reported, but authors stated there was "no significant difference"
	Mean Recipient hepatic enzymes ALT (U/L)	24 (SD: NR)	22 (SD: NR)	NC	These are medians. Dispersion not reported, but authors stated there was "no significant difference"
	Mean Recipient hepatic enzymes AST (U/L)	24 (SD: NR)	21 (SD: NR)	NC	These are medians. Dispersion not reported, but authors stated there was "no significant difference"
	Mean Recipient platelet concentration (10^9/L)	177 (SD: NR)	215 (SD: NR)	NC	These are medians. Dispersion not reported, but authors stated there was "no significant difference"
	Mean Total ischemia time (hours)	10.3 (SD: NR)	9.8 (SD: NR)	NC	Dispersion not reported, but authors stated there was "no significant difference"

Study	Characteristic	Mean (SD) or % for Recipients of D+ Organs	Mean (SD) or % for Recipients of D- Organs	Difference in percentage points (p.p.), or Hedges' g	Comments
	Mean Warm ischemia time (hours)	0.6 (SD: NR)	0.53 (SD: NR)	NC	These are medians. Dispersion not reported, but authors stated there was "no significant difference"
Vargas et al. (1999)[92]	Recipient % male	74% (17/23)	85% (144/169)	11 p.p.	
	Mean Recipient age	51.1 (SD: 10.4)	49.5 (SD: 11.7)	g = 0.14	SD of the age of recipients of infected organs was calculated by ECRI Institute based on Table 1 of the article. SD of the age of recipients of uninfected organs was calculated by ECRI Institute using the reported SEM of 0.9 and the N for that group which was 169

Study	Characteristic	Mean (SD) or % for Recipients of D+ Organs	Mean (SD) or % for Recipients of D- Organs	Difference in percentage points (p.p.), or Hedges' g	Comments
Testa et al. (1998)[89]	Recipient % male	50% (11/22)	73% (84/115)	23 p.p.	Large difference at baseline.
	Mean Recipient age	48.2 (SD: NR)	47.1 (SD: NR)	g = 0.08	Neither SD nor SEM were reported, and no statistical test reported. ECRI Institute estimated Hedges' g using an estimated SD of 14.1 for both groups, which was based on pooling on other studies' reported SDs for this characteristic.
Shah et al. (1993)[12,16]	Study only reported that "No statistical difference in disease indication for OLTx was evident between the 4 study groups"				

Note: Shaded cells denote comparisons for which the groups differed at baseline by 15 or more percentage points (dichotomous outcomes) or for which the groups differed at baseline by Hedges' g of 0.4 or more (continuous measures). Hedges' g is the difference between means divided by the pooled standard deviation. This was calculated by ECRI Institute.

NC – Not calculable
NR – Not reported
p.p. – Percentage points
SD – Standard deviation
SEM – Standard error of the mean

Table 67. Question 7: Quality Assessment

Study	7a	7b	7c	7d	7e	7f	7g	7h
Recipients Negative Before Transplant; Comparison of Clinical Outcomes After HBV+ Donor vs. HBV- Donor								
Fong et al. (2002)[55]			✓			✓		
Recipients Negative Before Transplant; Comparison of Clinical Outcomes After HCV+ Donor vs. HCV- Donor								
Abbott et al. (2003)[83,84]			✓		✓	✓	✓	✓
Velidedeoglu et al. (2002)[93,94]			✓			✓		
Shah et al. (1993)[12,16]						✓		
Haji et al. (2004)[77,79]						✓	✓	✓
Recipients Positive Before Transplant; Comparison of Clinical Outcomes After HBV+ Donor vs. HBV- Donor								
Fong et al. (2002)[55]			✓		✓	✓		
Madayag et al. (1997)[56]			✓		✓	✓	✓	✓
Lai et al. (1996)[95-97]			✓			✓		
Saab et al. (2003)[91]						✓		
Recipients Positive Before Transplant; Comparison of Clinical Outcomes After HCV+ Donor vs. HCV- Donor								
Kasprzyk et al. (2007)[98]			✓			✓	✓	✓
Abbott et al. (2003)[83,84]			✓		✓	✓	✓	✓
Woodside et al. (2003)[85]			✓			✓	✓	✓
Mandal et al. (2000)[86]			✓			✓	✓	✓
Ali et al. (1998)[99]			✓			✓	✓	✓
Morales et al. (1995)[87]			✓			✓	✓	✓
Saab et al. (2003)[91]						✓		
Velidedeoglu et al. (2002)[93,94]			✓	✓		✓		
Marroquin et al. (2001)[90]			✓	✓	✓	✓	✓	✓
Salizzoni et al. (2001)[88]						✓		
Vargas et al. (1999)[92]			✓	✓		✓	✓	✓
Testa et al. (1998)[89]			✓			✓	✓	✓
Shah et al. (1993)[12,16]						✓		

A checkmark (✓) means that the study met the quality criterion for this Question; the lack of a checkmark means that the study either did not meet the criterion, or it was unclear whether the study met the criterion. The criteria specific to this Question were:

7a. Were the patients randomly assigned to treatments?

7b. Was the study planned prospectively (i.e., before any data were collected)

7c. Were all consecutive patients enrolled (or a random sample of eligible patients)?

7d. Were the two groups comparable at baseline? (age, sex, comorbidities, indication for transplant, previous duration on waitlist)

7e. If not, were statistical adjustments performed to control for baseline differences?

7f. Were the two groups treated concurrently?

7g. Did at least 85% of the study enrollees provide data?

7h. Was the between-group difference in study completion rates less than 15%?

Table 68. Question 7: Reported Data

Study	Outcome	Timepoint	D+ Outcome	D- Outcome	Adjustment for Comorbidities	Statistical Test Result	Comments
Recipients Negative Before Transplant; Comparison of Clinical Outcomes After HBV+ Donor vs. HBV- Donor							
Fong et al. (2002)[55]	Graft survival	12	87% (N = Not reported [NR])	88% (N = NR)	None	Overall graft survival curve: p = 0.009 for D+R- vs. D-R-; p = 0.06 for D-R+ vs. D-R-; p = 0.69 for D+R+ vs. D-R-	Survival percentages estimated by ECRI Institute from Figure 1 in the article
	Graft survival	24	78% (N = NR)	83% (N = NR)	None	Overall graft survival curve: p = 0.009 for D+R- vs. D-R-; p = 0.06 for D-R+ vs. D-R-; p = 0.69 for D+R+ vs. D-R-	Survival percentages estimated by ECRI Institute from Figure 1 in the article
	Graft survival	36	72% (N = NR)	77% (N = NR)	None	Overall graft survival curve: p = 0.009 for D+R- vs. D-R-; p = 0.06 for D-R+ vs. D-R-; p = 0.69 for D+R+ vs. D-R-	Survival percentages estimated by ECRI Institute from Figure 1 in the article
	Patient survival	12	94% (N = NR)	94% (N = NR)	None	Overall patient survival curve: p = 0.01 for D+R- vs. D-R-	Survival percentages estimated by ECRI Institute from Figure 2 in the article

Study	Outcome	Timepoint	D+ Outcome	D- Outcome	Adjustment for Comorbidities	Statistical Test Result	Comments
	Patient survival	24	90% (N = NR)	92% (N = NR)	None	Overall patient survival curve: p = 0.01 for D+R- vs. D-R-	Survival percentages estimated by ECRI Institute from Figure 2 in the article
	Patient survival	36	86% (N = NR)	90% (N = NR)	None	Overall patient survival curve: p = 0.01 for D+R- vs. D-R-	Survival percentages estimated by ECRI Institute from Figure 2 in the article
Recipients Negative Before Transplant; Comparison of Clinical Outcomes After HCV+ Donor vs. HCV- Donor							
Abbott et al. (2003)[83,84]	Graft survival	NA	Relative risk was 0.97 (95% CI: 0.6 to 1.56) (very slightly in favor of recipients of positive organs)		None	n.s.	
	Patient survival, hazard ratio of death	NA	Unadjusted hazard ratio of death was 2.30 (95% CI: 1.75 to 3.26) in favor of recipients of negative organs.		None	Significant	
	Patient survival, hazard ratio of death	NA	Adjusted hazard ratio of death was 2.25 (95% CI: 1.56 to 3.24) in favor of recipients of negative organs.		Donor age, recipient age, HLA mismatch, elevated creatinine at 1 year post-transplantation, years of dialysis before transplantation, and albumin level.	Significant	

Study	Outcome	Timepoint	D+ Outcome	D- Outcome	Adjustment for Comorbidities	Statistical Test Result	Comments
Velidedeoglu et al. (2002)[93,94] UNOS data	Graft survival	12	80.9% (N = 29)	82.3% (N = 7,811)	None	NR	
	Graft survival	36	69.2% (N = NR)	76% (N = NR)	None	NR	
	Graft survival	60	69.2% (N = NR)	70.1% (N = NR)	None	NR	
Shah et al. (1993)[12,16]	Graft survival	24	60% (N = NR)	69% (N = NR)	None	n.s.	
	Patient survival	24	60% (N = NR)	75% (N = NR)	None	n.s.	

