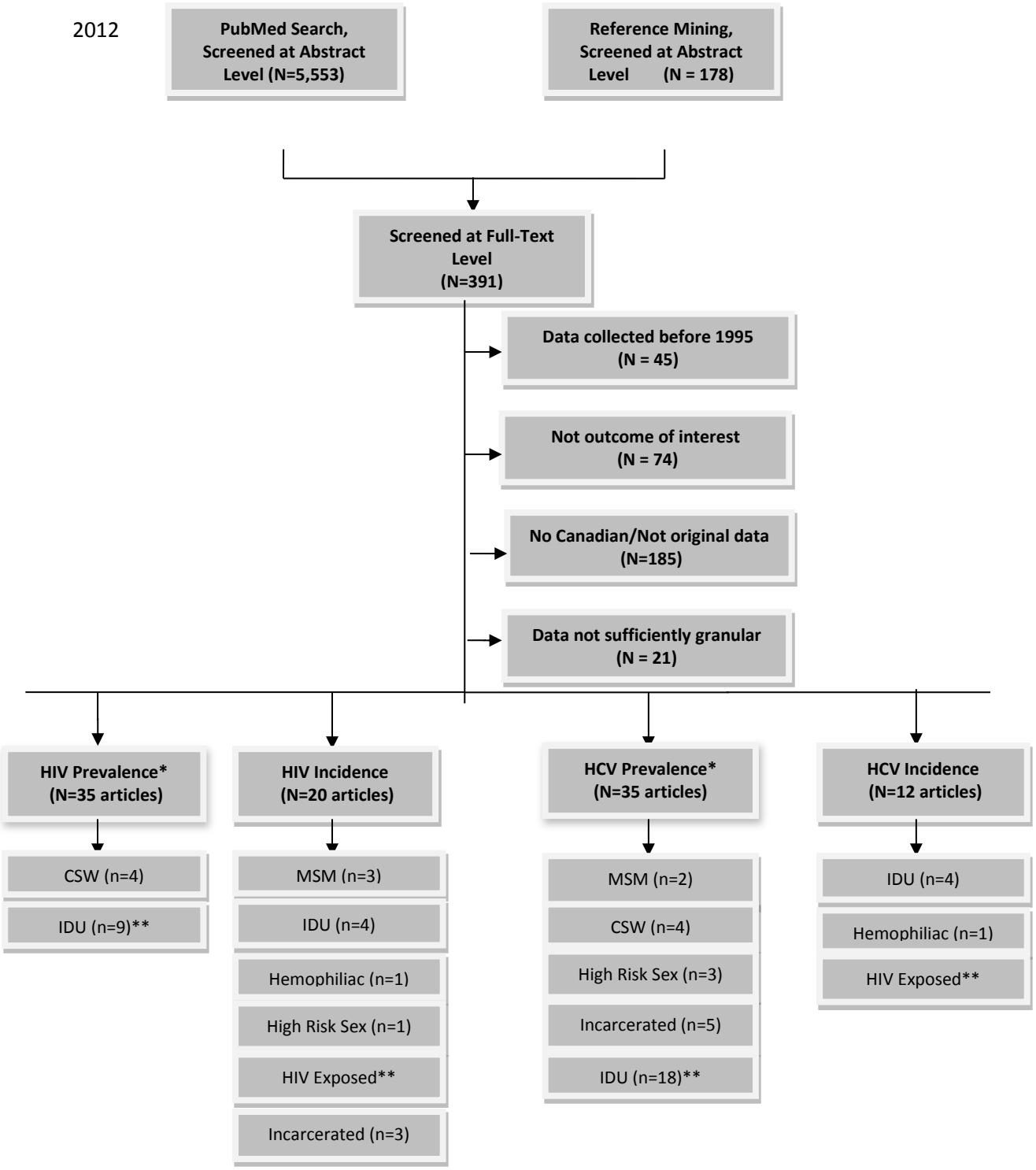
APPENDIX S1: Supplementary Material related to residual risk estimation:

Figure 1: Search/Selection of studies published between January 1st, 1995 and December 12th, 2012



*****Prevalence estimates were not included for HRD categories with sufficient incidence data available. **When estimating prevalence from incidence, IDU was the reference category as this category had the highest number of incidence and prevalence measurements.

Study selection, search strategy, and data abstraction

Any study reporting an original estimate of HIV of HCV prevalence or incidence in Canada after January 1st, 1995 was eligible. Prevalence/incidence had to be measured by detection of antibodies, proteins, or RNA; studies based on self-report alone were excluded, as were estimates without a defined denominator. We searched PubMed for studies meeting these criteria on December 12th, 2012. All abstracts were screened by 2 independent reviewers (EC and BB), and disagreements were adjudicated by another 2 (DS and LK). The following data were abstracted from each article: dates of recruitment, state, city, and specific location of recruitment, sampling method, inclusion criteria, testing methods, number of patients approached, eligible, tested, and positive. For incidence studies, the number of seronegative patients eligible for follow-up, the number tested at follow-up, the number of seroconversions, incidence rate, and total number of person-years at risk were all abstracted.

