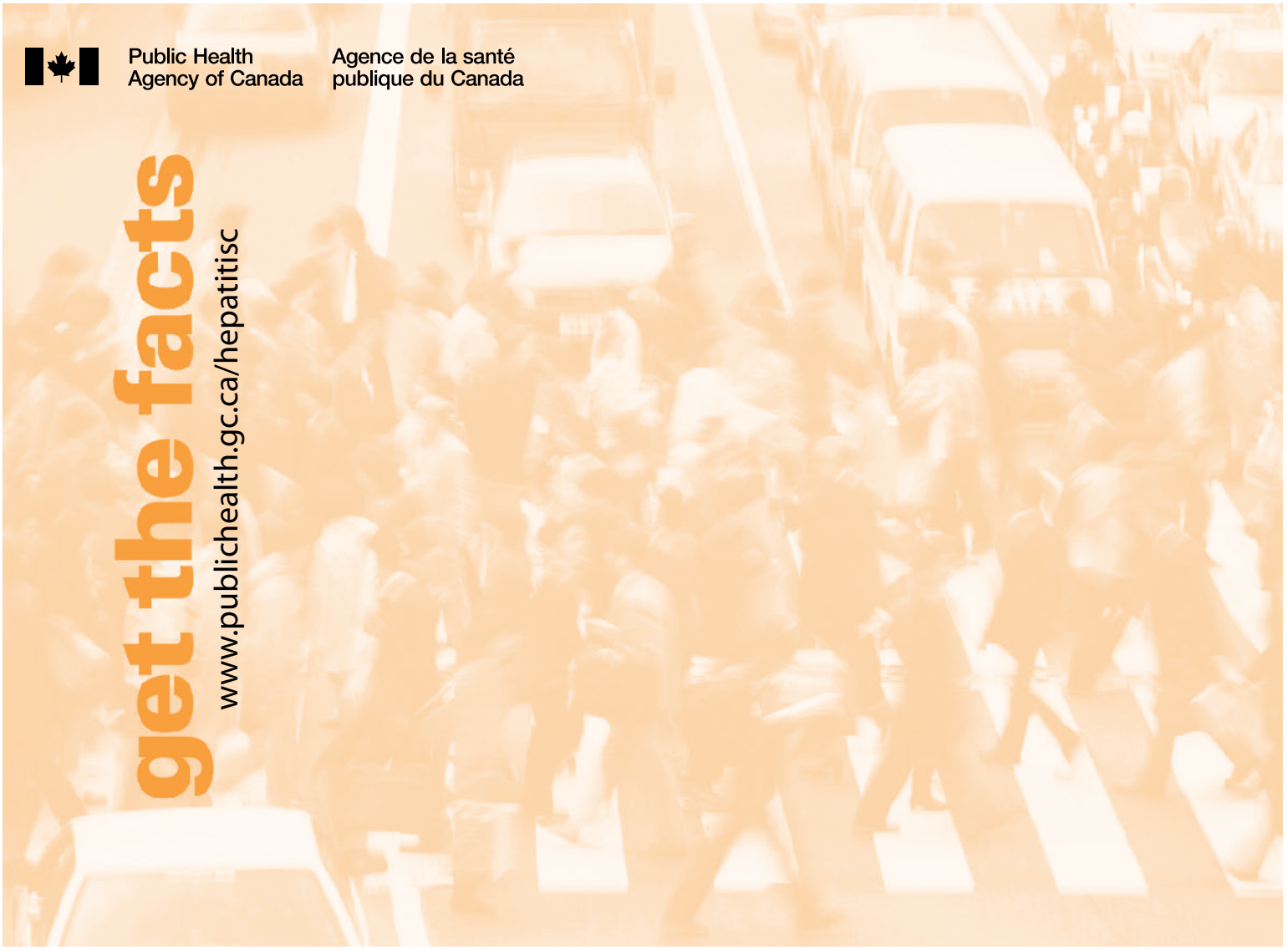

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A Study to Characterize the Epidemiology of Hepatitis C Infection in Canada, 2002

Final Report

Canada

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A Study to Characterize the Epidemiology of Hepatitis C Infection in Canada, 2002

Final Report

Hepatitis C Prevention, Support and Research Program
Community Acquired Infections Division
Centre for Communicable Diseases and Infection Control
Infectious Disease and Emergency Preparedness Branch
Public Health Agency of Canada

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Executive Summary

In 1998, a working group evaluated the extent of hepatitis C infection transmitted through blood transfusion in Canada. In the course of its work, the group estimated that, overall, about 240,000 persons were infected with hepatitis C virus (HCV) in Canada as of July 1998. The working group did not, however, examine the distribution of HCV infection among persons in other exposure categories (such as injection drug use, the most common source of infection), nor did it attempt to estimate the current or future impact of HCV infection. Given the elapsed time since this work was carried out and its limited scope, Health Canada wished to re-examine the estimated prevalence of HCV infection in Canada and to obtain more detailed estimates for each exposure category. This has become particularly pertinent since the Hepatitis C Prevention, Support and Research Program is scheduled to end in March 2004, and the Government of Canada is considering whether to renew this program.

The objectives of this HCV modeling study were to estimate the following parameters: hepatitis C incidence and prevalence (overall and by exposure category); the proportion of HCV infections diagnosed; the number of persons living with HCV infection by stage of disease; HCV-related morbidity; and the future occurrence of serious complications of HCV infection.

The study was carried out in three stages: (1) estimating the populations at risk by place of birth and exposure category; (2) modeling HCV incidence and prevalence among those born in Canada and, for persons born elsewhere, HCV prevalence at the time of arrival and subsequent HCV incidence ; and (3) projecting the outcomes of chronic HCV infection among those infected.

The population was stratified according to birth in Canada versus elsewhere. In each group, we estimated the numbers of persons in four mutually exclusive categories related to the acquisition of HCV infection: injection drug users, hemophilia patients, recipients of blood transfusions, and others. The "Other" category included persons infected by HCV primarily through sexual transmission, exposures of health care workers and non-injecting drug use. The model was run from 1960 to 2022. To estimate the population size in each year accurately, the multiple components of mortality were modeled specifically for each exposure category.

Data from the Enhanced Hepatitis Strain Surveillance System were used to help estimate HCV incidence and to determine the relative proportion of incident and prevalent HCV infections by exposure category and place of birth.

HCV-infected persons may eventually develop serious complications. This was assessed by estimating the number progressing through the following stages: cirrhosis, decompensated cirrhosis (liver failure), hepatocellular carcinoma, liver transplant and liver-related death. The model used annual transition parameters based on published data and modeling studies, incorporating important modifying factors such as age, sex and alcohol intake. The model was treated as an integrated continuum from entry through birth or immigration and then transition to exposure-related behaviours or experiences, mortality, HCV infection and progression to serious HCV disease.

To estimate the impact of HCV infection on increased morbidity, we estimated for each year and cumulatively the deficit in "quality-adjusted life years" (QALYs) in comparison to persons who were not infected with HCV, for each year from 1960 to 2022 and cumulatively since 1960. A questionnaire was sent to provincial representatives to obtain information on the reporting of HCV infection and details of notification programs that encourage transfusion recipients to be tested for HCV infection.

The results of our study may be summarized as follows. We estimated that approximately 251,000 persons in Canada were infected with HCV as of December 2002 and that about 5,000 persons are newly infected each year, mostly through injection drug use. The prevalence of HCV infection in Canada in 2002 was 4% higher than in 1998. The distribution of prevalent HCV infections by exposure category (to the nearest 1,000) was as follows: IDU 50,000, ex-IDU 89,000, hemophilia patients 1,200, blood transfusion recipients 33,000 and "Other" 74,000. In our analysis, IDU accounted for 55.6% of the prevalent HCV infections in Canada, hemophilia for 0.5%, blood transfusions 13.2% and other modes of transmission 29.6%. Overall, about 65% of HCV-infected persons in Canada have received a diagnosis to date.

The impact of the sequelae of hepatitis C infection on the health of Canadians appears to be considerable. In 2002, 9,400 persons were living with cirrhosis and 3,200 with liver failure. The annual incidence of newly developing cirrhosis appeared to peak in the late 1990s and early 2000s but, according to the results of our model, the incidence of the more serious outcomes of HCV infection will continue to rise, at least until 2022. Finally, our results also indicate that the impact of HCV disease on the health of Canadians has been and will continue to be dramatic: to 2002, almost 1,200,000 QALY have been lost from HCV infection and, by 2022, a cumulative total of almost 2,100,000 QALY will have been lost. These results should, nevertheless, be put in the context of other infectious and non-infectious conditions to be fully appreciated.

There are several important lessons to be learned from our study. Clearly, the impact of hepatitis C infection on the health of Canadians is considerable. Measures must be taken to encourage the estimated 90,000 HCV-infected persons whose condition remains undiagnosed to undergo HCV testing. Health care services to treat HCV-infected patients must be made available to all who may benefit from them; these include specialized physician and laboratory services and antiviral drugs. Further research is also required at many levels, including studies to (1) better evaluate the extent and the factors responsible for HCV infection in Canada, (2) develop more effective outreach programs to prevent new infection, (3) improve access to diagnosis and treatment services for underserved populations, (4) better understand HCV infection and disease and (5) develop more effective methods of treatment.

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1. Introduction

In June 1998, a working group evaluated the epidemiology of hepatitis C infection transmitted through blood transfusion in Canada from 1960 to 1992[1]. Although that study specifically focused on HCV transmission due to transfusion, in the course of its work the group used a model to estimate the number of HCV infections through blood transfusion as a proportion of total HCV infections in Canada. In this context, the working group estimated HCV prevalence in Canada and in each province, concluding that approximately 240,000 persons were infected with hepatitis C in Canada as of July 1998. It did not, however, examine the distribution of HCV infections among persons in other exposure categories (including injection drug use) nor did it attempt to estimate trends in HCV prevalence over time. In addition, HCV prevalence was not stratified by sex or age, except for those infected by blood transfusion.

Although the HCV prevalence estimate obtained still seems plausible, it is now appropriate to re-examine the estimated extent of HCV infection in Canada and attempt to obtain more detailed estimates stratified by exposure category. The present study is a response to a request for proposals from the Hepatitis C Division, Health Canada, to assess the epidemiologic situation in Canada as of 2002. This has become particularly pertinent since the special initiative on hepatitis C is scheduled to end in March 2004, and the Government of Canada is considering whether to renew this program.

2. Study Objectives

The objectives of the HCV modeling study were as follows:

1. to estimate hepatitis C incidence and prevalence;
2. to estimate the proportion of prevalent HCV infections that has been diagnosed;
3. to estimate the number of persons living with HCV infection by stage of disease;
4. to estimate HCV-related morbidity; and
5. to project the occurrence of serious sequelae of HCV infection, including cirrhosis, liver failure, hepatocellular carcinoma and liver-related death, into the future.

3. Methods

3.1 HCV Infection and Outcomes Model – Overview

The HCV modeling study was carried out in three stages using spreadsheet software (Excel 97, Microsoft Corporation 1999). In the first stage we obtained estimates of the population at risk, stratified by age and sex. The second stage modeled the HCV incidence rate among those born in Canada as well as HCV prevalence at the time of arrival and subsequent incidence for persons immigrating to Canada. The third stage projected outcomes of chronic HCV infection among those infected, as estimated in the second stage.