Study	Outcome	Timepoint	D+ Outcome	D- Outcome	Adjustment for Comorbidities	Statistical Test Result	Comments
Haji et al. (2004)[77,79]	Patient survival	12	80% (N = NR)	96% (N = NR)	Not reported. The methods section reported the use of Cox regression "to adjust for significant covariates", but authors did not report whether the hazard ratio of 2.8 was adjusted or unadjusted. They did report that "By univariate Cox regression, recipient and donor age, ischemia time, cumulative episodes of rejection, standard biopsy score, donor and recipient cytomegalovirus seropositivity, and post-transplant cytomegalovirus infection were not significant (All p-values >0.1) in determining mortality in our patient population." (page 280)	Overall p-value for the survival curves was reported as p = 0.004 in favor of D- recipients	Confounding by indication: "At our institution, an HCV-seropositive donor was used when, in the judgment of the transplant team, the recipient was critically ill and not a candidate for mechanical ventricular assist device (recurrent stroke, infections)" (page 278) However, one criterion for inclusion in the analysis was that all patients must have been discharged home successfully i.e., went home in stable condition. Survival percentages estimated by ECRI Institute from Figure 1 in the article

Study	Outcome	Timepoint	D+ Outcome	D- Outcome	Adjustment for Comorbidities	Statistical Test Result	Comments
	Patient survival	36	78% (N = NR)	92% (N = NR)	Not reported. The methods section reported the use of Cox regression "to adjust for significant covariates", but authors did not report whether the hazard ratio of 2.8 was adjusted or unadjusted. They did report that "By univariate Cox regression, recipient and donor age, ischemia time, cumulative episodes of rejection, standard biopsy score, donor and recipient cytomegalovirus seropositivity, and post-transplant cytomegalovirus infection were not significant (All p-values >0.1) in determining mortality in our patient population." (page 280)	Overall p-value for the survival curves was reported as p = 0.004 in favor of D- recipients	Survival percentages estimated by ECRI Institute from Figure 1 in the article

Study	Outcome	Timepoint	D+ Outcome	D- Outcome	Adjustment for Comorbidities	Statistical Test Result	Comments
	Patient survival	60	59% (N = NR)	88% (N = NR)	Not reported. The methods section reported the use of Cox regression "to adjust for significant covariates", but authors did not report whether the hazard ratio of 2.8 was adjusted or unadjusted. They did report that "By univariate Cox regression, recipient and donor age, ischemia time, cumulative episodes of rejection, standard biopsy score, donor and recipient cytomegalovirus seropositivity, and post-transplant cytomegalovirus infection were not significant (All p-values >0.1) in determining mortality in our patient population."(page 280)	Overall p-value for the survival curves was reported as p = 0.004 in favor of D- recipients	Survival percentages estimated by ECRI Institute from Figure 1 in the article
	Patient survival, rate	Mean: 50 months (SD: 23)	68% (23/34)	85% (155/183)	None	Relative risk or mortality: 2.8 (95% CI: 1.3-5.7; p = 0.006) in favor of D- recipients	

Study	Outcome	Timepoint	D+ Outcome	D- Outcome	Adjustment for Comorbidities	Statistical Test Result	Comments
Recipients Positive Before Transplant; Comparison of Clinical Outcomes After HBV+ Donor vs. HBV- Donor							
Fong et al. (2002)[55]	Graft survival	12	91% (N = NR)	86% (N = NR)	Adjusted for previous transplant, recipient age, recipient race, peak panel reactive antibody, recipient HCV, duration of dialysis, donor age, cold ischemia time, donor race, cause of donor death, ABDRMM (definition of this acronym not provided)	NR	Percentage estimated by ECRI Institute from Figure 1 in the publication
	Graft survival	24	80% (N = NR)	83% (N = NR)	Adjusted for previous transplant, recipient age, recipient race, peak panel reactive antibody, recipient HCV, duration of dialysis, donor age, cold ischemia time, donor race, cause of donor death, ABDRMM (definition of this acronym not provided)	NR	Percentage estimated by ECRI Institute from Figure 1 in the publication
	Graft survival	36	68% (N = NR)	75% (N = NR)	Adjusted for previous transplant, recipient age, recipient race, peak panel reactive antibody, recipient HCV, duration of dialysis, donor age, cold ischemia time, donor race, cause of donor death, ABDRMM (definition of this acronym not provided)	NR	Percentage estimated by ECRI Institute from Figure 1 in the publication

Study	Outcome	Timepoint	D+ Outcome	D- Outcome	Adjustment for Comorbidities	Statistical Test Result	Comments
	Patient survival	12	95% (N = NR)	94% (N = NR)	Adjusted for previous transplant, recipient age, recipient race, peak panel reactive antibody, recipient HCV, duration of dialysis, donor age, cold ischemia time, donor race, cause of donor death, ABDRMM (definition of this acronym not provided)	NR	Percentage estimated by ECRI Institute from Figure 1 in the publication
	Patient survival	24	94% (N = NR)	91% (N = NR)	Adjusted for previous transplant, recipient age, recipient race, peak panel reactive antibody, recipient HCV, duration of dialysis, donor age, cold ischemia time, donor race, cause of donor death, ABDRMM (definition of this acronym not provided)	NR	Percentage estimated by ECRI Institute from Figure 1 in the publication
	Patient survival	36	90% (N = NR)	88% (N = NR)	Adjusted for previous transplant, recipient age, recipient race, peak panel reactive antibody, recipient HCV, duration of dialysis, donor age, cold ischemia time, donor race, cause of donor death, ABDRMM (definition of this acronym not provided)	NR	Percentage estimated by ECRI Institute from Figure 1 in the publication

Study	Outcome	Timepoint	D+ Outcome	D- Outcome	Adjustment for Comorbidities	Statistical Test Result	Comments
Madayag et al. (1997)[56]	Graft survival	12	93.4% (N = 32)	100% (N = 37)	Adjusted for sex, pre-transplant HBsAg, pre-transplant anti-HBs, pre-transplant anti-HBc, organ type, and date of transplant	n.s.	Recipients of positive organs were significantly older (Mean: 49 vs. 44; p = 0.03).
	Graft survival	36	86.1% (N = 8)	100% (N = 11)	Adjusted for sex, pre-transplant HBsAg, pre-transplant anti-HBs, pre-transplant anti-HBc, organ type, and date of transplant	n.s.	Recipients of positive organs were significantly older (Mean: 49 vs. 44; p = 0.03).
	Graft survival, cumulative graft loss risk	Mean: 24 (Range: 2-64)	11% (5/45)	2% (1/45)	Adjusted for sex, pre-transplant HBsAg, pre-transplant anti-HBs, pre-transplant anti-HBc, organ type, and date of transplant	n.s.; Relative risk was 5.7 in favor (but not statistically significant) of the recipients of negative organs (95% CI: 0.52 to 52.17	Recipients of positive organs were significantly older (Mean: 49 vs. 44; p = 0.03).
Lai et al. (1996)[95-97]	Patient survival, living donor	12	100% (N = NR)	91.7% (N = NR)	None	p = 0.334 for the comparison of patient survival curves for D+ vs. D- when the donor was a living donor	
	Patient survival, deceased donor	12	76.5% (N = NR)	100% (N = NR)	None	p = 0.063 for the comparison of patient survival curves for D+ vs. D- when the donor was deceased	

Study	Outcome	Timepoint	D+ Outcome	D- Outcome	Adjustment for Comorbidities	Statistical Test Result	Comments
	Patient survival, living donor	60	100% (N = NR)	72.4% (N = NR)	None	p = 0.334 for the comparison of patient survival curves for D+ vs. D- when the donor was a living donor	
	Patient survival, deceased donor	60	58.8% (N = NR)	96.6% (N = NR)	None	p = 0.063 for the comparison of patient survival curves for D+ vs. D- when the donor was deceased	
	Graft survival, living donor	12	100% (N = NR)	91.6% (N = NR)	None	p = 0.0013 for the comparison of graft survival curves for D+ vs. D- when the donor was a living donor	
	Graft survival, deceased donor	12	76.5% (N = NR)	100% (N = NR)	None	p = 0.0035 for the comparison of graft survival curves for D+ vs. D- when the donor was deceased	
	Graft survival, living donor	60	100% (N = NR)	53.9% (N = NR)	None	p = 0.0013 for the comparison of graft survival curves for D+ vs. D- when the donor was a living donor	

Study	Outcome	Timepoint	D+ Outcome	D- Outcome	Adjustment for Comorbidities	Statistical Test Result	Comments
	Graft survival, deceased donor	60	58.8% (N = NR)	92.4% (N = NR)	None	p = 0.0035 for the comparison of graft survival curves for D+ vs. D- when the donor was deceased	
Saab et al. (2003)[91]	Patient survival	12	94% (N = NR)	91% (N = NR)	None	p = 0.65 comparing the survival curves	
	Patient survival	36	73% (N = NR)	81% (N = NR)	None	p = 0.65 comparing the survival curves	
	Patient survival	60	73% (N = NR)	81% (N = NR)	None	p = 0.65 comparing the survival curves	
	Graft survival	12	87% (N = NR)	84% (N = NR)	None	p = 0.94 comparing the survival curves	
	Graft survival	36	71% (N = NR)	75% (N = NR)	None	p = 0.94 comparing the survival curves	
	Graft survival	60	71% (N = NR)	75% (N = NR)	None	p = 0.94 comparing the survival curves	

Study	Outcome	Timepoint	D+ Outcome	D- Outcome	Adjustment for Comorbidities	Statistical Test Result	Comments
Recipients Positive Before Transplant; Comparison of Clinical Outcomes After HCV+ Donor vs. HCV- Donor							
Kasprzyk et al. (2007)[98]	Graft survival	Range: 12-156	78% (47/60)	70% (140/199)	None	n.s.; this statistical test result included recipients who were negative before transplant, but the percentages themselves in this table are restricted to those who were positive before transplant	
	Patient survival	Range: 12-156	95% (57/60)	85% (169/199)	None	n.s.; this statistical test result included recipients who were negative before transplant, but the percentages themselves in this table are restricted to those who were positive before transplant	

Study	Outcome	Timepoint	D+ Outcome	D- Outcome	Adjustment for Comorbidities	Statistical Test Result	Comments
Abbott et al. (2003)[83,84]	Patient survival	NR; see comments	Unadjusted hazard ratio of death was 1.43 (95% CI: 1.02 to 2.02) in favor of recipients of negative organs.		None	Significant	This comparison was restricted to the ~90% of patients who survived at least 2 years after transplant, because of the violation of the proportional hazards assumption. There was no difference between groups up to 2 years post-transplant.
	Patient survival	NR; see comments	Adjusted hazard ratio of death was 2.04 (95% CI: 1.20 to 3.45) in favor of recipients of negative organs.		Donor age, recipient age, HLA mismatch, elevated creatinine at 1 year post-transplantation, years of dialysis before transplantation, and albumin level.	Significant	This comparison was restricted to the ~90% of patients who survived at least 2 years after transplant, because of the violation of the proportional hazards assumption. There was no difference between groups up to 2 years post-transplant.
	Graft survival	NR	91.7% (542/593)	90.9% (769/846)	None	NR	Denominator for D- calculated by ECRI Institute based on reported percentage and number of events

Study	Outcome	Timepoint	D+ Outcome	D- Outcome	Adjustment for Comorbidities	Statistical Test Result	Comments
Woodside et al. (2003)[85]	Graft survival	12	89% (N = 19)	89% (N = 19)	None	NR	
	Patient survival	12	89% (N = 17)	89% (N = 17)	None	NR	
Mandal et al. (2000)[86]	Graft survival	Median: 16, Mean: 15 (standard error of the mean: 2), Range: 3-33	56% (11/19)	50% (5/10)	None	NR	In the D+ group, there were 19 operations in the 18 patients. Diabetes was more common in D+ recipients (5/18) than D- recipients (1/10). D+ recipients were significantly older (46 vs. 35). D+ recipients rate of antiCMV was higher (87% vs. 50%). Mismatching of HLA-A and HLA-B was higher in the D+ recipients (3.2 vs. 2.3).

