

## APPENDIX A

### ***ESTIMATING THE NUMBER OF BLOOD TRANSFUSION RECIPIENTS INFECTED BY HEPATITIS C VIRUS IN CANADA, 1960-85 AND 1990-92***

*Robert S. Remis MD, MPH, FRCPC  
Department of Public Health Sciences, University of Toronto*

*in collaboration with the  
Hepatitis C Working Group\* for Blood-borne Pathogens Division,  
Laboratory Centre for Disease Control, Health Canada*

*\*The members of the Hepatitis C Working Group are:*

*Robert Hogg, BA, MA, PhD, British Columbia Centre for Excellence in  
HIV/AIDS, St Paul's Hospital, Vancouver, BC;  
Murray D. Krahn, MD, MHSc, FRCPC, Toronto Hospital, Toronto,  
Ontario;  
Jutta K. Preiksaitis MD, FRCPC, Walter MacKenzie Health Sciences  
Centre, University of Alberta, Edmonton, Alberta;  
Morris Sherman, MB, BCh, PhD, FCP(SA), FRCPC, The Toronto Hospital,  
Toronto, Ontario.*

*The following persons were observers: JoAnne Chiavetta, PhD, Canadian  
Red Cross Society, Toronto, Ontario; Martin Tepper MD, Shimian Zou MD  
and Bob Slinger MD (Field Epidemiologist), Blood-borne pathogens,  
Laboratory Centre for Disease Control, Health Canada, Ottawa, Ontario.*

*The analysis was supported by Robert W.H. Palmer, Toronto, Ontario.*

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## EXECUTIVE SUMMARY

Under a mandate from the Blood-borne Pathogens Division, Laboratory Centre for Disease Control, we carried out a series of analyses to estimate the number of persons infected by hepatitis C virus (HCV) through blood transfusion from 1960 to 1992. Although the original request was limited to the periods 1960-85 and 1990-92, it became clear that, as a result of new insights into the per-unit risk of HCV infection and into the survival of HCV-infected transfusion recipients, it was important to reconsider the estimates carried out earlier for the period 1986-90.

We used three different models to estimate these numbers: Model 1 was a "transmission model" in which we multiplied the number of units transfused by the HCV per-unit risk to derive the number of HCV transmissions by blood, correcting for the possibility that a recipient might receive more than one infected unit. In the second stage, we estimated the survival of HCV-infected persons from the year of transfusion to mid-1998. In Model 2, we estimated the total number of HCV-infected Canadians in mid-1998 and, using the estimated proportion due to blood transfusion, we calculated the number of persons infected through transfusion. Finally, for Model 3, we derived the number of persons living in mid-1998 who had ever been transfused and, using the proportion who became infected with HCV due to blood, we calculated the number of persons infected through blood.

We were also interested to know how many Canadians were infected with HCV and had been transfused but were *not* infected through transfusion. This number could be important in the implementation of any potential compensation program. Each of the above three models was extended to obtain an estimate of the so-called "pre-existing" HCV infections.

Based on our analyses, we estimate that approximately 34,800 Canadians living as of mid-1998 were infected by HCV through blood transfusion from 1960 to 1992. The plausible limits for this estimate derived from Monte-Carlo simulation were 26,600 and 45,400. The distribution according to period of transfusion (with plausible limits) was as follows: 1960-85, 27,700 (19,800-38,200); 1986 to March 1990, 6,600 (5,200-8,100); and April 1990 to March 1992, 450 (390-520). In addition to these infections, we estimate that approximately 21,600 HCV-infected persons (plausible limits 15,700 to 28,700) were transfused but not infected through transfusion.

In all, about 3.3 million persons alive as of mid-1998 have been transfused at some time during their lifetime and about 240,000 Canadians are infected with HCV (population rate 0.8%), independent of the source of the infection. We believe that approximately 70,000 HCV-infected persons, or about 30% of all HCV-infected persons, have been diagnosed to date.

## **1. BACKGROUND**

Before 1990, when a specific serologic test became available to test for the presence of hepatitis C virus (HCV) among blood donors, many persons receiving transfusions in Canada were infected by HCV. During the period 1986 to 1990, blood banks in the United States used surrogate testing to reduce the risk of HCV infection from units from donors more likely to be infected with HCV. In January 1998, a working group was formed to determine the number of persons infected by hepatitis C virus through transfusion during the period 1986 to 1990.

Little is known directly about the trends in post-transfusion hepatitis in Canada in the distant past. Most transfusions are administered to older patients and mortality among transfusion recipients is substantially higher than that of the general population of the same age. Nevertheless, it is also true that over half of transfusions are administered to persons less than 65 years old and that the latency for disease from blood-borne infections and, in particular, for hepatitis C may be long. Thus, there may potentially be a large number of persons infected by hepatitis C in the years before 1986 who are still alive.

An estimate of the number infected during the period 1970-85 was carried out by the Laboratory Centre for Disease Control (LCDC) in March 1998, but this work included a number of simplifying assumptions, in particular, concerning HCV prevalence among donors and survival probabilities. In May 1998, LCDC invited the members of the Working Group who prepared the estimates for the 1986-90 to review these estimates and to undertake additional analytic techniques to independently assess the earlier and later transmission of hepatitis C. It had become apparent that other techniques may be available to independently estimate the number of persons infected in this way and, thus, to "triangulate" the results of different methodologic approaches to obtain a plausible estimate. In May 1998, the Working Group was re-convened to examine transmission of hepatitis C for the period 1960-85 and July 1990 to March 1992.

## 2. METHODS

### 2.1 Model description

Three different methods were used to estimate the number of persons infected by hepatitis C virus through transfusion in the pre-1986 period. The three methods may be briefly described as follows:

**Model 1:** This model may be referred to as a "transmission model". It is based on estimating that number of units of blood actually administered and multiplying by the per-unit risk of hepatitis C virus infection from donor units to obtain the number of transfusion recipients infected by HCV each year. Finally, by applying post-transfusion mortality probabilities, we calculated the number of persons surviving from the year of transfusion to mid-1998.

**Model 2:** This model is a prevalence, or cross-sectional, approach to estimation. We first estimated the number and prevalence of hepatitis C infections in Canada in 1998. In the second stage of analysis, the number of HCV-infected persons in Canada was multiplied by the proportion of HCV infections thought to be due to the receipt of a blood transfusion. This proportion is based on surveillance-based data and clinical series in which the risk factors of patients diagnosed with hepatitis C infection have been determined.

**Model 3:** This model is a cross-sectional approach somewhat similar to Model 2, except that it was carried out in the opposite direction. First, we estimated the number and proportion of persons living in 1998 who had ever been transfused. Second, we multiplied the number of transfusion recipients by the prevalence of HCV infection among transfusion recipients. The product of these two parameters provided an independent estimate of the number of persons infected with HCV through transfusion.

Besides estimating the number of persons infected by HCV through transfusion, we were also interested in evaluating the non-negligible number of persons who were transfused and HCV-infected but not infected by transfusion. The infection from another source (e.g. injection drug use) may have been before *or* after the transfusion but before the first HCV serologic test. This number could be important in the implementation of any program that may offer compensation to persons HCV-infected through transfusion. Methods used to estimate this number were incorporated into each of the three models.

## **2.2 DETERMINATION OF VALUES FOR MODEL PARAMETERS**

For the three models, we used data from the published literature, unpublished manuscripts, reports and analyses as well as information from key informants to establish the most likely values for the model parameters. We also established plausible limits (to incorporate a certainty of approximately 95%) for parameters with uncertain values such that the actual value fell within this range of these limits for use in a Monte-Carlo simulation. The Monte-Carlo simulation provides an estimate of the range in model outputs taking into account the uncertainty in the model parameter values. Further details on the technique used are provided in Section 2.3 below.

### **2.2.1 Model 1 parameters**

Model 1 was carried out by year of transfusion and incorporated age- and sex-specific parameters. The year of transfusion was grouped into the following periods: 1960 to 1985, 1985 to March 1990, and April 1990 to March 1992.

#### ***2.2.1.1 Units of blood administered 1960-92***

Administrative reports for blood transfusion service activities were available for the years 1960 to 1992 from the Canadian Red Cross Society. For the years for which such data were available, namely 1970 to 1992, we summed the different components administered indicated in the administrative reports (this included whole blood, red blood cells, platelets, fresh frozen plasma, frozen plasma, stored plasma and cryoprecipitate). We considered this approach to be the most accurate measure of the number of units of fresh blood and its components actually administered. We also calculated a ratio of the number of units administered to the number of units collected, for the period for which both numbers were available. For the period 1960 to 1969, when the data on the number of units administered were not available, we used the units administered to units collected ratio for 1970 to determine the number of units administered for this period. The number of units administered by year with the ratios is indicated in Table A1.

#### ***2.2.1.2 Distribution of number of units per recipient in Canada***

For several calculations within the model, it was important to have an estimate of the distribution of the number of units administered to blood transfusion recipients in Canada. For this purpose, we used the distribution developed for the study on HIV transmission by blood transfusion in Canada from 1978 to 1985 carried out by Remis and Palmer for Health Canada in 1994. Briefly, the distribution was derived from studies on each of the components including red cells, platelets and plasma, as well as from a study by Chiavetta on red cell distributions in hospitals in the Toronto region. For cryoprecipitate, key informants were used to estimate the number of persons who received cryoprecipitate and the mean number of units received in any given year. These

four distributions were overlaid and weighted according to their relative importance to obtain a final, overall distribution. The distribution by units is shown in Table A2.

### ***2.2.1.3 Age distribution of transfusion recipients***

It is clear that the distribution of units administered according to the age of the recipient is an important determinant of the final result, since mortality is intimately linked to the sex and, in particular, the age of the transfusion recipient. Limited data are available on the age distribution of persons receiving blood in Canada in recent years. Therefore, for this purpose, we began with the distribution of blood as reported by Vamvakas and Taswell (1) to establish a starting point to determine the most likely distribution. The distribution was then adjusted to fit the data from the study by Chiavetta on red blood cell administration in 45 hospitals in the Toronto region in the late 1980's (2). These distributions differed somewhat, especially for younger recipients. Since each of these studies may not be representative of the situation for Canada as a whole over the study period, we used a final distribution which was intermediate between the two studies.

Finally, to validate the distribution by age, we compared the age of transfusion generated by our model to the results of the age of transfusion age distribution observed by the British Columbia Provincial Notification Program (3). In carrying out this comparison, we took into account the fact that most HCV infections among young adults 20 to 39 years of age were acquired by routes other than blood transfusion.

The distribution according to age and sex is shown in Table A3 and illustrated in Figure 1. Note that the median age at transfusion was approximately 64 years for men and 63 for women. This is in agreement with data from other studies on the median age at transfusion.