Further details of the approach used in each of the three stages follow.

Stage 1

Stage 1 was carried out in two phases. In the first phase, we estimated the populations potentially at risk of HCV infection. The population was divided into two major categories, namely persons born in Canada and persons born elsewhere who immigrated to Canada. In the second phase, we estimated the numbers of persons in four mutually exclusive categories defined as a function of risk of HCV infection, both within each of these two subpopulations and together. The four exposure categories were injection drug users, recipients of blood transfusion, hemophilia patients, and others.

For those born in Canada, the birth cohort was modeled from 1960 to 2022. Life table values for mortality specific to sex and age were applied to obtain an estimate of the number of persons alive at each age, by sex, for each year from 1960 to 2022. Projections from Statistics Canada were used for the population after 2002[2]. Data from Statistics Canada and Citizenship and Immigration Canada were used to estimate the number of immigrants arriving in Canada and their distribution by age and sex for each of 84 major countries or groupings of countries. The resulting populations were compared with Census Canada data stratified by age, sex and birthplace (in Canada or elsewhere) and, for those who had immigrated, by country of birth, since 1961. Where digressions from census statistics were greater than 5%, the input parameters, including births, immigrants and life table mortality, were adjusted to fit the observed census data.

In the second phase, subpopulations in each of the four exposure categories were obtained using an approach specific to each category, as described later in this section. In general, the incidence of the risk behaviour/experience and mortality was incorporated to estimate the age and sex-specific prevalence of that behaviour/experience. These estimates were then compared with values from observed studies and from previous modeling exercises and adjusted accordingly.

Limited data are available to estimate the number of injection drug users (IDUs) in Canada. One study used the capture-recapture method to estimate the number of active IDUs in Montreal, Toronto and Vancouver[3]. In 2000, Eric Single estimated the number of IDUs in Canada to be 75,000 to 125,000[4], a number consistent with the results of the capture-recapture study.

Triangulation techniques involving HIV diagnostic data provided estimated HIV prevalence rates for the three major cities (Montreal, Toronto and Vancouver), the rest of the three provinces (Quebec, Ontario and British Columbia) and the other seven provinces, to help converge the estimate.

For IDUs, we took into account the proportion of the population initiating injection as a population rate and the proportion of drug users who stop injecting drugs in the course of each year to generate a second population of ex-IDUs. It is important to take this into account in estimating the extent of hepatitis C infection, since the burden of HCV infection is considerable among persons who are not actively injecting but may have injected at some time in the past. We had developed a preliminary model of this type for HIV infection among IDUs in New York City, Montreal and Toronto, which closely fit the observed HIV prevalence data. In this approach, the number of IDUs was obtained by varying the rates of initiation and cessation of injection drug use so as to generate estimates that approximated the existing, though imprecise, estimates of the number of IDUs in Canada. This analysis incorporated values for both active IDUs and ex-IDUs.

Patterns of blood transfusion were based on the modeling work carried out by the Working Group in 1998[1].

For hemophilia patients, a fixed proportion was initially applied to male births and then modified to fit the known numbers of hemophilia patients in Canada, after taking into account mortality rates.

The "Other" category included persons infected by HCV primarily through sexual transmission and health care workers infected through parenteral exposure, and was estimated by subtraction from the total population after accounting for persons in the three higher risk categories, namely IDUs, blood transfusion recipients and hemophilia patients.

To estimate the population size in each year accurately, the components and rates of mortality were modeled specifically for each of the three major exposure categories. For IDUs, mortality was considered in three categories, namely, (1) life table mortality; (2) mortality directly related to injection drug use, including overdose, serious systemic infections, infection and trauma, and (3) mortality due to HIV disease. HIV-related mortality among IDUs began, for the most part, around 1985. The excess mortality related to overdose, etc., was greater among those who were HIV-infected, since these persons tend to be more active injectors.

For blood transfusion recipients, we incorporated the high level of mortality following transfusion that was associated with the illness for which the patient was transfused. Mortality rates among blood transfusion recipients were based on the 1998 study[1], which incorporated a high level of mortality within the first 3 years following transfusion with gradually declining excess mortality until 10 years later, after which life table mortality was used. However, to simplify the model construction, we used a two- rather than a three-stage approach, with an appropriately high mortality in the year following the transfusion and a weighted mortality thereafter, to approximate the mortality rates from the 1998 study. The numbers specific for each year by age and sex were generated and then compared with available estimates of populations so that the size of the population at risk was plausible.

For hemophilia patients, data on mortality were derived from published studies[5,6] and included the effect of specific treatment for hemophilia, introduced in the 1970s, in decreasing the mortality rates. In this population, mortality due to HIV infections acquired in the period 1978-1985 was incorporated in the model.

For persons in all exposure categories, mortality based on life table values was applied. This was the only mortality applied to persons in the "Other" exposure category.

Stage 2

HCV incidence rates derived from published studies and previous modeling studies were used to estimate the number of HCV-infected persons for each of the four groups defined. With respect to immigrants, the HCV prevalence in their country of origin stratified by sex and appropriate for the age at arrival was used to generate initial estimates of the number of prevalent HCV infections at time of arrival.

Immigrant populations were also subjected to incident HCV infection related to injection drug use, blood transfusion and "Other" modes of transmission but not to risk associated with hemophilia. Many hemophilia patients may not be admissible for immigration into Canada. More importantly, the number of non-Canadian-born hemophilia patients would likely be small because of prior higher mortality in countries where limited specialty care is available and because of restricted admissibility for immigration. In any case, no data were available on hemophilia patients by region of birth. For these reasons and for the sake of simplicity, hemophilia patients were modeled within the Canadian-born population.

Data on HCV incidence rates from the Enhanced Hepatitis Strain Surveillance System[7] (Forrester L., Health Canada: personal communication, 2003) adjusted for under-reporting and asymptomatic infection were used for initial values of overall HCV incidence. In a second approach, data from the available epidemiologic studies were also used to guide initial HCV incidence values. In this approach, incidence was applied only to susceptible persons; this is particularly important for IDUs. The numbers of prevalent HCV infections were subsequently compared with available data from special studies and previous modeling exercises to fit with observed HCV prevalence data[8-25].

Stage 3

The progression of infection of HCV-infected persons was evaluated using annual transition parameters of a Markov model based on both observed data and modeling studies previously published. With respect to the natural history of HCV infection, the true transition probabilities and the important covariates are still somewhat incompletely characterized, but there is the emergence of a consensus around the likely values of many of these parameters. Several studies have examined or reviewed the progression from HCV infection through serious sequelae[25-31]. A recent critical review by Freeman et al.[31] of a large number of natural history studies was of particular interest in this regard, as was the modeling study by Salomon[32], which used observed data to constrain the true values of 5 these progression parameters. Finally, the report of Krahn and colleagues[33] was also extremely helpful, since it included a systematic review of transition parameters and the important modifying factors such as age, sex and alcohol intake.

For the purposes of this study, the following stages of HCV-related morbidity were included: cirrhosis, decompensated cirrhosis (liver failure), hepatocellular carcinoma, liver transplant and liver-related death. The final estimates were compared with reported and modeled numbers of liver-related deaths and the incidence of hepatocellular carcinoma published by investigators at Health Canada[34-36]. See Sections 3.6 and 3.7 for further details of the methods used to model HCV sequelae.

3.2 Modeling of HCV Prevalence

To estimate HCV prevalence in Canada in 2002, the reference year, we considered separately each population stratum defined by exposure category and place of birth (Canada versus elsewhere). We reviewed studies carried out in Canada, including those done in prisons[9-23]. We used HCV incidence among IDUs as observed in studies in Montreal[37] and Vancouver[8] as well as from studies in other countries.

The data for modeling HCV infection acquired through blood transfusion were based on work carried out in a previous study1 and integrated into the model of HCV prevalence and incidence.

A model that we had previously developed for hemophilia patients for the purpose of estimating HCV and HCV-HIV co-infection was adapted for the purposes of the present study. Data from two studies of hemophilia patients in the UK were also useful in this regard[5,6].

The number of HCV transmissions in the "Other" category was developed on a proportional basis to fix the percentage of infections related to non-parenteral drug use, sexual transmission and transmission in the health care setting according to data from the Enhanced Hepatitis Strain Surveillance System (EHSSS) as well as studies carried out in the United States.

3.3 HCV Infection Among Persons Not Born in Canada

Extensive analyses were carried out to determine the contribution to HCV infections in Canada of infections acquired before arrival by persons born elsewhere who had immigrated to this country. An initial model was developed for each country in the world using data from the World Health Organization on country-specific HCV prevalence and applied to the population of each country.

Adjustments were made as necessary such that the total world prevalence of HCV matched the 170 million HCV-infected persons estimated by the World Health Organization. Data from the 2001 census from Statistics Canada on persons living in Canada by country of birth were then applied to the HCV prevalence in the country of origin to determine the number of HCV-infected persons living in Canada, and, as well, to make a preliminary characterization of the extent of HCV infection among immigrants from the most important countries of origin.

3.4 Use of Data from the Enhanced Hepatitis Strain Surveillance System (EHSSS)

Health Canada kindly provided data on acute and chronic HCV infections collected at eight sentinel sites beginning in 1998. Investigators at the EHSSS kindly provided custom outputs on the distribution of cases by mutually exclusive risk factor by year, country of birth and acute versus chronic infection for each sentinel site. We performed a cross-tabulation of risk factors by country of birth. The purpose of this analysis was to compare, for each sentinel site, the EHSSS data with census data to determine the degree to which HCV prevalence may be different among persons born outside Canada. We also wished to validate the initial results from the country-specific HCV prevalence analysis as noted in Section 3.3 to identify the most important countries involved. Finally, we wished to test our initial hypothesis that the majority of HCV infection among persons born outside Canada was related to exposures other than injection drug use, the most important exposure for persons born in Canada.

3.5 HCV Incidence

HCV incidence is unknown for most groups in Canada with the possible exception of IDUs in Montreal and Vancouver. We used two approaches to obtain plausible estimates of the annual number of new HCV infections in Canada. The first approach consisted of examining the incidence of clinically apparent and reported cases of confirmed, acute HCV infection through the EHSSS project of the Centre for Infectious Disease Prevention and Control, Health Canada. The "true" HCV incidence was derived by dividing this rate by the proportion of acute HCV infections that are icteric (and therefore presumably severe enough to motivate the seeking of medical care and serologic diagnosis) reporting. The value for the proportion that would be symptomatic was 20%, and the proportion of symptomatic infections that would be reported was 75% since most of such infections would be laboratory diagnosed and thus reported.