Meta-Analysis

Studies of HIV and HCV incidence were pooled within each HRD behavioral category. Poisson exact confidence intervals were calculated for each pooled incidence estimate using STATA 12/MP (College Station, TX, USA). Studies in the same category that took place in the same geographic location were reevaluated to ensure that the estimates were not derived from the same cohort. For categories where incidence data was unavailable, incidence was estimated from prevalence using methods previously described, with the incidence and prevalence among IDUs, the category with the largest number of participants, used as a reference.

Estimating the risk of WP infection

Pooled incidence estimates were used to calculate the risk of WP infection using the equation below (Figure 2A). We used studies of HIV and HCV incidence in Canadian blood donors to estimate the risk of WP infection in hemophiliacs using the equation below (Figure 2B and 2C). To ensure conservative estimates, we used the upper bounds of the 95% CI of the HIV and HCV NATs used for screening the blood supply, and assumed a hemophiliac received one unit of blood per day for the entire duration of the WP. The risk of WP infection in the category "exposed to HIV (+) blood)" was calculated using estimates from a recent review of sharps injuries with HIV-infected blood that pooled 5810 participants from 25 studies. The per-exposure risk of transmission was estimated to be 0.24% (95% CI: 0.14-0.40). We assumed one exposure in the year prior to donation. Similarly, a recent 55-hospital prospective cohort study of workers percutaneously exposed to HCV-infected blood found a per-exposure risk of 0.85% when the blood was co-infected with HIV. To estimate the probability that HIV-infected blood was co-infected with HCV, we compiled prevalence studies of HCV among HIV-positive persons.

We used the per-exposure risk of transmission to calculate the risk of WP infection using the equation below (Figure 2D).

RESULTS

Men who have sex with men (MSM)

HIV: A pooled sample of 2216 MSMs with 28,517.4 person years (pys) of follow-up yielded a pooled HIV incidence of 0.97 per 100 pys (95% CI: 0.86-1.10, Table 1). Per 10,000 donors, the risk of an HIV WP infection was 5.8 if ELISA was used (range 5.2-6.6) and 2.4 if NAT was used (range 2.1-2.7).

HCV: No eligible incidence studies were identified; incidence was estimated from prevalence (see brief methods below) using a pooled sample of 3321 MSMs (Table 2). HCV incidence was estimated to be 0.79 per 100 pys (95% CI: 0.59-0.96). Per 10,000 donors, the risk of an HCV WP infection was 14.3 for ELISA (range 10.7-17.3) and 1.5 for NAT (range 1.1-1.8). .

Injection drug users (IDU)

HIV: A pooled sample of 4712 IDUs with 46,177.5 pys of follow-up yielded a pooled HIV incidence of 1.1 per 100 pys (95% CI: 1.0-1.2). Per 10,000 donors, the risk of an HIV WP infection was 6.6 for ELISA (range 6.1-7.2) and 2.7 for NAT (range 2.5-3.0).

HCV: A pooled sample of 1179 IDUs with 2332.1 pys of follow-up yielded a pooled HCV incidence of 21.3 per 100 pys. Per 10,000 donors, the risk of HCV WP infection was 377.4 for ELISA (range 346.0-412.1) and 40.8 for NAT (range 37.4-44.6).

Hemophiliacs

HIV: We used estimates of HIV incidence in Canadian blood donors to estimate the risk of WP infection in hemophiliacs (see methods for details). The most recent study in blood donors reported an HIV incidence of 0.00049 per 100 pys (95% CI: 0.00015-0.00089). Per 10,000 the risk of HIV WP infection was 0.028 for ELISA (range 0.009-0.059) and 0.014 for NAT (range 0.010-0.029).

HCV: The same study reported an HCV incidence of 0.0085 per 100 pys in Canadian blood donors (95% CI: 0.0011-0.0024). Per 10,000 the risk of HCV WP infection was 0.21 for ELISA (range 0.08-0.43) and 0.03 for NAT (0.02-0.05).

Commercial Sex Workers (CSW)

HIV: No eligible incidence studies were identified; incidence was estimated from prevalence using a pooled sample of 579 CSWs. HIV incidence was estimated to be 0.62 per 100 pys (95% CI: 0.5-0.8). Per 10,000 donors, the risk of an HIV WP infection was 3.7 for ELISA (range 3.0-4.8) and 1.5 for NAT (range 1.2-2.0).