Study	Outcome	Timepoint	D+ Outcome	D- Outcome	Adjustment for Comorbidities	Statistical Test Result	Comments
	Patient survival	Median: 16, Mean: 15 (standard error of the mean: 2), Range: 3-33	94% (17/18)	90% (9/10)	None	NR	In the D+ group, there were 19 operations in the 18 patients. Diabetes was more common in D+ recipients (5/18) than D- recipients (1/10). D+ recipients were significantly older (46 vs. 35). D+ recipients rate of antiCMV was higher (87% vs. 50%). Mismatching of HLA-A and HLA-B was higher in the D+ recipients (3.2 vs. 2.3).
Ali et al. (1998)[99]	Graft survival	Mean 36, Range: 12-60	50% (14/28)	31% (5/16)	None	p-value was reported as p >0.3. However the chi-squared test yields p = 0.23.	

Study	Outcome	Timepoint	D+ Outcome	D- Outcome	Adjustment for Comorbidities	Statistical Test Result	Comments
Morales et al. (1995)[87]	Graft survival	26 months (SD: 8) for those who received a positive organ, and 30 months (SD: 10) for those who received a negative organ	96% (23/24)	93% (37/40)	None	n.s.	Number of blood transfusions less in D+ recipients (7 vs. 21); p <0.05.
	Patient survival	26 months (SD: 8) for those who received a positive organ, and 30 months (SD: 10) for those who received a negative organ	100% (24/24)	98% (39/40)	None	n.s.	Number of blood transfusions less in D+ recipients (7 vs. 21); p <0.05.
Saab et al. (2003)[91]	Patient survival	12	89% (N = NR)	87% (N = NR)	None	p = 0.22 comparing the survival curves	
	Patient survival	36	89% (N = NR)	79% (N = NR)	None	p = 0.22 comparing the survival curves	
	Patient survival	60	89% (N = NR)	69% (N = NR)	None	p = 0.22 comparing the survival curves	

Study	Outcome	Timepoint	D+ Outcome	D- Outcome	Adjustment for Comorbidities	Statistical Test Result	Comments
	Graft survival	12	73% (N = NR)	78% (N = NR)	None	p = 0.77 comparing the survival curves	
	Graft survival	36	73% (N = NR)	70% (N = NR)	None	p = 0.77 comparing the survival curves	
	Graft survival	60	73% (N = NR)	59% (N = NR)	None	p = 0.77 comparing the survival curves	
Velidedeoglu et al. (2002)[93,94] Penn data	Graft survival	12	69.2% (N = 13)	79.6% (N = 103)	None	p-value comparing graft survival curves was p = 0.6778	These data refer to patients seen at Penn
	Graft survival	36	69.2% (N = NR)	71.6% (N = NR)	None	p-value comparing graft survival curves was p = 0.6778	These data refer to patients seen at Penn
	Graft survival	60	69.2% (N = NR)	61.2% (N = NR)	None	p-value comparing graft survival curves was p = 0.6778	These data refer to patients seen at Penn
	Patient survival	Mean: 23.4	77% (10/13)	78.7% (81/103)	None	NR	These data refer to patients seen at Penn

Study	Outcome	Timepoint	D+ Outcome	D- Outcome	Adjustment for Comorbidities	Statistical Test Result	Comments
Velidedeoglu et al. (2002)[93,94] UNOS data	Graft survival	12	76.9% (N = 190)	80.6% (N = 5,053)	None	p-value comparing graft survival curves was p = 0.965	These data refer to patients from UNOS
	Graft survival	36	72.6% (N = NR)	69.1% (N = NR)	None	p-value comparing graft survival curves was p = 0.965	These data refer to patients from UNOS
	Graft survival	60	69.3% (N = NR)	62.2% (N = NR)	None	p-value comparing graft survival curves was p = 0.965	These data refer to patients from UNOS
Marroquin et al. (2001)[90]	Patient survival	6	95% (N = NR)	85% (N = NR)	None	p = 0.01 for the comparison of patient survival curves	Recipients of positive organs were more likely to have liver cancer (8.3% vs. 3.1%; p = 0.01), more likely to have ABO incompatibility (4.2% vs. 1.3%; p = 0.04), and they had poorer waitlist status (see Table 5 in the publication).
	Patient survival	12	90% (N = NR)	82% (N = NR)	None	p = 0.01 for the comparison of patient survival curves	Recipients of positive organs were more likely to have liver cancer (8.3% vs. 3.1%; p = 0.01), more likely to have ABO incompatibility (4.2% vs. 1.3%; p = 0.04), and they had poorer waitlist status (see Table 5 in the publication).

Study	Outcome	Timepoint	D+ Outcome	D- Outcome	Adjustment for Comorbidities	Statistical Test Result	Comments
	Patient survival	18	90% (N = NR)	79% (N = NR)	None	p = 0.01 for the comparison of patient survival curves	Recipients of positive organs were more likely to have liver cancer (8.3% vs. 3.1%; p = 0.01), more likely to have ABO incompatibility (4.2% vs. 1.3%; p = 0.04), and they had poorer waitlist status (see Table 5 in the publication).
	Patient survival	24	90% (N = NR)	77% (N = NR)	None	p = 0.01 for the comparison of patient survival curves	Recipients of positive organs were more likely to have liver cancer (8.3% vs. 3.1%; p = 0.01), more likely to have ABO incompatibility (4.2% vs. 1.3%; p = 0.04), and they had poorer waitlist status (see Table 5 in the publication).

Study	Outcome	Timepoint	D+ Outcome	D- Outcome	Adjustment for Comorbidities	Statistical Test Result	Comments
	Patient survival, overall	Median was 34 months for those who received a positive organ, and 37 months for those who received a negative organ	90% (86/96)	77% (2194/2827)	None	NR	Recipients of positive organs were more likely to have liver cancer (8.3% vs. 3.1%; p = 0.01), more likely to have ABO incompatibility (4.2% vs. 1.3%; p = 0.04), and they had poorer waitlist status (see Table 5 in the publication).
	Graft survival	6	88% (N = NR)	81% (N = NR)	None	NR	Data estimated by ECRI Institute from Figure 3 in the publication. Recipients of positive organs were more likely to have liver cancer (8.3% vs. 3.1%; p = 0.01), more likely to have ABO incompatibility (4.2% vs. 1.3%; p = 0.04), and they had poorer waitlist status (see Table 5 in the publication).

Study	Outcome	Timepoint	D+ Outcome	D- Outcome	Adjustment for Comorbidities	Statistical Test Result	Comments
	Graft survival	12	76% (N = NR)	76% (N = NR)	None	NR	Data estimated by ECRI Institute from Figure 3 in the publication. Recipients of positive organs were more likely to have liver cancer (8.3% vs. 3.1%; p = 0.01), more likely to have ABO incompatibility (4.2% vs. 1.3%; p = 0.04), and they had poorer waitlist status (see Table 5 in the publication).
	Graft survival	18	76% (N = NR)	72% (N = NR)	None	NR	Data estimated by ECRI Institute from Figure 3 in the publication. Recipients of positive organs were more likely to have liver cancer (8.3% vs. 3.1%; p = 0.01), more likely to have ABO incompatibility (4.2% vs. 1.3%; p = 0.04), and they had poorer waitlist status (see Table 5 in the publication).

Study	Outcome	Timepoint	D+ Outcome	D- Outcome	Adjustment for Comorbidities	Statistical Test Result	Comments
	Graft survival	24	76% (N = NR)	70% (N = NR)	None	NR	Data estimated by ECRI Institute from Figure 3 in the publication. Recipients of positive organs were more likely to have liver cancer (8.3% vs. 3.1%; p = 0.01), more likely to have ABO incompatibility (4.2% vs. 1.3%; p = 0.04), and they had poorer waitlist status (see Table 5 in the publication).
	Graft survival, adjusted odds	3	0.7	See previous column	Adjusted for sex/age/weight of both donor and recipient, ABO incompatibility, coexisting diseases, change in liver function tests, immunosuppressive regimens, causes of graft failure, UNOS status at time of transplant, ICU length of stay, hospital length of stay	n.s.	

Study	Outcome	Timepoint	D+ Outcome	D- Outcome	Adjustment for Comorbidities	Statistical Test Result	Comments
	Graft survival, adjusted odds	6	0.66	See previous column	Adjusted for sex/age/weight of both donor and recipient, ABO incompatibility, coexisting diseases, change in liver function tests, immunosuppressive regimens, causes of graft failure, UNOS status at time of transplant, ICU length of stay, hospital length of stay	n.s.	
	Graft survival, adjusted odds	12	1	See previous column	Adjusted for sex/age/weight of both donor and recipient, ABO incompatibility, coexisting diseases, change in liver function tests, immuno-suppressive regimens, causes of graft failure, UNOS status at time of transplant, ICU length of stay, hospital length of stay	n.s.	
	Graft survival, adjusted odds	24	0.88	See previous column	Adjusted for sex/age/weight of both donor and recipient, ABO incompatibility, coexisting diseases, change in liver function tests, immuno-suppressive regimens, causes of graft failure, UNOS status at time of transplant, ICU length of stay, hospital length of stay	n.s.	

Study	Outcome	Timepoint	D+ Outcome	D- Outcome	Adjustment for Comorbidities	Statistical Test Result	Comments
	Patient survival, adjusted odds	3	0.37	See previous column	Adjusted for sex/age/weight of both donor and recipient, ABO incompatibility, coexisting diseases, change in liver function tests, immuno-suppressive regimens, causes of graft failure, UNOS status at time of transplant, ICU length of stay, hospital length of stay	n.s.	
	Patient survival, adjusted odds	6	0.39	See previous column	Adjusted for sex/age/weight of both donor and recipient, ABO incompatibility, coexisting diseases, change in liver function tests, immuno-suppressive regimens, causes of graft failure, UNOS status at time of transplant, ICU length of stay, hospital length of stay	n.s.	
	Patient survival, adjusted odds	12	0.56	See previous column	Adjusted for sex/age/weight of both donor and recipient, ABO incompatibility, coexisting diseases, change in liver function tests, immuno-suppressive regimens, causes of graft failure, UNOS status at time of transplant, ICU length of stay, hospital length of stay	n.s.	