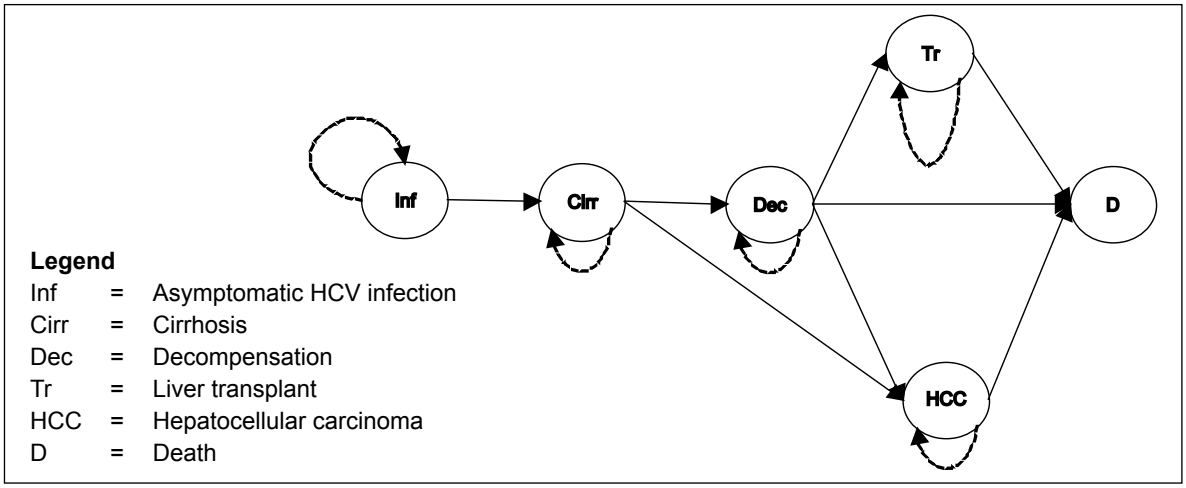
We also used a second, independent, approach to estimate HCV incidence. We estimated the proportion and number of active IDUs in Canada who would be susceptible to HCV infection (i.e. not already HCV infected) and multiplied this number by the HCV incidence observed among IDUs in epidemiologic studies[8,37]. This number of new infections among IDUs was then divided by the estimated proportion of new HCV infections that are thought to occur among IDUs, largely on the basis of the observations at the eight sites of the EHSSS from 1998 to 2002.

The methods for estimating HCV incidence were based on collaborative work carried out with Dr. Shimian Zou in 2001, who worked at Health Canada at the time[38].

3.6 Modeling HCV Outcomes

We carried out an extensive review of the medical literature to determine the annual rates of transition from initial HCV infection to the more advanced stages of HCV disease and its sequelae. We took into account the proportion of persons newly infected with HCV who remained viremic (i.e. had detectable HCV RNA) and, subsequently, the annual rate of HCV RNA loss and the rate of HCV antibody loss. Thus, the model incorporated three stages of HCV serologic status: RNA+ Ab+, RNA- Ab+, and RNA- Ab-. The natural history of hepatitis C after infection was simulated using a Markov model through the following stages: infection (pre-cirrhotic), cirrhosis, decompensation, transplantation, hepatocellular carcinoma and death. The values of the annual transition probabilities were obtained from published studies and reports[25,30,32,33,36,39-42]. The schematic model and the transition probabilities used are shown in Figure 1.

Figure 1: Markov Model of Transition Through Stages of HCV Infection



Summary of Annual HCV Stage Transition Probabilities									
		HIV negative				HIV positive			
		Female		Male		Female		Male	
From:	To:	< 40	40+	< 40	40+	< 40	40+	< 40	40+
Inf	Cirr	0.0025	0.0038	0.0035	0.0052	0.0036	0.0054	0.0050	0.0075
Cirr	Dec	0.0450	0.0450	0.0450	0.0450	0.1350	0.1350	0.1350	0.1350
Cirr	HCC	0.0210	0.0210	0.0210	0.0210	0.0210	0.0210	0.0210	0.0210
Dec	HCC	0.0300	0.0300	0.0300	0.0300	0.0300	0.0300	0.0300	0.0300
Dec	Transplant	0.0500	0.0500	0.0500	0.0500	0.0500	0.0500	0.0500	0.0500
Dec	Death	0.2500	0.2500	0.2500	0.2500	0.8200	0.8200	0.8200	0.8200
HCC	Death	0.5000	0.5000	0.5000	0.5000	0.5000	0.5000	0.5000	0.5000
Transplant	Death	0.0570	0.0570	0.0570	0.0570	0.0570	0.0570	0.0570	0.0570

Inf – infection, Cirr – Cirrhosis, Dec – Decompensation, HCC – Hepatocellular carcinoma

3.7 The Integrated Analytic HCV Model

The entire model was treated as a Markov model in an integrated continuum from entry through birth or immigration and then transition to exposure-related behaviours or experiences, mortality, HCV infection and progression to HCV disease.

All tables and rates were developed in Excel spreadsheets. Required parameters were consolidated in a consistent and usable format in two Excel "input" spreadsheets.

The model engine was written in the programming language APL+Win Version 4.0.03 supplied by APL2000 Inc. Data from the two spreadsheets of parameters were copied into the APL workspace and saved. Any subsequent changes were recopied and saved. Adjustment and control parameters were developed and stored directly in the APL workspace.

The raw product of the model was a series of arrays of the subpopulations, as defined already, and the decrements of every type to which each population is subjected. For example, the shape of the array of Male Results is 63 (years 1960-2022) by 111 (ages 0-110) by 386 (number of population and decrement columns). Note that, except for death, each decrement column is the new-entrant column for a subsequent subpopulation.

Subsidiary programs condensed and consolidated the raw output in various ways, such as by 5-year periods, summing over age and combining some columns. Finally, selected condensed and consolidated data were exported directly by program to Excel spreadsheets. In the spreadsheets, further simple calculations, such as summing and ratio calculation, plus formatting were performed.

For immigrants, a "super-model" was developed that ran the basic model for each country/region and summed the results. It differed in basic model processes only as follows:

- Instead of births at age zero each year, new immigrants entered the model at age of arrival.

- A proportion of new immigrants were considered to be infected with HCV on arrival.

- Hemophilia patients were all modeled within the Canadian-born population for the reasons stated in Section 3.1 and because modeling this group as one rather than two populations simplified the analysis.

To account for competing mortality, HIV infection (including HIV incidence and HIV-related mortality) was incorporated into the model. This was carried out only for IDUs and hemophilia patients, since the contribution of mortality due to HIV was minimal among blood transfusion recipients (likely fewer than 100 persons also infected with HIV among an estimated 35,000 HCV-infected blood transfusion recipients) and other persons (likely fewer than 1,000 persons co-infected with HIV and HCV among the estimated 74,000 HCV-infected persons in the "Other" category). Among ex-IDUs, HIV incidence was considered to be zero, since essentially all their HIV risk is related to active drug injection.

As indicated in Section 3.1 in the description of Stage 1, we also incorporated mortality due to other causes than HCV and HIV infection into the final model. For this purpose, we used life table values specific for each age and sex.

To model populations at risk and HCV incidence and prevalence, we adjusted model parameters so that model estimates were within 2% of the epidemiologically modeled estimates for these values.

3.8 Estimating HCV-Related Morbidity: Calculation of Quality-Adjusted Life Years Lost

To estimate the impact of HCV infection on increased morbidity, we estimated the deficit in quality-adjusted life years (QALY) in comparison to persons who were not infected with HCV for each year from 1960 to 2022 and cumulatively since 1960.

We calculated the annual and cumulative quality-adjusted life years lost (QALYL) from 1962 to 2022 based on the modeled distribution of persons by HCV disease stage: HCV-negative (uninfected), infected pre-cirrhosis, cirrhosis, decompensated, transplantation and hepatocellular carcinoma (HCC). To estimate the annual population in the absence of HCV, the model was re-run with an HCV incidence of zero.

Quality of life utility scores were taken from a study that asked an expert panel of hepatologists to use the time trade-off method to estimate the quality of life or utility for each of these disease stages[43]. The utility scores are measured on a scale of 0 to 1, where 0 indicates dead and 1 indicates perfect health.

The total annual QALYL were calculated by adding up the products of the modeled population prevalence in each of the disease stages (n_i) by the utility score for that stage (q_i). Since the uninfected stage has a utility score of 1, the total QALYL in the absence of HCV were the modeled population for that year (N). The annual QALYL were calculated by subtracting the total annual QALYL in the absence of hepatitis C from the QALYL modeled in the presence of hepatitis C.

$$QALYL = N - \sum_{i=1}^{6} n_i q_i$$

Annual QALYL were calculated at 5-year intervals from 1977 to 2022. The QALYL values for other years were interpolated linearly within the 5-year period. The cumulative QALYL from 1977 to 2022 were calculated as the sum of the QALYL for all of the years.

3.9 Proportion of HCV Infections Diagnosed and Reported

One of the objectives of the present study was to estimate the proportion of HCV-infected persons living in Canada as of 2002 whose condition had been diagnosed to date. To estimate this, data on HCV cases (including both acute and chronic HCV infections) reported from 1991 to 2002 were extracted from the Notifiable Disease Reporting System (Carole Scott, Health Canada: personal communication, 2003). For provinces in which HCV was not reportable from 1991 (most provinces, in fact), the number of HCV diagnoses before case reporting data were available was estimated by using relative weights among the provinces derived from years for which data on reported cases were available. Data for 2002 were unavailable for one province and, for the others, were available only until September 2002. Values for the provinces with data to September 2002 were extrapolated on the basis of the proportion reported up to September in previous years. The value for the province without data for 2002 was imputed using the same method as for the years before data were available, as described.

3.10 Survey of Provincial Health Departments

A questionnaire was sent to representatives of all provinces, and the study research assistant ensured follow-up and completion of the questionnaires. When necessary, telephone interviews were carried out to complete the collection of information. Certain questions related to the reportable disease surveillance system, including when HCV was made reportable, what precise data were collected and what the quality of the data was, e.g. reporting rates and duplication rates. A section of the questionnaire dealt with the generalized "lookback" campaigns to contact, by registered letter, persons identified as having been transfused usually, but not always, from 1986 to 1990, as conducted early on in British Columbia and Nova Scotia. This was to obtain a more precise appreciation of the proportion of HCV-infected transfusion recipients whose condition was likely to have been diagnosed and also to characterize the extent of efforts being made to ensure that latent hepatitis C was being diagnosed in the province in general. The questionnaire also served to identify additional studies carried out within the province that might shed further light on the epidemiology of HCV.

4. Results

4.1 HCV Prevalence Among Persons Immigrating to Canada

Table 1 shows the distribution of HCV infections by continent for persons born outside Canada who now live here. This table indicates that 98,400 immigrants to Canada are infected with hepatitis C, and 42% of them are immigrants from Southeast Asia. Nevertheless, there are many problems in interpreting these results. First, HCV prevalence among those who immigrate to Canada is likely different compared to that in the country of origin and is likely to be lower. An analysis carried out several years ago 44 of HIV infection in persons immigrating from countries where HIV infection is hyperendemic indicated that HIV prevalence among those immigrating to Canada was from 20% to 90% that of persons living in the country of origin. In addition, the distribution by age and sex of immigrants to Canada is likely different from that in the country of origin. This is because of selective factors related to the decision and the ability to immigrate to Canada.

