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Known and Unknown Risk Factors for Hepatitis B and Hepatitis C Infections in Ottawa (1998-2002)

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KNOWN AND UNKNOWN RISK FACTORS FOR HEPATITIS B AND HEPATITIS C INFECTIONS IN OTTAWA

Dr. Lilian Arakelyan

Thesis submitted to the
Faculty of Graduated and Postdoctoral Studies
in partial fulfillment of the requirements for the degree of
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ABSTRACT

Title: Known and unknown risk factors of viral hepatitis B (HBV) and hepatitis C (HCV) in Ottawa, 1998-2002.

Objectives: Investigate, describe and evaluate HBV and HCV cases with known and unknown risk factors and propose modifications to the Enhanced Surveillance questionnaire based on the results of an exploratory study.

Design: 1) Enhanced Surveillance database analysis; 2) Exploratory Study of hepatitis patients with unknown risk factors (URF) at the Ottawa site.

Methods: Demographic and epidemiologic data analysis of HBV/HCV cases. Telephone interview with cases having unknown risk factors, using an open-ended questionnaire.

Results: Medical/health care acquired, sexual transmission, healthcare and other work related and other recognised and potential new risk factors for contracting HBV/HCV were revealed. Some of the cases with URF could have been identified at the Enhanced Surveillance.

Conclusions: The open-ended questions from the Exploratory Study should be incorporated into the Enhanced Surveillance questionnaire. The newly identified potential risk factors deserve further assessment through analytical studies.

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TABLE OF CONTENTS

LIST OF TABLES

Chapter 1. Introduction

Chapter 2. Enhanced Surveillance

Chapter 3. Exploratory Study

LIST OF FIGURES

Chapter 1. Introduction

Chapter 2. Enhanced Surveillance

Chapter 3. Exploratory Study

LIST OF SCHEMAS

Chapter 1. Introduction

Chapter 2. Enhanced Surveillance

Chapter 3. Exploratory Study

LIST OF ABBREVIATIONS

ALT	Alanine-Amino-Transferase (a type of liver enzyme)
Anti-HBc	Antibody to HBcAg
Anti-HBe	Antibody to HBeAg
Anti-HBs	Antibody to HBsAg
Anti-HCV	Antibody to hepatitis C virus
AST	Aspartame-Amino-Transferase (a type of liver enzyme)
BBPD	Blood-Borne Pathogens Division (Health Canada)
CDC	Centers for Disease Control and Prevention (Atlanta, USA)
CI(s)	Confidence interval(s)
DNA	Desoxyribo-nucleic acid
EEG	Electro-encephallography
EHSSS	Enhanced Hepatitis Strain Surveillance System, Enhanced Surveillance
ELISA	Enzyme linked immunoassay
HAV	Hepatitis A virus
HBcAg	Hepatitis B core antigen from the nucleocapsid core
HBeAg	Hepatitis B "e" antigen from the nucleocapsid core of the virus
HBsAg	Hepatitis B surface antigen from the glycoprotein coat of the virus
HBV	Hepatitis B virus
HCAID	Health Care Acquired Infections Division
HCC	Hepato-cellular carcinoma
HCV	Hepatitis C virus
HIB	Hemophilius influenza B
HIV	Human immunodificiency virus
IDU	Injection drug use or users
IgM anti-HAV	Immunoglobulin M antibody to HAVAg
IgM anti-HBc	Immunoglobulin G antibody to HBcAg
IgM anti-HBc	Immunoglobulin M antibody to HbcAg
K	Kappa coefficient

LCDC	Laboratory Centre for Disease Control
MoU	Memorandum of Understanding
MSM	Men sex with men
NDRS	National Notifiable Diseases Reporting System at Health Canada
NML	National Microbiology Laboratory
OHU	Ottawa Health Unit
PCR	Polymerase chain reaction
PPHB	Population and Public Health Branch
PTH-NANB	Post-transfusion non-A, non-B hepatitis infection
RD(s)	Risk difference(s)
RNA	Ribo-nucleic acid
RF(s)	Risk factor(s)
RR(s)	Relative risk(s)
STD	Sexually transmitted disease
URF(s)	Unknown risk factor(s)
USA	United States of America
WHO	World Health Organization
%(s)	Percent(s), percentage(s)

1. INTRODUCTION

1.1 Overview of Viral Hepatitis

Hepatitis B and hepatitis C are viral infections of the liver caused by the hepatitis B virus (HBV) and hepatitis C virus (HCV), respectively. The viruses are spread by direct exposure to the blood, blood products or body fluids (such as semen, saliva etc.) of those infected with the viruses. Symptoms include loss of appetite, nausea and vomiting, abdominal pain, extreme fatigue, dark urine, and jaundice.

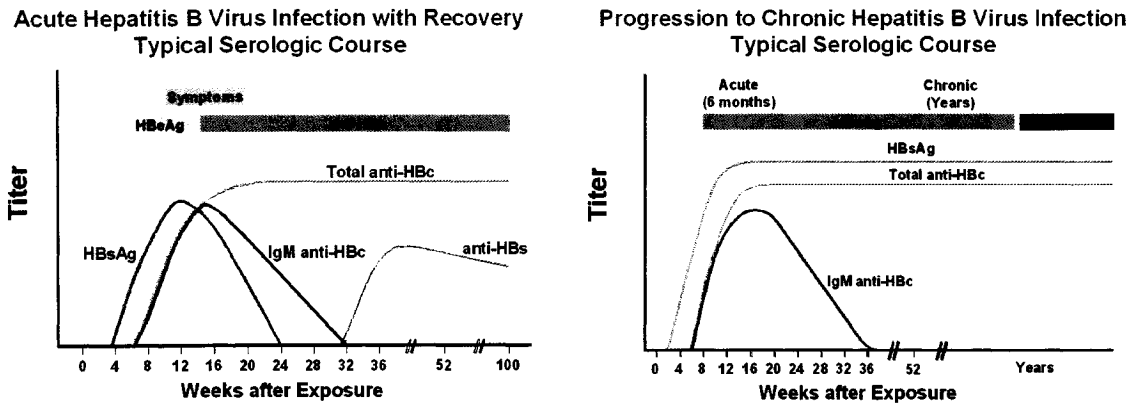
1.1.1 Natural history of HBV.

HBV was the first human hepatitis virus from which the proteins and genome could be clearly identified and characterised. In 1963, Blumberg et al. [1] discovered a previously unknown antigen that was first called "Australia antigen" and later was recognised by its specific association with hepatitis B. In 1970, Dane and colleagues [2] first described the 42 nm particles that are the hepatitis B virions. The term Australia antigen was later replaced with HBsAg to denote its association with the envelope of HBV. Now, it is the primary component of the hepatitis B vaccine. In 1973, an endogenous desoxyribo-nucleic acid (DNA) dependant DNA polymerase within their core was detected [3]. Subsequently, the HBV was found to be a small, circular, partly double-stranded DNA virus of the class Hepadnaviridae (Figures 1.1 a-b). [4, 5].

Figure 1.1a-b Hepatitis B virus.

The natural history of chronic HBV infection can be divided into three phases based on virus-host interactions: high replicative or immune tolerant, low replicative or immune clearance, and "acute exacerbations" phases with an incubation period of about 4 weeks [6].

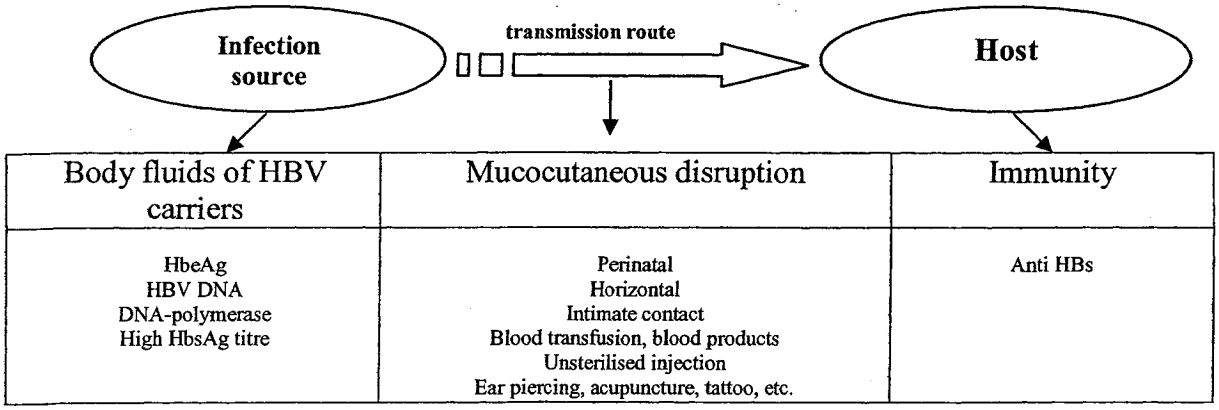
About 30% of persons infected with hepatitis B virus have no signs or symptoms, 90% of cases recover completely and become immune to the virus, and 10% develop a chronic infection with ongoing symptoms and continue to be infectious for a variable length of time. Chronic infection is defined as having hepatitis B present for six months or more. People with a chronic hepatitis infection are at high risk of liver damage; 20-30% of those will progress to cirrhosis. The serological progression of the HBV infection is illustrated in Figures 1.2 a-b.



a **b**

Figures 1.2 a-b Serologic course of acute HBV infection with recovery (a) and with progression into chronic infection (b).

Like other infectious agents, successful HBV infection requires three components: an infection source, a susceptible host, and an established route of infection (Schema 1.1) [7]. Rather then treating those who are already infected, the most effective ways to control hepatitis B are to prevent any susceptible person from virus infection by: 1) interrupting the route of transmission; 2) immunising the susceptible host. Among them, immunisation and public education are the most essential tools.



Schema 1.1 Components of hepatitis B virus infection.

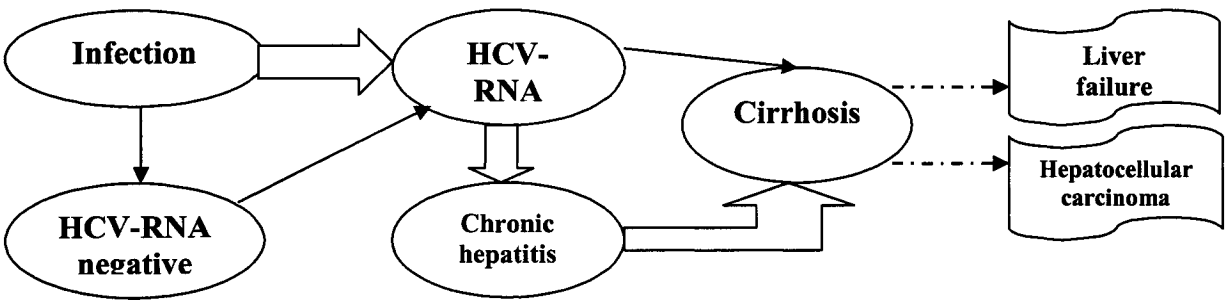
Since introduction of a vaccine against hepatitis B in 1991, its prevention in Canada includes the following (Source: Health Canada website, atURL http://www.hc-sc.gc.ca/pphb-dgspsp/dird-dimr/vpd-mev/hepatitis-b_e.html, last update - October 23, 02): 1) publicly funded universal immunisation of children offered in all provinces and territories of Canada including Ontario; 2) universal screening of all pregnant women for HBsAg at the first prenatal visit or at the time of delivery, at latest; 3) pre-exposure immunisation of high-risk groups of people who are at increased risk of occupational infection such as those exposed frequently to blood, blood products and bodily fluids that may contain the virus (health care and emergency service workers) and others at increased risk (homosexual men, injection drug users, haemophiliacs, household contacts, travelers to endemic areas); 4) post-exposure intervention for those exposed to disease, particularly infants born to HBV+ mothers.