Study	Outcome	Timepoint	D+ Outcome	D- Outcome	Adjustment for Comorbidities	Statistical Test Result	Comments
	Patient survival, adjusted odds	24	0.51	See previous column	Adjusted for sex/age/weight of both donor and recipient, ABO incompatibility, coexisting diseases, change in liver function tests, immuno-suppressive regimens, causes of graft failure, UNOS status at time of transplant, ICU length of stay, hospital length of stay	n.s.	
Salizzoni et al. (2001)[88]	Patient survival	12	83.3% (N = NR)	82.4% (N = NR)	None	n.s.	
	Graft survival	12	83.3% (N = NR)	79.8% (N = NR)	None	n.s.	
Vargas et al. (1999)[92]	Graft survival	NR	87% (20/23)	91% (154/169)	None	n.s.	
	Patient survival	12	89% (N = NR)	88% (N = NR)	None	n.s.	
	Patient survival	60	72% (N = NR)	73% (N = NR)	None	n.s.	
Testa et al. (1998)[89]	Graft survival	48	71.9% (N = NR)	76.2% (N = NR)	None	n.s.	
	Patient survival	48	83.9% (N = NR)	79.1% (N = NR)	None	n.s.	

Study	Outcome	Timepoint	D+ Outcome	D- Outcome	Adjustment for Comorbidities	Statistical Test Result	Comments
	Patient survival	40 months (Range: 12-58) for those who received a positive organ, and 36 months (Range: 17-135) for those who received a negative organ	82% (18/22)	81% (93/115)	None	n.s.	
Shah et al. (1993)[12]	Graft survival	24	80% (4/5)	70% (N = NR)	None	n.s.	
	Patient survival	24	100% (N = NR)	80% (N = NR)	None	n.s.	

NR – Not reported
n.s. – Not statistically significant

Evidence Reviews: V. Potential risks and benefits of transplanting, or not transplanting, solid organs from donors with risk factors for HIV, HBV, or HCV

Question 8. How do the clinical outcomes of transplant recipients who receive organs from donors with behavioral or nonbehavioral risk factors compare to those who remain on the transplant list?

This question is similar to Question 7, however, Question 7 involved the use of an organ *known* to be infected, whereas Question 8 involves an organ from a donor at *increased risk* of infection. Some individuals may test negative for HIV/HBV/HCV and yet have the virus (possibly due to the window period for virus detection, or because of test insensitivity).

Two studies met the inclusion criteria (Schweitzer et al. [2007][203] and Freeman and Cohen [2009][204]). Both performed simulations on the key dilemma of whether to use organs from serologically negative donors who have behavioral risks of infection. The two studies, however, made different comparisons, and so they were considered separately. Schweitzer et al. (2007)[203] estimated mortality after transplanting the kidneys vs. keeping patients on the waitlist. Freeman and Cohen (2009)[204] estimated waitlist mortality rates, however they did not estimate mortality of all who received organs from at-risk donors. Instead, they reported the overall prevalence of infection among recipients of organs from at-risk donors (which was exceedingly low), and then estimated mortality just for infected recipients. Both studies are described in more detail in the sections below.

Due to the small amount of evidence, we also looked for studies comparing the clinical outcomes of two types of recipients: recipients of organs from at-risk donors, and recipients of organs from not-at-risk donors (these donors may or may not have been infected). We defined "at risk" for this question as having a potential behavioral risk factor, or having a clinical symptom/physical finding associated with infection, or having a medical comorbidity associated with infection. No such comparative studies were identified.

Schweitzer et al. (2007)[203]

This simulation addressed the question: *Should the kidneys of negative-serology donors who are at increased risk of infection based on 1994 CDC criteria be* transplanted *or* discarded*?* Authors constructed a complicated Markov model of these two alternatives. They considered four types of increased-risk donors (IRDs): intravenous drug users (IDU), men who have sex with men (MSM), commercial sex workers (CSW), and prison inmates. The authors' methods, our quality assessment, and study results are detailed in the text below, as well as in Table 69 through Table 75.

The model considered a 20-year interval, with one-year cycles. During each year, each simulated patient was in one of nine states:

	Recipient HIV status	Recipient HCV status
1) On the waitlist	HIV-	HCV-
2) Received a kidney	HIV-	HCV-
3) On the waitlist	HIV+	HCV-
4) On the waitlist	HIV-	HCV +
5) On the waitlist	HIV +	HCV +
6) Received a kidney	HIV +	HCV-
7) Received a kidney	HIV-	HCV +
8) Received a kidney	HIV +	HCV +
9) Dead		

Each of the first eight health states was associated with a different death rate, a different quality-of-life, and a different cost of care. For simplicity, authors assumed that all recipients were immune to acute HBV infection, which explains why none of the nine states involve HBV status. Transition probabilities between states were based on various assumptions using the published literature (see Table 69 through Table 71 below).

The epidemiology assumptions listed in Table 70 and Table 71 can be compared informally with the corresponding estimates in Question 1 of this evidence review. For HIV, the incidence estimates matched closely (Schweitzer assumed 0.02 per 100 person-years, and the estimate in Question 1 was 0.019 per 100 person years). However, the prevalence of HIV was about one-third of the estimate from Question 1 (0.128% vs 0.37%). Also, for HCV, the incidence rates were very different (Schweitzer assumed 0.11 cases per 100 person-years but in Question 1 the estimate was 0.057 per 100 person-years). For HCV prevalence, the assumed 1.8% was within the range of estimates from Question 1 (1.3% to 1.9%).

The base case simulation assumed that the CDC-IRD donors were all seronegative injection drug users, and the results appear in Table 72. The transplant strategy resulted in lower mortality, more quality-adjusted life-years (QALYs), and also lower cost. There were more HIV infections using the transplant strategy, but the number of them was too small (and the resulting health problems not severe enough) to overcome the advantages of transplantation. Interestingly, with HCV, there were actually more infections with the discard strategy. This was because the discard strategy led to more time on hemodialysis than the transplant strategy; the assumed incidence of HCV when on hemodialysis (0.34 per 100 patient-years) was 30 times higher than the assumed incidence of HCV after kidney transplant (0.011 per 100 patient-years; see the bottom two rows of Table 71).

Authors performed separate analyses for three other types of increased-risk donors (MSM, CSW, and inmates); results were very similar to the base case for outcomes such as the number of transplants,

survival, QALYs, and costs. There were some differences, however, regarding HIV and HCV infections (Table 73). Infection counts due to the use of kidneys from MSM or inmates were low for both HIV and HCV. The counts for CSW were somewhat higher, but even for this subgroup the total number of infections using the transplant strategy (13.7, comprised of 3.4 HIV and 9.3 HCV) was still lower than the total number of infections using the discard strategy (14.8, comprised of 1.9 HIV and 12.9 HCV).

Authors conducted numerous one-way sensitivity analyses (in which a single assumption is altered and all others left unchanged), and they stated that in most cases the conclusions of the base case "were not substantially changed". They did note that the number of HCV infections was strongly influenced by assumptions about incidence rates, but concluded that "the 'Discard' policy would yield fewer HCV infections only in a setting where a recipient's risk of infection on dialysis is very low, while the probability of CDC-IRD infection in a donor is high".[203]

Authors also conducted a "worse-case scenario" analysis that used the following alternate assumptions:

- That CDC-IRD donors have much higher HIV incidence (25 per 100 person-years) and HIV prevalence (50%) than assumed in the base case analysis (2 per 100 person-years, and 18%, respectively)
- That CDC-IRD donors have higher HCV incidence (25 per 100 person-years) and HCV prevalence (50%) than assumed in the base case analysis (21 per 100 person-years, and 38%, respectively)
- While on the waitlist, the risk of HCV is much lower (0.1 infections per 100 person-years instead of the 0.34 assumed in the base case)
- Lower chance of an individual receiving an offer of a CDC-IRD kidney because of increased number of eligible individuals for those kidneys (30% instead of the base case 5%)
- Lower percentage of CDC-IRD kidneys (2% of donors instead of 5%)
- Higher cost associated with HIV or HCV infection ($30,000/year instead of $21,000)
- Lower utility associated with HIV or HCV infection (0.45 instead of 0.78 for HIV and 0.82 for HCV)

Interestingly, even though these assumptions were slanted against the Transplant strategy, it still was preferable to the discard strategy, resulting in more transplants, less time on the waitlist, more time with a functioning transplant, lower mortality, more QALYs, and lower cost.

Finally, because NAT testing may not be widely available, authors also modeled a scenario where only antibody testing was available, lengthening the window period for HIV to 22 days from 11; lengthening the window period for HCV to 70 days from 10). Results still favored the transplant strategy for all outcomes except the number of infections, which rose to 2.6 HIV infections per 1,000 patients and 27.7 HCV infections per 1000 patients. These additional infections were not sufficient to overcome the overall advantages of the transplant strategy.

The GRADE evidence profile appears in Table 76. The evidence was rated as Very Low, because this was a simulation and not an empirical study. The GRADE system does not consider simulations as informative as empirical studies.

Table 69. Assumptions in the Schweitzer et al. (2007) Model

Key Assumptions about Donors
• Deceased donors only • All donors tested negative on antibody and nucleic amplification tests (NAT) for both HIV and HCV. NAT has a relatively short window period (i.e., the duration when it cannot detect the virus), so it would be relatively unlikely to miss a virus for this reason. • 5% of donors are classified as “CDC-IRD” (IRD = increased risk donor; sensitivity analyses ranging 2%-8%), defined as being in one of the seven categories in the 1994 CDC guideline on HIV.
Key Assumptions about Recipients
• 50-year old hemodialysis patients (sensitivity analyses ranging from 18-65) • All recipients were willing to accept kidneys from CDC-IRDs. • All recipients were immune to “acute HBV infection”. Thus if any donor were HBV+, this had no impact on the analysis. • In any given year, a recipient could acquire either HIV or HCV, but not both. They could acquire the other one in subsequent years. • 5% of patients on waitlist would be candidates for CDC-IRD kidney (sensitivity analyses ranging from 1%-30%) • Number of patients on the waitlist at the end of 2002 was 50,535 • Annual number of standard deceased donor kidney transplants in 2002 was 8,288 • Median time to transplant for new waiting list registrants was 3.5 years • Annual standard donor kidney transplant rate was 20% (sensitivity analyses ranging 2%-53% • Median waiting time for CDC-IRD kidney transplants was 3.5 years
Key Assumptions about Death Rates
• Annual death rate among all patients on the U.S. kidney waitlist was 3.7% for those 18-34; 5.4% for those aged 35-49; 9.2% for those aged 50-64; and 12.9% for those aged 65+ • Annual death rate in the first year after kidney transplant was 2.3% for those 18-34; 3.9% for those aged 35-49; 8.0% for those aged 50-64; and 11.6% for those aged 65+ • Annual death rate in all subsequent years after kidney transplant was 2.1% for those 18-34; 2.3% for those aged 35-49; 4.0% for those aged 50-64; and 7.2% for those aged 65+ • Relative risk of death due to HIV infection was 1.5 • Relative risk of death due to HCV infection was 1.7