### ***2.2.1.4 Per-unit risk of HCV infection, 1960-1992***

The other important component of the model, namely the per-unit risk of HCV infection, is not precisely known during the period of the analysis. In fact, no studies of post-transfusion hepatitis (PTH) were carried out in Canada until the 1980's. During the course of the study, however, we were able to obtain data from six studies, five of which were from Canada, which examined HCV transmission by transfusion from 1983 through 1990 (4-12), helping us to derive a reasonable estimate of HCV prevalence among donors and, therefore, the per-unit risk for recipients. The prospective studies in which recipients infected by HCV before the transfusion could be eliminated from the analyses were given more weight than data from the observational, lookback studies.

For the purposes of this analysis, we used the observed HCV prevalence in the spring of 1990 when HCV screening of blood units began in Canada. It allowed us to assess the per-unit HCV risk for 1990 using observed data. Since the initial screening was carried out with the first

generation EIA test (EIA1), we calculated the "true" HCV prevalence by dividing by the sensitivity. One must also take into account the observation that not all donors with anti-HCV antibody (for the most part, presumed infected) result in HCV transmission to the recipient. A number of studies have addressed this question (13-16); many of the issues are complex. We carefully reviewed several studies which examined PTH among blood transfusions, and re-analysed them using the following assumptions: (1) all HCV transmissions would be identified among those with PTH; and (2) the second-generation EIA test has essentially 100% sensitivity. Based on this analysis, we concluded that EIA1 sensitivity was 80% and overall infectivity 92%. Thus, the proportion of *infectious units* that would be detected by EIA1 is 87%. This value corresponded closely to the observations of both Aach (13) and the Gonzales (15). Based on these parameters, the per-unit infectious HCV risk in Canada just before HCV testing began would be 0.185% (0.161%/0.87).

A number of studies carried out in 1980's were examined to attempt to estimate the per-unit risk of HCV infection associated with blood transfusion in earlier years. A summary of the studies used to estimate the per-unit infectivity from HCV derived by the authors or by our own calculation is shown in Table A4.

A prospective study by Feinman and colleagues in Toronto carried out in 1983 to 1985 (4) observed a rate of PTH of 9.2%. Later, stored specimens from this study were examined for EIA1 (5) and subsequently by EIA2 (6) for HCV antibody. A per-patient risk of HCV of 3.1% was observed (18 of 576). It is not clear from either of the two latter reports whether the repeat reactive EIA results were confirmed by immunoblot. We were also unable to determine precisely the mean number of units administered per patient due to inconsistencies in the data as presented. However, the authors present data on administrations in the Discussion that seemed plausible, which yielded an estimate of mean the number of units per patient received of 4.26, with a resulting per-unit risk of 0.73%.

A study carried out by Preiksaitis in blood transfusion recipients in Edmonton in 1983 to 1985 (9) calculated a per-unit HCV risk of 0.17%. Finally, a study carried out in Vancouver, British Columbia at the BC Women's and Children's Hospital (10) provided data that allowed us to estimate the per-unit HCV risk; this was 0.60%. The results of fitting a curve using the formula  $1 - [(1-p)^n]$  (where  $p$  is the risk per-unit and  $n$  is the number of units) suggested that there was minimal pre-existing HCV infection in this population (about 63% of patients were under 20 and 77% under 30 years of age). We plotted the estimates from different centres, adjusting for the relative prevalence of HCV when HCV screening began in 1990 (see Table A5). HCV prevalence decreased by a factor of about 2.5 fold from 1984 to 1990 for British Columbia and Edmonton. Before 1983, it appears that HCV prevalence was stable; this appeared to be the case as in the United States, based on several studies in that country summarized recently by Tobler and Busch (17). We assumed, based on the prevalence of HBsAg among persons at high risk for HCV and HBV, that the implementation of HBsAg testing in 1973 reduced the HCV prevalence by 5%.

We compared the U.S. experience with hepatitis C virus with that in Canada. All indications, including a population-based study from NHANES in the U.S. (18) and a population-based estimate in Quebec by Joly and colleagues (19) appeared to indicate that population prevalence, donor HCV prevalence and the incidence of HCV-PTH are each approximately double in the U.S. compared to Canada. Our estimate of a per-unit HCV risk of 0.40% for Canada in 1982 and a per-transfusion episode risk of 2 to 3% is consistent with this observation. The estimate for 1984 appears to be from 0.3% to 0.5%; it is difficult, given the lack of studies from other centres in Canada and the limited study years, to be more precise than this. The uncertainty in the HCV per-unit risk is incorporated in the Monte-Carlo simulations (see below).

We derived an estimate for the national per-unit risk for the median year when the study was carried out by weighting the per-unit risk observed in the study using the relative prevalence of HCV among blood donors donating in 1990. Table A5 shows the summary results of this exercise and Figure 2 depicts this in graphic form. The final per-unit risk of HCV for the entire study period, i.e. from 1960 to 1992, used in Model 1 is shown in Table A6.

#### ***2.2.1.5 Correction for multiple exposures to HCV-infected units***

When prevalence is low, the number of persons infected by any blood-borne pathogen can be derived simply by multiplying the number of units administered times the risk per unit due to that pathogen. However, when prevalence is more than negligible, this simple relationship no longer holds, since in such a case more than one infected unit may be transfused into any given recipient. The correct formula for calculating this risk is  $1 - [(1-p)^n]$  (where  $p$  is the risk per-unit and  $n$  is the number of units). To correct for this potential source of error, we adjusted the final number of persons infected by HCV according to the prevalence for each of the years in the final spreadsheet model. The correction was minimal for the per-unit HCV risk since 1990 where the correction factor was less than 1.0%. However, for the per-unit risk of 0.40% before 1983, the correction factor was about 8%. The correction factor used at each level of per-unit HCV risk is shown in Column 5 of Table A6.

#### ***2.2.1.6 Survival of transfusion recipients***

The mortality among transfusion recipients in Canada is not well characterized. No prospective studies in this group have been carried out which ensure active follow-up to determine vital status for an extended period of time following transfusion. It is clear that patients who are transfused have markedly reduced survival, related mostly of course to the medical or surgical condition for which the transfusion was required. For a minority of patients (e.g. obstetrical cases, some trauma patients), life expectancy may return to virtually normal after the acute period of care (and transfusion), but for most patients survival remains compromised for a long and probably indefinite period following transfusion. The study by Chiavetta in 45 acute-care hospitals in the Toronto region observed an in-hospital (immediate) mortality of transfusion recipients of 13%,



compared to 2% for patients admitted to the same hospitals who were not transfused (2). This is obviously much greater than for an age-matched cohort during the same, relatively brief period.

Only one population-based cohort study has been carried out to date, in Olmstead County, Minnesota, USA (20,21), in which 802 patients transfused in 1981 were followed for a period of 10 years. This study observed a crude 10-year survival of 48%, compared to the survival of an age-matched population of about 70%. Survival was a function of age at transfusion, gender and number of units received. In a program to notify transfusion recipients in British Columbia to encourage HCV testing, approximately 60% of recipients identified were alive at about 9.5 years. This translates into a 10-year survival of about 58%. According to the principal investigator (22), approximately 5% of transfusion recipients overall who died in hospital or otherwise soon after transfusion were excluded. Thus, the corrected survival at 10 years among those transfused in B.C. from 1985-90 is probably about 55%.

There is reason to believe that mortality among residents of Olmstead County may be somewhat greater than that among Canadian transfusion recipients. According to information provided by Dr. Vamvakas (23), one of the two authors of the study, the transfusion service at one of the major hospitals providing care in Olmstead County adopted a conservative transfusion policy such that transfusion was reserved for patients for whom the need was life-saving and beyond doubt. Preliminary comparative calculations of transfusion intensity revealed that the transfusion rates (patients transfused/population) in 1981 using Canadian Red Cross administrative data were in fact about 10% lower in Olmstead County than in Canada as a whole. Thus, transfusion patients included in the Minnesota study may have been, on the whole, more severely ill than patients in Canada and therefore their survival would be less favourable. Thus, a 10-year survival of transfusion recipients in Canada of 55% is very plausible. This was used for the base-case analysis in Model 1.

In addition to the above considerations, any estimation of the mortality experience of transfusion recipients must take into consideration the distribution of number of units received by the recipients. Because the occurrence of an HCV infection is a probabilistic event, it follows that the distribution of number of units among those who are HCV-infected will be different from that among all transfusion recipients. HCV-infected recipients will have received a substantially higher mean and median number of units.

We carried out preliminary calculations using the distribution of number of units administered in Canada in 1985 from a study of HIV transmission by blood transfusion carried out by Remis and Palmer in 1994 for Health Canada (24). The number of units varied from 1 to 500 plus. For all transfusion recipients, the mean was 5.8 units per patient and the median, 3 units. We applied the formula  $1 - [(1-p)^n]$  using a risk per unit (p) of 0.40% to examine the distribution of number of units received by HCV-infected recipients. As expected, the distribution was very different, with HCV-infected recipients having received a mean of 37 and a median of 8 units. Though only about 2% of recipients were infected, HCV-infected recipients received almost 14% of all units administered. This phenomenon is dependent on the distribution of units to recipients and on the

risk per unit. In the study of Donahue in Baltimore in 1985-86 (12), uninfected recipients received 8.3 units whereas HCV-infected recipients received 24.0 units (the degree of "shift" is probably underestimated since only persons surviving the first month or two following transfusion are included in such an analysis and those having received more units were more likely to have died [see below]). A similar observation was made in the B.C. hospital lookback study (3), with means of 6.1 and 22.7 units among all recipients and HCV-infected recipients, respectively.

The above observation is of critical importance because the mortality experience of transfusion recipients is strongly correlated with the number of units administered, with those receiving more units having poorer survival. Thus, mortality among HCV-infected transfusion patients will be substantially higher than transfusion recipients as a whole; this is independent of HCV-status of these recipients (i.e. it is a statistical phenomenon). In the prospective study of survival by Vamvakas (20), only 22% of recipients receiving more than 10 units survived to 10 years compared to about 40% of those receiving 4-10 units study and 55% of those receiving less than 4 units. This is not surprising since patients who are more severely ill tend to receive more units (e.g. patients with disseminated intravascular coagulation, serious trauma with uncontrollable bleeding, etc.). Therefore, to properly apply the appropriate survival curves, in the final analysis, we weighted the survival curves using the data of Vamvakas and colleagues according to the aggregated sub-groups stratified by number of units received.

Survival has improved over the duration of the study, with mortality being lower especially for persons 60 years of age and older. Therefore, the lifetable for the years 1960-65 was used for the survival function after 10 years for the years 1960-77 and 1991 lifetable for the years 1978-92.