1.1.2 Natural history of HCV

Hepatitis C virus is a positive strand RNA virus that is related to the Flavi and Pestiviruses family. It was first identified in the USA in 1989 as a major causative agent of post transfusion non-A, non-B hepatitis [8]. Like many RNA viruses, HCV displays a high mutation rate which produces: 1) protection against immunological detection and destruction which leads to its

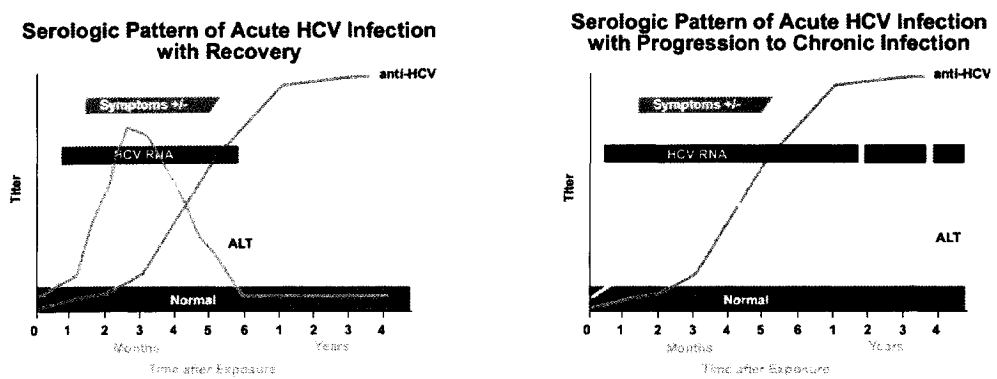
persistence, flare up and transmission of disease; 2) unreliability of antibody tests; 3) higher reinfection rate due to incomplete immunity; 4) variable clinical expression; 5) variable and unpredictable response to treatment; 6) difficulty in development of a reliable vaccine [9-11].

Hepatitis C has clinical symptoms similar to hepatitis B. HCV infection leads to acute hepatitis in 20% of cases and chronic hepatitis in 50% of cases, 20% of whom develop cirrhosis [12, 13]. There is also a strong relationship between HCV and hepatocellular carcinoma [14, 15]. Schema 1.2 represents an overview of the natural history of hepatitis C.



Schema 1.2 Overview of the natural history of hepatitis C.

Hepatitis C is considered more dangerous than hepatitis B in its development and outcome since 80% of infected persons have no signs or symptoms of a disease and there is no vaccine. The serologic patterns of acute HCV are depicted in Figure 1.3 a-b.



a **b**

Figure 1.3 a-b. Serologic pattern of acute HCV infection with recovery (a) and with progression to chronic infection (b).

1.2 Epidemiology of Hepatitis B and Hepatitis C

1.2.1 World data

HBV and HCV infections are a major challenge and an important public health concern in the contemporary world. According to World Health Organisation (WHO) data, the prevalence of these infections in the world is very high and varies from region to region [16]. Based on those levels, WHO has defined regions and countries with high, intermediate and low endemicity (Figure 1.4).

HBV is prevalent in Asia, Africa, southern Europe, and Latin America, where the rate of hepatitis B surface antigen (HBsAg) carriage in the general population ranges from 2% to 20% [17, 18]. About one third of the world's population (2 billion people) have serologic evidence of being exposed to HBV, of which more than 350 million suffer from chronic infection. These people have a 15% to 25% risk of dying from HBV related liver disease, including end-stage cirrhosis and hepatocellular carcinoma (HCC) [6, 19]. Each year, acute and chronic HBV infection causes roughly one million deaths [18].

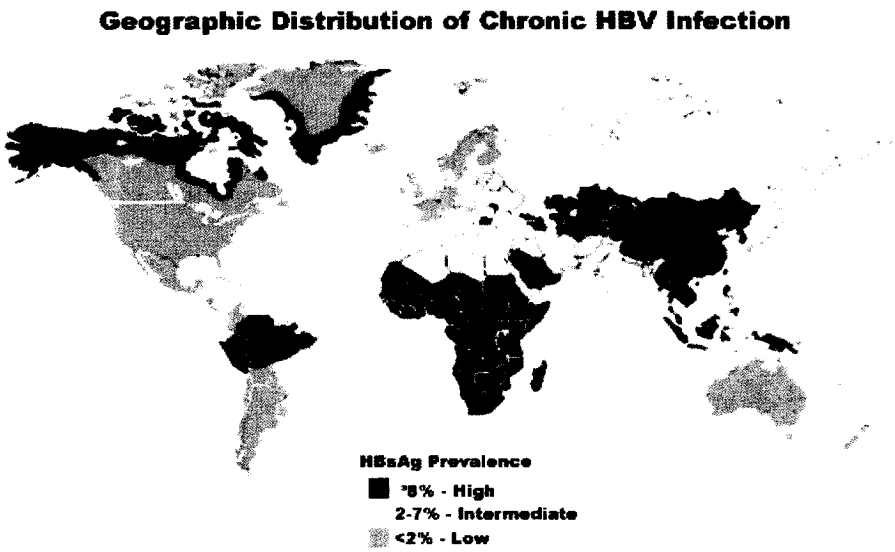


Figure 1.4 Prevalence of HBV infection in the world.

Although the published numbers for HCV are much smaller due to the lack of screening programs and incomplete data reporting, they are also very alarming. According to the WHO, of the total population of 5,811 million in the world, 169.7 million (or 3.1% as reported in website, which is actually 2.9%) are infected with HCV, and that number does not include the infected population from 57 countries where data are not available [20, 21]. In the USA, antibodies to HCV are encountered in 0.1% to 1.8% of the general population. In healthy volunteer blood donors the incidence of HCV in the USA varies from 0.17 % to 1.4% and in the UK is 0.35%. However in other parts of the world, the incidence of HCV infection both in the general population and blood donors may be much higher.

1.2.2 Canada and USA

The Centers for Disease Control and Prevention (CDC) has declared that although the annual incidence of newly acquired HCV has declined substantially in the USA, from 180,000 to 300,000 in the past decade, there still remains a large reservoir of chronically infected population (estimated to be 3.9 million, or 1.8%) who can serve as a source of transmission to others and who are at risk of severe consequences of chronic liver disease [22].

In Canada, it is estimated that over 100,000 people are infected with HBV [23] and about 240,000 with HCV [24]. Examination of the rates of HBV and HCV infections in Canada over the last 12 years (Figure 1.5) shows that reported incidence rates for HBV have decreased slightly (probably due to vaccination strategies), but identification rates for HCV have increased very sharply. However, the later figures may include many newly reported chronic cases.

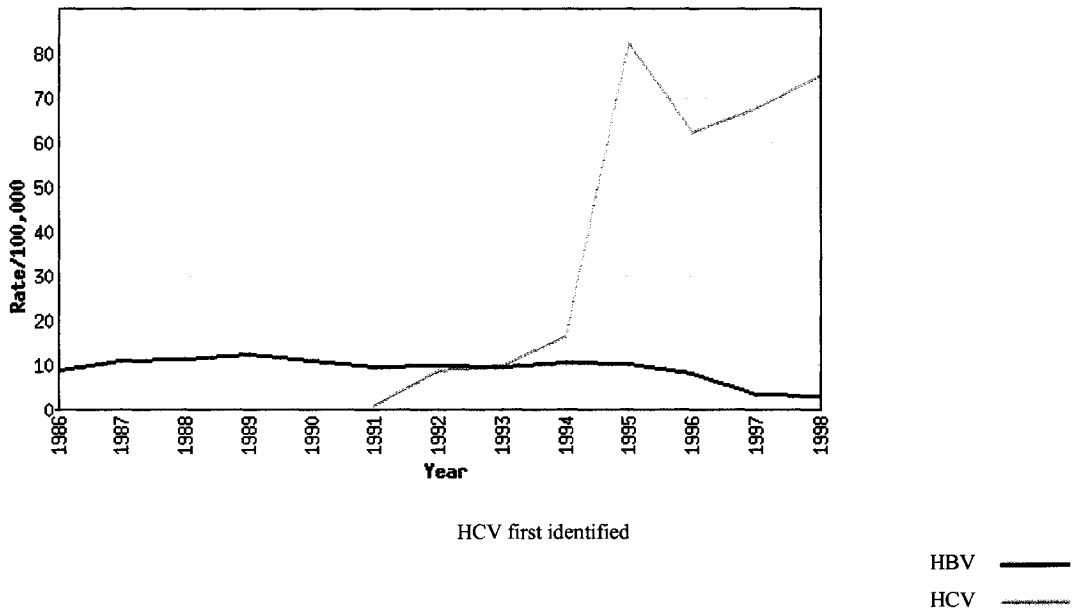
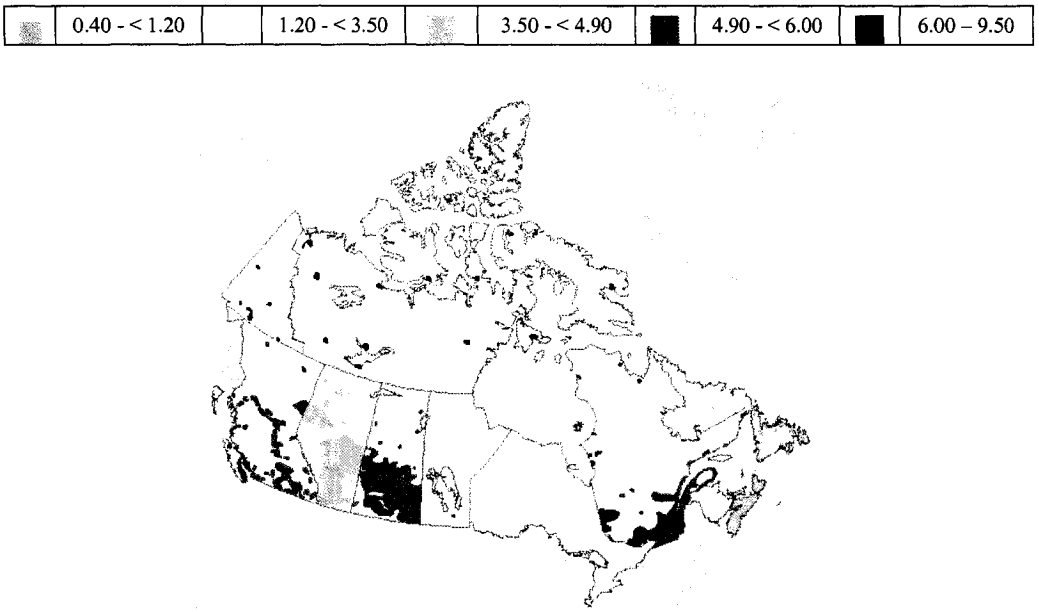