Key Assumptions about Costs and Quality-Adjusted-Life-Years (QALYs)
• Costs in 2002 dollars, adjusted using the medical care component of the consumer price index • Cost of "Stat HIV" and HCV nucleic acid testing (NAT) were estimated at $500/donor or $250/kidney was added to the cost when the donor was CDC-IRD • Cost of hemodialysis $61,000/year (sensitivity analyses ranging from) (sensitivity analyses ranging from $49,000-$71,000) • Cost of care of kidney recipient in the first year after transplant $97,000/year (sensitivity analyses ranging from $76,000-$177,000) • Cost of care kidney recipient in all subsequent years $21,000/year (sensitivity analyses ranging from $17,000-$38,000) • Cost of care for HIV infection was $21,000/year (sensitivity analyses ranging from $19,000-$23,000) • Cost of care for HCV infection was $2,000/year (sensitivity analyses ranging from $1,000-$30,000) • Utility of being on hemodialysis was 0.57 (0 denotes death, 1 denotes perfect) (sensitivity analyses ranging from 0.41-0.64) • Utility of post-transplant quality-of-life was 0.70 (0 denotes death, 1 denotes perfect) (sensitivity analyses ranging from 0.62-0.82) • Utility of HIV was 0.82 (0 denotes death, 1 denotes perfect) (sensitivity analyses ranging from 0.45-1.00) • Utility of HCV was 0.78 (0 denotes death, 1 denotes perfect) (sensitivity analyses ranging from 0.60-0.86) • Discounting of both costs and QALYs at 3%
Other Assumptions
• Overall risk of graft failure after kidney transplant was 6% in the first year (sensitivity analyses ranging from 4%-7%), and 4% in subsequent years (sensitivity analyses ranging from 2%-6%). After graft failure, the patient returned to one of the waitlist health states. • Relative risk of graft failure specifically due to HIV infection was 1.0 (sensitivity analyses ranging from 1.0 to 1.3) • Relative risk of graft failure specifically due to HCV infection was 1.6 (sensitivity analyses ranging from 1.4 to 1.8) • The window period for HIV antibody testing alone was 22 days; for HIV antibody plus NAT was 11 days; for HCV antibody alone was 70 days; for HCV antibody plus NAT was 10 days • The false-negative rate for pre-transplant serological testing of CDC-IRDs donors was 5%. Together with the window period, this incorporated the possibility of missed viruses.

Table 70. HIV Epidemiology Assumptions in the Schweitzer et al. (2007) Model

HIV	Incidence[a]		Prevalence	
Population	**Base Case**	**Sensitivity Range**	**Base Case**	**Sensitivity Range**
General population	0.02	N.A.	0.128%	N.A.
Potential Donors				
Intravenous drug users	2	1-3	18%	1-49
Men who have sex with men	3	1-12	25%	0-40
Commercial sex workers	10	3-30	24%	0-60
Inmates	0.2	0-0.4	2%	1-17
Potential Recipients				
Hemodialysis patients	0.02	N.A.	N.E.	N.E.
Kidney transplant patients	0.02	N.A.	N.E.	N.E.

[a] Incidence is the number of new cases per 100 patient-years.

N.A. – Not applicable because no sensitivity analysis of this parameter was performed.
N.E. – Not estimated, because the model did not require estimates of the prevalence of HIV or HCV among recipients.

Table 71. HCV Epidemiology Assumptions in the Schweitzer et al. (2007) Model

HIV	Incidence[a]		Prevalence	
Population	**Base Case**	**Sensitivity Range**	**Base Case**	**Sensitivity Range**
General population	0.011	N.A.	1.8%	N.A.
Potential Donors				
Intravenous drug users	21	10-45	38%	10-90
Men who have sex with men	0.2	0-1	4%	2-18
Commercial sex workers	10	5-23	12%	6-45
Inmates	1	0.3-6	23%	16-41
Potential Recipients				
Hemodialysis patients	0.34	0.1-3	N.E.	N.E.
Kidney transplant patients	0.011	N.A.	N.E.	N.E.

[a] Incidence is the number of new cases per 100 patient-years.

N.A. – Not applicable because no sensitivity analysis of this parameter was performed.
N.E. – Not estimated, because the model did not require estimates of the prevalence of HIV or HCV among recipients.

Table 72. Base Case Results of the Schweitzer et al. (2007) Model

Outcome	Transplant	Discard
Number of kidney transplants per 1,000 patients	Total: 990 Standard donors: 495 CDC-IRD donors: 495	Total: 740, all standard donors
Survival	1-year: 91% 5-year: 68% 10-year: 49% 20-year: 23%	1-year: 91% 5-year: 65% 10-year: 45% 20-year: 20%
Quality-adjusted life-years	5.6	5.1
Cost of care over 20 years for a typical patient	$338,000	$363,000
HIV infections per 1,000 patients over 20 years	2.3, comprising 1.9 infections when on the waitlist or community acquired, and 0.3 from window-period CDC-IRD donations (these do not add to 2.3 due to rounding)	1.9, all while on the waitlist or community-acquired
HCV infections per 1,000 patients over 20 years	10.8*, comprising 7.9 infections when on the waitlist or community acquired, and 2.9 from window-period CDC-IRD donations	12.9*, all while on the waitlist or community-acquired

CDC-IRD – CDC increased-risk donor

*The reason that there were actually more HCV infections using the discard strategy is that the discard strategy led to more time on hemodialysis than the transplant strategy; the assumed incidence of HCV when on hemodialysis (0.34 per 100 patient-years) was 30 times higher than the assumed incidence of HCV after kidney transplant (0.011; see the bottom two rows of Table 71).

Table 73. HIV and HCV Infection Results in Recipients of Kidneys from CDC-IRD Donors

Outcome	HIV			HCV		
	Total	Waitlist or Community Acquired	Transplant-Acquired	Total	Waitlist or Community Acquired	Transplant-Acquired
Injection drug users (base case)	2.3*	1.9	0.3	10.8	7.9	2.9
Men who have sex with men	2.4	1.9	0.5	8.0	7.9	0.1
Commercial sex workers	3.4	1.9	1.5	9.3	7.9	1.4
Prison inmates	2.0	1.9	0.1	8.1	7.9	0.2

*All numbers are the number of infections per 1,000 patients, all in the Transplant group willing to receive kidneys from CDC increased-risk donors. Due to rounding, numbers in the two columns "Waitlist or community acquired" and "Transplant-acquired" may not add up exactly to the numbers in the Total column.

Freeman and Cohen (2009)[204]

This study was a comprehensive risk analysis of numerous considerations pertaining to solid organ donation. Authors emphasized that the risk of transmitting an infection to a recipient is only one among a set of competing risks, including the risk of dying while on the waitlist, the risk of dying after the transplant (regardless of the donor's status), and risks of dying from medications, employment, transportation, and recreation. Taking this broad perspective, the authors provided real-world context to critical decisions about organ donation.

Most of the data reported in the article did not address this particular research question. These include data on the transmission of other pathogens or conditions (e.g., CMV), mortality risks after receiving an organ from an extended-criteria kidney or a standard criteria kidney, and everyday mortality risks. This question specifically involves the comparison of the clinical outcomes (e.g., mortality rates) of two types of potential recipients: 1) those who remained on the waitlist, and 2) those who received organs from at-risk donors. For at-risk donors, the study only addressed mortality after HIV (see Table 3 of the article; a row for "High risk donors" appears in the HIV section).

The waitlist mortality estimates are reproduced in Table 74 below. These were based on the authors' Markov model that utilized 90-day waitlist mortality and transplantation probabilities from the OPTN/SRTR 2007 Annual Report. Authors reported rates separately for 12 different types of recipients (see table). Three-year estimates were also provided for kidney recipients. For confirmation, ECRI Institute replicated the reported results using the reported probabilities using TreeAge Pro (TreeAge Software Inc., Williamstown, MA).

The GRADE evidence profile appears in Table 76; the evidence was rated as Very Low, because it was a simulation; the GRADE rating system provides higher ratings to empirical studies.

Table 74. Waitlist Mortality Estimates by Freeman and Cohen (2009)

Type of Recipient	1-year Estimated Waitlist Mortality	3-year Estimated Waitlist Mortality
Kidney recipient, age 18-34	2.7%	9.8%
Kidney recipient, age 35-49	4.6%	17.2%
Kidney recipient, age 50-64	7.5%	28.0%
Kidney recipient, age 65+	10.5%	40.3%
Liver recipient, Model for End-Stage Liver Disease (MELD) score 10 or less	4.1%	NR
Liver recipient, MELD score 11-14	7.1%	NR
Liver recipient, MELD score 15-20	11.4%	NR
Liver recipient, MELD score 21-30	18.5%	NR
Liver recipient, MELD score 31+	37.1%	NR
Heart recipient, status 2	5.9%	NR
Heart recipient, status 1B	13.6%	NR
Heart recipient, status 1A	21.8%	NR

NR – Not reported.

Note: These data are from Table 3 of the Freeman and Cohen article.[204] Other data in that table (such as one-year mortality after receiving an immediate extended-criteria kidney, and one-year mortality after receiving an immediate standard-criteria kidney, liver or heart) do not address Question 8 of this evidence review, and therefore are not included in this table.

For consideration of at-risk donors, authors stated that "The 2,189 CDC 'high-risk' donors since 2004 have resulted in 1 HIV positive donor, corresponding to an infection risk of 46 per 100,000."(footnote b of Table 3 of the article)[204] In a conservative analysis, they assumed that HIV is 100% fatal, and therefore estimated that the HIV-related mortality per 100,000 recipients of organs from at-risk donors was 46 in 100,000. This corresponds to 0.046%, which is much lower than all of the waitlist mortality rates in Table 74 (the lowest in the entire table is 2.7%, which is 59 times higher than HIV-related mortality after receiving organs from at-risk donors). The authors concluded that the waitlist mortality risk far outweighs the risk of HIV-related mortality associated with receiving an organ from a serologically negative donor with a behavioral risk factor. They did not attempt to make mortality estimates for either HBV or HCV due to insufficient documentation in the literature regarding the mortality rate for infected recipients.