Table 1: HCV Prevalence by Continent and Among Immigrants to Canada

Continent	Population (millions)	Immigrated to Canada	HCV Prevalence	HCV Number Country	HCV Number Canada	HCV Prevalence Canada
Western Europe	456.2	1,685,395	0.8%	3,650,200	8,349	0.5%
Eastern Europe	450.2	626,820	1.7%	7,792,000	10,257	1.6%
SS Africa	669.9	188,720	3.8%	25,236,300	5,634	3.0%
Southeast Asia	1,982.1	1,196,280	3.2%	64,301,500	40,857	3.4%
South Asia	1,380.3	514,120	1.9%	26,025,600	9,555	1.9%
North America	309.2	237,920	1.3%	4,128,600	3,331	1.4%
Latin America	518.0	599,680	1.7%	8,687,500	8,108	1.4%
Middle East	338.5	34,485	4.8%	16,084,700	10,597	3.1%
Oceania	24.7	47,965	1.6%	406,500	1,725	3.6%
Total	6,129.1	5,439,385		156,312,900	98,414	1.8%

Note: This table is for illustrative purposes only.

Table 2 shows the countries of birth of persons who have immigrated to Canada, ranked by the number of these persons with HCV infection living in Canada. The four highest ranking countries of origin were China, Viet Nam, the Philippines and Egypt, accounting together for 34% of HCV-infected immigrants to Canada in this analysis.

Table 2: HCV Number by Country of Birth, Selected Countries by Ranking, Canada, 2002

	Cumulative		
Country of Birth	**HCV Number**	**HCV Number**	**Number of Countries**
Group 1 (5,000-9,999)			
China	9,985		
Vietnam	9,053		
Philippines	8,376		
Egypt	6,476	3,890	4
Group 2 (2,000-4,999)			
India	5,664		
South Korea	4,232		
Taiwan	4,026		
United States	3,331		
Trinidad	3,192		
Romania	2,707		
Poland	2,526	25,678	7
Group 3 (1,000-1,999)			
Pakistan	1,904		
Germany	1,741		
Italy	1,577		
Fiji	1,340		
Sri Lanka	1,310		
United Kingdom	1,212		
Guyana	1,253		
Hong Kong	1,178		
Tanzania	1,159		
Greece	1,137		
Russia	1,083		
Iran	1,080		
Haiti	1,053		
Lebanon	1,008	18,033	15
Total	77,601	77,601	26

Note: This table is for illustrative purposes only.

4.2 Analysis of EHSSS Data

The results of the analysis of the EHSSS database by sentinel site (aggregate data) and continent of birth are shown in Table 3 for acute HCV infections and Table 4 for chronic HCV infections (Table 4 also includes those whose phase of infection was unknown). Overall, as seen in Table 3, 93% of persons with a diagnosis of acute HCV infection were born in Canada, though this varied by site, from 83% at the British Columbia Centre for Disease Control (BCCDC, which reports data from British Columbia outside Vancouver) to 100% in New Brunswick.

The data on the distribution of chronic HCV infections are shown in Table 4. Note that there were very limited data from BCCDC and Halifax, the most recent additions to the surveillance system. The proportion born in Canada was much lower than for acute infection, at 79%. Only persons from Southeast Asia accounted for a substantial proportion of chronic HCV infections. There were also marked variations by site: in Vancouver, 60% of persons with chronic HCV infection were born in Canada, and 28% were born in Southeast Asia.

The results of the EHSSS data analysis by mutually exclusive risk factor and place of birth for acute HCV infections are shown in Table 5. Injection drug use accounted for 58% of cases overall among persons born in Canada, but the proportion was somewhat lower (47%) among persons not born in Canada; this difference was not, however, statistically significant. Interestingly, the proportion indicating injection drug use represented 67% and 56% of those with known risk factors for persons born in Canada and elsewhere respectively.

Table 6 presents a similar analysis for reported HCV infections that were chronic or unknown. Here the difference in the proportion of IDUs by place of birth was more dramatic: 57% of chronic HCV infections were assigned to IDU for those born in Canada compared with 33% for those not born in Canada. This difference was statistically significant ($p < 0.0001$).

The EHSSS data and analyses were critical to the development of the final HCV prevalence model. As initially hypothesized, we found that injection drug use was responsible for a lower proportion of prevalent HCV infections among persons born elsewhere compared with those born in Canada, 33% versus 57% respectively.

Table 3: Cases and Proportions of Acute HCV Infection by Sentinel Site and Region of Birth, Enhanced Hepatitis Strain Surveillance System (EHSSS), 1998-2002

	Cases	Proportion Known
Canada	317	92.7%
United States	3	0.9%
Latin America	4	1.2%
Western Europe	1	0.3%
Eastern Europe	0	0.0%
Middle East	0	0.0%
Africa	2	0.6%
South Asia	0	0.0%
Southeast Asia	3	0.9%
Other regions	12	3.5%
Total, other	**25**	**7.3%**
Total known	**342**	**100.0%**
Region unknown	**49**	
Total	**391**	

Table 4: Cases and Proportions of Chronic HCV Infection by Sentinel Site and Region of Birth, Enhanced Hepatitis Strain Surveillance System (EHSSS), 1998-2002

	Cases	Proportion Known
Canada	6,503	78.9%
United States	79	1.0%
Latin America	50	0.6%
Western Europe	54	0.7%
Eastern Europe	22	0.3%
Middle East	17	0.2%
Africa	125	1.5%
South Asia	25	0.3%
Southeast Asia	619	7.5%
Other regions	744	9.0%
Total, other	**1,735**	**21.1%**
Total known	**8,238**	**100.0%**
Region unknown	**2,817**	
Total	**11,055**	

Table 5: Cases and Proportions of Acute HCV Infection by Mutually Exclusive Risk Category and Birthplace (Canada versus Elsewhere), Enhanced Hepatitis Strain Surveillance System (EHSSS), 1998-2002

	Canada	Not Canada	Unknown	Total
Injection drug use	154	9	1	164
Drug snorting	18	1	0	19
Blood contact	6	0	0	6
Tattooing	7	0	0	7
Incarceration	8	0	0	8
Sex with person with HCV	9	0	0	9
Hepatitis C in family	12	1	0	13
Dental care	5	2	0	7
Unknown	35	3	1	39
Other	12	3	0	15
Total	266	19	2	287

	Canada	Not Canada	Unknown	Total
Injection drug use	57.9%	47.4%	50.0%	57.1%
Drug snorting	6.8%	5.3%	0.0%	6.6%
Blood contact	2.3%	0.0%	0.0%	2.1%
Tattooing	2.6%	0.0%	0.0%	2.4%
Incarceration	3.0%	0.0%	0.0%	2.8%
Sex with person with HCV	3.4%	0.0%	0.0%	3.1%
Hepatitis C in family	4.5%	5.3%	0.0%	4.5%
Dental care	1.9%	10.5%	0.0%	2.4%
Unknown	13.2%	15.8%	50.0%	13.6%
Other	4.5%	15.8%	0.0%	5.2%
Total	100.0%	100.0%	100.0%	100.0%

	Canada	Not Canada
Injection drug use	67.0%	56.0%
Drug snorting	8.0%	6.0%
Blood contact	3.0%	0.0%
Tattooing	3.0%	0.0%
Incarceration	3.0%	0.0%
Sex with person with HCV	4.0%	0.0%
Hepatitis C in family	5.0%	6.0%
Dental care	2.0%	13.0%
Other	5.0%	19.0%
Total	100.0%	100.0%

Table 6: Cases and Proportions of Chronic HCV Infection by Mutually Exclusive Risk Category and Birthplace (Canada versus Elsewhere), Enhanced Hepatitis Strain Surveillance System (EHSSS), 1998-2002

	Canada	Not Canada	Unknown	Total
Injection drug use	2,529	318	81	2,928
Blood transfusion	1,099	250	15	1,364
Hemophilia	23	7	2	32
Other	755	342	6	1,103
Unknown	45	47	4	96
Total	4,451	964	108	5,523

Column percent	Canada	Not Canada	Unknown	Total
Injection drug use	56.8%	33.0%	75.0%	53.0%
Blood transfusion	24.7%	25.9%	13.9%	24.7%
Hemophilia	0.5%	0.7%	1.9%	0.6%
Other	17.0%	35.5%	5.6%	20.0%
Unknown	1.0%	4.9%	3.7%	1.7%
Total	100.0%	100.0%	100.0%	100.0%

Row percent (among those with known country of birth)	Canada	Not Canada
Injection drug use	88.8%	11.2%
Blood transfusion	81.5%	18.5%
Hemophilia	76.7%	23.3%
Other	68.8%	31.2%
Unknown	48.9%	51.1%
Total	82.2%	17.8%
Other/unknown	67.3%	32.7%

4.3 Results of Epidemiologic Modeling: HCV Prevalence

Preliminary estimates of the prevalence of HCV by exposure category and country of birth, i.e. Canada or elsewhere, are shown in Table 7. We estimate that, overall, approximately 251,000 Canadians were infected with hepatitis C as of December 2002. Of these, 202,000 were born in Canada and 49,000 elsewhere. Note that the estimates of HCV-infected immigrants are only one half of the preliminary estimate shown in Tables 1 and 2. Although the HCV prevalence rate was only slightly higher (0.90% vs 0.79%) among those born elsewhere, the distribution by source of infection was quite different. For those born outside Canada, only 33% of infections were related to injection drug use and 55% related to other sources compared with 63% and 23% respectively for Canadian-born HCV-infected persons.

4.4 Results of Epidemiologic Modeling: HCV Incidence

Table 8 shows the estimate of HCV incidence by exposure category using the two methods described earlier. As seen in this table, we estimate that approximately 5,000 new HCV infections occur every year in Canada. Although 72% of new HCV infections occur in IDUs, we believe that a non-negligible proportion of transmissions occurs by other routes. These include non-parenteral drug exposure (in particular, snorting cocaine), exposure in high-risk health care settings such as hemodialysis units, intensive care units, surgery and pathology, and through sexual contact and mother-infant transmission. It is difficult to be precise about the distribution of these quite distinct routes of transmission among the estimated 1,400 new infections occurring annually in the "Other" category.