A summary of 40-year survival according to the different functions described in this section is shown in Figure 3. The curve indicated as "Model 1" was that applied to transfusion recipients as a whole. The survival function used in Model 1 to estimate the number of surviving HCV-infected transfusion recipients is the curve with the steepest mortality, indicated as "unit-adjusted".

## **2.2.2 MODEL 2 PARAMETERS**

### ***2.2.2.1 HCV prevalence in Canada, 1998***

For the purposes of Model 2, it was important to have as precise an estimate as possible of HCV prevalence in the general population. To do this, we used two independent methods: we used the results of the number of seroepidemiologic studies in selected populations taking into account the strength and direction of biases in the population samples as well as the region in which the study was carried out (25-32). Secondly, HCV prevalence in the United States (based on actual measurement in a population-based sample) was prorated based on the relative prevalence of HCV in blood donors and also taking into account the number and prevalence of hepatitis C virus in injection drug users.

The only data available on HCV prevalence derived from a large, population-based sample were from a study by Joly and colleagues in Quebec in 1990-92; the study investigators kindly provided us with data from this study (19). This study measured HCV prevalence among 10,000 patients attending day surgery in 19 sentinel hospitals throughout the province of Quebec from November 1990 to October 1992 (33). We obtained custom outputs of this study which allowed us to standardize the final results for sex, age group, region of residence and HIV-positivity. Overall, we obtained a standardized HCV prevalence of about 0.64%. In discussions with Dr. Alary, one of the principal investigators in this study, and in the light of other considerations, we believe that this is likely a modest underestimate of the true population prevalence since injection drug users, comprising by far the largest single group affected by HCV (with HCV prevalence of 40-80%), both with respect to prevalence within the group and the proportion of total HCV infections, would be less likely to attend day surgery, tending rather to use emergency rooms for their medical services. On the other hand, transfusion recipients would likely be over-represented in this sample. This latter population would have an HCV prevalence of about two to three times that of the general population.

The Alary study also provided important indicators concerning the variation in HCV prevalence by age and sex and region of residence. More specifically, HCV prevalence appears to peak among persons 20 to 49 years of age, is about 1.5-2.0 times more prevalent in men than in women and is 2 to 3 times more prevalent in Montreal than outside this major urban centre. These observations are similar to those in several studies in the United States including the NHANES (18) study and a study of blood donors by Murphy (34).

A summary of the results of studies measuring HCV prevalence in selected populations in Canada is shown in Table A7. Based on these studies, we estimate that the overall prevalence of HCV infection in Canada is about 0.8%.

We developed a model for HCV prevalence by province in Canada, using HCV prevalence among donors when screening began, the population-based estimates from Quebec and data from other studies of special populations. The results of this analysis shown in Table A8. This type of analysis also allowed us to calculate the total number of HCV infections for each province and the proportion of all infections comprised in each province. According to these calculations, Ontario accounts for 44% of all Canadian HCV infections, British Columbia for 22%, Quebec for 15% and Alberta, 11%. The other six provinces, namely Manitoba, Saskatchewan and the Atlantic provinces and the territories together account for only about 8% of HCV infections in Canada. The age and sex specific HCV prevalences, derived from the assumption noted above, were used to develop the first part of Model 2, namely the prevalence of HCV by age group and sex. The population estimates for 1996 were obtained from Statistics Canada.

Data were available from Ontario (35) and from six provinces and both territories in which hepatitis C was reportable since 1994 or earlier (36). Correcting for the provinces for which hepatitis C is not yet reported, it appears that approximately 70,000 HCV infections have been diagnosed in Canada to 1997.

### ***2.2.2.2 Proportion of HCV infections due to transfusion***

Limited data are available on the proportion of HCV infections caused by transfusion or in which transfusion was named as a possible source (35,37,38). Custom outputs from the 8-city sentinel study on reported HCV cases carried out by LCDC in 1993-95 (38) and expert opinion within the working group allowed us to develop working estimates of the proportion of HCV infections by age and sex that were likely due to transfusion. Custom outputs were also available the surveillance program of the Ontario Ministry of Health and from a study of blood donors. The studies and databases examined are summarized in Table A9.

All data examined contained important biases that were difficult to characterize or quantify. Some analyses contained both prevalent and incident cases (with the proportion of each not known) and since, the incidence of HCV infection due to transfusion changed dramatically from 1983 to 1992, these data are difficult to interpret. Nevertheless, based on careful review of these studies, the available data is consistent with an estimate of 15% of *prevalent* HCV infections being due to transfusion, with a plausible range of 10 to 20%.

### **2.2.3 MODEL 3**

#### ***2.2.3.1 Number of transfusion recipients in Canada***

There is limited data available on the proportion of the Canadian population that has been transfused; therefore, we also used indirect methods allowed us to obtain plausible estimates of this number. According to a study of U.S. blood donors in the U.S. by Murphy (34), 6.0% of donors have been transfused. However, this is likely to be an underestimate since blood donors are generally under 65 and many of the transfusion recipients are 65 or older. Also, blood donors tend to be in better health than the population as a whole since blood transfusion recipients would be more likely to have contra-indications for donating blood. A survey in Alberta on a population sample of 1,200 adults found a lifetime history of receipt of blood or blood products of 22%. This appears to be higher than is likely in our opinion perhaps in part because of the form of the question (“Have you ever received blood or blood products?”) which may have led to some misunderstanding.

A study from the Canadian Health Monitor (39) on the proportion of Canadians transfused between 1978 and 1985 provided for estimates in the range of 5% to 7%. The question asked in this survey was “Have you been transfused from 1978 to 1985”. A similar study carried out in Quebec in the context of the *Operation Transfusion* program in 1993 (40) found a substantially lower number when the same question was asked: only 3% of adults asked reported a history of transfusion during the same 1978 to 1985 period.

We also used an independent method to estimate the number of persons receiving transfusions as an extension of the calculations for Model 1. We used the number of units administered in

Canada from 1960 to 1992 and adjusted for the number of recipients using a mean number of units received between 6 and 7 units and subjected the recipients to a survival curve derived from our final model for survival. This survival was somewhat better than that observed by Vamvakas and only slightly lower than the British Columbia hospital-based HCV notification program; thus, we used a ten-year survival of 55%. According to this approach, from 2.3 to 2.7 million Canadians living in 1998 were transfused between 1960 and 1992, for a rate of about 7% to 9%.

Chiavetta carried out a survey on 6,000 blood donors to the Canadian Red Cross (41). Overall, 9.7% of donors reported ever having been transfused; this was similar for men and women.

The National Health Study (42), which surveyed 26,000 Canadian adults in 1996, included the following question: "Between 1978 and 1985, did you receive a blood transfusion?" The results were standardized for persons 18 years and older in Canada. Overall, 3.8% of women and 2.9% of men responded affirmatively, for a weighted estimate of 3.4% or 752,000 persons in Canada. In Model 1, we estimated that 33% of persons transfused from 1960 to 1992 were transfused from 1978 to 1985. Based on this, an estimated 2.28 million adults were transfused from 1960 to 1992. This figure does not include persons under 18 years of age; however, based on the data from Vamvakas (1), from Chiavetta (2) and from our own analysis, children represent about 4% of transfusion recipients. In addition, a substantial proportion of transfusion recipients do not realize they have been transfused (perhaps as many as 30% according to one HCV hospital-based HCV lookback program carried out in Hamilton in 1995 [43]), so the 2.28 million is probably an underestimate.

In summary, we feel that the limited data available and our own calculations in Model 1 support the belief that about 11% of Canadians have ever received a transfusion, with a plausible range of about 9% to 13%. This translates into an absolute number of 3.0 million persons, with a plausible range of 2.6 million to 3.8 million persons.

### ***2.2.3.2 HCV prevalence among blood transfusion recipients***

It is clear from the literature and the experience of the members of the Working Group that a not insignificant proportion of persons transfused are already infected before a transfusion. There is some data from a number of studies which provide an indication of the importance of this phenomenon. A reasonable estimate for this number would be about 1.0 to 1.2% based on data from Alberta (44). However, some of these pre-existing infections would be due to previous transfusion episodes, either during the same hospitalization or more importantly in earlier hospitalizations or medical treatments. For the sake of our study, we estimated it at approximately two-thirds of these infections would be due to sources other than blood transfusion. This allowed us, in Model 3, to calculate the number of infected transfusion recipients and apportion them according to whether or not the transfusion was the source of the infection.

## **2.3 DETERMINING PLAUSIBLE RANGES FOR POINT ESTIMATES OF MODEL OUTPUTS**

For all three models, there was uncertainty about the actual values for many of the parameters. However, the degree of imprecision varied across the model parameters. Some were known with relative certainty (e.g. the number of units of blood components administered) and others were derived through indirect methods sometimes involving speculative assumptions.

Therefore, to better reflect the uncertainties involved and to provide plausible limits around our point estimates, we subjected all three models to Monte-Carlo simulation. This involves assigning a frequency distribution for each model parameter which is not precisely known and carrying out a large number of iterative calculations of model outputs using values of the model parameters sampled according to their frequency distribution. For this purpose, we used commercial software (Crystal Ball, Version 4.0, Decisioneering, Inc, Aurora, Colorado, USA) and performed 10,000 iterations for each output.

The values for the plausible range for each parameter were based on a review of all data taking into account its precision, the laboratory and sampling methods used and the representativeness of the population studies. A summary of the point estimates and plausible range used for all model parameters is shown in A10.

### 3. RESULTS

#### 3.1 MODEL 1 OUTPUTS

The summary results of Model 1 are shown in Table 1. A total of 122,500 persons were infected with HCV through transfusion in Canada from 1960 to 1992: 920 persons were infected in 1990 to 1992, 15,700 from 1986 to 1990 and 105,900 from 1960 to 1985. The total number of HCV-infected recipients alive as of mid-1998 was 34,800 of whom 450 were infected in 1990-92, 6,600 in 1986-90 and 27,700 in 1960-85. Mortality in this population was substantial since less than 30% of HCV-infected transfusion recipients (34,800 of 122,500) are alive as of mid-1998. The numbers of infections in each of the three periods is shown in the lower right-hand corner of Table 1 in Column 6. The proportion of persons infected according to the period of infection is shown at the bottom of Column 7: 1.3% of HCV-infected persons living as of mid-1998 were infected in 1990 to 1992, approximately 19% for the period 1986 to 1990 and 80% for those infected in 1960 to 1985. The distribution of HCV-infected and surviving recipients is presented in Figure 5.

Table 2 shows the calculation of the most likely number of recipients who received blood and in the right columns of the table, those surviving to 1998 (using the overall survival probabilities for all transfusion recipients as indicated in Section 2.2.1.6 above). Using the range of 6 to 7 units, a plausible range for the mean number of units received, we observed that approximately 2.3 to 2.7 million Canadians living as of mid-1998 were transfused at some time in their life.