Table 75. Questions 8/9: Quality Assessment

Study	8a or 9a	8b or 9b	8c or 9c	8d or 9d	8e or 9e	8f or 9f	8g or 9g	8h or 9h
Schweitzer et al. (2007)[203]	Simulation							
Freeman and Cohen (2009)[204]			✓			✓	✓	✓

The Schweitzer et al. (2007)[203] article was not assessed with these items because it was a simulation rather than a study enrolling patients. Extensive details about this simulation appear in the text for Question 8. A checkmark (✓) means that the study met the quality criterion for this Question; the lack of a checkmark means that the study either did not meet the criterion, or it was unclear whether the study met the criterion. The criteria specific to this Question were:

8a. Were the patients randomly assigned to treatments?

8b. Was the study planned prospectively (i.e., before any data were collected)

8c. Were all consecutive patients enrolled (or a random sample of eligible patients)?

8d. Were the two groups comparable at baseline? (age, sex, comorbidities, indication for transplant, previous duration on waitlist)

8e. If not, were statistical adjustments performed to control for baseline differences?

8f. Were the two groups treated concurrently?

8g. Did at least 85% of the study enrollees provide data?

8h. Was the between-group difference in study completion rates less than 15%?

Table 76. GRADE Table for Question 8 (Clinical Outcomes of At-risk Organs vs. Waitlist or Not-at-risk Organs)

Comparison	Outcome	Quantity and Type of Evidence	Findings	Starting Grade	Decrease GRADE					Increase GRADE			GRADE of Evidence for Outcome	Overall GRADE of Evidence Base
					Study Quality	Consistency	Directness	Precision	Publication Bias	Large Magnitude	Dose Response	Confounders would reduce the effect		
Transplant vs. discard kidneys from at-risk donors who test negative	Recipient survival	One simulation[203]	91% survival in both groups at one year. At five years, survival was 68% for the transplant group and 65% for the discard group. At 10 years, survival was 49% for the transplant group and 45% for the discard group. At 20 years, survival was 23% for the transplant group and 20% for the discard group.	Very Low	0	-1	0	0	0	0	0	0	Very Low	Very Low
	Quality of life	One simulation[203]	5.6 QALYs for the transplant strategy, compared to 5.1 QALYs for the discard strategy	Very Low	0	-1	0	0	0	0	0	0	Very Low	

Comparison	Outcome	Quantity and Type of Evidence	Findings	Starting Grade	Decrease GRADE					Increase GRADE			GRADE of Evidence for Outcome	Overall GRADE of Evidence Base
					Study Quality	Consistency	Directness	Precision	Publication Bias	Large Magnitude	Dose Response	Confounders would reduce the effect		
Waitlist survival vs. survival of infected recipients of at-risk organs	Recipient survival	One simulation[204]	One-year waitlist mortality for kidneys was 3% to 11% (increasing with age); for livers it was 4% to 37% (increasing with MELD score); for hearts it was 6% to 22% (increasing with criticality status). No mortality estimates provided for all those who received at-risk organs. Of 2,189 'high-risk' donors, there was only one confirmed cases of HIV infection.	Very Low	0	-1	0	0	0	0	0	0	Very Low	Very Low

Question 9. What is the impact of excluding potential solid organ donors with behavioral or nonbehavioral risk factors on the organ donor pool?

The exclusion of any potential donors, if employed, would reduce the size of the organ donor pool. This question is intended to quantify the size of that potential reduction if exclusion were based on the presense of a risk factor for HIV, HBV, or HCV. One study was included for this question (Schweitzer et al. (2007).[203] This simulation study was described in great detail under Question 8.

Over a 20-year period, the simulation estimated that if at-risk kidneys were excluded from transplantation, there would only be 740 transplanted kidneys per 1,000 patients, instead of 990 if at-risk donors were included in the pool. Thus 250 fewer kidneys would have been transplanted. This is a reduction of 25.3% (250/990). Note that the study only considered four types of behavioral exclusions (IDU, MSM, CSW, and prison inmates), and furthermore the study considered only HIV and HCV. Exclusions for other reasons (e.g., HBV risk, or nonbehavioral risk factors for HIV or HCV) would mean a larger reduction in the organ donor pool.

Question 10. What is the impact of false positive tests on the organ donor pool?

No studies were identified that met the inclusion criteria.

Gaps in the Current Literature

This systematic review uncovered numerous gaps in the literature about the possible transmission of HIV, HBV, or HCV through solid organ transplantation. This section describes the most prominent gaps.

In Question 1, we sought to identify literature on the prevalence and incidence of HIV, HBV, and HCV among people whose organs are being considered for donation. Only four small studies of this population were identified, and two involved living relatives wishing to donate solid organs to children, which comprise only a small proportion of potential organ donors. None of the studies reported incidence, and only two of the four studies reported rates of HIV.

In Question 2, the major gap was the lack of studies of the rate of HIV transmission. This is likely because federal regulations prohibit the use of organs from donors testing positive for HIV for transplant..

Several important gaps affect the usefulness of the current evidence for Questions 3 and 4. Very little literature on potential organ donors exists, and the applicability of data from other populations is unclear. In addition, almost no information on children was found, and there is very little information on HBV. Nearly all of the studies focused on risk factors for prevalent infection; little information on factors for incident infection, including signs and symptoms, has been published. Differentiating dependent from independent risk factors was inconsistent. Most of the information on identification of factors came from self-report, and the reliability of next-of-kin interviews on highly private and personal behavioral factors is brought into question by the sole study of potential tissue donors.

Data on performance of diagnostic tests in potential organ donors is lacking for Question 5. For some of the tests, there is no data at all. For many tests, some or most of the data is from analytic validation studies and may not be applicable to real-world use. Study of the test in relevant clinical applications, or at least reasonably similar applications or populations, is needed to draw strong conclusions regarding the 'real-world' use of these tests in this context. This is also needed to enable the calculation of useful statistics including predictive values, likelihood ratios, and post-test probabilities of diseases.

Question 6, on inactivation, only yielded a single uncontrolled study that had been published in 1994; no additional studies of the inactivation of solid organs have appeared since then. The last three questions (8 through 10) all contained low amounts of evidence, and are all potential targets for future research.

In Question 7, only one included study had a waitlist control group. Numerous studies used a control group of recipients who received organs from negative donors, however, those studies had various quality problems (e.g., differing pre-transplant characteristics, without statistical adjustment) that limit the interpretability of their results. More comprehensive analyses of competing risks (of both transplanting and discarding organs from infected donors) would help inform critical decision making.

Question 8 included only two studies, both of which estimated survival on the waitlist using Markov models. One of them also provided data for Question 9 on the size of reduction in the organ donor pool, and no studies addressed Question 10.

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Appendix A

Details of Literature Search

Electronic Database Searches

The following databases have been searched for relevant information:

Table 77. Electronic Databases Searched

Database	Date Limits	Platform/Provider
The Cochrane Central Register of Controlled Trials (CENTRAL)	Through 2009, Issue 3	www.thecochranelibrary.com
The Cochrane Database of Methodology Reviews (Methodology Reviews)	Through 2009, Issue 3	www.thecochranelibrary.com
The Cochrane Database of Systematic Reviews (Cochrane Reviews)	Through 2009, Issue 3	www.thecochranelibrary.com
Database of Abstracts of Reviews of Effects (DARE)	Through 2009, Issue 3	www.thecochranelibrary.com
EMBASE (Excerpta Medica)	1990 – July 13, 2009	OVID
Health Technology Assessment Database (HTA)	Through 2009, Issue 3	www.thecochranelibrary.com
Healthcare Standards	Searched February 10, 2009	ECRI Institute
MEDLINE	1990 – July 13, 2009 Searches for some key questions not limited by date	OVID
PreMEDLINE	Searched July 13, 2009	OVID
U.K. National Health Service Economic Evaluation Database (NHS EED)	Through 2009, Issue 3	www.thecochranelibrary.com
U.S. National Guideline Clearinghouse™ (NGC)	Searched February 10, 2009	www.ngc.gov

Hand Searches of Journal and Nonjournal Literature

Journals and supplements maintained in ECRI's collections were routinely reviewed. Nonjournal publications and conference proceedings from professional organizations, private agencies, and government agencies were also screened. Other mechanisms used to retrieve additional relevant information included review of bibliographies/reference lists from peer-reviewed and gray literature. (Gray literature consists of reports, studies, articles, and monographs produced by federal and local government agencies, private organizations, educational facilities, consulting firms, and corporations. These documents do not appear in the peer-reviewed journal literature.)

Grey Literature Searches

The following resources have been searched for information relevant to specific diagnostic tests:

Resource	Date Limits	Platform/Provider
Google *("CE Mark" OR "CE marked" OR registered) (test name)*	Searched August 8, 2009	www.google.com
Health Protection Agency Microbiological Diagnostics Assessment Service Evaluations	Searched August 7, 2009	www.hpa-midas.org.uk
HealthCanada	Searched August 8, 2009	http://www.hc-sc.gc.ca/dhp-mps/index-eng.php
Manufacturer Web sites	Searched August 8, 2009	www.abbottdiagnostics.com www.abbott.com www.abbottdiagnostics.com.au www.beckman.com www.bio-rad.com www.biomerieux.com www.biomerieux-diagnostics.com www.chiron.com www.gen-probe.com www.innogenetics.be www.orthoclinical.com www.roche.com www.roche-diagnostics.com www.siemens.com www.diagnostics.siemens.com
National Serology Reference Laboratory	Searched August 7, 2009	www.nrl.gov.au
U.S. Food and Drug Administration (FDA) Web site	Searched August 6, 2009	www.fda.gov
World Health Organization Web site	Searched August 7, 2009	www.who.int/en/

Search Strategies

The search strategies employed combinations of free text keywords as well as controlled vocabulary terms including (but not limited to) the following concepts. The strategy below is presented in OVID syntax; the search was simultaneously conducted across EMBASE, MEDLINE, and PsycINFO.
A parallel strategy was used to search the databases comprising the Cochrane Library.