Table 7: Estimated Population at Risk and HCV prevalence by Exposure Category and Place of Birth (Canada versus Elsewhere) Canada, 2002

	Born in Canada				Born Elsewhere				Total			
	Population	HCV Prevalence Rate	HCV Prevalence Number	Proportion	Population	HCV Prevalence Rate	HCV Prevalence Number	Proportion	Population	HCV Prevalence Rate	HCV Prevalence Number	Proportion
IDU	80,000	80%	64,000	32%	10,000	80%	8,000	16%	90,000	80%	72,000	29%
Ex-IDU	160,000	40%	64,000	32%	20,000	40%	8,000	16%	180,000	40%	72,000	29%
IDU, total	240,000		128,000	63%	30,000		16,000	33%	270,000		144,000	57%
Transfusion	2,200,000	1.2%	27,000	13%	500,000	1.2%	6,000	12%	2,700,000	1.2%	33,000	13%
Hemophilia	1,700	59%	1,000	0.50%	300	47%	140	0.29%	2,000	57%	1,140	0.5%
Other	23,000,000	0.20%	46,000	23%	4,900,000	0.55%	26,950	55%	27,900,000	0.26%	72,950	29%
Total	25,441,700	0.79%	202,000	100%	5,430,300	0.90%	49,090	100%	30,872,000	0.81%	251,090	100%

IDU = Injection drug user

Table 8: Estimated HCV Incidence by Exposure Category and Place of Birth, Canada 2002

Born in Canada	Population	HCV Prevalence Rate	HCV Prevalence Number	HCV Incidence Rate	HCV Incidence Number	Proportion
IDU	80,000	80%	64,000	20%	3,200	74%
Other	25,360,000	0.20%	50,720	0.0045%	1,139	26%
Total	25,440,000				4,339	100%

Born elsewhere	Population	HCV Prevalence Rate	HCV Prevalence Number	HCV Incidence Rate	HCV Incidence Number	Proportion
IDU	10,000	80%	8,000	20%	400	62%
Other	5,420,000	0.55%	29,810	0.0045%	243	38%
Total	5,430,000				643	100%

Total Canada	Population	HCV Prevalence Number	HCV Incidence Number	Proportion
IDU	90,000	72,000	3,600	72%
Other	30,780,000	80,530	1,381	28%
Total	30,870,000		4,981	100%

An analysis of yearly trends taking into account mortality, and new and imported HCV infections indicates that the prevalence of HCV in Canada is increasing. To calculate the net increase, we subtracted mortality among those HCV infected, including excess mortality in IDUs as well as life table mortality in each of the other populations. The excess transfusion-related mortality has also been taken into account since this is an older population; annual mortality among HCV-infected blood transfusion recipients was estimated in the 1998 report1. As seen in Table 9, HCV prevalence appears to increase by approximately 2,300 cases per year, representing an annual increase in HCV prevalence of about 1%. This estimate must be considered as an order of magnitude approximation at the present time. The increase is related to the incidence of HCV infection, primarily among injection drug users, and HCV infection among persons arriving in Canada.

Table 9: Modeled Trends in HCV Prevalence, Canada, 1998 to 2002 Increase in HCV Prevalence

Increase in HCV prevalence						
New infections		5,000				
Immigration HCV-infected persons		2,000				
Total		7,000				
Decrease in HCV prevalence						
		Mortality among HCV-infected persons				
		Lifetable 0.005	**Excess IDU 0.02**	**HIV Mortality**	**HCV Mortality**	**Total**
IDU	72,000	360	1,440	100		1,900
Ex-IDU	72,000	360		50		410
		0.030				
Transfusion	33,000	990		15		1,005
Hemophilia	1,140	6		17		23
Other	39,000	195				195
Immigrants other only	27000	135				135
					1,000	1,000
Total	244,140	2,046		182	1,000	4,668
		July 1998	240,000			
		Annual net increase	2,332			
		Total net increase	10,494			
		Dec 2002	250,494			

4.5 Results of Epidemiologic Modeling: HCV Outcomes

The review of published studies and available unpublished reports allowed us to estimate the so-called transition parameters as described in Section 3.6. In summary, we estimated annual transition rates from initial HCV infection to cirrhosis, decompensation, hepatocellular carcinoma, liver transplantation and death. The structure of the model is illustrated in Figure 1 and the actual transition parameter values used are shown below the schematic diagram. The transition from infection to cirrhosis was modeled as a function of sex, age and HIV infection status. The values and sources of the transition parameters used in the model are shown in more detail in Table 10.

The final estimates for the populations at risk, HCV incidence and HIV incidence were incorporated into a model programmed in APL as described earlier. The modeled estimates of the size of the populations at risk and the HIV and HCV prevalence and incidence for 2002 among those born in Canada, among immigrants and in both groups together are shown in Tables 11, 12 and 13 respectively.

Table 10: Parameters of Transition from Initial HCV Infection Through to Death: Data Sources and Calculations

Annual Transition Probabilities (base case: female, < 40, HIV-)						
	From: Infect*	Cirr	Decomp	HCC	Transplant	Death
To: Infection	0.998	0.000	0.000	0.000	0.000	0.000
Cirrhosis	0.003	0.934	0.000	0.000	0.000	0.000
Decompensation	0.000	0.045	0.670	0.000	0.000	0.000
Hepatocellular carcinoma	0.000	0.021	0.030	0.500	0.000	0.000
Transplant	0.000	0.000	0.050	0.000	0.943	0.000
Death	0.000	0.000	0.250	0.500	0.057	0.000
*Note: Transition from Infect to Cirr (only) is age group and sex specific (see table below)						

Annual Transition Probabilities (base case: female, < 40, HIV-)				
Population	From:	To:	Value	References
Young women	*Infect	Cirr	0.0025	Weighted estimate from Wiese[39], Kenny-Walsh[40] [in Krahn 2002, Table 433, p.6]
General	Cirr	Decomp	0.045	Salomon[32], Table 1, [page 764, ref 51-55]
General	Cirr	HCC	0.021	Krahn, weighted rate, Table 4.4-1 (page 12) [in Salomon 2002, Table 1, ref 51-53,55,56]
	Decomp	HCC	0.030	Modeled from Zou[36]
	Decomp	Transplant	0.050	Modeled from Zou[36]
General	Decomp	Death	0.250	Salomon[32], Table 1, ref 51-58
General	HCC	Death	0.500	Salomon[32], Table 1, ref 59,60
	Transplant	Death	0.057	Wong JB25, (death after first year [0.21 in first year])
*Note: Transition from Infect to Cirr (only) is age group and sex specific (see table below).				

Relative risks (RRs) for Transition Probability from Infection To Cirrhosis by Age Group and Sex (vs. female, < 40)				
		Age <40	40+	Reference
	RR	1	1.5	Poynard 1997[42] [Krahn ref. 8.]
Sex Male	1.39	0.003475	0.005213	
Female	1.00	0.0025	0.00375	

Table 10: Parameters of Transition from Initial HCV Infection Through to Death: Data Sources and Calculations (continued)

Annual Transition Probabilities (base case: female, < 40, HIV+)						
	From: Infect*	Cirr	Decomp	HCC	Transplant	Death
To: Infection	0.996	0.000	0.000	0.000	0.000	0.000
Cirrhosis	0.004	0.844	0.000	0.000	0.000	0.000
Decompensation	0.000	0.135	0.100	0.000	0.000	0.000
Hepatocellular carinoma	0.000	0.021	0.030	0.500	0.000	0.000
Transplant	0.000	0.000	0.050	0.000	0.943	0.000
Death	0.000	0.000	0.820	0.500	0.057	0.000
*Note: Transition from Infection to Cirrhosis (only) is age group and sex specific.						

HIV/HCV Co-Infection: Relative Risk for Annual Transitional Probabilities Relative Risk (HIV+/HIV-)				
Population	**From:**	**To:**	**Value**	**References**
Hemophilia	*Infection	Cirrhosis	1.44	Krahn[33] ref 14, table 4.3-3 p.10
Hemophilia	Cirrhosis	Decompensation	3.00	Ragni[41] table 1, page 1113
	Cirrhosis	Hepatocellular carinoma	1.00	Assume no effect from HIV+
	Decompensation	Hepatocellular carinoma	1.00	Assume no effect from HIV+
	Decompensation	Transplant	1.00	Assume no effect from HIV+
Hemophilia	Decompensation	Death	3.28	Lower limit Ragni[41] Table 1, page 1113
General	Hepatocellular carinoma	Death	1.00	Assume no effect from HIV+
	Transplant	Death	1.00	Assume no effect from HIV+

Table 11: Prevalence and Incidence of HCV Infection by Sex and Exposure Category Among Persons Born in Canada, Canada, 2002

IDU Prevalence						IDU Incidence				
	Population	HCV Number	Rate	HIV Number	Rate		HCV Number	Rate	HIV Number	Rate
Male	54,518	29,782	54.6%	4,081	7.5%	Male	3,018	12.2%	701	2.8%
Female	26,357	14,327	54.4%	1,928	7.3%	Female	1,424	11.8%	330	2.7%
Total	80,875	44,109	54.5%	6,009	7.4%	Total	4,442	12.1%	1,031	2.8%
Ex-IDU Prevalence						**Ex-IDU Incidence**				
Male	107,813	53,072	49.2%	2,238	2.1%	Male	0	0.0%	0	0
Female	52,910	25,903	49.0%	1,067	2.0%	Female	0	0.0%	0	0
Total	160,723	78,975	49.1%	3,305	2.1%	Total	0	0.0%	0	0
Hemophilia Prevalence						**Hemophilia Incidence**				
Male	2,079	1,156	55.6%	309	14.9%	Male	5	0.5%	0	0
Female	–	–	–	–	–	Female	0	0.0%	0	0
Total	2,079	1,156	55.6%	309	14.9%	Total	5	0.5%	0	0

Transfused Prevalence				Transfused Incidence			
	Population	HCV Number	Rate		Transfused	HCV Number	Rate
Male	1,050,570	12,995	1.2%	Male	73,638	55	0.07%
Female	1,159,102	14,003	1.2%	Female	85,193	63	0.07%
Total	2,209,672	26,998	1.2%	Total	158,831	118	0.07%

Other Prevalence				Other Incidence		
	Population	HCV Number	Rate		HCV Number	Rate
Male	11,347,259	24,979	0.22%	Male	676	0.006%
Female	11,452,481	21,947	0.19%	Female	571	0.005%
Total	22,799,740	46,926	0.21%	Total	1,247	0.005%

Total Prevalence						Total Incidence				
	Population	HCV Number	Population Total	HIV Number	Population Total		HCV Number	Population Total	HIV Number	Population Total
IDU	80,875	44,109	22.3%	6,009	62.4%	IDU	4,442	76.4%	1,031	100.0%
Ex-IDU	160,723	78,975	39.9%	3,305	34.3%	Ex-IDU	0	0.0%	0	0.0%
Hemophilia	2,079	1,156	0.6%	309	3.2%	Hemophila	5	0.1%	0	0.0%
Transfused	2,209,672	26,998	13.6%	–	0.0%	Transfused	118	2.0%	–	0.0%
Other	22,799,740	46,926	23.7%	–	0.0%	Other	1,247	21.5%	–	0.0%
Total	25,253,089	198,164	100.0%	9,623	100.0%	Total	5,812	100.0%	1,031	100.0%

Table 12: Prevalence and Incidence of HCV Infection by Sex and Exposure Category Among Persons Born Outside Canada, Canada, 2002

IDU Prevalence						IDU Incidence				
	Population	HCV Number	Rate	HIV Number	Rate		HCV Number	Rate	HIV Number	Rate
Male	6,836	3,910	57.2%	370	5.4%	Male	449	15.3%	71	2.4%
Female	3,337	1,902	54.4%	180	5.4%	Female	219	15.3%	34	2.4%
Total	10,173	5,812	57.1%	550	5.4%	Total	668	15.3%	105	2.4%
Ex-IDU Prevalence						**Ex-IDU Incidence**				
Male	13,919	7,033	50.5%	199	1.4%	Male	0	0.0%	0	0.0%
Female	6,763	3,411	50.4%	97	1.4%	Female	0	0.0%	0	0.0%
Total	20,682	10,444	50.5%	296	1.4%	Total	0	0.0%	0	0.0%
Hemophilia Prevalence*						**Hemophilia Incidence**				
Male	–	–	–	–	–	Male	–	–	–	–
Female	–	–	–	–	–	Female	–	–	–	–
Total	–	–	–	–	–	Total	–	–	–	–

Transfused Prevalence				Transfused Incidence			
	Population	HCV Number	Rate		Transfused	HCV Number	Rate
Male	245,073	2,889	1.2%	Male	22,825	21	0.09%
Female	293,482	3,048	1.0%	Female	28,199	23	0.08%
Total	538,555	5,937	1.1%	Total	51,024	44	0.09%

Other Prevalence				Other Incidence		
	Population	HCV Number	Rate		HCV Number	Rate
Male	2,518,655	13,312	0.53%	Male	42	0.002%
Female	2,705,481	13,515	0.50%	Female	69	0.003%
Total	5,224,136	26,827	0.51%	Total	111	0.002%

Total Prevalence						Total Incidence				
	Population	HCV Number	Population Total	HIV Number	Population Total		HCV Number	Population Total	HIV Number	Population Total
IDU	10,173	5,812	11.9%	550	65.0%	IDU	668	81.2%	1051	100.0%
Ex-IDU	20,682	10,444	21.3%	296	35.0%	Ex-IDU	0	0.0%	0	0.0%
Hemophilia	–	–	–	–	–	Hemophilia	–	–	–	–
Transfused	538,555	5,937	12.1%	–	–	Transfused	44	5.3%	–	–
Other	5,224,136	26,827	54.7%	–	–	Other	111	13.5%	–	–
Total	5,793,546	49,020	100.0%	846	100.0%	Total	823	100.0%	105	100.0%

* For simplicity, all persons with hemophilia were considered Canadian born.