HCV: No eligible incidence studies were identified; incidence was estimated from prevalence using a pooled sample of 479 CSWs. HCV incidence was estimated to be 15.2 per 100 pys (95% CI: 13.6-16.8). Per 10,000 donors, the risk of HCV WP infection was 270.8 per 10,000 for ELISA (range 242.6-298.9) and 29.1 per 10,000 for NAT (range 26.1-32.2).

Sex with a partner in previous four categories

HIV: Only 1 eligible incidence study was identified for this category; the number of participants was not specified but they contributed 29,695 pys of follow-up for an HIV incidence of 0.11 per 100 pys (95% CI: 0.08-0.2). Per 10,000 donors, the risk of WP HIV infection was 0.7 for ELISA (range 0.5-0.9) and 0.3 for NAT (range 0.2-0.4).

HCV: No eligible incidence studies were identified; incidence was estimated from prevalence using a pooled sample of 541 persons with high risk sexual behavior. HCV incidence was estimated to be 9.4 per 100 pys (95% CI: 8.8-10.7). Per 10,000 donors, the risk of HCV WP infection was 168.3 for ELISA (range 157.7-191.4) and 18.0 for NAT (range 16.9-20.5).

HIV exposed through blood

HIV: The risk of WP infection in this category was calculated using estimates from a recent review of sharps injuries with HIV-infected blood that pooled 5810 participants from 25 studies. The per-exposure risk of transmission was estimated to be 0.24% (95% CI: 0.14-0.40). Assuming one exposure in the year prior to donation, the risk per 10,000 donors was 1.5 for ELISA (range 0.8-2.4) and 0.6 for NAT (range 0.4-1.0).

HCV: A recent 55-hospital prospective cohort study of workers percutaneously exposed to HCV-infected blood found a per-exposure risk of 0.85% when the blood was co-infected with HIV (Table 14A). To estimate the probability that HIV-infected blood was co-infected with HCV, we compiled prevalence studies of HCV among HIV-positive persons. From a pooled sample of 121 HIV (+) persons, we found a prevalence of 90.1%. It is important to note that all persons included were also drug users (Table 14B); the prevalence of HCV may be lower in HIV (+) persons who do not use drugs. Per 10,000, the risk of WP HCV infection was 13.9 for ELISA (range 2.9-44.6) and 1.4 for NAT (range 0.3-4.3).

Incarcerated

HIV: No eligible incidence studies were identified; incidence was estimated from prevalence using a pooled sample of 3942 incarcerated persons. HIV incidence was estimated to be 0.16 per 100 pys (95% CI: 0.13-0.19). Per 10,000 donors, the risk of HIV WP infection was 1.0 for ELISA (range 0.8-1.2) and 0.4 for NAT (range 0.3-0.5).

HCV: No eligible incidence studies were identified; incidence was estimated from prevalence using a pooled sample of 3727 incarcerated persons. HCV incidence was estimated to be 6.0 per 100 pys (95% CI: 5.7-6.5). Per 10,000 donors, the risk of HCV WP infection was 107.8 for ELISA (range 102.4-116.7) and 11.5 for NAT (range 10.9-12.5).

Table S1: Risk per 10,000 of an HIV infection occurring during the Window Period, by ELISA and NAT

HRD Category	# Patients	# HIV Seroconverted	Person-Years	Pooled Incidence per 100 pys (95% CI)	ELISA Per 10,000	NAT Per 10,000
MSM	>2216	277	28517.4	0.97 (0.86-1.10)	5.8 (5.2-6.6)	2.4 (2.1-2.7)
IDU	>4712	513	46177.5	1.1 (1.0-1.2)	6.6 (6.1-7.2)	2.7 (2.5-3.0)
Hemophiliac **	4,140,862	6	1,469,070	0.00049 (0.00015-0.00089)	0.028 (.009-0.059)	0.014 (0.010-0.029)
Commercial sex worker	579	52	*	0.62 (0.5-0.8)	3.7 (3.0-4.8)	1.5 (1.2-2.0)
Sex with a partner in categories 1-4	Unk.	33	29695	0.11 (0.08-0.2)	0.7 (0.5-0.9)	0.3 (0.2-0.4)
HIV Exposed through blood***	5810			.0024 (0.0014-0.0040)	1.5 (0.8-2.4)	0.6 (0.4-1.0)
Incarcerated	3942	90	*	0.16 (0.13-0.19)	1.0 (0.8-1.2)	0.4 (0.3-0.5)

Table S2: Risk per 10,000 of an HCV infection occurring during the Window Period, by ELISA and NAT