Medical Subject Headings (MeSH), EMTREE and Keywords

Conventions:

OVID

$	=	truncation character (wildcard)
exp	=	"explodes" controlled vocabulary term (e.g., expands search to all more specific related terms in the vocabulary's hierarchy)
/	=	limit controlled vocabulary heading
.fs.	=	floating subheading
.hw.	=	limit to heading word
.md.	=	type of methodology (PsycINFO)
.mp.	=	combined search fields (default if no fields are specified)
.pt.	=	publication type
.ti.	=	limit to title
.tw.	=	limit to title and abstract fields

Dialog

?	=	truncation character (wildcard)
!	=	"explodes" controlled vocabulary term (e.g., expands search to all more specific related terms in the vocabulary's hierarchy)
/de	=	limit controlled vocabulary heading
pt	=	publication type
/ti	=	limit to title
/ti,ab	=	limit to title and abstract fields

Topic-specific Search Terms

Concept	Controlled Vocabulary	Keywords
Analytic validity	Accuracy Diagnostic accuracy Exp diagnostic error/ Exp diagnostic errors/ Likelihood Observer variation Precision Exp Prediction and forecasting/ Predictive value of tests Receiver operating characteristic ROC curve Sensitivity and specificity	Accurate Accuracy Analytic adj2 valid$ Borderline Concordance False negative False positive Intraobserver Intra-observer Interobserver Inter-observer Interpret$ Kappa Likelihood Observer bias Observer variability Observer variation Precision Predict$ Reader$ Reader concordance Receiver operating characteristic Reliab$ Repeatab$ Replicabil$ ROC True negative True positive Valid$ Window$ WPRT$
Diagnosis	Exp diagnosis/ di.fs. (diagnosis)	Diagnos$
Disease transmission	Disease transmission/pc Disease transmission, horizontal/pc Transmission.fs.	

Concept	Controlled Vocabulary	Keywords
Donors	Cadaver Cadaver donor Donor Kidney donor Living donor Living donors Organ donor Exp tissue/ Exp Tissue donors/ Exp Tissue and organ procurement/ Exp Transplantation Classification.fs. Supply & distribution.fs.	Donor$ Donat$
Epidemiology	eh.fs. (ethnology) ep.fs. (epidemiology) prevalence exp United States/	Epidemiol$ Incidence Prevalen$ US.ti. United States USA.tw.
Risk	Exp Anamnesis/ Behavioral risk factor surveillance system High risk behavior High risk patient High risk population Exp Medical history taking/ Medical record review Medical records Exp Physical examination/ Population characteristics Risk factor Risk factors Risk reduction behavior Risk-taking Sexual behavior Substance abuse, intravenous Unsafe sex	Behavior Chart review Gaol Haemophilia$ Hemophilia$ High adj2 risk$ Intravenous drug$ IV drug$ Incarcerat$ Inmate$ Injectable drug$ Jail$ MSM Medical history Multiple adj2 partner$ Needle adj shar$ Patient history Penitentiary Prison$ Risk (in the title) Sex
Screening	Exp Mass screening/ Exp screening/	Screen$

Concept	Controlled Vocabulary	Keywords
Solid organ & tissue transplantation	Allotransplantation Exp organ transplantation/ Transplantation, homologous Tr.fs. (transplantation)	Allograft$ Bone$ Bowel$ Composite vascular Cornea$ Face$ Hand$ Heart Homograft$ Intestin$ Kidney Liver Lung$ Ovar$ Pancreas Solid organ Testes Testicl$ Tissue$ Transplant$
Specific infections	Communicable diseases Hepatitis antigens Hepatitis b Hepatitis c Exp hepatitis b antigen/ Exp hepatitis b antigens/ Exp hepatitis c antigens/ Exp HIV Infections/ HTLV-1 infections Exp human immunodeficiency virus Human immunodeficiency virus antigen Exp human immunodeficiency virus infections/	hepatitis Hepatitis B Hepatitis C HIV$ HBV HCV
Specific publications	MMWR morbidity & mortality weekly report.jn.	

Concept	Controlled Vocabulary	Keywords
Testing	DNA microarray Exp gene amplification/ Exp hybridization/ Exp in situ hybridization/ Microarray analysis Exp Microarray analysis/ Molecular diagnostic techniques Exp molecular probe/ Exp molecular probe techniques/ Exp nucleic acid amplification techniques/ Exp nucleic acid hybridization/ Serological tests	ADVIA Centaur AMRAD anti-p22 antibody test Architect Assay$ AxSYM Blot Borderline Centaur COBAS Amplicor COBAS AmpliScreen Core Corecell haemagglutination assay CORZYME Coulter antigen Coulter p24 Elecsys Enzygnost Genetic$ adj System$ Genscreen HBsAG HIVAB INNOTEST MATRIX HCV Monolisa Murex NAT Nucleic acid amplification NucliSens-AmpliScreen Occult Ortho ELISA PCR$ PRISM ProCleix Qiagen QIAmp Roche combo Roche modular TaqMan Test$ Uni-Form VERSANT HCV VIDAS DUO Vironostika Virus BioRobot Vitros Window$ WPRT$

Concept	Controlled Vocabulary	Keywords
Virus inactivation	Exp *antiviral agents/ Exp*antivirus agent/ Virus inactivation Organ perfusion Organ preservation exp Organ preservation/ Perfusion Tissue perfusion Tissue preservation	Deactivat$ Inactivat$ Irrigat$

Searches

Unless otherwise specified, all searches were limited to human population and by date range 1990 – 2009.

Donor 1966 – 2009

Set Number	Concept	Search Statement
1	Transplantation	exp organ transplantation/
2		(((transplantation, homologous or allotransplantation).de. or tr.fs.) and (solid organ or heart or lung$ or kidney$ or liver or intestin$ or bowel$ or pancreas or face or hand$ or (composite adj vascular) or ovar$ or testes or testicl$))
3		Exp tissue transplantation/
4	Combine sets	or/1-3
5	Donors	exp tissue donors/ or exp tissue/ or living donors/ or donor/ or kidney donor/ or living donor/ or organ donor/ or cadaver donor/ or cadaver/
6		donor$.ti.
7		6 and (solid organ or heart or lung$ or kidney$ or liver or intestin$ or bowel$ or pancreas or face or hand$ or (composite adj vascular) or ovar$ or testes or testicl$)
8	Combine sets	or/5-7
9	Combine sets (tissue donors)	4 and 8
10	Specific infections	exp HIV infections/ or exp human immunodeficiency virus infections/ or exp hepatitis b antigens/ or exp hepatitis c antigens/ or exp hepatitis b antigen/ or (hepatitis b or hepatitis c or hepatitis c antigen).de. or (hepatitis adj (b or c) or HIV$)
11	Combine sets (Infections and tissue transplantation)	9 and 10
13	Limit by publication type	12 not (letter/ or editorial/ or news/ or comment/ or note/ or conference paper/ or (letter or editorial or news or comment).pt.)
14	Eliminate overlap	Remove duplicates from 13

Epidemiology (Q1) (2004-2009)

Set Number	Concept	Search Statement
1	Specific infections	exp HIV infections/ or exp human immunodeficiency virus infections/ or exp hepatitis b antigens/ or exp hepatitis c antigens/ or exp hepatitis b antigen/ or (hepatitis b or hepatitis c or hepatitis c antigen).de. or (hepatitis adj (b or c))
2	Epidemiology	1 and ep.fs.
3		1 and eh.fs.
4		1 and prevalence.de.
5		1 and (prevalen$ or incidence or epidemiol$).ti.
6	Combine sets	or/2-5
7	Reviews	6 and review$.ti,de,pt.
8	RCTs *Narrow filter*	6 and (random$.ti. or randomized controlled trial.pt.)
9	Limit by publication type	6 not (letter/ or editorial/ or news/ or comment/ or note/ or conference paper/ or case reports/ or (letter or editorial or news or comment or case reports).pt.))
10	Systematic reviews *Broad filter*	9 and ((research synthesis or pooled).mp. or review.ti,pt. or (systematic review or meta analysis or meta-analysis).de. or ((evidence base$ or methodol$ or systematic or quantitative$ or studies).mp. and (review.de. or review.pt.)))
11	Eliminate overlap	Remove duplicates from 10
		The retrieval was still too large so we used another approach
12		5 and 11
13	Limit by region	12 and (exp United States/ or United States.tw. or us.ti. or usa.ti.)
14	HIV infections as major topic	Exp *HIV infections/ep,eh
15		Exp *human immunodeficiency virus infection/ep
16	Hepatitis infection as major topic	*hepatitis b/ep or *hepatitis c/ep
17	Combine sets	or/15-17
18	Systematic reviews *Broad filter*	17 and ((research synthesis or pooled).mp. or review.ti,pt. or (systematic review or meta analysis or meta-analysis).de. or ((evidence base$ or methodol$ or systematic or quantitative$ or studies).mp. and (review.de. or review.pt.)))
19	Limit by region	18 and (exp United States/ or United States.tw. or us.ti. or usa.ti.)

Set Number	Concept	Search Statement
20	Limit by concept	18 and prevalence.ti.
		One more another approach
21	Limit by concept	17 and prevalence.ti.
22		21 and (hepatitis or HIV$ or HBV$ or HCV$).ti.
23	Limit by publication type	22 not ((letter or editorial or news or comment or case reports or note or conference paper).de. or (letter or editorial or news or comment or case reports).pt.)
24	Limit by region	23 and (exp United States/ or United States.tw. or us.ti. or usa.tw.)
25	Limit by publication	23 and mmwr morbidity & mortality weekly report.jn.
25	Author search	(Armstrong$ and Wasley$ and Simard$).au.
26	Related articles search	Find articles related to *The prevalence of hepatitis C virus infection in the United States, 1999 through 2002*

Inactivation (Q6) – includes animal population

Set Number	Concept	Search Statement
1	Transplantation	exp organ transplantation/
2		(((transplantation, homologous or allotransplantation).de. or tr.fs.) and (solid organ or heart or lung$ or kidney$ or liver or intestin$ or bowel$ or pancreas or face or hand$ or (composite adj vascular) or ovar$ or testes or testicl$))
3		Exp tissue transplantation/
4		(((transplantation, homologous or allotransplantation).de. or tr.fs.) and (tissue$ or bone$ or allograft$ or homograft$))
5	Combine sets	or/1-4
6	Organ donors	((exp tissue donors/ or exp tissue/) and organ procurement/) or (living donors or donor or kidney donor or living donor or organ donor).de.
7		donor$.ti.
8		7 and (solid organ or heart or lung$ or kidney$ or liver or intestin$ or bowel$ or pancreas or face or hand$ or (composite adj vascular) or ovar$ or testes or testicl$ or tissue or bone or allograft$ or homograft$)
9	Combine sets	6 or 8
10	Combine sets	5 or 9
11	Specific infections	exp HIV infections/ or exp human immunodeficiency virus infections/ or exp hepatitis b antigens/ or exp hepatitis c antigens/ or exp hepatitis b antigen/ or (hepatitis b or hepatitis c or hepatitis c antigen).de. or (hepatitis adj (b or c)) or HIV$
12	Infections and transplantation Combine sets	10 and 11
13	Limit by publication type	12 not ((letter or editorial or news or comment or case reports or note or conference paper).de. or (letter or editorial or news or comment or case reports).pt.)
14	Virus inactivation	13 and (Virus inactivation.de. or (inactivat$ or deactivat$).tw.)
15		13 and (Exp *antiviral agents/ or exp *antivirus agent/)
16		13 and irrigat$
17	Combine sets	or/14-16
18	Eliminate overlap	Remove duplicates from