Figure 4 shows the distribution by age and sex of HCV-infected transfusion recipients as of mid-1998. Compared to the distributions of transfusion recipients, the age is shifted to the right and, due to their lower mortality, HCV-infected women predominate even more than for recipients as a whole.

Table A11 shows, as an example, the worksheet for 1984 from which the data were incorporated into the final summary sheet shown in Table 1. As seen in Table A11, the analysis was carried out by five-year age strata for males and females separately. The same per-unit risk of HCV as indicated on the bottom of the table was used for all age strata as was the correction factor for multiple exposures. The respective proportions surviving to mid-1998 are shown in Column 6 to obtain the final number of HCV-infected persons surviving to mid-1998 (Column 7) and then summed for both men and women across all ages. The final adjustment for unit-specific survival, as discussed in Section 2.2.1.6 above, is indicated at the bottom.

Column 6 of Table 2 indicates the number of HCV-infections among transfused persons who were *not* infected by transfusion by year of transfusion. In all, based on the analysis in Model 1, we estimate that 21,600 persons were in this category.

### **3.2 MODEL 2 RESULTS**

As noted above, Model 2 attempts to estimate the number of persons infected by HCV through blood by first estimating the number of HCV infections and then the proportions of HCV-infected persons who were infected through blood transfusion. The output is shown in Table 3.

Overall, we estimate that approximately 0.8% of Canadians are infected with HCV, for a total 240,000 persons. Of these, 155,000 are male and 85,000 female. The highest rates, and the greatest proportion of those infected, are in the age group 20 to 39: 144,000 or 60% of all infected persons were in this age category.

Overall, we estimate from this model that 36,000 persons were infected by HCV through blood transfusion. This includes persons infected before 1960 and since 1992. Neither of these are likely to be very important because of the low incidence of HCV transmission by blood since 1992 and the low proportion of persons surviving who were infected before 1960.

From the outputs from Model 2, an estimated 204,000 people were infected through other sources. Based on a lifetime transfusion rate of 12%, approximately 24,000 persons would be infected by HCV and transfused but not infected by transfusion.

### **3.3 MODEL 3 RESULTS**

The results of the estimation based on Model 3 are shown in Table 4. From this calculation, we observe that approximately 3.0 million persons in Canada have received a transfusion in Canada. This is slightly higher than the 2.3 to 2.7 million estimated from Model 1, but within the same order of magnitude. Based on estimate of an HCV prevalence of 2.0% among transfusion recipients alive as of mid-1998, 64,400 transfusion recipients are infected with HCV.

Based on the (imprecise) assumption that 70% were infected from transfusion and 30% from other causes, 45,000 recipients were infected through transfusion and 19,300 from other causes.

### **3.4 SUMMARY OF FINDINGS**

A summary of the three model outputs including the plausible range generated by the Monte-Carlo simulation is shown in Table 6. The outputs for Model 1 by year of transfusion are presented in Table 7.



## 4. DISCUSSION

A modelling exercise involving three different approaches to estimate the number of persons infected by HCV through blood transfusion in Canada yielded an overall estimate of 34,800 persons, of whom 27,700 were infected from 1960 to 1985, 6,600 from 1986 to March 1990 and about 450 from April 1990 to March 1992. In addition to these persons infected by transfusion, an additional approximately 22,200 persons were HCV-infected and transfused but not infected through transfusion.

We believe that Model 1 provides the most plausible estimates of the extent of HCV transmission by blood in Canada, both because of the simplicity of the theoretical model used and the relative precision of the parameter values available. With the data available to the Working Group at present, Models 2 and 3 could not provide a truly independent estimate since, for each of these models, one of the two principal parameters was not known and could not be estimated with precision. Nevertheless, both Models 2 and 3 added useful information about the distribution of blood transfusion and about the epidemiology of HCV in Canada. They also lent some credence to the results of Model 1 since the values for the parameters which generate comparable results were plausible.

There are a number of important limits to our study. For many of the parameters used in our models, data for Canada for the period of study were not available. Therefore, indirect methods had to be used to derive these parameters based on expert opinion, studies from other places at other times and on general principles. To deal with the uncertainty around each of the parameters, we used Monte-Carlo simulation to obtain a range of plausible estimates around the point estimates presented in our study.

We carried out our analysis of HCV transmission and survival of HCV-infected recipients from 1960 to 1992. The estimated number of persons infected in 1960 and surviving to 1998 was not negligible (about 340 persons). Applying a back-projection to estimate cases for the period 1950 to 1959 would add approximately 2,000 additional HCV-infected persons surviving to 1998.

In addition to the uncertainty around several of the parameters used in the model, we were obliged by the limited data available as well as limited time allotted to this study to make a number of assumptions. For the purposes of Model 1, we assumed that the number of units received did not vary by age or sex. This assumption is supported by the study of Chiavetta (2) which showed approximately equal mean number of units for each of the age strata presented, at least for red blood cells in the Toronto region in the late 1980's. We also assumed that the distribution of units received according to age and sex and also the overall proportions for each number of each of the levels of transfusion intensity were stable over time. This is clearly not the case since transfusion practice changed substantially during the period 1960 to 1992. In particular, new indications were developed that inclusion the administration of blood components and component therapy essentially replaced whole blood administrations in the 1980's, resulting in a much more efficient use of blood. In addition, following the recognition of the HIV problem, physicians

became more conservative about the use of blood. In the 1980's and early 1990's, there was also a decrease in blood donor availability and therefore a decrease in overall collections. This latter phenomenon was particularly important in the early 1990's but, given the relatively small number of transmissions during this period, this probably affected the study results only minimally.

In our study, we did not take into account any increased mortality that may be due to liver disease from HCV among infected transfusion recipients. Although the transfusion-related survival functions and the mortality tables do take this into account, the former includes follow-up only to 10 years before such mortality would be expected, and the latter includes only a small proportion of HCV-infected persons. The effect of this mortality would not necessarily be negligible. In the United States, an estimated 8,000 to 10,000 persons are thought to die each year from the complications of hepatitis C infection (45). Extrapolating this figure to Canada would give 500 to 600 hepatitis C-related deaths a year; 15% or 75 to 90 would be among persons infected through transfusion. Assuming minimal mortality in the first 20 years, such deaths would begin in 1980 for a total of approximately 1,350 to 1,650 cumulative deaths to 1998. This would result in an overall 5% lower number of surviving HCV-infected transfusion recipients. All of the HCV-related excess deaths would occur among persons transfused before 1980. The decrease in the number of surviving recipients due to HCV-related deaths is approximately the same as the number of surviving transfusion recipients infected in the 1950s not accounted for in our analysis.

In our study, we estimated that about 6,600 persons were infected by transfusions received from January 1986 and April 1990. This is substantially less than the approximately 12,400 incident infections estimated surviving to mid 1997 for the same period by the LCDC HCV Working Group convened in January 1998 (of which all of the current Working Group were members). There are several possible reasons for this difference. First, we projected the survivors to mid-1998, one year later than the earlier study. This, however, would result in only about 400 deaths during the additional year. We used additional data not available to the first Working Group to assess the per-unit HCV risk, resulting in a lower estimate, approximately 75% of the previous analysis. Finally and most importantly, we used a mortality function which took into account the latest results from the BC Notification Program and the results from the Olmstead County study and also were adjusted for the greater mortality associated with the substantially higher mean number of units received by HCV-infected persons compared to all recipients. The means were 37 versus 5.8 units per patient, respectively. Mortality is significantly greater for persons receiving a greater number of units. Thus, we used a 10-year survival of about 43% compared to about 68% survival used by the January Working Group.

It will be interesting to obtain and evaluate data on persons coming forward for HCV testing in the next few years. This will help validate the modelled estimates presented in this report. However, such observational data will have to be interpreted with caution. A lookback program may be carried through a public information campaign or through an archival search and active follow-up of transfused patients. The latter will be severely limited by the availability of hospital records for the distant past and the difficulty of locating recipients, given the long time lapse. Not all transfused patients will undergo HCV testing; based on the experience from the BC Program

(3) and the Hamilton hospital-based program (43), about 70% might be expected to do so. However, this proportion might not be a reliable indication of what might happen. If there were a pecuniary incentive, the proportion may be greater but, on the other hand, for periods in the more remote past, hospital records may be poorer and the knowledge or recollection of having been transfused less reliable. Finally, there may be a significant number of HCV-infected transfusion recipients for whom the assessment of transfusion as the source of the infection may be difficult.

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## **TABLES**

**Table 1**  
**Summary of HCV infections and number of surviving HCV-infected recipients Canada, 1960-92**

1	2	3	4	5	6	7
Year	Number of units admin	Per-unit HCV risk	HCV infections	Proportion surviving to 1998	Number surviving to 1998	Cumulative number surviving to 1998
1992	449 995	0,00017	75,2	0,543	40,9	40,9
1991	1 899 981	0,00017	317,7	0,502	159,4	200,3
1990b	1 424 985	0,00037	524,1	0,479	251,2	451,4
1990a	474 995	0,00185	852,1	0,457	389,8	389,8
1989	1 570 984	0,00201	3046,7	0,439	1338,6	1 728,5
1988	1 602 984	0,00223	3425,0	0,425	1455,6	3 184,1
1987	1 656 983	0,00246	3882,2	0,412	1600,9	4 785,0
1986b	641 243	0,00278	1687,7	0,400	674,6	5 459,6
1986a	1 068 739	0,00278	2812,9	0,400	1124,4	6 584,0
1985	1 745 182	0,00317	5191,9	0,387	2009,1	2 009,1
1984	1 702 183	0,00356	5631,0	0,375	2109,0	4 118,0
1983	1 576 084	0,00383	5582,8	0,362	2022,1	6 140,1
1982	1 458 885	0,00400	5383,7	0,350	1884,2	8 024,3
1981	1 378 686	0,00400	5087,7	0,338	1719,5	9 743,8
1980	1 296 687	0,00400	4785,1	0,325	1556,1	11 299,9
1979	1 268 078	0,00400	4679,6	0,314	1469,0	12 768,9
1978	1 255 403	0,00400	4632,8	0,303	1402,9	14 171,8
1977	1 176 288	0,00400	4340,8	0,292	1267,3	15 439,1
1976	1 231 887	0,00400	4546,0	0,281	1279,0	16 718,0
1975	1 218 688	0,00400	4497,3	0,250	1125,2	17 843,2
1974	1 166 088	0,00400	4303,2	0,241	1038,0	18 881,2
1973	1 210 088	0,00400	4465,6	0,232	1037,1	19 918,3
1972	1 089 089	0,00420	4202,6	0,223	938,2	20 856,5
1971	1 002 890	0,00420	3869,9	0,214	829,2	21 685,7
1970	930 520	0,00420	3590,7	0,207	742,0	22 427,7
1969	948 690	0,00420	3660,8	0,199	728,6	23 156,4
1968	946 890	0,00420	3653,8	0,191	699,5	23 855,9
1967	897 991	0,00420	3465,2	0,184	637,0	24 492,8
1966	856 391	0,00420	3304,6	0,176	582,3	25 075,2
1965	819 392	0,00420	3161,9	0,170	538,7	25 613,9
1964	804 392	0,00420	3104,0	0,164	510,4	26 124,2
1963	765 392	0,00420	2953,5	0,158	468,1	26 592,3
1962	726 393	0,00420	2803,0	0,153	427,5	27 019,8
1961	663 193	0,00420	2559,1	0,147	375,1	27 395,0
1960	626 294	0,00420	2416,7	0,142	342,5	27 737,5
<b>1990-92</b>	3 774 961		917		451	0,013
<b>1986-90</b>	7 015 928		15 707		6 584	0,189
<b>1960-85</b>	28 761 743		105 873		27 737	0,798
<b>1960-92</b>	39 552 632		122 497		34 773	1,000