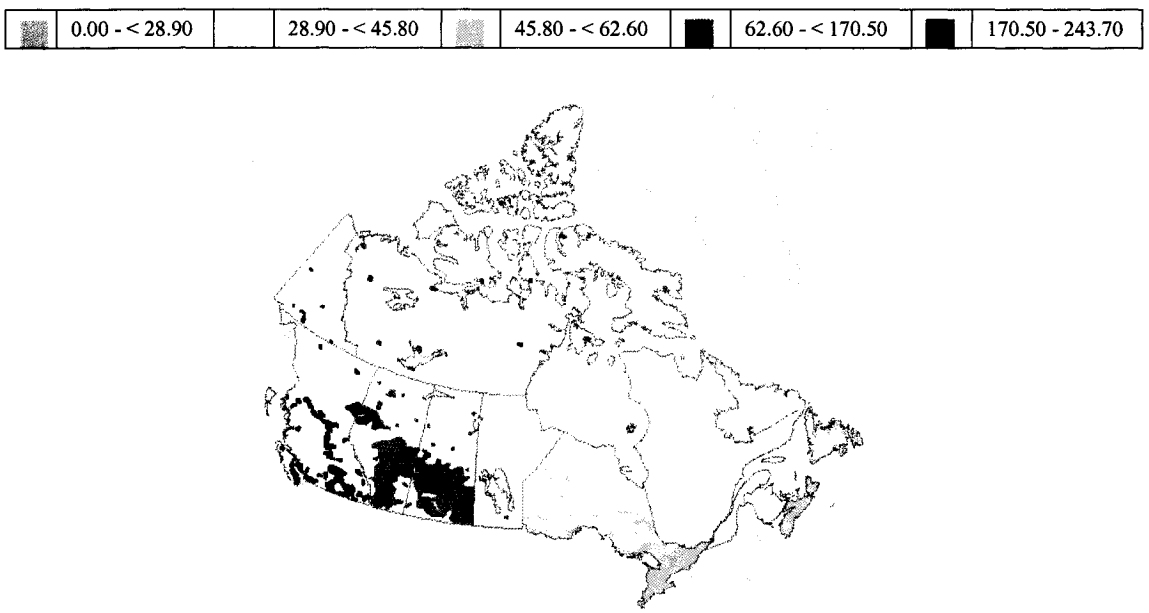
Figure 1.5 Incidence of HBV and identification rates for HCV over time for both sexes and all ages combined, Canada, 1986-1998 (Source: Health Canada).

The prevalence of hepatitis B and hepatitis C infections varies considerably across Canada because of the heterogeneity of the Canadian population (Figure 1.6 a-b). If the Canadian population can be described by three groups - Native/Inuit, Immigrant and Non-immigrant, then the estimated numbers and prevalence of HBV cases in Canada would be the following [25-30] 154,160 (or 4.3%) among Immigrants, particularly those from regions with high endemic rates of HBV, such as Asia; 1,640 (or 4%) among Native/Inuit; and 49,862 to 124,655 (or 0.2-0.5%) among Non-immigrants. The proportion of HBV infected patients who are HBeAg-positive also varies amongst the different groups [25]. HBeAg-positivity ranges from <9% in the Inuit population, to <15% for non-immigrants, to 46% for Asian immigrants and 55% for Indochinese immigrants. The majority of HBeAg-positive cases occur in the young immigrant population.

Hepatitis B
Both Sexes and All Ages Combined, 1998*
(Rate per 100,000)



Hepatitis C
Both Sexes and All Ages Combined, 1998*
(Rate per 100,000)



*Source: Health Canada

Figure 1.6 Prevalence of hepatitis B and hepatitis C in Canadian provinces/territories.

It is not possible to cite population-specific estimates for HCV infection, since the only major source of Canadian data is the Enhanced Surveillance (described in Chapter 2) that was established at the end of 1998 and is not nation-wide. It can only provide preliminary and approximate numbers which imply the highest rates of HCV in the Native/Inuit population [29-32]. Subsequently, wherever these groups of populations are mostly located, those regions have highest rates of infections. Therefore, HBV is highest in North West Territories and HCV is highest in British Columbia (Figure 1.6).

As a leading cause of chronic liver disease and hepatocellular carcinoma, and because of the magnitude of the infection worldwide, HBV and HCV have important implications for public health [33-36]. For instance, chronic liver disease is the tenth leading cause of death among adults in the United States, and accounts for approximately 25,000 deaths annually, or approximately 1% of all deaths. Population-based studies indicate that 40% of chronic liver disease is HCV-related, resulting in an estimated 8,000 to 10,000 deaths each year.

According to Statistics Canada data, 2,030 deaths in 1997 occurred from chronic liver diseases, which comprise a noticeable proportion of all the leading causes of deaths and are 3.2 times as common as deaths from HIV (Table 1.1; note that chronic liver disease and cirrhosis may have causes other than HBV or HCV, such as alcohol-related cirrhosis etc.).

Table 1.1 Age-standardised mortality rates from chronic liver diseases and HIV*

Causes of Death	1997				
	Number	%	Both sexes	Males	Females
			Rate**		
All causes	215,669	100.0	658.7	844.0	521.6
Chronic liver diseases and cirrhosis	2,030	0.9	6.4	8.9	4.2
HIV infection	626	0.3	2.0	3.6	0.5

*Source: Statistics Canada
** Age-standardized mortality rate per 100,000 population

Over the next 10 to 20 years chronic hepatitis C is predicted to become a major burden on the health care system in Canada as patients who are currently asymptomatic with relatively mild disease progress to end-stage liver disease and develop hepatocellular carcinoma. Predictions in the USA indicate that there will be a 60% increase in the incidence of cirrhosis, a 68% increase in hepatoma incidence, a 279% increment in incidence of hepatic decompensation, a 528% increase in the need for transplantation, and a 223% increase in liver death rate [37]. There are no comparable studies to assess the future health burden in Canada, but since the demographics in the US and Canada are similar, we can expect a similar increase in Canada.

1.2.3 Risk factors for HBV and HCV

The epidemiology of HBV and HCV infections in developed countries has changed. Formerly, the main source of HCV infection was transfusion of contaminated blood and/or blood products (before 1992), but now injection-drug use accounts for the majority of new infections [33, 37-38]. For instance, the trends of well-established groups of risk factors responsible for acute hepatitis C over time are reflected in Figure 1.7.

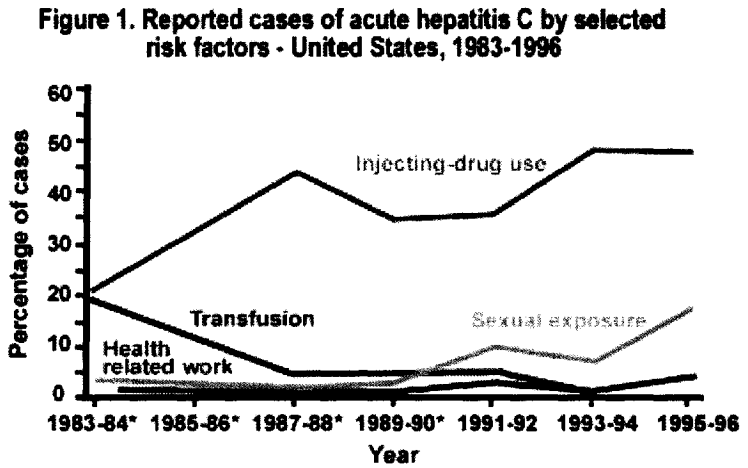


Figure 1.7 Major groups of risk factors for HCV over time (Source: CDC, USA).

On the other hand, Alter MJ et al. (1999, USA) found that the factors with the strongest independent associations with HCV infection among persons 17 to 59 years old were: 1) illegal drug use (ever used cocaine or marijuana-smoking 100 or more times); 2) high-risk sexual behaviour (an early age at first intercourse or 50 or more lifetime sexual partners) in the absence of illegal drug use; 3) marital status (divorced or separated); 4) income (below poverty level); and 5) the number of years of education (12 and fewer) [39].

Risk factors associated with HBV and HCV in Canada have been studied by Tepper [40], Gully [41], Roy E. et al. [42], Delage G. et al [43]. For HBV, they were: injection drug use, multiple sex partners, sexual contact with hepatitis carriers, high risk homosexual activity of men, and possibly tattooing and body piercing. For HCV, the known risk factors were injection drug use, history of blood transfusion or receipt of blood products prior to 1992, and sexual contact with an infected drug user. Occupational blood exposure, history of surgery and hospitalisation/institutionalisation (including prisons) may be related to an increased risk of acquiring HCV in Canada [41, 43].

According to the majority of world literature, between 19 to 50% of adults with acute hepatitis (HBV and possibly HCV) infection in low-endemic countries have been recorded to have no known risk factor for their infection [24, 44-54]. In some of the studies, less well-established (i.e., supported only by anecdotal, case report or case-series studies) transmission routes (for example, needle-stick injuries, organ transplantation, renal hemodialysis, non-sterile tattooing/body piercing, contact with contaminated surfaces, being a health care worker, and having visited a foreign country) were also recorded [55].

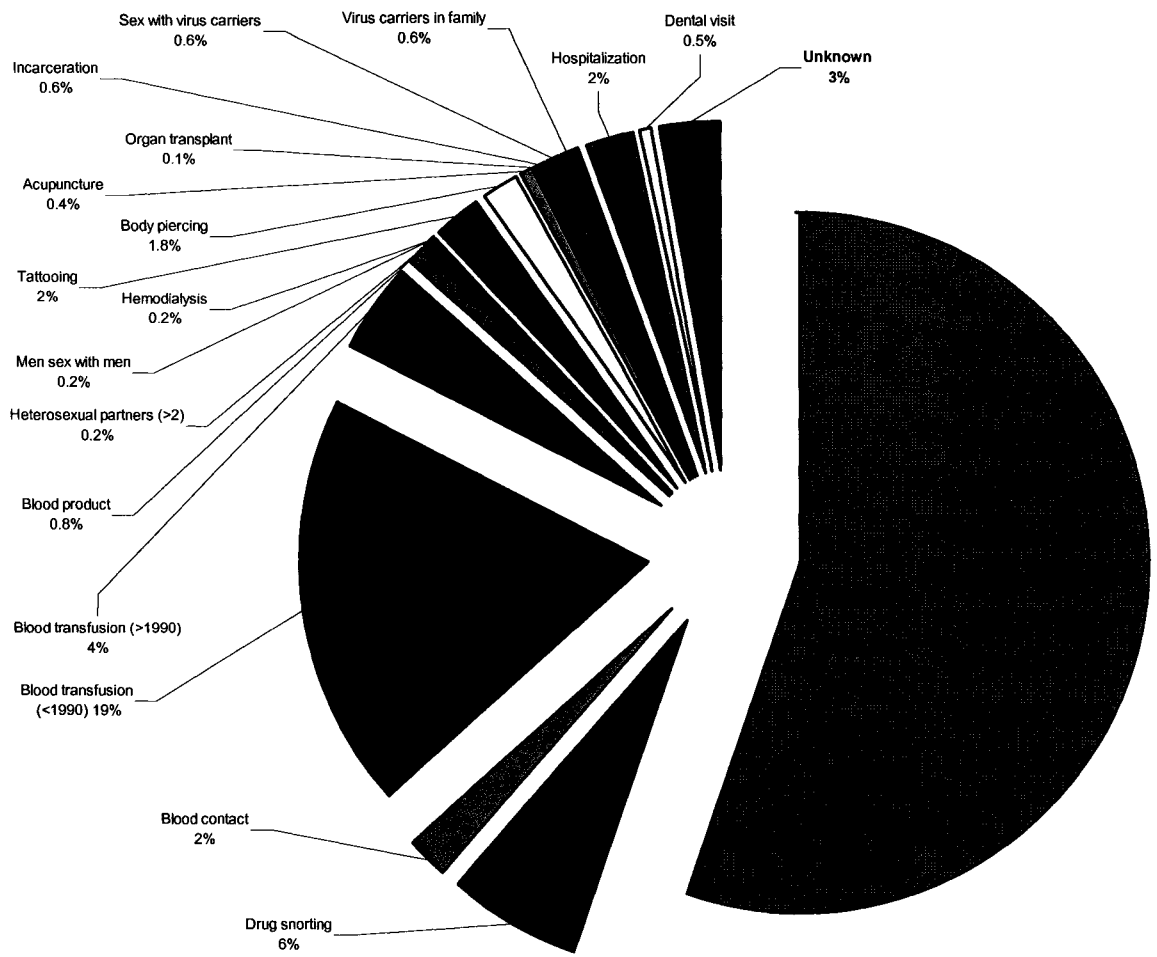
1.3 Enhanced Surveillance of Hepatitis B and Hepatitis C in Canada