Table 13: Prevalence and Incidence of HCV Infection by Sex and Exposure Category Among All Persons, Canada, 2002

IDU Prevalence						IDU Incidence				
	Population	HCV Number	Rate	HIV Number	Rate		HCV Number	Rate	HIV Number	Rate
Male	61,354	33,692	54.9%	4,451	7.3%	Male	3,467	12.5%	772	1.4%
Female	29,694	16,229	54.4%	2,108	7.1%	Female	1,643	12.2%	364	1.3%
Total	91,048	49,921	54.8%	6,559	7.2%	Total	5,110	12.4%	1,136	1.3%
Ex-IDU Prevalence						**Ex-IDU Incidence**				
Male	121,732	60,105	49.4%	2,437	2.0%	Male	0	0.0%	0	0.0%
Female	59,673	29,314	49.1%	1,164	2.0%	Female	0	0.0%	0	0.0%
Total	181,405	89,419	49.3%	3,601	2.0%	Total	0	0.0%	0	0.0%
Hemophilia Prevalence						**Hemophilia Incidence**				
Male	2,079	1,156	55.6%	309	14.9%	Male	5	0.0%	0	0.0%
Female	–	–	–	–	–	Female	–	–	–	–
Total	2,079	1,156	55.6%	309	14.9%	Total	5	0.0%	0	0.0%

Transfused Prevalence				Transfused Incidence			
	Population	HCV Number	Rate		Transfused	HCV Number	Rate
Male	1,295,643	15,884	1.2%	Male	96,463	76	0.08%
Female	1,452,584	17,051	1.2%	Female	113,392	86	0.08%
Total	2,748,227	32,935	1.2%	Total	209,855	162	0.08%

Other Prevalence				Other Incidence		
	Population	HCV Number	Rate		HCV Number	Rate
Male	13,865,914	38,291	0.3%	Male	718	0.002%
Female	14,157,962	35,462	0.3%	Female	640	0.003%
Total	28,023,876	73,753	0.3%	Total	1,358	0.002%

Total Prevalence						Total Incidence				
	Population	HCV Number	Population Total	HIV Number	Population Total		HCV Number	Population Total	HIV Number	Population Total
IDU	91,048	49,921	20.2%	6,559	62.7%	IDU	5,110	77.0%	1,136	100.0%
Ex-IDU	181,405	89,419	36.2%	3,601	34.4%	Ex-IDU	0	0.0%	0	0.0%
Hemophilia	2,079	1,156	0.5%	309	3.0%	Hemophilia	5	0.1%	0	0.0%
Transfused	2,748,227	32,935	13.3%	–	–	Transfused	162	2.4%	–	–
Other	28,023,876	73,753	29.8%	–	–	Other	1,358	20.5%	–	–
Total	31,046,635	247,184	100.0%	10,469	100.0%	Total	6,635	100.0%	1,136	100.0%

* For simplicity, all persons with hemophilia were considered Canadian born.

The modeled HCV infection outcomes, including annual incidence of transitions and prevalence of HCV clinical stages, are shown in Table 14 at 5-year intervals from 1962-2022 and graphically in Figure 2. The annual incidence of HCV-induced cirrhosis increased from 0 in 1960 to a peak of over 800 cases per year in the late 1990s and early 2000s; the model predicts that annual incidence of cirrhosis will subsequently decrease somewhat over the following 20 years. According to the model, approximately 9,400 HCV-infected persons were living with cirrhosis in 2002. In contrast, the incidence of the more advanced sequelae of hepatitis C infection will continue to increase through the early part of the 21st century. According to the model, for example, hepatocellular carcinoma will increase by about 15% from 2002 to 2022, whereas HCV-related deaths will increase by almost 40%.

The results of our model were compared with some Canadian data on the incidence of hepatocellular carcinoma (HCC), the modeled burden of HCV in Canada and models from other industrialized countries; this comparison is summarized in Table 15. Interestingly, the number of modeled new HCC cases in 1997 matched relatively closely the actual numbers of HCC cases in 1997, assuming that one-third of HCC cases were due to HCV, as per Wong[25] and the number modeled by Zou[36]. Nevertheless, our model predicts substantially fewer prevalent cases of cirrhosis due to HCV than the Zou model (for example, 9,835 cases of cirrhosis in 2007 compared with 33,076 cases predicted for 2008 by Zou).

Figure 2: Modeled Outcomes of HCV Infection, Canada, 1962-2022

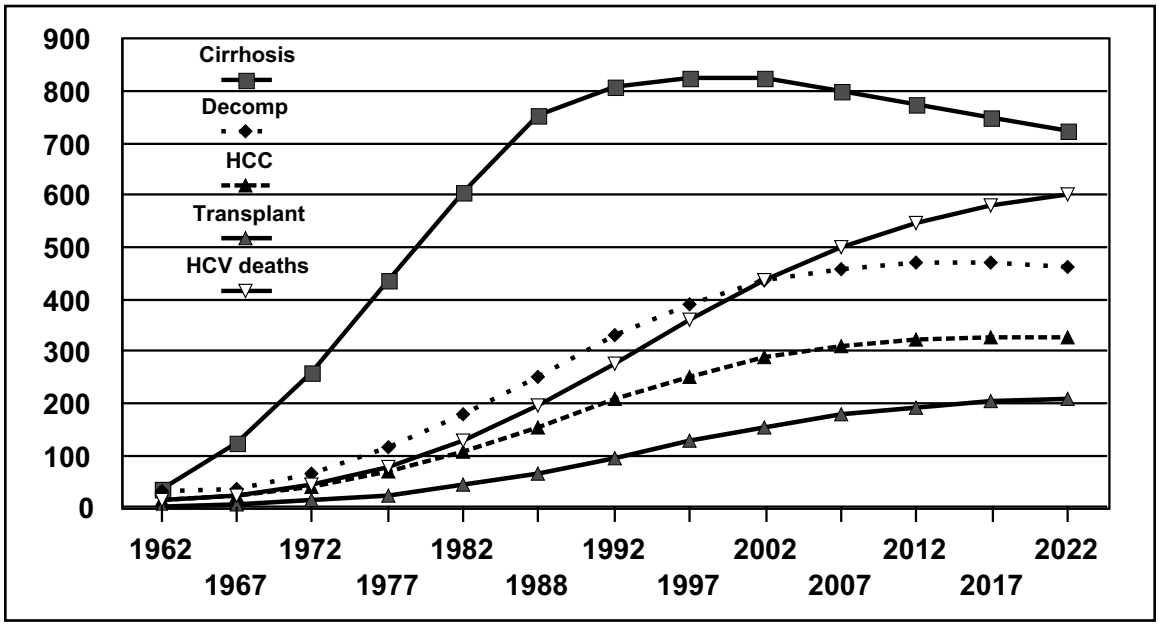


Table 14: Modeled Outcomes of HCV Infection Canada, 1962-2022

Incidence during year:

	Infection	Cirrhosis	Decomp	HCC	Transplant	Decomp Death	HCC Death	Transplant Death	HCV Deaths Total
1962	5,428	37	30	16	3	2	11	0	13
1967	16,069	126	38	23	8	4	19	1	25
1972	20,492	259	66	39	15	8	31	3	44
1977	24,213	437	115	68	25	14	56	8	77
1982	25,318	606	179	108	43	24	91	14	129
1988	19,052	753	252	156	67	37	136	24	196
1992	10,032	811	330	208	95	53	188	37	277
1997	8,401	828	392	253	127	70	236	55	362
2002	6,633	827	436	288	155	85	274	76	437
2007	7,274	802	460	310	178	98	302	99	499
2012	7,502	777	471	323	194	107	319	120	547
2017	7,650	751	471	328	205	113	326	139	579
2022	7,559	726	463	326	210	116	328	155	600

Prevalence (exclusive) at year end:

	Infection	Cirrhosis	Decomp	HCC	Transplant
1962	18,048	654	82	27	4
1967	61,766	896	181	41	31
1972	113,461	1,595	323	71	76
1977	178,575	2,767	571	124	149
1982	233,986	4,227	946	200	271
1988	264,582	5,848	1,440	292	459
1992	259,640	7,481	2,035	396	717
1997	248,130	8,683	2,651	490	1,047
2002	232,585	9,444	3,198	562	1,422
2007	222,005	9,835	3,636	613	1,812
2012	214,493	9,930	3,944	643	2,184
2017	208,344	9,820	4,131	655	2,515
2022	202,077	9,561	4,213	654	2,788

Table 15: HCV Clinical Sequelae: Comparison of Values

	United States		France	Australia	Canada			
	Kim[24]	Wong[25]	Grittiths[48]	NCHECR[50]	Zou[7]	Zou[36]	Saadany[34]	Pohani[35]
Reference year	1999	1997	1999	2001	1998	2008	1997	1997
Population	280,000,000	280,000,000	59,200,000	19,600,000	29,800,000	32,100,000	29,800,000	29,800,000
HCV infections	3,900,000	3,900,000	650,000	210,000	240,000	270,000	240,000	240,000
HCV rate	1.39%	1.39%	1.10%	1.07%	0.81%	0.84%	0.81%	0.81%
Cirrhosis, incidence					2,547	3,360		
Cirrhosis, prevalence				6,500	17,216	33,076		
Cirrhosis prev/1,000 infections				31.0	71.7	122.5		
Decompensation				185	524	1,275		
Decomp/1,000 infections				0.88	2.6	4.7		
Transplants – HCV	1,100				55	137		
Transplants/1,000 infections	0.28				0.23	0.51		
HCC – cases							850	
Cases/1,000 infections							3.5	
HCC – HCV cases		1,747*		50			490	
Cases/1,000 infections		0.45		0.24			2.0	
HCC – HCV deaths		1,600			269	524	283	
Deaths/1,000 infections		2.5			1.12	1.94	1.18	
Liver deaths								
Deaths/1,000 infections								
Liver deaths – HCV	5,000				608	1,377		125
Deaths/1,000 infections	1.3				2.5	5.1		0.52