Hepatitis B (1966 – 2009)

Set Number	Concept	Search Statement
1	Hepatitis B	Exp hepatitis b antigens/ or exp hepatitis b antigen/ or hepatitis b/ or hepatitis b or HBV
2	Diagnosis	1 and (exp diagnosis/ or di.fs. or receiver operating characteristic/ or ROC curve/ or sensitivity and specificity/ or accuracy/ or diagnostic accuracy/ or precision or exp prediction and forecasting/ or likelihood or ((false or true) adj (positive or negative)) or predictive value of tests/)
3	Molecular testing (EMTREE)	2 and (exp molecular probe/ or exp hybridization/ or exp molecular probe/ or exp gene amplification/ or Microarray analysis/ or DNA microarray/)
4	Molecular testing (MeSH)	2 and (molecular diagnostic techniques/ or exp molecular probe techniques/ or exp nucleic acid amplification techniques/ or exp nucleic acid hybridization/ or exp in situ hybridization/ or exp microarray analysis/)
5	Specific tests	((HBsAg adj2 (Elecsys or AxSYM or Architect or Centaur or Enzygnost or Vitros)) or AMRAD or NucliSens-AmpliScreen or VERSANT HCV PRISM HCV or anti-p22 antibody test or NAT or nucleic acid amplification technology or Cobas Amplicor or Qiagen QIAamp or Virus BioRobot or PCR or TaqMan or MATRIX HCV or western blot or corecell haemagglutination assay).mp,df, dm.
6	Combine sets	or/3-5
7	Eliminate overlap	Remove duplicates from 6
8	Limit by publication type	12 not ((letter or editorial or news or comment or case reports or note or conference paper).de. or (letter or editorial or news or comment or case reports).pt.)

Risk (Q3 and Q4) 7/2/09

Set Number	Concept	Search Statement
1	Specific infections	exp HIV infections/ or exp human immunodeficiency virus infections/ or exp hepatitis b antigens/ or exp hepatitis c antigens/ or exp hepatitis b antigen/ or (hepatitis b or hepatitis c or hepatitis c antigen).de. or (hepatitis adj (b or c) or HIV)
2	Donors	((exp tissue donors/ or exp tissue/) and organ procurement/) or (living donors or donor or kidney donor or living donor or organ donor or cadaver donor or cadaver).de. or donor$ or donat$
3	Risk	(risk-taking or risk reduction behavior or behavioral risk factor surveillance system or risk factors or population characteristics or sexual behavior or unsafe sex or substance abuse, intravenous).de.
4		(high risk behavior or risk factor or high risk population or high risk patient).de.
5		(high adj2 risk$).ti. or (multiple adj2 partner$) or ((intravenous or iv or injectable) adj drug$) or (needle adj shar$) or hemophilia$ or haemophilia$ or incarcerat$ or prison$ or gaol or jail$ or inmate$ or MSM.tw.
6	Donor history	(exp Medical history taking/ or exp Physical examination/ or exp Anamnesis/ or exp Physical examination/ or (medical records or medical record review).de. or ((Medical or patient) adj history) or chart review)
7	Combine sets	or/3-6
8	Combine sets	1 and 2 and 6
9	Eliminate overlap	Remove duplicates from 7
10	Limit by publication type	8 not ((letter or editorial or news or comment or case reports or note or conference paper).de. or (letter or editorial or news or comment or case reports).pt.)
11	Limit by major concept	10 and (*risk factor/ or *risk factors/ or *risk-taking/ or *high risk behavior/)
12	Limit by concept	10 and risk$.ti.
14	Limit by concept	10 and (behavio?r$ or sex$)
15	Combine sets	6 and 10
16	Combine sets	or/11-15

Screening

Set Number	Concept	Search Statement
1	Specific infections	exp HIV infections/ or exp human immunodeficiency virus infections/ or exp hepatitis b antigens/ or exp hepatitis c antigens/ or exp hepatitis b antigen/ or (hepatitis b or hepatitis c or hepatitis c antigen).de. or (hepatitis adj (b or c))
2	Screening	1 and (screen$.ti. or exp screening/ or exp mass screening/)
3	Limit by publication type	2 not ((letter or editorial or news or comment or note or conference paper).de. or (letter or editorial or news or comment).pt.)
6	Eliminate overlap	Remove duplicates from 5
7	Analytic validity of tests	6 and (Analytic adj2 valid$)
8		Exp “prediction and forecasting”/
9		6 and 8
10		6 and ((predictive value of tests or receiver operating characteristic or ROC curve or sensitivity and specificity or accuracy or diagnostic accuracy or precision or likelihood).de. or ((false or true) adj (positive or negative)))
11		6 and Valid$.ti,ab.
12		6 and ((intraobserver or intra-observer or interobserver or inter-observer or interpret$ or kappa or observer bias or observer variability or reader$ or reader concordance or reliab$ or repeatab$ or replicat$).tw. or observer variation.de.)
13	Combine sets	or/7,9-12
14	Donors	13 and ((Living donor or cadaver donor).de. or exp Tissue donors/ or exp transplantation/ or donor$ or donat$)
15		exp “Tissue and organ procurement”/
16	Combine sets	13 and 15
17	Combine sets	14 or 16
18	Combine sets	13 not 17

Specific Tests (Q5)

Set Number	Concept	Search Statement
1	Genetics System (GS) HIV 1-1/HIV-2 Plus 0 EIA	((genetic$ adj system$) and ((HIV$ or HBV$ or HCV$ or HbsAg or anti-HB$ or anti-HC$ or HBc$) or Bio-Rad or Biorad).mp.) or (genetic$ adj system$).dv.
2	HIVAB HIV-1/HIV-2 (rDNA) EIA	HIVAB$.mp,dv.
3	AxSYM	(AxSYM and (core$ or HIV$ or HBV$ or HCV$ or HbsAg or anti-HB$ or anti-HC$ or HBc$)).mp,dv.
4	ADVIA Centaur	(ADVIA Centaur and (core$ or HIV$ or HBV$ or HCV$ or HbsAg or anti-HB$ or anti-HC$ or HBc$)).mp,dv.
5	PRISM	(PRISM and (core$ or HIV$ or HBV$ or HCV$ or HbsAg or anti-HB$ or anti-HC$ or HBc$)).mp,dv.
6	CORZYME	(CORZYME and (core$ or HIV$ or HBV$ or HCV$ or HbsAg or anti-HB$ or anti-HC$ or HBc$)).mp,dv.
7	COBAS AmpliScreen	((COBAS and (core or AmpliScreen)) and (core$ or HIV$ or HBV$ or HCV$ or HbsAg or anti-HB$ or anti-HC$ or HBc$)).mp,dv.
8	ProCleix HIV-1/HCV	(ProCleix and (core$ or HIV$ or HBV$ or HCV$ or HbsAg or anti-HB$ or anti-HC$ or HBc$)).mp,dv.
9	VIDAS DUO	((VIDAS and DUO) and (core$ or HIV$ or HBV$ or HCV$ or HbsAg or anti-HB$ or anti-HC$ or HBc$)).mp,dv.
10	ARCHITECT	(ARCHITECT and (core$ or HIV$ or HBV$ or HCV$ or HbsAg or anti-HB$ or anti-HC$ or HBc$)).mp,dv.
11	Genscreen	(Genscreen and (core$ or HIV$ or HBV$ or HCV$ or HbsAg or anti-HB$ or anti-HC$ or HBc$)).mp,dv.
12	Murex	(Murex and (core$ or HIV$ or HBV$ or HCV$ or HbsAg or anti-HB$ or anti-HC$ or HBc$)).mp,dv.
13	Enzygnost	(Enzygnost and (core$ or HIV$ or HBV$ or HCV$ or HbsAg or anti-HB$ or anti-HC$ or HBc$)).mp,dv.
14	Vironostika	((Vironostika or Uni-Form) and (core$ or HIV$ or HBV$ or HCV$ or HbsAg or anti-HB$ or anti-HC$ or HBc$)).mp,dv.
15	INNOTEST	(INNOTEST and (core$ or HIV$ or HBV$ or HCV$ or HbsAg or anti-HB$ or anti-HC$ or HBc$)).mp,dv.
16	Monolisa	(Monolisa and (core$ or HIV$ or HBV$ or HCV$ or HbsAg or anti-HB$ or anti-HC$ or HBc$)).mp,dv.
17	Ortho ELISA v 3	(Ortho and ELISA and (core$ or HIV$ or HBV$ or HCV$ or HbsAg or anti-HB$ or anti-HC$ or HBc$)).mp,dv.
18	Coulter HIV-1 p24 Antigen Assay	(Coulter and (antigen$ or p24) and (core$ or HIV$ or HBV$ or HCV$ or HbsAg or anti-HB$ or anti-HC$ or HBc$)).mp,dv.

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19	Modular HIV Combo	(Roche and (modular or combo) and (core$ or HIV$ or HBV$ or HCV$ or HbsAg or anti-HB$ or anti-HC$ or HBc$)).mp,dv.
20	HCV EIA 2.0	(Abbot and EIA and 2$ and (core$ or HIV$ or HBV$ or HCV$ or HbsAg or anti-HB$ or anti-HC$ or HBc$)).mp,dv.
21	Combine sets	or/1-20
22	Eliminate overlap	Remove duplicates from 21
23	Limit by publication type	22 not ((letter or editorial or news or comment or case reports or note or conference paper).de. or (letter or editorial or news or comment or case reports).pt.)
24	Limit to diagnosis & screening	23 and (screen$ or diagnos$.tw. or exp diagnosis/ or di.fs. or receiver operating characteristic.de. or ROC curve.de. or sensitivity and specificity/ or accuracy.de. or diagnostic accuracy.de. or precision or exp prediction and forecasting/ or exp diagnostic errors/ or exp diagnostic error/ or likelihood or ((false or true) adj (positive or negative)) or predictive value of tests.de.)
25	Window	23 and (window$ or WPRT$).tw.
26	Combine sets	24 or 25
27		23 and borderline$
28	Combine sets	26 or 27
29		23 and occult$
30	Combine sets	28 or 29