To overcome some limitations associated with disease notification and to monitor the incidence and risk factors associated with acute hepatitis B and hepatitis C, an Enhanced Surveillance System was established in two regions of Canada (Ottawa and Edmonton) by Health Canada in October 1998.

In the summer of 2002, the enhanced surveillance was renamed Enhanced Hepatitis Strain Surveillance System (EHSSS) and expanded to include seven sites: Ottawa, Edmonton, Calgary, Vancouver, Winnipeg, New Brunswick, and Nova Scotia; covering approximately 5.5 million people. It is performed as a part of the mandate of the Health Care Acquired Infections Division (HCAID) and National Microbiology Laboratory (NML) of Health Canada (see the Protocol for the Enhanced Surveillance System in Appendix I). Relevant demographic, clinical, laboratory and potential RF data are collected using pre-defined questionnaires (Appendix II).

One of the major concerns revealed by the initial analysis of the enhanced surveillance was a relatively significant percentage of cases with unknown risk factors (URF): about 27% of all interviewed cases with acute HBV and 21% with acute HCV did not report any known risk factors (October, 1998 – December, 1999). On the other hand, the analysis of year 2000 data revealed a significant drop in the proportion of cases with unknown risk factors to approximately 3% for both infections combined, with a slightly higher number for HBV (Figure 1.8). For now, it is unclear whether the observed decline is a true reflection of the proportion of cases with URF, a chance variation, or, which is more likely, changes in the interview procedures. Previous data with a much higher proportion of the cases with URF are consistent with what is reported elsewhere in the world.

Figure 1.8 Distribution of main risk factors for HBV and HCV at Ottawa site of Enhanced Surveillance, 2000



1.4 Rationale, Objectives and Overview of the Thesis

1.4.1 Rationale

Reducing the burden of HBV and HCV infections and their related disease requires implementation of primary prevention activities to reduce the risk for contracting HBV/HCV infections and secondary prevention activities to reduce the risk for liver and other chronic diseases in infected persons. Therefore, to follow the trends and to comprehensively explain the numbers and the features of risk factors for HBV and HCV seem to be imperative issues for public health in Canada. A preliminary analysis of the enhanced surveillance data revealed a wide variety of known risk factors, on one hand, and a considerable number of unknown risk factors, on the other. Therefore, a serious and thorough analysis of risk factors for viral hepatitis B and C based on the results of the enhanced surveillance was undertaken in order to achieve the following: 1) better understanding the epidemiology of HBV and HCV and its risk factor profile; 2) further exploring unknown risk factors; 3) finding possible new risk factors; 4) improving and implementing preventive measures against those infections.

Despite the fact that the number of cases with URF has diminished over time, the analysis of 5-year cumulative enhanced surveillance data showed that the proportion of URF comprises over 10% of all interviewed cases on average, therefore the rationale of further exploring URF cases still holds.

1.4.2 Aim and Objectives

The aim of this thesis is to describe and evaluate the epidemiology of viral hepatitis B and viral hepatitis C in Ottawa during 1998-2002 in order to support effective measures for their prevention in the community.

The objectives of the thesis are:

1. To determine the detailed social-demographic, behavioral, and cultural characteristics of HBV/HCV cases identified at the Ottawa site of the enhanced surveillance during 1998-2002 through quantitative analysis as a basis for improving control programs.
2. To design and conduct an exploratory study of URF for HBV and HCV transmission cases captured by the enhanced surveillance at the Ottawa site in 1998-2002, in order to reveal potential new risk factors.
3. To propose modifications to the enhanced surveillance questionnaire based on the results of the exploratory study as an appropriate tool for comprehensively identifying risk factors for HCV and HBV infection cases captured by the enhanced surveillance.

The following three hypotheses were cautiously tested wherever it was found feasible: 1) cases with unknown risk factors differ from those with known RFs with respect to age, gender, and birthplace; 2) cases' individual risk factor characteristics differ by age and gender; 3) risk factors cluster, i.e., exhibit associations greater than expected from chance alone.

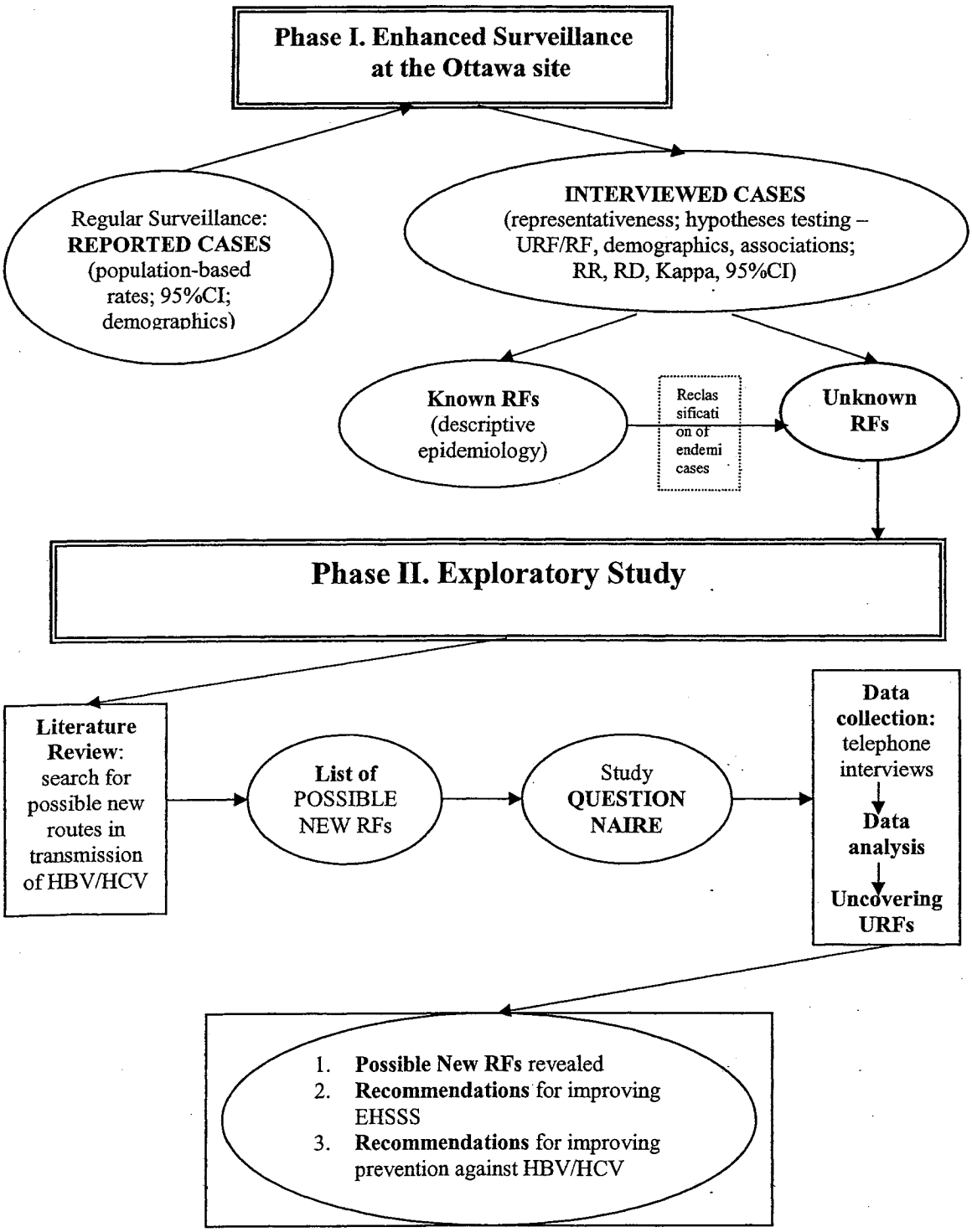
1.4.3 Overview

An overall description of the study design and analysis strategy is given in the Schema 1.3. It shows that the thesis contains two major components:

1. Analysis of the epidemiology of viral hepatitis B and viral hepatitis C infections in Ottawa and evaluation of the risk factor patterns based on the Enhanced Surveillance System for newly identified HBV and HCV infections at the Ottawa site (objective 1).
2. Investigation and possible identification of the unknown risk factors for acute and chronic HBV and HCV infections by designing and conducting an exploratory study in collaboration

with the Blood-Borne Pathogens Division of Health Canada and the Public Health Branch of the City of Ottawa (objectives 2, 3).

Schema 1.3 Overview of research design and analysis strategy.



2. ENHANCED HEPATITIS STRAIN SURVEILLANCE SYSTEM (EHSSS)

2.1 Methods and Procedures

Hepatitis B and hepatitis C are reportable diseases in Canada through the National Notifiable Diseases Reporting System (NDRS). Hepatitis B has been reportable since 1969 whereas reporting of hepatitis C began in 1992 in the province of British Columbia and has been implemented by all provinces and territories since January 1999.

The usefulness of the data obtained through this routine surveillance, however, was limited and affected by the nature of the infections, the inconsistency in reporting practices of provinces and territories (with some reporting case-by-case data and others reporting only aggregate data stratified by age and sex), and by the lack of information on the risk factors associated with transmission. To overcome some of the limitations associated with the NDRS, an Enhanced Surveillance System for hepatitis B and hepatitis C was established by the former Laboratory Centre for Disease Control (LCDC) of Health Canada.

The system was implemented to address the following issues/objectives: 1) estimate the incidence of HBV and HCV infection and monitor rates over time and across population groups; 2) investigate the risk factors associated with viral transmission; 3) monitor the distribution of genotypes over time, by mode of transmission, population group and geography; 4) provide data to support the development and evaluation of prevention and control programs, as well as identify at-risk populations for targeted research and intervention.