**Table 2**  
**Number of persons infected and surviving to mid-1998 assuming the mean number of units received**  
**(and number of "pre-existing" HCV infections from a source other than transfusion)**

1 Number of people transfused assuming a mean number of units received of:		2		3 Proportion recipients surviving to 1998		4 Number of recipients surviving to 1998, assuming a mean number of units received of:		5		6 Number of recipients surviving with pre-existing HCV infection from other sources (assuming a mean of 6 units)	
6		7				6		7			
74 999,2	64 285,1			0,662		49 648,4	42 555,7				399,2
316 663,4	271 425,8			0,635		201 083,7	172 357,4				1616,7
237 497,6	203 569,3			0,611		145 178,9	124 439,1				1167,2
79 165,9	67 856,4			0,584		46 196,9	39 597,3				371,4
261 830,7	224 426,3			0,566		148 248,8	127 070,4				1191,9
267 163,9	228 997,7			<b>0,550</b>		146 916,7	125 928,6				1181,2
276 163,8	236 711,9			0,534		147 347,8	126 298,1				1184,7
106 873,9	91 606,2			0,517		55 274,2	47 377,9				444,4
178 123,2	152 677,0			0,517		92 123,7	78 963,2				740,7
290 863,7	249 311,7			0,501		145 632,1	124 827,6				1170,9
283 697,1	243 168,9			0,485		137 476,9	117 837,3				1105,3
262 680,6	225 154,8			0,469		123 100,4	105 514,6				989,7
243 147,5	208 412,2			0,453		110 108,2	94 378,4				885,3
229 781,0	196 955,1			0,437		100 479,3	86 125,1				807,9
216 114,5	185 241,0			0,421		90 934,9	77 944,2				731,1
211 346,3	181 154,0			0,406		85 840,6	73 577,7				690,2
209 233,9	179 343,3			0,392		81 979,7	70 268,3				659,1
196 048,0	168 041,1			0,378		74 056,9	63 477,3				595,4
205 314,6	175 983,9			0,364		74 738,6	64 061,7				600,9
203 114,6	174 098,2			0,324		65 754,1	56 360,7				528,7
194 348,0	166 584,0			0,312		60 657,2	51 991,9				487,7
201 681,3	172 869,7			0,300		60 601,8	51 944,4				487,2
181 514,8	155 584,1			0,289		52 432,4	44 942,0				421,6
167 148,3	143 270,0			0,277		46 339,7	39 719,7				372,6
155 086,7	132 931,5			0,267		41 467,1	35 543,2				333,4
158 115,0	135 527,2			0,258		40 720,4	34 903,2				327,4
157 815,1	135 270,0			0,248		39 089,6	33 505,4				314,3
149 665,1	128 284,4			0,238		35 597,7	30 512,3				286,2
142 731,9	122 341,6			0,228		32 543,6	27 894,5				261,7
136 565,3	117 055,9			0,220		30 104,5	25 803,8				242,0
134 065,3	114 913,1			0,213		28 521,9	24 447,4				229,3
127 565,4	109 341,7			0,205		26 157,7	22 420,9				210,3
121 065,4	103 770,4			0,197		23 893,4	20 480,1				192,1
110 532,2	94 741,9			0,190		20 964,2	17 969,3				168,6
104 382,3	89 470,5			0,183		19 141,5	16 407,0				153,9
				<b>1990-92</b>		395 911	339 352				3 183
				<b>1986-90</b>		636 108	545 236				5 114
				<b>1960-85</b>		1 648 334	1 412 858				13 253
				<b>1960-92</b>		2 680 354	2 297 446				21 550

Table 3

Model 2 output: Number of transfusion-associated HCV infections, by sex and age group Derived from proportion of HCV-infected persons infected by transfusion Canada, 1998

	1	2	3	4	5	6	7	8
	Population (000s)	HCV prevalence (%)	HCV infections (number)	Proportion HCV infections transfused (%)	Transfusion associated HCV infections (number)	Number HCV infected by other sources	Proportion transfused (%)	Number other HCV-infected transfused
<b>Males</b>								
0-5	1212	0,3	3636	95,0	3454	182	0,5	1
6-14	1857	0,05	929	95,0	882	47	1,0	0
15-19	1026	0,1	1026	12,0	123	903	4,0	36
20-39	4833	2	96660	9,0	8699	87961	8,0	7037
40-64	4373	1	43730	13,0	5685	38045	16,0	6087
65+	1544	0,6	9264	20,0	1853	7411	22,0	1630
Total	14845	1,05	155245	13,3	20696	134549	11,0	14792
<b>Females</b>								
0-5	1152	0,1	1152	95,0	1094	58	0,5	0
6-14	1775	0,05	888	95,0	843	45	1,0	0
15-19	977	0,1	977	18,0	176	801	3,0	24
20-39	4725	1	47250	13,0	6143	41107	10,0	4111
40-64	4392	0,5	21960	18,0	3953	18007	18,0	3241
65+	2098	0,6	12588	25,0	3147	9441	24,0	2266
Total	15119	0,56	84815	18,1	15356	69459	13,9	9643
<b>Both sexes</b>								
0-5	2364	0,2	4788	95,0	4548	240	0,5	1
6-14	3632	0,05	1816	95,0	1725	91	1,0	1
15-19	2003	0,1	2003	14,9	299	1704	3,5	60
20-39	9558	1,51	143910	10,3	14842	129068	8,6	11148
40-64	8765	0,75	65690	14,7	9638	56052	16,6	9328
65+	3642	0,6	21852	22,9	5000	16852	23,1	3896
Total	29964	0,8	240059	15,0	36052	204007	12,0	24435
Crude HCV prevalence (%)				0,8				
Proportion HCV infection due to transfusion (%)				15				
Proportion of other HCV-infected persons transfused (%)				12				



Table 4

Model 3 output: Number of transfusion-associated HCV infections, by sex and age group Derived from proportion HCV-infected among persons ever transfused Canada, January 1998

	1	2	3	4	5	6	7	8	9
	Population (000s)	Proportion ever transfused (%)	Persons ever transfused (number)	Proportion HCV infected	Proportion HCV+ recip infected by transfusion	Proportion HCV+ recip infected by other sources	Transfusion associated HCV infections (number)	Other HCV infections (number)	Total HCV infections (number)
Males									
0-5	1212	0,5	6060	0,002					
6-14	1857	1,0	18570	0,010					
15-19	1026	1,5	15390	0,015					
20-39	4833	6,0	289980	0,020					
40-64	4373	18,0	787140	0,022					
65+	1544	24,0	370560	0,027					
Total	14845	10,0	1487700	0,023	0,7	0,3	23485	10065	33550
Females									
0-5	1152	0,5	5760	0,001					
6-14	1775	1,5	26625	0,002					
15-19	977	2,0	19540	0,010					
20-39	4725	8,0	378000	0,012					
40-64	4392	20,0	878400	0,017					
65+	2098	24,0	503520	0,022					
Total	15119	12,0	1811845	0,017	0,7	0,3	21560	9240	30801
Both sexes									
0-5	2364	0,5	11820	0,000					
6-14	3632	2,0	45195	0,000					
15-19	2003	1,7	34930	0,000					
20-39	9558	7,0	667980	0,000					
40-64	8765	19,0	1665540	0,000					
65+	3642	24,0	874080	0,000					
Total	29964	11,0	3299545	0,020	0,7	0,3	45046	19305	64351
Proportion transfused (%)			11						
Proportion HCV infected (%)			2						
Proportion HCV+ from transfusion			0,7						

**Table 5**  
**Modelled transfusion-associated HCV infections and other HCV-infected persons transfused**  
**by province, Canada, 1998**

<i>Province</i>	<i>1</i> <i>Population</i> <i>(000s)</i>	<i>2</i> <i>Number</i> <i>transfusion-</i> <i>associated</i> <i>HCV infection</i> <i>number</i>	<i>3</i> <i>Prevalence</i> <i>transfusion-</i> <i>associated</i> <i>HCV infection</i> <i>(/1000 pop'n)</i>	<i>4</i> <i>Proportion</i> <i>of TA-HCV</i> <i>infections</i> <i>Canada</i> <i>(%)</i>	<i>5</i> <i>Number</i> <i>other</i> <i>HCV -infected</i> <i>persons</i> <i>transfused</i>
British Columbi	3860	7656	1,98	22,0	4752
Alberta	2790	3705	1,33	10,7	2300
Saskatchewan	1020	634	0,62	1,8	394
Manitoba	1140	902	0,79	2,6	560
Ontario	11250	15365	1,37	44,2	9537
Quebec	7390	5290	0,72	15,2	3284
New Brunswick	760	415	0,55	1,2	258
Nova Scotia	940	699	0,74	2,0	434
Prince Edward	140	50	0,36	0,1	31
Newfoundland	570	67	0,12	0,2	42
Canada	29860	34784	1,16	100,0	21590

**Note:** These estimates are subject to uncertainty; they are based on the assumption including that both transfusion-associated HCV infection and other HCV-infected persons who were transfused vary across provinces as does the relative HCV prevalence among blood donors in Canada in 1990

Number of TAI-	34800
Other HCV trar	21600

**Table 6**  
**Summary of point estimates and plausible limits of HCV-infected transfusion recipients obtained from Models 1, 2 and 3 (rounded)**  
**Persons surviving as of mid-1998**  
**Canada**

	<i>Transfusion-associated infections</i>		<i>Other HCV-infected recipients</i>	
	<i>Point estimate</i>	<i>Plausible limits</i>	<i>Point estimate</i>	<i>Plausible limits</i>
Model 1	34,800	26,600 - 45,400	21,600	15,700 - 28,700
Model 2	36,000	25,300 - 49,600	24,400	19,000 - 31,000
Model 3	45,000	29,000 - 67,700	19,300	3,400 - 34,600