HRD Category	# Patients	# HCV Seroconverted	Person-Years	Pooled Incidence per 100 pys (95% CI)	ELISA Per 10,000	NAT Per 10,000
MSM	3321	143	*	0.79 (0.59-0.96)	14.3 (10.7-17.3)	1.5 (1.1-1.8)
IDU	>1179	497	2332.1	21.3 (19.5-23.3)	377.4 (346.0-412.1)	40.8 (37.4-44.6)
Hemophiliac **	4,140,862	24	1,469,063	0.00163 (0.0011-0.0024)	0.21 (0.08-0.43)	0.03 0.02-0.05)
CSW	417	192	*	15.2 (13.6-16.8)	270.8 (242.6-298.9)	29.1 (26.1-32.2)
Sex with a partner in	541	154	*	9.4 (8.8-10.7)	168.3 (157.7-	18.0 (16.9-20.5)

categories 1-4					191.4)	
HIV Exposed through blood* **	121	110		0.0085 (0.0018-0.0247)	13.9 (2.9-44.6)	1.4 (0.3-4.3)
Incarcerated	3727	683	*	6.0 (5.7-6.5)	107.8 (102.4-116.7)	11.5 (10.9-12.5)

*Incidence estimated from prevalence

**Pooled incidence among blood donors was used to calculate residual risk of infection in blood supply using the upper estimate of the WP of the NAT used in blood screening (n=11 days). Residual risk in the blood supply was used to calculate the risk of WP infection in hemophiliacs, making the very conservative assumption that they received 1 unit of blood per day for the duration of WPs.

***per exposure estimate taken from a systematic review of post-needlestick HIV seroconversion. Risk of WP infection was calculated using per needlestick risk x risk of exposure occurring during the WP.

Figure S2: Equations Used in Meta-Analysis

(a) Calculating the Probability of Window Period Infection Using Pooled Incidence Estimates*

$$\textit{Risk of WP Infection} = 1 - e^{-\textit{Pooled IR*WP duration}}$$

(b) Calculating Residual Risk of Infection in Blood Donors

$$\textit{Residual Risk in Blood Donors} = 1 - e^{-\textit{IR*WP duration of blood screening test}}$$

(c) Probability that a Hemophiliac was Infected During the WP

$$\textit{P(at least 1 unit infected)} = 1 - \textit{P(unit uninfected)}^{\#\textit{Units Received in WP}}$$

(d) Risk of WP infection among persons with percutaneous exposure to known HIV infected blood

$$\textit{Risk of WP Infection} = \textit{P(infection per exposure)} \times \textit{P(exposure occurred during WP)}$$

*Within each category, the total number of PYs at risk and the total number of sero-conversions were combined to derive pooled estimates for that category. Poisson exact 95% confidence intervals (CIs) were calculated for each pooled estimate; pooled incidence estimates and the

bounds of their 95% CIs were used to derive the expected number of WP infections using the equation shown in (A)

Appendix S2: General information to be included in the patient manual / information package provided at time of the transplant evaluation or listing.

Offer of an Organ classified "at Increased Risk".

All organs transplant carry some risk of infection. All donors undergo screening tests for HIV, HBV and HCV, but none of these screening tests are able to completely eliminate the possibility of an infection. You might be offered an organ from a deceased donor that the Canadian Standards Association guidelines define as being at increased risk for transmitting infections, such as HIV, HBV, and HCV. You will be informed if this is an increased risk organ when it is offered to you. The actual risk will vary by the type of organ donor. These risks can be discussed in more detail with your transplant team. The potential advantage to accepting such an organ may include earlier access to transplantation. *Will an Increased Risk Organ Work Well?*

The increased risk does not affect how well the organ will work. It means that the donor engaged in behaviors before their death that increase the chances of having an infection. All donors are screened for infections. This includes testing for HIV, Hepatitis B, and Hepatitis C. An organ will only be offered if the results are negative. However, even with negative test results, there is still a very small chance that an organ from an increased risk donor has an infection such as HIV or Hepatitis. These are chronic diseases that are treatable though not curable. On average increased risk donors tend to be of younger age with better organ function.

Why would I be offered an Increased Risk Organ?

You will only be offered an increased risk organ if a transplant physician at your hospital feels that the benefits of transplanting you with the organ outweigh this risk. Otherwise the organ will not be offered to you. The physician will review with you the likely risks and benefits to you of accepting the increased risk organ versus waiting for another organ.

Will we know if I develop an Infection?

If you decide to accept the organ, you will be monitored after your transplant to be sure that you did not get an infection. In the unlikely case that you do get an infection, treatments are available. The infectious disease doctors will treat you, if needed.

Who decides if I should accept an Increased Risk Organ?

The decision to accept the increased risk organ is YOURS. If you decide NOT to accept the organ, you will not lose your place on the waiting list. If you have questions about organs from increased risk donors, discuss this with a member of your healthcare team while you are waiting for your transplant. IF you are offered an organ from an increased risk donor, it will be helpful to have already thought about this information.