2.1.1 Design

A collaborative undertaking, this sentinel site surveillance was first implemented in Edmonton and Ottawa in October 1998. Three months later, in January 1999, the project was expanded to

include the Calgary and Winnipeg Health Authorities. In April of 2000, Vancouver-Richmond Health Board joined the Enhanced Surveillance system followed by the province of New Brunswick in August 2000 and the capital region of Nova Scotia in summer 2002 (Schema 2.1).

Schema 2.1 The sentinel site history of the Enhanced Surveillance system.

Epidemiologic Data		Laboratory Data
Coordinator: Health Care Acquired Infections Division (HCAID) of Health Canada		Coordinator: National Microbiology Laboratory (NML)
Sentinel sites	Date joined into EHSSS	Site Laboratories
Ottawa	October, 1998	National Microbiology Laboratory (NML)
Edmonton	October, 1998	Alberta North Provincial Laboratory
Calgary	January 1999	Alberta South Provincial Laboratory
Winnipeg	January 1999	Cadham Provincial Laboratory, Manitoba
Vancouver	April 2000	British Columbia Centre for Disease Control
New Brunswick	August 2000	Queen Elizabeth II Hospital, Nova Scotia
Halifax (Capital Region)	Summer 2002	Queen Elizabeth II Hospital, Nova Scotia

With the start of 2002 fiscal year, an Enhanced Hepatitis Strain Surveillance System (EHSSS) was implemented that brought together the laboratory and epidemiologic sciences. The new system integrated the Hepatitis Strain Surveillance System of the National Microbiology Laboratory (NML) in Winnipeg and the enhanced Surveillance System of the Health Care Acquired Infections Division (HCAID) of Health Canada. The collection of the epidemiologic data is coordinated by the HCAID whereas the retrieval, shipment and genotype analysis of acute specimens for HBV and HCV is coordinated by the NML.

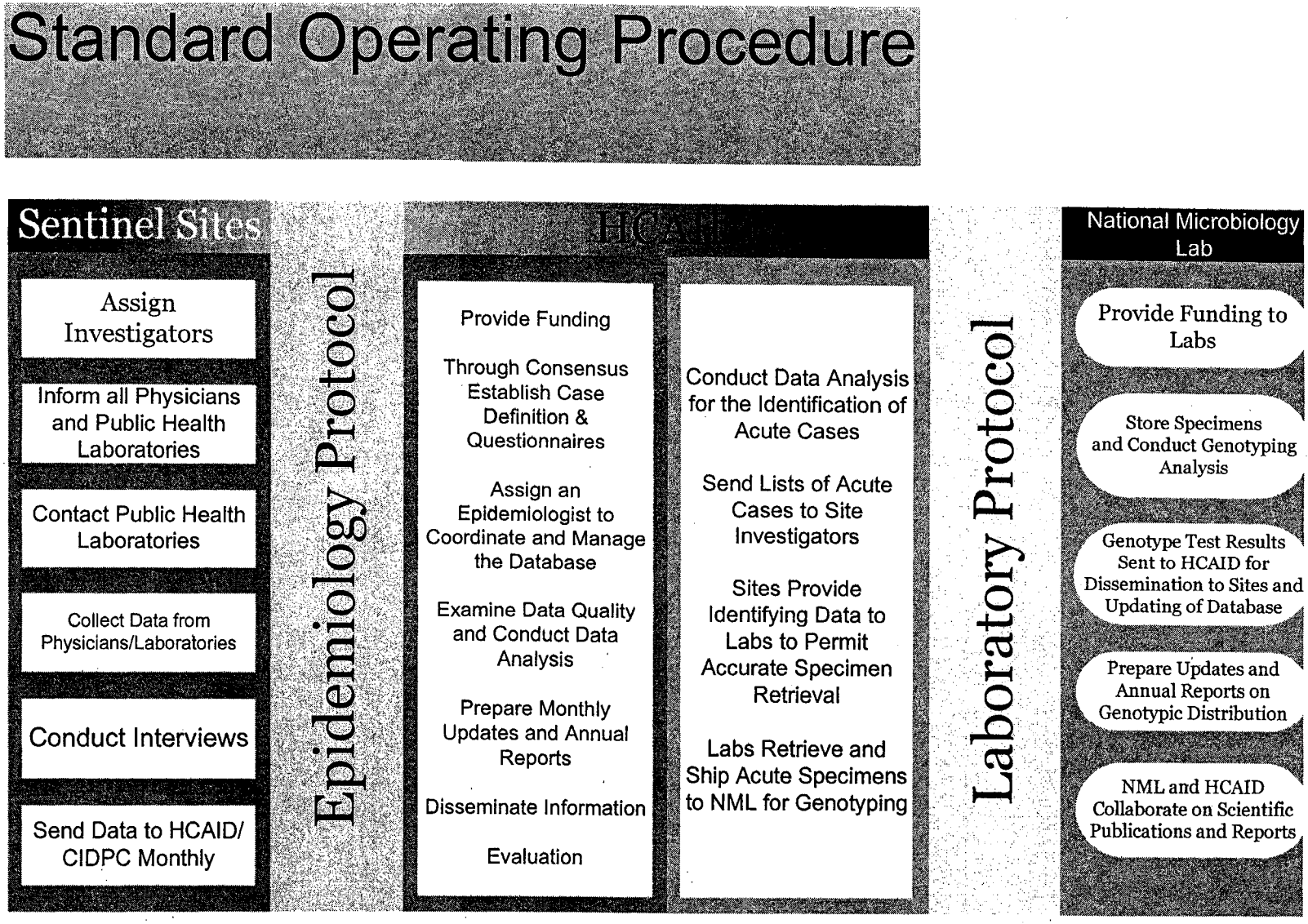
The protocol for the collection of the epidemiologic data (Appendix I) is specified in a Memorandum of Understanding (MoU) between each participating site and the HCAID. In each site, the Enhanced Surveillance system essentially piggy-backs on the normal public health follow up that would occur when a new case of hepatitis B or hepatitis C infection is reported to the health region. Schema 2.2 explains the standard operational procedures for the EHSSS. Full

details are found in Appendix I. Participating sites are provided with funding which contributes to the salary support for the investigator. Site investigators are either public health nurses or environmental health officers. It is the responsibility of the site investigator to contact the laboratories to ensure that laboratory confirmed positive cases are reported to their public health office for appropriate follow up.

Identified cases are interviewed (as they would normally be) but through a standardized telephone interview. Cases are asked for consent to share their risk factor information with health Canada. It should be highlighted that because hepatitis B and hepatitis C are reportable diseases, individuals who do not consent to sharing of their risk factor information (very few) with Health Canada are still included in the database. The only difference between consenting and non-consenting individuals is in the transfer of their risk factor information. All of the other data are transferred, with the exception of personal data such as names, and incorporated into the national database.

In terms of the laboratory protocol (Schema 2.2), HCAID worked collaboratively with participating sites and the NML for the timely and accurate identification, retrieval and shipment of specimens from cases that meet the definition for an acute case. Specifically, the analyses were conducted for the identification of acute cases. This analysis is conducted routinely, approximately every 2 to 3 months. This is important because participating laboratories have varying degrees of capacity to store specimens. Once the analysis is complete, a site-specific list of cases is prepared and sent to the respective site investigator. The site investigator, in turn, provides "identifiable" information to the participating laboratory so that the correct specimen is retrieved. In the event that the case is a seroconverter (conversion within previous 12 months) both previous negative specimen and current positive specimen are retrieved and sent to NML.

Schema 2.2 Operational procedures for the Enhanced Hepatitis Strain Surveillance System.



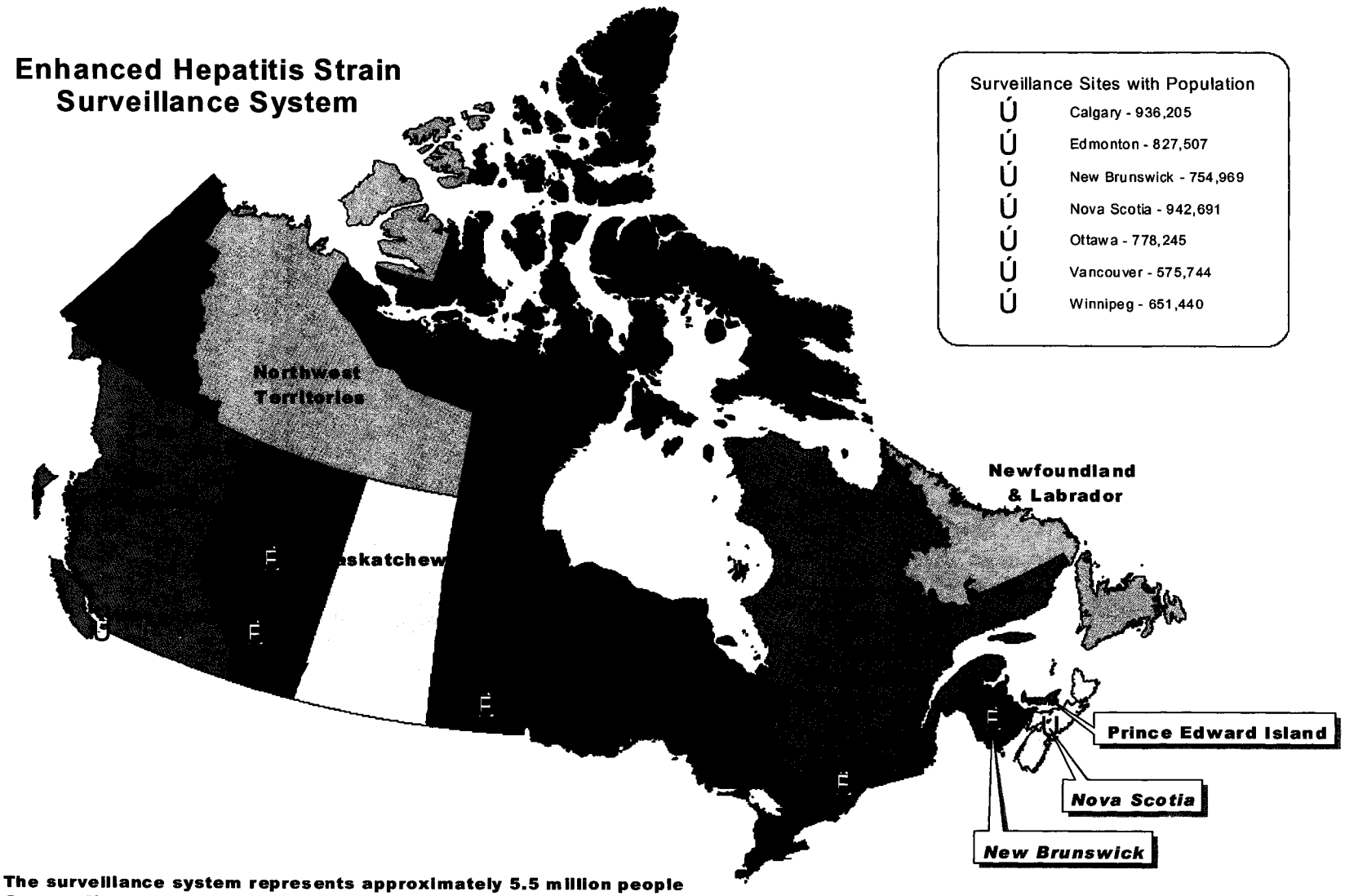
The NML funds participating laboratories. The NML stores and conducts the genotype analyses on the specimens. Test results are forwarded to HCAID of Health Canada for dissemination to each of the sites. The NML is responsible for the preparation of updates and annual reports on the genotypic distribution of HBV and HCV in Canada. There is no laboratory test currently available to differentiate acute HCV infection from chronic. As a result, the case definition in Schema 2.3 was adopted for determination of an acute case. It should be noted that this case definition is consistent with the definition employed by the Centers for Disease Control (CDC) in Atlanta.