**Table 7**

**Summary of point estimates and plausible limits of HCV-infected transfusion recipients obtained from Model 1 (rounded)  
By period of transfusion  
Persons surviving as of mid-1998, Canada**

	<i>Transfusion-associated infections</i>		<i>Other HCV-infected recipients</i>	
	<i>Point estimate</i>	<i>Plausible limits</i>	<i>Point estimate</i>	<i>Plausible limits</i>
<b>1960-85</b>	27,700	19,800 - 38,200	13,300	9,700 - 17,600
<b>1986-90</b>	6,600	5,200 - 8,100	5,100	3,700 - 6,800
<b>1990-92</b>	450	390 - 520	3,200	2,300 - 4,200
<b>Total</b>	34,800	26,600 - 45,400	21,600	15,700 - 28,700

## **FIGURES**

FIGURE 1

Age distribution of patients  
at time of transfusion

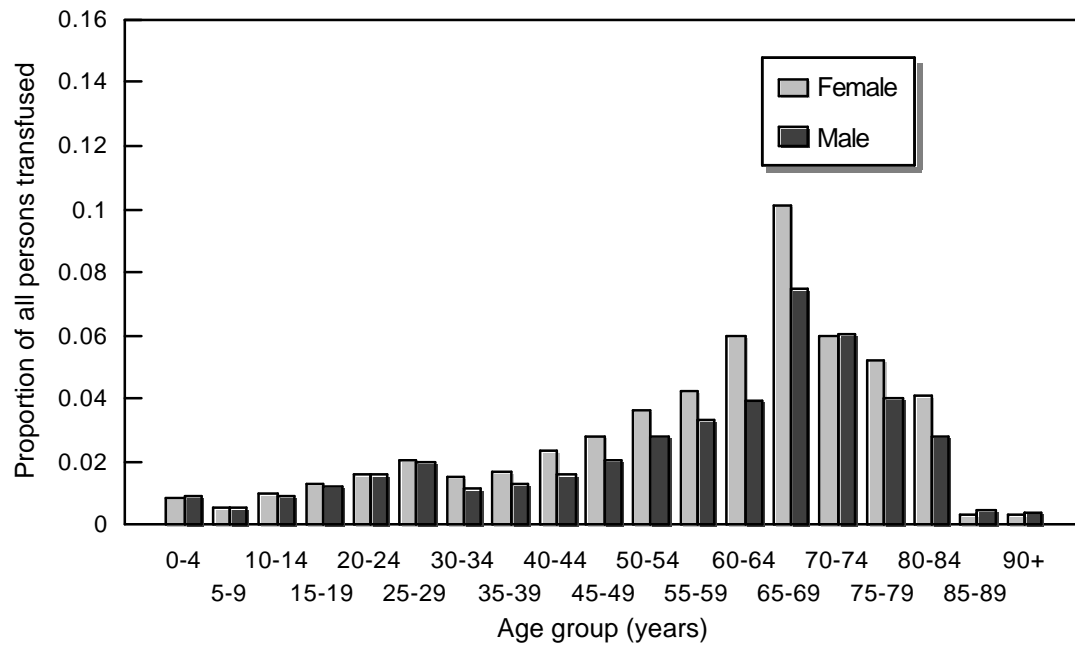


FIGURE 2

### Estimation of per-unit risk of HCV infection through transfusion Canada, 1980-90

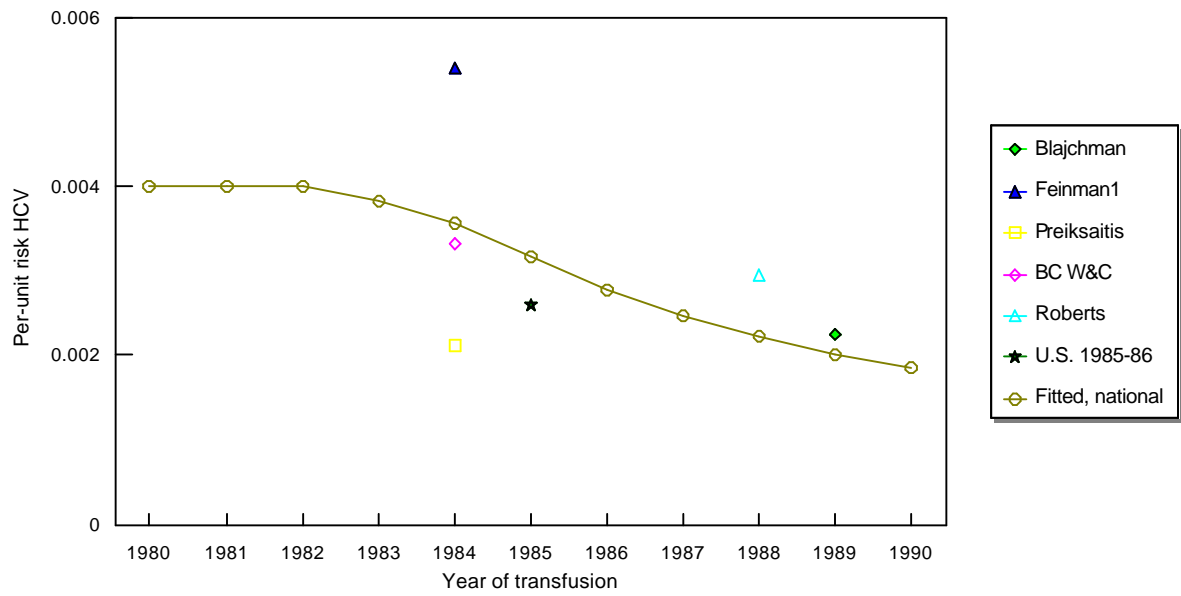


Figure 3

### Survival following transfusion

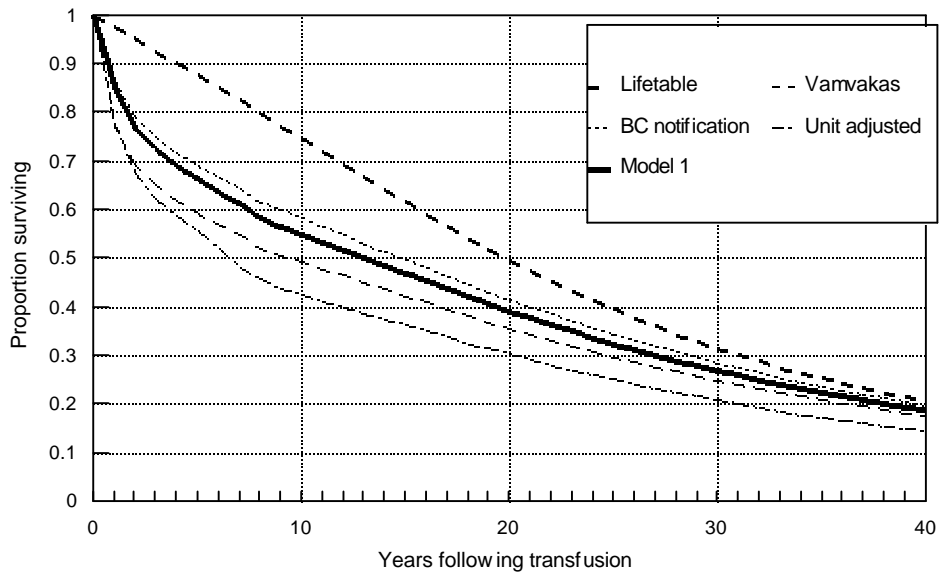




FIGURE 4

**Age distribution of HCV-infected recipients  
surviving to 1998**

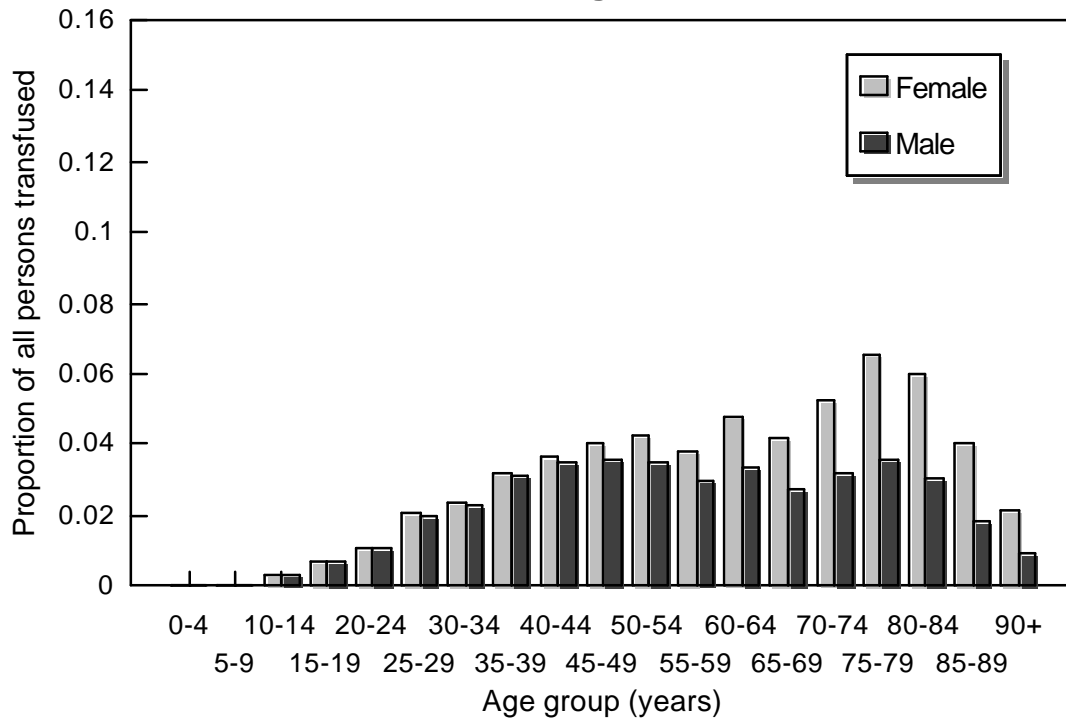
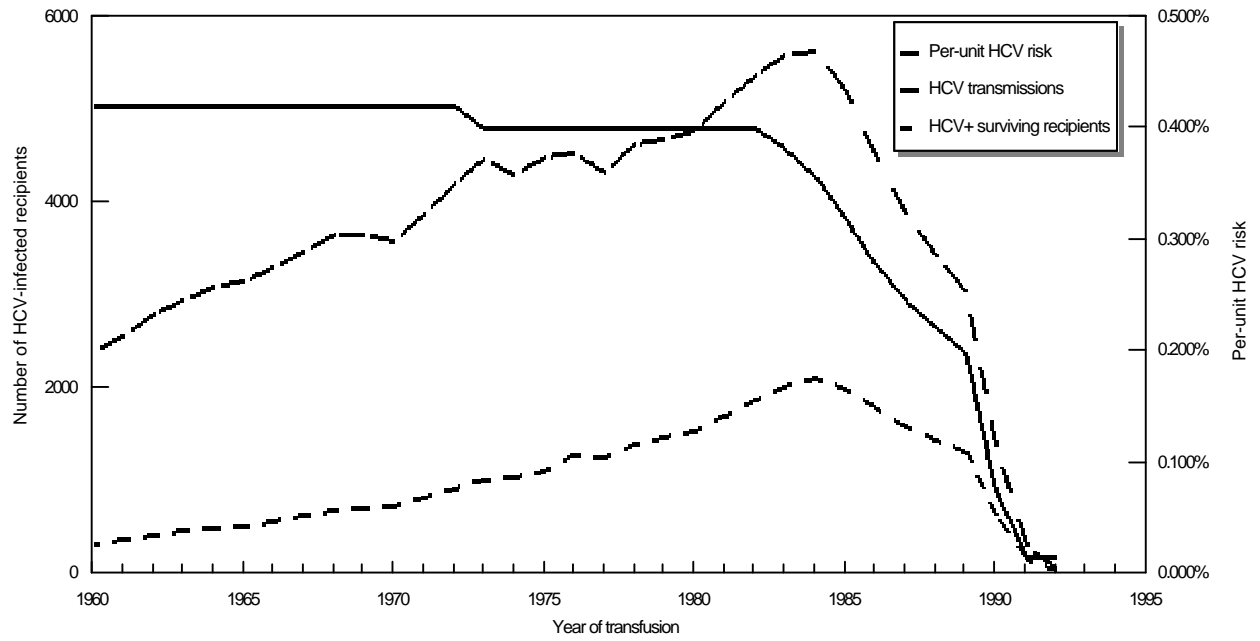