Note: Reference year refers to year indicated on top row for all figures unless otherwise stated.
* Reference year 1992

Table 15: HCV Clinical Sequelae: Comparison of Values (continued)

	Canada Remis			
Reference year	1992	1997	2002	2007
Population	28,100,000	29,800,000	31,000,000	32,100,000
HCV infections	220,000	240,000	250,000	270,000
HCV rate	0.78%	0.81%	0.81%	0.84%
Cirrhosis, incidence	810	828	827	802
Cirrhosis, prevalence	7,481	8,683	9,444	9,835
Cirrhosis prev/1,000 infections	34.0	36.2	37.8	36.4
Decompensation	330	393	436	288
Decomp/1,000 infections	1.50	1.64	1.74	1.07
Transplants – HCV	95	127	155	178
Transplants/1,000 infections	0.43	0.53	0.62	0.66
HCC – cases				
Cases/1,000 infections				
HCC – HCV cases	208	253	288	310
Cases/1,000 infections	0.95	1.05	1.15	1.15
HCC – HCV deaths	236	274	302	319
Deaths/1,000 infections	1.07	1.14	1.21	1.18
Liver deaths				
Deaths/1,000 infections				
Liver deaths – HCV	277	362	437	499
Deaths/1,000 infections	1.3	1.5	1.7	1.8

Note: Reference year refers to year indicated on top row for all figures unless otherwise stated.

4.6 Results of Epidemiologic Modeling: HCV Morbidity

The results of the calculation of QALY lost due to the hepatitis C epidemic in Canada are shown in Table 16. This analysis suggests that the impact of HCV disease on the health of Canadians is dramatic. Since 1987, 40,000 to 45,000 QALY have been lost each year; this trend appears to continue at least until 2022. To date (2002), 1,179,000 QALY have been lost and, by 2022, a cumulative total of 2,052,000 QALY will have been lost.

4.7 HCV Infections Diagnosed and Reported

Table 17 shows the reported diagnosed cases of HCV provided by the Notifiable Disease Reporting System, Health Canada. For most provinces, the data for 2002 were complete to September 2002; however, data from Nova Scotia were not yet available. Thus, 141,000 HCV infections had been reported in Canada to September 2002. Ontario accounted for 36% and British Columbia for 34% of reported infections. According to the analyses carried out in 1998, Ontario accounted for 45% and British Columbia 22% of the prevalent HCV infections in Canada.

Table 18 presents the modeled "true" numbers of HCV diagnoses from 1991 to 2002 using interpolation as described in Section 3.9. Overall, we estimate that 156,000 persons have received a diagnosis of HCV infection. In the lower part of the table, we compare the numbers of persons with diagnosed HCV with the prevalent HCV infections modeled in 1998. This comparison indicates that 65% of prevalent infections have been diagnosed in Canada, but this varies from 50% in Ontario to 141% in Saskatchewan.

It should be noted that the numbers of persons with diagnosed HCV infection have not been adjusted for under-reporting or duplicate reporting, which would, in fact, operate in opposite directions. Data from the questionnaire completed by all but one of the provinces indicated that HCV reporting rates were likely very high, since reporting is mostly laboratory-based. Although duplicate rates were less likely to be known by the provincial authorities, the provinces that did estimate the extent of duplicate reporting indicated that measures were being taken systematically to eliminate duplicates and that the residual duplicate rate was less than 10%.

Table 16: Quality-Adjusted Life Years (QALY) Lost Due to HCV Infection, Canada, 1962-2022

	Model with HCV, QALY						Model without HCV, QALY				
Year	HCV-negative	Pre-cirrhosis	Cirrhosis	Decomp	HCC	Transplant	HCV-negative	QALY Model with HCV	QALY Model no HCV	QALY lost	Cumulative QALY lost
1962	18,909,206	18,048	654	82	27	4	18,927,850	17,600,414	17,602,901	2,486	2,486
1967	20,671,925	61,766	896	181	41	31	20,733,936	19,274,563	19,282,560	7,997	31,450
1972	22,091,682	113,461	1,595	323	71	76	22,205,565	20,636,475	20,651,175	14,701	91,547
1977	23,527,988	178,575	2,767	571	124	149	23,708,072	22,024,857	22,048,507	23,650	191,898
1982	24,829,022	233,986	4,227	946	200	271	25,068,342	23,280,130	23,313,558	33,428	339,483
1987	26,074,392	264,582	5,848	1,440	292	459	26,348,987	24,464,290	24,504,558	40,268	527,142
1992	27,860,581	259,640	7,481	2,035	396	717	28,135,664	26,123,467	26,166,168	42,700	735,779
1997	29,508,539	248,130	8,683	2,651	490	1,047	29,776,104	27,647,449	27,691,777	44,328	954,163
2002	30,799,425	232,585	9,444	3,198	562	1,422	31,054,381	28,835,148	28,880,574	45,426	1,179,098
2007	31,881,396	222,005	9,835	3,636	613	1,812	32,128,318	29,832,723	29,879,336	46,613	1,409,790
2012	32,812,665	214,493	9,930	3,944	643	2,184	33,053,997	30,697,580	30,740,217	42,637	1,630,927
2017	33,595,319	208,344	9,820	4,131	655	2,515	33,831,481	31,420,862	31,463,277	42,415	1,843,447
2022	34,174,815	202,077	9,561	4,213	654	2,788	34,404,320	31,954,880	31,996,018	41,137	2,051,690

	HCV Negative	Pre-cirrhosis	Cirrhosis	Decomp	Transplant	HCC
Utility	0.93	0.79	0.80	0.60	0.73	0.72

Source: Chong CA, et al.[43]
Mittmann N, et al.[45]
Note: QALY values for inter-model output years interpolated linearly within the five-year period.

Table 17: Reported Cases of Hepatitis C Infection by Province/Territory 1991-2002, Incomplete

	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	Total
British Columbia	197	1,089	1,071	2,232	5,153	6,626	8,282	6,819	5,016	4,733	3,665	3,681	48,564
Alberta	–	–	–	–	–	–	1,666	2,992	2,705	2,253	1,963	1,003	12,582
Saskatchewan	25	74	343	337	583	524	604	917	537	720	680	438	5,782
Manitoba	–	–	–	–	–	–	–	–	573	505	695	361	2,134
Ontario	0	155	124	174	8,234	8,212	6,472	7,087	6,520	5,767	4,325	3,309	50,379
Quebec	–	–	–	–	–	22	1,693	3,207	3,397	4,209	1,973	2,140	16,641
New Brunswick	–	–	93	62	143	160	177	218	186	211	144	111	1,505
Nova Scotia	–	–	–	–	–	336	528	429	305	254	73	–	1,925
PEI	2	1	1	3	0	0	0	59	26	11	27	32	162
Newfoundland	–	–	2	19	41	36	43	38	45	52	46	30	352
Nunavut	–	–	–	–	–	–	–	–	–	–	–	–	–
NWT	–	–	5	15	23	35	20	42	42	35	50	29	296
Yukon	–	–	–	14	55	77	87	77	45	47	45	36	483
Total	224	1,319	1,639	2,856	14,232	16,028	19,572	21,885	19,397	18,797	13,686	11,170	140,805

* Data complete to September 2002; Nova Scotia data were not yet available.

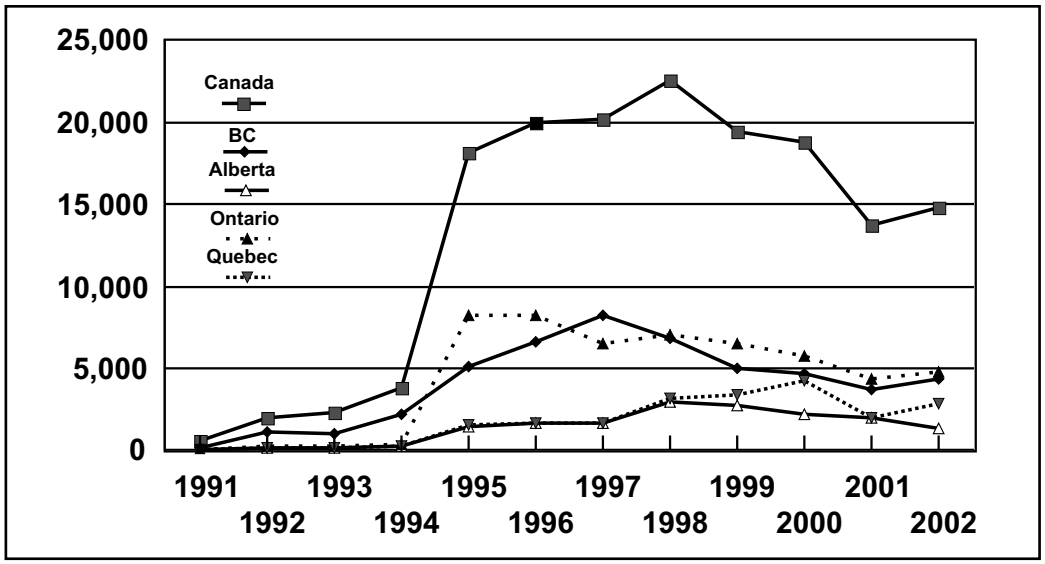
Table 18: Modeled Number of Diagnosed Hepatitis C Infections by Province/Territory 1991-2002

	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002*	Total
British Columbia	197	1,089	1,071	2,232	5,153	6,626	8,282	6,819	5,016	4,733	3,665	4,326	49,209
Alberta	70	166	187	318	1,495	1,645	1,666	2,992	2,705	2,253	1,963	1,306	16,766
Saskatchewan	25	74	343	337	583	524	604	917	537	720	680	785	6,129
Manitoba	60	60	68	114	535	588	597	666	573	505	695	417	4,878
Ontario	70	310	248	348	8,234	8,212	6,472	7,087	6,520	5,767	4,325	4,797	52,390
Quebec	70	169	190	323	1,518	1,670	1,693	3,207	3,397	4,209	1,973	2,815	21,234
New Brunswick	40	82	93	62	143	160	177	218	186	211	144	132	1,648
Nova Scotia	10	34	39	65	305	336	528	429	305	254	73	79	2,457
PEI	4	5	6	10	48	52	53	59	26	11	27	37	338
Newfoundland	5	10	11	19	41	36	43	38	45	52	46	24	370
Nunavut												6	6
NWT	0	8	9	15	23	35	20	42	42	35	50	50	329
Yukon	5	7	8	14	55	77	87	77	45	47	45	38	834
Total	556	2,014	2,273	3,857	18,133	19,961	20,222	22,551	19,397	18,797	13,686	14,776	156,590

	Diagnosed to 2002	Modeled 1998	Proportion Diagnosed Modeled
British Columbia	49,209	52,546	94%
Alberta	16,766	25,380	66%
Saskatchewan	6,129	4,343	141%
Manitoba	4,878	6,178	79%
Ontario	52,390	105,242	50%
Quebec	21,234	36,235	59%
New Brunswick	1,648	2,844	58%
Nova Scotia	2,457	4,791	51%
PEI	338	343	99%
Newfoundland	370	460	80%
Total	155,421	238,362	65%

Figure 3 presents graphically the data in Table 18, which estimates the number of HCV infections reported annually. It suggests that we do not yet appear to be close to exhausting the pool of chronic HCV infections in Canada.