Schema 2.3 Acute viral hepatitis B and acute viral hepatitis C case definitions

Case definition criteria		Acute HBV	Acute HCV
1.	Discrete onset of clinical symptoms	✓	✓
2.	Serum aminotransferase (ALT/AST) levels 2.5 times the upper limit of normal	✓	✓
3.	HBsAg or IgM anti-HBs (if done)	Positive	Negative
4.	IgM anti-HAV (if done)	Negative	Negative
5.	Anti-HCV (confirmed by a supplemental test)	N/A	Positive
6.	Seroconversion within 12 months	✓	✓
7.	Likely acute: Does not have symptoms or elevated ALT/AST but is IgM anti-HBc positive	✓	N/A

2.1.2 Population/Eligibility criteria

The total number of people covered by the surveillance is approximately 5.5 million or 18 % of the Canadian population (Schema 2.4).



Schema 2.4 Canadian population under Enhanced Hepatitis Strain Surveillance System

2.1.2.1 Study population

The study population comprised all acute and chronic HBV and HCV cases reported at the Ottawa site of the Enhanced Surveillance during October, 1998 – March, 2002, that met the eligibility criteria.

2.1.2.2 Eligibility criteria

Inclusion criteria:

- **Case definition.** Persons with clinical diagnosis of hepatitis B or hepatitis C by physicians, or identification of hepatitis C or B infections by laboratories
- Consent to participate in the study

Exclusion criteria:

- Inability to communicate in English or French
- Inability to provide an informed consent with the Study Protocol and the absence of a person with power of attorney

2.1.3 Sample size

The detailed numbers on the sample size of the enhanced surveillance including overall reported and interviewed cases are presented in Appendix V.

Sampling strategy. The following selection strategy was adopted by the team of the Enhanced Surveillance based on its relevance to the task of better controlling viral hepatitis B and C infection. Priorities were set to put an emphasis on investigating/interviewing cases in the following order of preference, which noticeably influenced the results of EHSSS:

a) Hepatitis C cases, due to a fact that the Enhanced Surveillance was the first and only national surveillance system to investigate the situation with HCV in Canada, given its relatively recent (in comparison with hepatitis B) discovery and screening (from 1992).
b) Acute cases, whether for HCV or for HBV, since the investigation of acute infection sheds more light on the epidemiological characteristics of a particular infection and is of more importance for public health.
c) Canadian-born cases, since it was believed that the investigation of their epidemiological characteristics would help in developing more effective preventive measures in Canadian communities and in controlling the infection.

2.1.4 Data collection

2.1.4.1 Data collection tools – the Enhanced Surveillance questionnaires

Two separate questionnaires for hepatitis B and hepatitis C (Appendix II a-b) were designed to be used for interviewing the cases that met the eligibility criteria.

2.1.4.2 Data collection procedures – telephone interviewing

The questionnaires were administered through telephone interviews by a Public Health Nurse of the City of Ottawa, the site investigator for the Enhanced Surveillance. The interviewer told the interviewee that he/she (or his/her children) was recently found to have viral hepatitis B and/or hepatitis C infections. In order to investigate risk factors for contracting the disease and possibly elaborate preventive measures in the community, an enhanced surveillance was launched to ask a number of questions that would take some 30-40 minutes to answer. Then, the interviewee was asked whether that was an appropriate time to talk. If the answer was "Yes", the consent form

was read to the interviewee over the phone and the interview proceeded. Otherwise, the interviewer would call back later, at a mutually convenient time, to conduct the interview.

2.1.5 Data analysis

Analysis strategy. An overview of the analysis strategy was given in Schema 1.3. A thorough quantitative analysis of overall reported and interviewed cases of the Enhanced Surveillance was done by calculating: 1) population-based rates of incidence of acute/chronic HBV/HCV cases by age and gender, with 95% confidence intervals (CI); 2) response, or interview, "rates" to unveil the extent of previously mentioned selection bias and its possible influence on results of the enhanced surveillance; 3) prevalence proportions of RFs, or percent (%) among all cases, with total number of cases as a denominator in formula; 4) frequency distributions of RFs, or percent (%) among all risk factors, with total number of all RFs as a denominator in formula. Hypotheses regarding the known and unknown risk factor profiles by age and gender and the clustering of RFs were examined by calculating: relative risks (RR), risk differences (RD), kappa coefficients (K), with 95% confidence intervals (CI).

Results of analysis are presented in cross-tabulation, charts, and figures. All tables and figures contain data for both diseases: acute/chronic HBV and acute/chronic HCV. Demographic and epidemiologic characteristics of cases were analysed for all 3.5 years combined (October, 1998 - March, 2002) and are presented in tables. Prevalence proportions are presented in tables, whereas frequency distributions are presented in charts. The time-trends were analysed for 14 quarters or for three separate years (1999, 2000, and 2001) and are presented in figures. Zero values could not be plotted in semi-logarithmic graphs.

The following software was used to manage, analyse and present data: Epi-Info version 6.0 and Microsoft Office (Access, Excel, Word, Power Point) version 7.0 (for database management and data presentation), SAS version 8.0 (for "Frequency Proc."), and Confidence Interval Analysis (CIA) version 2.0.0 (for RR, RD, K, CI) [56].

Selection bias. To examine the extent of a bias in the sampling strategy and the representativeness of the interviewed population (and thus the extent to which the hypotheses testing can be done) the interview rates were calculated across demographic groups, with the following comparison and interpretation principles:

1) For comparison, the percentages interviewed among all reported cases within age groups, sexes and birthplaces were calculated in order to understand whether a biased selection of reported cases for interviewing (acute, HCV, Canadian-born) affected the representativeness of the sample that was selected for the Enhanced Surveillance.
2) If there was any substantive difference in interview rates between age groups or sexes or birthplaces, it was taken as evidence that the biased sampling did affect the representativeness of the selected population with respect to the demographic where the difference was found. Therefore, characteristics of cases with known and unknown risk factors might not reflect the real picture in the general population, making the results of any hypothesis testing questionable.

Hypotheses testing. We have stated three hypotheses. In assessing the hypotheses, an inferential approach based on confidence interval estimation was considered and not a decision making approach based on hypotheses testing. That is, we did not formally assess them for a significance by means of the "level of significance" in a test of hypotheses. Having in mind that a non-significant result (conventionally, $P>0.05$) does not necessarily mean that there is no real

effect, we decided to evaluate the hypotheses calculating the 95% confidence intervals for relative (sometimes attributable) risks, and kappa coefficients.

Confidence intervals can be more helpful in interpretation of results, as they show the degree of uncertainty related to a result whether or not it was statistically significant. On one hand, there is a close relation between the results of a test of hypothesis and the associated confidence interval: if the difference between groups is significant at the 5% level then the associated 95% confidence interval excludes the value of 1.0 for the RR and value of zero for the RD and K. On the other hand, confidence intervals convey more information because they indicate a range of true values, which is compatible with the sample observations. A wide confidence interval points to lack of information, whether the difference is statistically significant or not, and is a warning against overinterpreting results from small studies as ours.

Main and all RFs. Analysis of risk factors was done by differentiating main, or mutually exclusive, and all RFs. The terminology "mutually exclusive risk factor" came from the Enhanced Surveillance program, which defines it for each case of infection as the one that has highest priority in a ranking of all risk factors, so that each case is assigned only one risk factor. The ranking of a RF was based on exposure of the general population to that particular RF and the probability of acquiring the infection. This hierarchy (different for HBV and HCV) was used to identify the mutually exclusive RFs, which were later renamed to "main" for simplicity of use. All risk factors in that hierarchy are well-known and largely accepted by world scientists as major causes for HBV and HCV. An algorithm was used to identify the main, or mutually exclusive, RF for each case (Appendix VI). Thus, the main RF indicates the probable way that the infection was actually contracted.

Initially we considered focusing on all RFs since most cases have more than one RF, and looking at multiple (or all) RFs would present a more complete picture of risk factor epidemiology. However, we switched the emphasis to main risk factors in order to avoid the implication that a case might have more than one route of transmission, and to be consistent with the Enhanced Surveillance methods and procedures.

2.1.5.1 Analysis of demographic characteristics

Analysis of demographic characteristics included analysis of age-gender-birthplace of the cases. In particular, the following were calculated: 1) frequency distribution of the study population by eligibility and recruitment status; 2) frequency distribution of reported HBV and HCV cases by demographic characteristics of age, gender, and country of birth; 3) time trends in demographic characteristics of reported HBV and HCV cases; 4) demographic characteristics of interviewed coinfected cases (people with both HBV and HCV).

2.1.5.2 Analysis of epidemiological data

The following analysis was done to unveil the epidemiologic characteristics of acute/chronic HBV and HCV cases: 1) population based rates per 100,000 person-years, with 95% CIs; 2) comparison of cases with unknown and known RFs by age/gender/birthplace with RRs and 95% CIs; 3) prevalence proportions and frequency distributions of main, or mutually exclusive, RFs for interviewed cases; 4) prevalence proportions of all RFs for acute/chronic HBV and HCV cases; 5) comparison of cases with different RFs by age/gender with RDs and 95% CIs; 6) aggregation of individual categories of risk factors into larger groups with similar or close routes of viral transmission such as drug use (injection, snorting), medical/health care acquired (blood

transfusion, hemodialysis, organ transplant, dental, surgery, hospitalisation, institutionalisation), sexual transmission (heterosexual partners, MSM, sex with carrier), other subcutaneous (tattooing, body piercing, acupuncture), and URF; 7) time-trends in prevalence proportions of all RFs for acute HBV and HCV cases; 8) number of RFs per interviewed case; 9) average numbers of other risk factors by main exposure; 10) assessing associations between pairs of RFs by calculating ratios and kappa coefficients with 95% confidence intervals for acute/chronic HBV/HCV cases; 11) epidemiologic characteristics of reported and interviewed cases coinfected with HBV and HCV.

Population-based rates. The incidence (acute) and identification rates (chronic) for HBV and HCV were calculated for 3 years (1999-2001) using the following formula:

$$\text{Population based rates} = \frac{\sum \text{Numbers of cases in Ottawa for 1999-2001 X 100,000 person-years}}{\sum \text{Ottawa population for 1999-2001}}$$

As denominators, we used the Statistics Canada estimates for Ottawa population (Schema 2.5). Since it was after amalgamation of the new city of Ottawa, the denominator in the formula for calculation of population-based rates reflected the population of the former Regional Municipality of Ottawa-Carleton. We understand that those numbers may not accurately represent the real denominator. On one hand, it might have been underestimated since some people from outside of the national capital region (e.g., from Eastern Ontario) may have come to Ottawa for testing, driven by a number of reasons. For example, it might have been related to unwillingness to be tested locally, particularly, wherever an exposure to injection drug use (IDU) and/or sexually transmitted disease (STD) had occurred. On the other hand, the denominator may have also been overestimated due to fluctuation of the population numbers in migration process. Nevertheless, we thought that this was a reasonable approach to choosing the denominator given the circumstances.