FIGURE 5

HCV transmissions by blood transfusion  
Canada, 1960-92



## **APPENDICES**

**Table A1**  
**Units of blood and its components collected and administered**  
**Canada, 1960 to 1990**

Year	Units collected	Units administered	Ratio	Partial years		
				Units collected	Units administered	
				<b>1992</b>	1 218 000	1 800 000
1992a	304 500	450 000	1,48	0,25	304 500	450 000
1991	1 283 000	1 900 000	1,48			
1990b	939 000	1 425 000	1,52	0,75	939 000	1 425 000
				<b>1990</b>	1 252 000	1 900 000
1990a	313 000	475 000	1,52	0,25	313 000	475 000
1989	1 013 000	1 571 000	1,55			
1988	1 034 000	1 603 000	1,55			
1987	1 070 000	1 657 000	1,55			
1986b	689 375	1 068 750	1,55	0,625	689 375	1 068 750
				<b>1986</b>	1 103 000	1 710 000
1986a	413 625	641 250	1,55	0,375	413 625	641 250
1985	1 124 000	1 745 200	1,55			
1984	1 117 700	1 702 200	1,52			
1983	1 063 600	1 576 100	1,48			
1982	1 129 200	1 458 900	1,29			
1981	1 107 300	1 378 700	1,25			
1980	1 066 300	1 296 700	1,22			
1979	1 040 800	1 268 091	1,22			
1978	1 019 000	1 255 416	1,23			
1977	1 005 400	1 176 300	1,17			
1976	1 022 700	1 231 900	1,20			
1975	1 044 400	1 218 700	1,17			
1974	1 000 900	1 166 100	1,17			
1973	974 000	1 210 100	1,24			
1972	936 000	1 089 100	1,16			
1971	936 100	1 002 900	1,07			
1970	953 100	930 530	0,98			
1969	971 700	948 700				
1968	969 900	946 900				
1967	919 800	898 000				
1966	877 200	856 400				
1965	839 300	819 400				
1964	823 900	804 400				
1963	783 950	765 400				
1962	744 000	726 400				
1961	679 300	663 200				
1960	641 500	626 300				

**Notes:** 1. Number of units collected for 1963 was interpolated from 1962 and 1964  
2. Number of units administered for 1960-69 based on ratio in 1970

**Source:** Canadian Red Cross Society

Table A2

**Modelled distribution of number of units administered  
to transfusion recipients, Canada, 1985**

<i>Number of units</i>	<i>Patients</i>	<i>Total units administered</i>	<i>Proportion of patients</i>	<i>Cumulative proportion of patients</i>
1	21940	21940	0,083	0,083
2	83463	166926	0,314	0,397
3	38488	115464	0,145	0,541
4	34351	137404	0,129	0,671
5	21166	105830	0,080	0,750
6	15427	92562	0,058	0,808
7	8892	62244	0,033	0,842
8	7420	59360	0,028	0,870
9	5472	49248	0,021	0,890
10	4618	46180	0,017	0,908
11	3683	40513	0,014	0,921
12	2936	35232	0,011	0,933
13	2536	32968	0,010	0,942
14	2162	30268	0,008	0,950
15	1815	27225	0,007	0,957
16	1415	22640	0,005	0,962
17	1068	18156	0,004	0,966
18	801	14418	0,003	0,969
19	587	11153	0,002	0,972
22	2349	51678	0,009	0,980
27	1495	40365	0,006	0,986
38	1948	74024	0,007	0,993
65	908	59020	0,003	0,997
200	507	101400	0,002	0,999
300	267	80100	0,001	1,000
550	80	44000	0,000	1,000
Total	265794	1540318		
Mean units / patient		5,80		

**Source:** Remis RS, Palmer RWH. The epidemiology of transfusion-associated HIV infection in Canada, 1978-85

**Table A3**  
**Distribution of sex and age of transfusion recipients**  
**Canada, 1960-92**

		Proportion of recipients			Proportion of recipients
<b>Males</b>	0-4	0,0089	<b>Females</b>	0-4	0,0087
	5-9	0,0053		5-9	0,0054
	10-14	0,0096		10-14	0,0096
	15-19	0,0125		15-19	0,0129
	20-24	0,0163		20-24	0,0159
	25-29	0,0200		25-29	0,0202
	30-34	0,0118		30-34	0,0150
	35-39	0,0127		35-39	0,0165
	40-44	0,0159		40-44	0,0232
	45-49	0,0202		45-49	0,0279
	50-54	0,0284		50-54	0,0360
	55-59	0,0332		55-59	0,0421
	60-64	0,0394		60-64	0,0598
	65-69	0,0749		65-69	0,1011
	70-74	0,0603		70-74	0,0596
	75-79	0,0399		75-79	0,0525
	80-84	0,0283		80-84	0,0410
85-89	0,0044	85-89	0,0035		
90+	0,0038	90-94	0,0030		
Total	0,4459	Total	0,5541		

		Proportion of recipients
<b>Both sexes</b>	0-4	0,0176
	5-9	0,0107
	10-14	0,0192
	15-19	0,0254
	20-24	0,0322
	25-29	0,0403
	30-34	0,0268
	35-39	0,0292
	40-44	0,0391
	45-49	0,0481
	50-54	0,0644
	55-59	0,0754
	60-64	0,0993
	65-69	0,1760
	70-74	0,1199
	75-79	0,0924
	80-84	0,0693
85-89	0,0079	
90+	0,0068	
Total	1,0000	

**TABLE A4**  
**SUMMARY OF ESTIMATES OF POST-TRANSFUSION HEPATITIS DUE TO HCV AND PER-UNIT HCV RISK, CANADA AND USA, 1983-90**

Ref	Author	Location	Period	N	n	HCV PTH	Units/patient	Per unit HCV risk	95%CL
4, 6	Feinman	Toronto	83/12-85/10	576	18	0.031	4.26	0.0073	0.0043 - 0.0114
9	Preiksaitis	Edmonton	83/10-85/05	279	5	0.018	10.9	0.0017	0.0005-0.0039
10	Mathias	BC	82/??-85/??	1118	45	0.040	6.4	0.0061	0.0045-0.0081
7	Blajchman	To/Ha/Wp	88/??-90/04	397	5	0.0126	4.76	0.0026	0.0008-0.0060
11	Roberts	Toronto	85/12-90/05	4500?	64	0.014	?	0.0025	?
12	Donahue	Baltimore	85/??-86/??	488	19	0.039	8.91	0.0052	0.0032-0.0080

Table A5

Risk per unit of HCV PTH, Canada 1980-90

	Blajchman (multicentre study)		Winnipeg	Feinman Toronto	Preiksaitis Edmonton	Forbes BC	Roberts Toronto	Donahue U.S.	Fitted curve Canada
	Toronto	Hamilton							
Centre weight	1,35	1,2	0,4	1,35	0,8	1,8	1,35		2
Proportion	0,5	0,35	0,15	1	1	1	1		1
Weight	1,16			1,35	0,8	1,8	1,35		2
Observed	<b>0,0026</b>			<b>0,0073</b>	<b>0,0017</b>	<b>0,0060</b>	<b>0,004</b>	<b>0,0052</b>	
1980									0,00400
1981									0,00400
1982									0,00400
1983									0,00383
1984				0,0054					0,00356
1985					0,0021	0,0033		0,0026	0,00317
1986									0,00278
1987									0,00246
1988							0,0030		0,00223
1989	0,0023								0,00201
1990									0,00185



**Table A6**

**Per unit risk of HCV infection from blood Canada, 1960-92**

<b>Year</b>	<b>Measured HCV prevalence</b>	<b>True HCV prevalence</b>	<b>Per-unit HCV risk</b>	<b>Correction factor for multiple exposures</b>
1992	0,00073	0,00091	0,000168	0,996
1991	0,00073	0,00091	0,000168	0,996
1990	0,00161	0,00201	0,000370	0,993
1990	0,00161	0,00201	0,00185	0,969
1989	0,00175	0,00219	0,00201	0,964
1988	0,00194	0,00243	0,00223	0,958
1987	0,00214	0,00268	0,00246	0,952
1986	0,00242	0,00303	0,00278	0,946
1986	0,00242	0,00303	0,00278	0,946
1985	0,00276	0,00345	0,00317	0,937
1984	0,00310	0,00387	0,00356	0,929
1983	0,00333	0,00416	0,00383	0,925
1982	0,00348	0,00435	0,00400	0,922
1981	0,00348	0,00435	0,00400	0,922
1980	0,00348	0,00435	0,00400	0,922
1979	0,00348	0,00435	0,00400	0,922
1978	0,00348	0,00435	0,00400	0,922
1977	0,00348	0,00435	0,00400	0,922
1976	0,00348	0,00435	0,00400	0,922
1975	0,00348	0,00435	0,00400	0,922
1974	0,00348	0,00435	0,00400	0,922
1973	0,00348	0,00435	0,00400	0,922
1972	0,00365	0,00456	0,00420	0,919
1971	0,00365	0,00456	0,00420	0,919
1970	0,00365	0,00456	0,00420	0,919
1969	0,00365	0,00456	0,00420	0,919
1968	0,00365	0,00456	0,00420	0,919
1967	0,00365	0,00456	0,00420	0,919
1966	0,00365	0,00456	0,00420	0,919
1965	0,00365	0,00456	0,00420	0,919
1964	0,00365	0,00456	0,00420	0,919
1963	0,00365	0,00456	0,00420	0,919
1962	0,00365	0,00456	0,00420	0,919
1961	0,00365	0,00456	0,00420	0,919
1960	0,00365	0,00456	0,00420	0,919