Figure 3: Modeled diagnosed HCV Infections for Selected Provinces and Canada, 1991-2002



4.8 Summary of Generalized Lookback Programs

A summary of the notification programs related to blood transfusion carried out by the provincial authorities is shown in Table 19. As seen in this table, generalized lookback programs have been carried out in all provinces but Newfoundland and Ontario. In Ontario, as best we could determine, lookback programs have been carried out only in three hospitals, namely the Hamilton-Chedoke Regional Hospital[46], the Hospital for Sick Children[47] and Sunnybrook Health Sciences Centre[48].

Table 19: Summary of Generalized Lookback Programs for Hepatitis C Carried Out to Date by Province, Canada, 2002

Province	GLBP*	Period covered		Lookback period		Recipients	Letters	Tested	HCV+	Proportion previously known
		From	To	Start date	End date					
British Columbia	Yes	1985-01	1990-06	1997-04	1997-11	137,207	60,398	38,989	1,945	
Alberta	Yes	1986	1990	2001-04	present					
Saskatchewan	Yes	1986	1990	1998						
Manitoba	Yes	1978	1992-04	2001-05	2002-03					
Ontario	No									
Quebec	Yes	1960	1990-06	2000-12	2003-12		112,221			
New Brunswick	Yes	1986	1990	1999	2001		17,813	6,847	38	N/A
Nova Scotia	Yes	1984-01	1990-06	1997-10	1999-04	38,244	17,395	9,942	125	48%
PEI	Yes	1984-01	1990-06	1998-02	1998-09	6,086	2,451	1,953	43	34%
Newfoundland	No									

* GLBP = generalized lookback program.

5. Discussion

We carried out an epidemiologic modeling study to determine the number and distribution of prevalent and incident HCV infections in Canada. We estimated that approximately 251,000 persons in Canada were infected with HCV as of December 2002 and that about 5,000 persons are newly infected each year, mostly through injection drug use. The prevalence of HCV infection in Canada was 4% higher than in 1998. The distribution of prevalent HCV infections by exposure category (to the nearest 1,000) was as follows: IDUs 50,000, ex-IDUs 89,000, hemophilia patients 1,200, blood transfusion recipients 33,000 and "Other" 74,000. In our analysis, IDU accounted for 56% of the prevalent HCV infections in Canada, hemophilia 0.5%, blood transfusion 13% and other modes of transmission 30%.

The impact of the sequelae of hepatitis C infection on the health of Canadians was considerable. In 2002, 9,400 persons were living with cirrhosis and 3,200 with liver failure. The annual incidence of newly developing cirrhosis appeared to peak in the late 1990s and early 2000s but, according to the results of our model, the incidence of the more serious outcomes of HCV infection will continue to rise, at least until 2022. Finally, our results also indicate that the impact of HCV disease on the health of Canadians has been and will continue to be dramatic: to 2002, almost 1,200,000 QALY have been lost because of HCV infection and, by 2022, a cumulative total of almost 2,100,000 QALY will have been lost. Nevertheless, these results should be put in the context of other infectious and non-infectious conditions to be fully appreciated.

To carry out the present study, we relied heavily on data from the EHSSS sentinel program. However, there are a number of limitations to these data. Although eight sites were included, data were from six sites, and there were still very limited data from British Columbia outside Vancouver, and no data from Montreal or Toronto. HCV infection in Toronto and Montreal represents an important component of the Canadian situation, given the large, urban population of these cities and the concentration of injection drug use. Patterns of HCV infection in Montreal and Toronto may differ from those in the rest of the country.

Within the EHSSS, interviews were not conducted for a substantial proportion of reported cases, thus resulting in an incomplete data set on risk factors related to the acquisition of HCV infection. From those interviewed, the rates for acute and chronic cases were approximately 80% and 50%, respectively. A large proportion of the risk factors for hepatitis C infection were reported as "Other" and as "unknown". In previous studies, this proportion of "Other" and unknown risks has been documented as ranging from 10% to 20% of acute cases. Risk factor data, reported by patients, are often difficult to interpret and evaluate. Some reported risk factors are unlikely to represent the true source of HCV infection since socially undesirable behaviours such as injecting drugs may not be disclosed. A substantial proportion of people interviewed did not provide risk factors and country of birth; accordingly, the direction and strength of biases contained in the data are difficult to evaluate without additional studies. Also, people who use injection drugs are probably less likely to complete an interview for several reasons (including, for example, not having a telephone or even a fixed address), and those who do consent to an interview may under-report injection drug use. Thus, the relative importance of injection drug use in our model is likely under-estimated.

Aside from persons who are not interviewed and those who deny risk factors but may, in fact, have injected drugs are persons classified as having being infected by other modes of transmission, representing almost 30% of the estimated prevalent infections and 21% of the acute infections. Some of these may have also injected drugs. Such misclassified cases would lead to underestimation of the number of persons infected through injection as well as overestimation of those infected by other routes.

The classification of reported cases into acute versus chronic infection is often difficult in the context of a surveillance study such as this. (The challenge of correct classification applies to clinical diagnoses as well). Cases may be misclassified in both directions; a new HCV infection may be diagnosed without good clinical or serologic evidence of recent acquisition, and chronic HCV infections may be diagnosed only after an exacerbation of chronic hepatitis leading to jaundice, which can be interpreted as evidence of a new infection. The relative degree of misclassification is difficult to quantify and, even if misclassifications did balance out, the misclassified cases in one direction may have different epidemiologic characteristics than cases misclassified in the opposite direction.

To calculate HCV incidence, we assumed that persons whose condition was diagnosed during the acute phase of infection were all symptomatic. This may not always be the case. Some recently infected persons may, in fact, have been tested as a result of reported risk behaviours rather than because of symptoms. If this occurred to a significant extent, it would have the effect of biasing our estimate of HCV incidence upward.

Another difficulty was the limited availability of detailed and reliable data on the extent and dynamics of drug injection. Thus, the number of IDUs, and especially of ex-IDUs, is difficult to estimate with precision. The group of ex-IDUs, which is difficult to define and track, is particularly problematic. For example, persons undergoing diagnostic testing for bloodborne viruses such as HCV or HIV may report injection drug use without indicating whether such exposure was recent. These persons are often assumed to be active IDUs. Thus, HCV prevalence among ex-IDUs is particularly difficult to estimate since few studies stratify results according to recency of drug use. The HCV prevalence rates ultimately used for active and ex-IDUs were chosen because they were consistent with the limited data showing that about one-third of persons with a lifetime history of drug injection are active IDUs and because they yielded plausible estimates of HCV prevalence for IDUs.

Our model began in 1960, and we established a "starting" population for each stratum defined by country of birth and exposure category. However, HCV incidence was applied only beginning in 1960 with application of our model. This may have produced some underestimation of HCV prevalence, especially in the early years. However, the "left-truncation effect" would have diminished with time and would have had little impact on the estimates for the period of interest, i.e. 1990 to 2022. In addition, HCV incidence appears to have been low before 1960 according to modeling studies carried out in the United States[32], France[49] and Australia[50], and was probably also low in Canada at that time.

In the course of this study, we examined the prevalence of HCV infection among persons born outside of Canada. When we carried out our initial calculation by multiplying the immigrant populations in Canada by the WHO estimate of HCV prevalence in the country of origin, we obtained an estimate of 98,400 HCV-infected persons. However, in our final model, using data on the country of birth reported to the EHSSS, the estimated number was markedly lower; in fact, in the final analysis, we estimated the number to be 49,000, or one-half of the preliminary estimate. This would yield an HCV prevalence among persons born outside Canada of 0.90%, only slightly higher (14% higher) than the HCV prevalence of 0.79% estimated for persons born in Canada. Although the EHSSS data are incomplete with respect to country of birth (country of birth was unavailable for 23% of cases with chronic or unknown HCV infection), we feel that the final estimate is likely to be closer to the true situation. First, the preliminary analysis of country-specific HCV prevalence for persons in Canada born elsewhere is subject to considerable uncertainty. The estimates developed by the WHO are imperfect, in part because many countries do not have a reliable surveillance system for hepatitis C, and only limited population-based studies have been carried out. In addition, the country-specific HCV prevalence rate we use here does not take into account possible HCV prevalence changes in each country over the past 40 years. Finally, the lower HCV prevalence observed in the final analysis compared with the preliminary analysis may have been due, in part, to selective factors in immigration to Canada.

The estimates of the number of incident HCV infections was based on a number of assumptions that could not be independently validated. Our analysis generated an estimated 160 annual HCV infections due to blood transfusion. Although this represents only a small fraction of the estimated 5,000 new HCV infections in Canada and therefore would not overly affect the total estimated total number of new HCV infections, other information suggests our estimate of the number of HCV infections due to transfusion is likely far too high. Beginning in October 1999, the Canadian Blood Service has used nucleic acid testing (NAT) for HCV, an assay that is considered to be almost 100% sensitive; since then, only a single donation has been found to be NAT-positive for HCV but negative by the EIA screening assay currently in use (Saldanah J., Canadian Blood Services: personal communication, 2003). Thus, it is likely that the number of HCV infections transmitted by blood transfusion in Canada is very small and much lower than the 160 transmissions yielded by our analysis. The precise estimation of this number is beyond the scope of the present study.

To estimate the occurrence and prevalence of serious outcomes of HCV infection, we applied annual transition probabilities to strata of HCV-infected persons. The values of these probabilities were obtained through a review of published studies and consultation with experts in the field. Nevertheless, these values are subject to considerable uncertainty. Studies of the natural history have attempted to quantify the rate of progression of HCV disease from HCV infection and have observed varying results. These differences could be due to the different methods used or to differences in the populations studied. Such populations could vary by source of infection, sex, age, genetic predisposition, alcohol intake, other medical conditions and the use of medications, among other factors, which could well influence the likelihood of, say, the rate of development of cirrhosis. It is impossible to know whether their distribution in the Canadian population is similar to that of the populations studied. Nevertheless, it is interesting that our estimate of the incidence of HCV-related HCC was consistent with the observed incidence reported by El Saadany[34] as well as that modeled by Zou[36]. On the other hand, our estimate of the incidence and prevalence of cirrhosis was considerably lower than that estimated in Zou's model using a very different approach from ours.

The progression and the models we used did not take into account the possible impact of treatment on HCV infection outcomes. This would likely have had little impact on the results to the present time since, to the best of our knowledge, only a few thousand HCV-infected persons have been treated with antiviral drugs in Canada to date, representing only 1% to 2% at most of infected persons. If, on the other hand, new treatment regimens for HCV infection are developed that are highly effective, safe, relatively cheap and easy to administer and are made widely available, the negative impact of chronic HCV infection in Canada could be significantly lower than our estimate.

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