Schema 2.5 Population in Ottawa-Carleton area by age groups and by gender

Year	Age				Sex		Total
	0-19	20-39	40-59	60+	Male	Female	
1999	192900	241422	217885	113895	375873	390229	766102
2000	195033	241170	225570	116472	382031	396214	778245
2001	194854	241785	230568	122930	389557	400580	790137
Total	582787	724377	674023	353297	1147461	1187023	2334484

The point estimates of the crude population rates were calculated for each year separately and the results were presented in a chart with a logarithmic scale. The population rates for age groups and gender were estimated for all 3 years combined and were presented in a table.

Also 95% CIs were calculated for estimating the population-based rates using the substitution method: **95% CI = [XL/n, XU/n],**

where XL and XU are values from the table of Poisson distributions when X <100;

$XL= (Z_{1-\alpha/2}/2 - \sqrt{X})^2$ and $XU= (Z_{1-\alpha/2}/2 + \sqrt{X+1})^2$ when X >100, with X = incidence or reported numbers, $Z_{1-\alpha/2} = 1.96$, n = population in person-years [56].

The **first hypothesis** was the assumption that cases with known RFs and URFs differ by demographic characteristics, particularly, by age, gender, and birthplace. To evaluate that hypothesis, the proportion of cases with URF among all interviewed patients in each demographic group (the denominator) was calculated.

In order to evaluate differences in the frequency of URFs, the RRs of having URF were calculated along with their 95% CIs. As reference groups, males in gender, and Canadian-born in birthplace were chosen. A multiple comparison was done in age groups. Relative risks for acute HBV and acute HCV were not calculated due to small numbers. Evaluation of RRs was based on the results of the 95% CIs, with the RRs considered statistically significant when the confidence intervals excluded one.

To test the **second hypothesis** that the distribution of risk factors differs by age and gender, the frequency distributions of main RFs in each age or gender group (or column %s) were calculated, along with RDs and their 95% CIs using reference groups as above. We wanted to be consistent and use RRs for evaluating the 2nd hypothesis as was done for the 1st hypothesis, but due to many zero-values in distribution of RFs, it was more appropriate to use risk differences. No RD was calculated for age, since due to very small numbers no statistical significance was expected.

For analysing whether the distribution of RFs is supported by age/gender characteristics of interviewed cases, frequency distributions of cases by age or gender in individual RFs were calculated using the "row %" formula:

$$\text{Row \% formula} = \frac{\text{Number of cases with a specific RF in a particular demo- group}}{\text{Number of all cases with that RF}}$$

As in the column % calculations, combined numbers of RFs for 1998-2002 were used due to small numbers.

Ratios and kappa coefficients with 95% CI were calculated for the **third hypothesis** for assessing the strength of associations between pairs of risk factors [57-61]. Although it was expected that there is some clustering of RFs, it was still relevant to define particular clusters and strength of associations in them. Ratios of proportion agreements were calculated based on fourfold tables,

	Risk factor #1		
Risk factor #2	Yes	No	Total
Yes	a	B	g_1
No	c	D	g_2
Total	f_1	f_2	N

using the following formula: $\mathbf{R = P(o)/P(e) = [(a+d)/N]/[(f_1 g_1 + f_2 g_2)/N],}$

where P(o) is the observed proportion of agreement and P(e) is the expected proportion of agreement by chance. Criteria for ratios were set arbitrarily, ignoring negative concordance (see below): 1.01-1.24 as poor, 1.25-1.49 as moderate, and ≥1.5 as strong associations between pairs of RFs. Cohen's kappa statistic is a measure of agreement beyond the level of agreement expected by chance alone, and was also used to determine whether RFs exhibited strong associations [57-60]. This chance-corrected index of agreement (K) was calculated for all pairs of RFs using the following formula [58, 61]: $\mathbf{K= [P(o) - P(e)]/[1 - P(e)]}$

The values of kappa can range from –1 to +1 with the following interpretation: a) when kappa is equal to 1, there is complete agreement; b) when kappa is greater than 0, the observed proportion of agreement is greater than chance; c) if kappa is less than 0, the observed agreement is worse than chance. To evaluate the results Landis and Koch [62] suggested the following interpretation scale for kappa:

Kappa statistics	Strength of agreement
<0.00	Poor
0.00-0.20	Slight
0.21-0.40	Fair
0.41-0.60	Moderate
0.61-0.80	Substantial
>0.80	Almost perfect

Although these divisions are arbitrary, they provide useful benchmarks and have been used in research. Therefore, we used a simplified for of this scale for interpretation of RF agreements as follows: a) 0.21-0.40 – fair; b) >0.41 moderate or better agreement. For purpose of our study, we ignored negative values of kappas (as was done for ratios) since worse than chance associations between RFs do not contribute much to the knowledge of RF epidemiology and are not interesting from the public health point of view.

Also, 95% confidence intervals for kappa were calculated:

$$\mathbf{CI\ (k) = K \pm Z_{1-\alpha/2} \times SE(k)\ ,}$$

where K = kappa coefficient, $Z_{1-\alpha/2} = 1.96$ for 95% confidence (from the table), SE(k) = Standard error of the kappa and SE (k) = $\sqrt{p_o(1 - p_o)/n(1 - p_c)}$. If 95% CI did not include null value, then we could be reasonably sure that agreement between that particular pair of RFs was better than by chance alone.

2.2 Results of the Enhanced Surveillance

2.2.1 Numbers and rates of reported and interviewed cases of acute/chronic HBV and HCV

2.2.1.1 Time-trends in numbers of acute/chronic HBV and HCV cases, 1999-2001

Figure 2.1 presents quarterly numbers of reported acute/chronic HBV and HCV cases in Ottawa between October, 1998 and March, 2002 in a logarithmic scale that allowed the observation of the following time-trends in development of the diseases. For acute diseases, the quarterly numbers of cases moderately varied between 1 and 7 with the exception of hepatitis C in October -December, 2000. The plots show stability in time for both acute HBV and acute HCV with numbers of acute HCV being slightly higher. The largest numbers for acute HBV were reported in January – March, 2000 and for acute HCV – in October-December, 2000. For chronic HBV, the number of cases showed only a slight increase over time. It stayed relatively stable from quarter to quarter during the last 10 quarters (or two and half years) with some fluctuations in the first four quarters at the beginning of the Enhanced Surveillance. Comparison of chronic HBV and chronic HCV revealed a rise in reported numbers of HBV and a decline in numbers of HCV, with a slight variation between quarters. Overall 3-year (1999-2001) trends showed a 74% absolute increase in numbers of reported chronic HBV and 72% absolute drop in chronic HCV.

2.2.1.2 Population-based rates: incidence of acute and identification rates of chronic HBV and HCV cases

Analysis of population-based rates in Ottawa (Figure 2.2) revealed that incidence of acute HBV was stable in the beginning of the surveillance, then decreased from 2000 to 2001. In contrast, incidence of acute HCV increased in 1999-2000, then stabilised from 2000 to 2001. Analysis of patterns in identification rates of both chronic infections showed a slight but prominent decrease in HCV and stabilization after initial increase in HBV.

2.2.1.3 Population-based rates of acute/chronic HBV and HCV cases by age and gender

Overall the population-based rates (Table 2.1) showed over 1.5-fold greater incidence in acute HCV than in acute HBV and 2-fold greater identification rates in chronic HCV than in chronic HBV. Analysis of rates by age and gender revealed much higher rates in HCV than in HBV in all age/gender groups, in particular, about a 5-fold increased incidence in the younger population of 0-19 years of age and 2-fold increased incidence in females. Across-groups comparison showed that the highest rates of both acute/chronic HBV and acute HCV were among 20-39 year old people, whereas the identification rates in chronic HCV were the highest in the middle aged population. Across-gender comparison revealed rates 2 to 3 times higher in males than females for both diseases.

2.2.1.4 Overall trends in numbers of reported and interviewed cases of acute/chronic HBV and HCV, 1998-2002

Table 2.2 presents the overall numbers of reported/interviewed cases by year and provides a reflection of the sampling strategy adopted by the Enhanced Surveillance team. The interview

rates for all acute cases of HBV and HCV were quite high with slightly higher rates for acute HCV than for acute HBV. For most of the five years of the enhanced surveillance, the rates were consistently high (varying from 79.2% to 100.0%), with the exceptions of years 2000 and 2001 when the interview rates for acute HBV dropped to about a half of reported cases. For chronic cases the interview rates were much lower, averaging 12.2% for HBV and 38.2% for HCV, with the interview rates in the first year (October-December, 1998) being substantially lower.

2.2.2 Demographic characteristics of reported cases of acute/chronic HBV and HCV

2.2.2.1 Overall demographic characteristics of acute/chronic HBV/HCV cases, 1998-2002

Distributions of cases by demographic characteristics (Table 2.3) revealed the following:

1) **Age** analysis - the majority of reported cases of both diseases were in age group 20-39 except for chronic HCV. The second largest age group was 40-59 year old patients.
2) **Gender** analysis - both acute/chronic HBV and HCV were more common in male than female population, and the differences in same instances were quite large: over 3-fold higher in both acute HBV/HCV, and over 2-fold higher in chronic HCV. Among cases of chronic HBV, the difference in proportions of men and women was less drastic.
3) Analysis of reported cases by **birthplace** uncovered an interesting picture: the Canadian-born population constituted the largest group in three categories of diseases of our interest (vs. Africa-, Asia-, and Europe-born population). Only cases with chronic HBV fell out of that trend, with Asian- and African-born cases constituting the highest proportions.

2.2.2.2 Interview rates among reported acute/chronic HBV and HCV cases by age/gender/birthplace

Analysis of interview rates by age, gender and birthplace (Table 2.4) showed similar percentages of interviewed cases among all reported within gender (all categories of both diseases) and in age groups, except over 40 years old (in acute HBV) and 40-59 years old (in chronic HCV) population. The interview rates by birthplace revealed an unbalanced structure of the selected sample with a significant excess of Canadian-born population in chronic HBV, acute/chronic HCV versus to a slightly bigger percentage of non Canadian-born population in acute HBV.

2.2.2.3 Time-trends in demographic characteristics of acute/chronic HBV and HCV cases, 1999-2001

Time-trends in demographic characteristics of reported cases are presented in Figures 2.3 a-c.

Analysis of **age** characteristics (Figure 2.3 a) showed that for acute HBV the young population of 20-39 year olds had an irregular trend, while the middle aged group fell, and there were no under 20 or over 60 years old cases at all. There was an absolute rise (about 63%) in the number of 20-39 years old cases over the 3 years in chronic HBV. The youngest and middle aged groups showed an irregular pattern while the 60+ age group showed a 57% absolute rise. In acute HCV the number of 20-39 years old noticeably increased from 1999 to year 2000 (3.7 fold), then decreased in 2001 (1.4 fold). Among chronic HCV cases, the same age group exhibited an almost 2-fold drop by 2001 yielding the place of the largest age group to the middle-aged population (40-59).