**Note:** HCV prevalence for period blood HCV screened, infectious prevalence was calculated as prevalence of undetected HCV (i.e. [measured HCV/sensitivity]-[measured HCV])

**Sensitivity** 0,8  
**Infectivity** 0,92

Table A7

## Parameter values: Prevalence of hepatitis C infection in selected populations

Reference	Population	Type of study	Year(s)	N	Result	Comments
Romanowski	STD clinic patients	Seroepid	1994-95	3765 2903	4.4% 2.0%	Men (approx) Women (approx)
Chaudhary	"Normal individuals"	Lab-based	?	256	2.0%	95% CL: 0.64%-4.5%
Roberts	Transfusion recipients, HSC	Lookback	1986-90	4496	1.4%	"Minimum estimate"
Armstrong	Cornea donors Ontario	Screening	1993-95	3228	1.0%	Mean age 75 years old
Joly	Sentinel hospitals Quebec	Anonymous	1990-92	4445 5631	0.89% 0.46%	Males Females
Johnson	EEG patients Scarborough	Outbreak investigation	1996	6000	1.3% 0.85%	Males Females
Pi	Pregnant women, BC	Prenatal sera	1994	15,000	0.9%	95% CL: 0.76%-1.1%
Louie	Teaching hospital Toronto	Anonymous	1990	1306	0.5%	EIA1 confirmed
CRCS	Volunteer blood donors	Transfusion	1990	10 <sup>6</sup>	0.124%	National prevalence

Table A8

Modelled HCV infections (all sources), number and prevalence  
by province and sex, Canada, 1998

<i>Province</i>	<i>Population (000s)</i>	<i>HCV infections, number</i>	<i>HCV prevalence (%)</i>	<i>Proportion total HCV infections (%)</i>	<i>HCV prevalence (%) Males</i>	<i>HCV prevalence (%) Females</i>
British Columbia	3860	52546	1,36	22,0	1,75	0,97
Alberta	2790	25380	0,91	10,6	1,17	0,65
Saskatchewan	1020	4343	0,43	1,8	0,55	0,30
Manitoba	1140	6178	0,54	2,6	0,70	0,39
Ontario	11250	105242	0,94	44,2	1,20	0,67
Quebec	7390	36235	0,49	15,2	0,63	0,35
New Brunswick	760	2844	0,37	1,2	0,48	0,27
Nova Scotia	940	4791	0,51	2,0	0,66	0,36
Prince Edward Island	140	343	0,25	0,1	0,32	0,18
Newfoundland	570	460	0,08	0,2	0,10	0,06
Canada	29860	238362	0,80	100	0,96	0,53

**Note:**

These estimates must be considered somewhat speculative; they are based on several assumptions including that the relative HCV prevalence in blood donors in 1990 reflect the relative HCV prevalence in the population as a whole, and that the male:female HCV prevalence ratio is constant across all provinces

Table A9

Parameter values: Proportion of hepatitis C infections with transfusion history

Author	Population	Type of study	Year(s)	Value	Comments
Stratton	PEI	Reported	1990-	39%	Blood/blood products
		cases	1995	46%	IDU
				6%	Both of above
Darling	Victoria, BC	General	1996	12%	Received blood/blood products
				62%	IDU
RDIS	Ontario	Reported cases	1997	7.0%	Blood recipients
			1996	7.8%	"
			1995	6.3%	"
			1994	6.7%	"
			1993	9.9%	"
			1992	9.8%	"
			1991	16%	"
			1990	20%	"
LCDC	8 health units BC/AL/SK/MN ON/PQ/PEI	Reported cases	1993-	30%	Blood transfusion ever (216/718)
			1995	69%	IDU (494/715)
Delage	Quebec?	Blood donors	?	22%	Blood transfusion
				45%	IDU
Scully	Ottawa	Clinical series	?	33%	Blood transfusion (21/63)
				43%	IDU (27/63)

**Table A10**  
**Point estimates and plausible range for model parameters**

			<i>Point estimate</i>	<i>Lower limit</i>	<i>Upper limit</i>
<b>Model 1:</b>	Per-unit HCV risk (%)	1990	0,143	0,129	0,159
		1989	0,166	0,149	0,184
		1988	0,195	0,156	0,244
		1987	0,225	0,180	0,281
		1986	0,260	0,208	0,325
		1985	0,310	0,217	0,443
		1984	0,356	0,249	0,509
		1983	0,383	0,268	0,547
		1982	0,400	0,280	0,571
	Survival following transfusion		0,425	0,383	0,472
<b>Model 2:</b>	HCV prevalence (%)		0,80	0,68	0,94
	Proportion HCV+ from transfusion		0,15	0,11	0,21
	Proportion other HCV+, transfused		0,12	0,096	0,15
<b>Model 3:</b>	Proportion persons transfused		0,11	0,094	0,129
	HCV prevalence among transfused		0,02	0,015	0,027
	Proportion due to transfusion		0,70	0,56	0,88

**Table A11**  
**Worksheet to calculate number of HCV-infected recipients surviving to mid-1998**

1984	1	2	3	4	5	6	7
Gender	Age group	Population	Proportion of units admin	Number of units admin	HCV infections	Proportion surviving to 1998	Number surviving to 1998
Males	0-4	1005,9	0,0089	15 166	54,0	0,936	50,5
	5-9	1031,3	0,0053	9 100	32,4	0,931	30,2
	10-14	1031,9	0,0096	16 304	58,0	0,927	53,8
	15-19	1026,3	0,0125	21 233	75,6	0,923	69,8
	20-24	1033,5	0,0163	27 678	98,5	0,923	90,9
	25-29	1121,5	0,0200	34 124	121,5	0,920	111,7
	30-34	1334	0,0118	20 055	71,4	0,914	65,3
	35-39	1343,9	0,0127	21 598	76,9	0,902	69,3
	40-44	1191,8	0,0159	27 074	96,4	0,658	63,4
	45-49	1084,8	0,0202	34 433	122,6	0,629	77,1
	50-54	838,2	0,0284	48 315	172,0	0,584	100,5
	55-59	661,9	0,0332	56 592	201,4	0,522	105,0
	60-64	596,2	0,0394	67 105	238,8	0,436	104,0
	65-69	536,2	0,0749	127 499	453,8	0,276	125,0
	70-74	432,8	0,0603	102 713	365,6	0,175	63,8
	75-79	289,2	0,0399	67 887	241,6	0,088	21,4
	80-84	174,9	0,0283	48 147	171,4	0,037	6,3
85-89	78,3	0,0044	7 543	26,8	0,000	0,0	
90+	32,5	0,0038	6 420	22,8	0,000	0,0	
	Total	14845,1	0,4459	758 985	2 701	0,447	1 208
Female	0-4	955	0,0087	14 803	52,7	0,947	49,9
	5-9	984,5	0,0054	9 159	32,6	0,946	30,9
	10-14	987,7	0,0096	16 424	58,5	0,945	55,3
	15-19	976,5	0,0129	22 019	78,4	0,944	74,0
	20-24	1002,9	0,0159	27 063	96,3	0,943	90,8
	25-29	1102,1	0,0202	34 431	122,6	0,940	115,2
	30-34	1297,2	0,0150	25 568	91,0	0,936	85,2
	35-39	1322,5	0,0165	28 161	100,2	0,927	93,0
	40-44	1195,7	0,0232	39 519	140,7	0,696	97,9
	45-49	1074,7	0,0279	47 423	168,8	0,679	114,7
	50-54	834	0,0360	61 339	218,3	0,655	143,0
	55-59	670,7	0,0421	71 719	255,3	0,617	157,6
	60-64	616,9	0,0598	101 867	362,6	0,561	203,3
	65-69	593,1	0,1011	172 125	612,6	0,392	240,3
	70-74	547,1	0,0596	101 429	361,0	0,291	105,0
	75-79	415,1	0,0525	89 385	318,1	0,170	54,1
	80-84	292,7	0,0410	69 733	248,2	0,072	17,8
85-89	162,3	0,0035	5 959	21,2	0,000	0,0	
90-94	88	0,0030	5 071	18,1	0,000	0,0	
	Total	15118,7	0,5541	943 197	3 357	0,515	1 728
Both sexes	0-4	1960,9	0,0176	29 969	106,7	0,942	100,4
	5-9	2015,8	0,0107	18 259	65,0	0,939	61,0
	10-14	2019,6	0,0192	32 728	116,5	0,936	109,0
	15-19	2002,8	0,0254	43 252	153,9	0,934	143,8
	20-24	2036,4	0,0322	54 742	194,8	0,933	181,7
	25-29	2223,6	0,0403	68 556	244,0	0,930	227,0
	30-34	2631,2	0,0268	45 624	162,4	0,926	150,4
	35-39	2666,4	0,0292	49 759	177,1	0,916	162,3
	40-44	2387,5	0,0391	66 593	237,0	0,680	161,2
	45-49	2159,5	0,0481	81 856	291,3	0,658	191,8
	50-54	1672,2	0,0644	109 654	390,3	0,624	243,5
	55-59	1332,6	0,0754	128 310	456,7	0,575	262,7
	60-64	1213,1	0,0993	168 971	601,4	0,511	307,3
	65-69	1129,3	0,1760	299 624	1066,4	0,343	365,3
	70-74	979,9	0,1199	204 142	726,6	0,232	168,8
	75-79	704,3	0,0924	157 272	559,8	0,135	75,4
	80-84	467,6	0,0693	117 879	419,6	0,058	24,1
85-89	240,6	0,0079	13 502	48,1	0,000	0,0	
90+	120,5	0,0068	11 491	40,9	0,000	0,0	
	Total	29963,8	1,0000	1 702 183	6058,5	0,485	2935,9
	Corrected for double inf. & unit-specific survival				5631,0	0,375	2109,0
	Number of units administered			1 702 200			
	HCV prevalence			0,00355925			
	Correction factor			0,92944351			
	Unit-specific survival adjustment			0,772867644	14	14	