Analysis of **gender** characteristics (Figure 2.3 b) revealed a 50% drop in male numbers from 1999 to 2001. For chronic HBV, the number of male cases constantly increased from year 1999 to year 2001, whereas the number of female cases had a dramatic and unexplainable 6-fold

drop from year 1999 to year 2000 and then a 7.5-fold rise in year 2001. For chronic HCV, the numbers of male and female cases gradually decreased, especially for males, which was consistent with the decline in the total numbers of reported cases during the 3 years of observation. Comparison between chronic diseases revealed an increasing numbers of male cases in HBV in contrast to HCV.

Time-trends in characteristics of cases by **birthplace** were the following (Figure 2.3 c). For acute HBV, there was a slight decline in the number of Canadian-born cases whereas for chronic HBV, there was an obvious increase in the numbers of African and Asian-born cases and an almost stable number of Canadian-born and other cases. For acute HCV, there was a slight initial increase in numbers of Canadian-born cases, whereas for chronic HCV there was a moderate increase in numbers of Asian-born and other cases with stable numbers of African-born and a 2-fold decrease in Canadian-born cases.

2.2.3 Epidemiologic characteristics of interviewed cases of acute/chronic HBV and HCV, 1998-2002 combined

2.2.3.1 Analysis of interviewed acute/chronic HBV and HCV cases with known and unknown risk factors by age/gender/birthplace

The comparison of URF and known RFs by demographic characteristics was done in order to assess **the first hypothesis** that the cases with URF and RF differ by age/gender/birthplace (Table 2.5). Although calculated RRs were elevated in many demographic groups indicating an increased "risk" for URF, differences whose CIs excluded the "null" value were found only in the following situations: 1) non-Canadian born cases – for acute/chronic HBV; 2) females – for

acute HCV; 3) 60+ vs. 20-39 and 60+ vs. 40-59 age groups, females, and non-Canadian born cases – for chronic HCV.

2.2.3.2 Distribution of main risk factors for acute/chronic HBV and HCV cases

Frequency distributions and prevalence proportions have the same values and meaning for main RFs since each case has only one designated main RF. We present here a table called distribution of the main risk factors.

Main risk factors for acute and chronic HBV (Table 2.6 a-b). The largest group of interviewed acute HBV cases had no known risk factors (URF). Among those with known RF, injection drug use (IDU) and men having sex with men (MSM) were the most prevalent RFs for acute HBV infection. Sexual risk factors were also very common modes of transmission for chronic HBV, with the highest proportion for multiple heterosexual partners (≥2). Other common main risk factors among chronic HBV were IDU, blood transfusion and body piercing. In contrast to acute HBV, the proportion of chronic HBV cases with URF was over 20-fold less.

Analysis of **main risk factors for acute and chronic HCV** (Table 2.6 b) revealed IDU and snorting as the most prevalent main RFs for acute HCV, with the latter being about 7-fold lower. For chronic HCV, the most common modes of transmission were IDU, as for acute HCV, and blood transfusion. The proportions of cases with URF were small for both acute and chronic HCV in contrast to acute HBV.

2.2.3.3 Distribution of main risk factors for interviewed acute/chronic HBV and HCV cases by age and gender

The **column %s** of RF distribution by age/gender with risk differences and 95% CIs (for gender) were calculated (Table 2.7 a-b) to assess the **second hypothesis** that the risk factors differ by age/gender. The only main RFs in the youngest age range of 0-19 years for both diseases were IDU, carrier in family, blood transfusion, body piercing, blood product, and snorting. The predominant main RFs for 20-39-year old cases were IDU, snorting, sexual (only for acute/chronic HBV), and tattooing/body piercing and blood transfusion (only for acute/chronic HCV). For middle age group of 40-59, the leading RFs were: IDU for acute diseases; sexual, IDU, blood transfusion for chronic HBV, and IDU, blood transfusion, snorting for chronic HCV. The very few main RFs for 60+ cases were sexual, dental for acute HBV and blood transfusion, hemodialysis, dental for acute HCV.

The RF structure of cases by gender (Table 2.7 b) showed that the most frequent exposures for men were sexual RFs and IDU for acute HBV and IDU, snorting, and blood transfusion for acute HCV. Similar RFs were prominent in female population, such as IDU, sexual, hospitalisation in acute HBV (plus body piercing in chronic HBV) and IDU, blood transfusion in HCV. The 95% CIs for differences in RF distributions by gender excluded zero for the acute diseases. The excess of IDU in males (RD=-19.7 and -23.1) and body piercing in females (RD=25.6 and 10.0) for both chronic infections and of blood transfusion in females (RD=14.2) for chronic HCV were the only statistically significant differences in gender distribution of RFs. A small excess of blood contacts (RD=1.8) in women was also revealed for chronic HCV. We did not analyse the distribution RFs by birthplace due to the biased selection of interviewed cases for that demographic characteristic.

The results of the risk factor distribution by age, or **row %** calculations, (Table 2.8 a-b) indicated that the younger groups were more prevailing for IDU, snorting, sexual contacts,

tattooing/body piercing, household contacts, and incarceration (except in chronic HBV), whereas the middle-aged and older groups were more common for blood transfusion, blood product, acupuncture, institutionalisation, hospitalisation, and dental visits. These observations were mostly based on acute diseases since it provides more timely and realistic picture of RFs and since it is difficult to interpret the chronic numbers. RF distribution by gender showed that male cases were more common in all RFs except body piercing and blood contact for both diseases.

Based on parallels to the interview rates, or to the structure of the interviewed sample in comparison to reported cases, we have to interpret these results with a great caution. They might be biased due to the fact that middle aged and older populations had higher interview rates, so a greater representation in the structure of the selected sample. There was no imbalance in response rates of the male and female cases, therefore the results on gender distribution of risk factors is more valid.

2.2.3.4 Prevalence proportions of all risk factors for acute/chronic HBV and HCV cases

The prevalence proportions and frequency distributions of all RFs are given in Table 2.9 a-b. The prevalence proportions revealed that MSM, dental visits, IDU, and snorting were the most frequent multiple RFs for acute HBV. For chronic HBV, dental visits overwhelmingly predominated among all cases, then hospitalisation, surgery, and multiple heterosexual partners were next most prevalent RFs for contracting the disease. For both acute and chronic HBV, dental visits/procedures were on the top of the list of risk factors, whereas IDU and drug snorting were lower down on the list for chronic HBV, in contrast to the acute disease. For acute HCV, the category of IDU was the most prevalent RF among all cases. The next most frequent RFs were snorting, hospitalisation, sex with HCV carrier, incarceration, and carrier in family. For

chronic HCV, the list of most frequent RFs was similar to that of chronic HBV, except for the presence of IDU/snorting and absence of heterosexual partners≥2.

The comparison of parallel groups of diseases showed that drug use (injection and snorting) was among the most frequently reported risk factors for both acute infections, and dental, hospitalisation, and surgery were the most predominant modes of transmission in development of both chronic infections. The results of frequency distribution of all RFs had similar patterns, therefore, they are not discussed here.

2.2.3.5 Time-trends in prevalence proportions of risk factors for acute HBV and HCV cases, 1999-2001

To follow the time-trends in RFs of both acute diseases, the prevalence proportions were calculated for each of 3 years of the Enhanced Surveillance (1999-2001) and presented in Figure 2.4 a-b. The results were assessed for overall trends from the year 1999 to the year 2001, unless there was an outstanding pattern in the middle point of 2000.

For acute HBV, cases with URF had the highest prevalence for the first 2 years then dropped sharply. IDU, with the second highest prevalence in 1999, dropped down to 0 and then increased to a higher level than in 1999. Sex with carrier dropped from the third highest in 1999 to 0 in 2000-2001. Prevalence of MSM gradually increased and became the most prevalent RF by 2001. The proportion of cases with snorting and MSM proportions sharply increased.

For acute HCV (Figure 2.4 b), the most frequently occurring RFs over time were IDU, snorting, carrier in family, and incarceration. Also we observed drops of 47% in sex with carrier, 30% in IDU, 36% in hospitalisation, 20% in Institutionalisation vs. increases of15% in incarceration and 9% in body piercing and dental. In general, there was a decreasing pattern in

the prevalence of most RFs over time, particularly in the medical/health care acquired group of RFs.

2.2.3.6 Associations between risk factors for acute/chronic HBV and HCV cases: ratios and kappa coefficients

For assessing the third hypothesis about clustering and strength of associations between pairs of RFs, ratios and kappa coefficients were calculated (Table 2.10 a-d). According to calculated ratios, the following pairs of RFs were identified as having fair and moderate associations and were supported by kappa coefficients: snorting/MSM and sex with HBV carrier/dental visits for acute HBV; IDU/snorting and hospitalisation/surgery for chronic HBV; sex with HCV carrier/HCV carrier in family for acute HCV; and tattooing/incarceration for chronic HCV.

All the values for ratios/kappas with fair, moderate agreements between pairs of RFs are bolded in the tables for ratio/kappa coefficients, but only those with 95% confidence intervals that did not include zero are noted here.

The kappa coefficients identified the following additional pairs of RFs which cluster with a strength ranging from a perfect agreement between carrier in family/incarceration for acute HBV (only 1 case) to moderate/better agreement between sex with HCV carrier/carrier in family for acute HCV; IDU/snorting, IDU/prison, snorting/prison, snorting/institutionalisation, hospitalisation/ surgery, tattoo/prison, and sex with carrier/carrier in family for chronic HBV; hemodialysis/ organ transplant, sex with hepatitis C carrier/carrier in family, blood product with hemodialysis and with organ transplant, and tattoo/prison for chronic HCV.

2.2.3.7 Overall and average number of risk factors per interviewed case of acute/chronic HBV and HCV

The number of RFs per interviewed case are presented in Table 2.11. The majority of acute HBV cases had either no RF or two RFs per case, and no cases with ≥5 RFs. The results for acute HCV cases were fairly similar, except for the much lower proportion with URF, and correspondingly larger proportions with numerous risk factors. The chronic cases of both HBV and HCV were characterised by an opposite pattern. The average number of multiple RFs per case were much bigger for chronic cases than for acute cases of both HBV and HCV (about 4 and 2-fold, respectively).

Analysis of **average total numbers of risk factors by main exposure** for acute/chronic HBV and HCV is presented in Figure 2.5 a-b. For acute HBV, the total numbers of RFs varied between 1 (for multiple heterosexual partners and dental visits as main risk factors) and 3 (for snorting). For chronic HBV, cases with IDU, snorting, tattooing, blood transfusion, acupuncture, or MSM as main RF had 5 or more RFs on average. Cases whose main RF was snorting had more numerous total RFs on average for acute/chronic HBV.

For acute HCV, the average number of total RFs also varied between 1 and 3, with the average of more than 2 for those whose main risk factor was: IDU, blood transfusion, incarceration, tattooing, or snorting. For both acute and chronic HCV, cases with IDU, snorting drugs, blood transfusion, or tattooing as main RF had a higher number of total RFs on average.

2.2.3.8 Demographic and epidemiological characteristics of coinfected HBV/HCV cases

Prevalence proportions of coinfected cases among all reported were calculated in a detailed analysis of HBV and HCV coinfection, and the results are presented in Table 2.12. Analysis of

overall numbers of HBV and HCV coinfection showed that the highest prevalence of coinfection was among acute HBV cases. Analysis of demographic characteristics of coinfected HBV and HCV cases revealed the following patterns. **Age analysis:** The highest prevalence proportions of coinfection were in 20-39 (for acute HBV) and in 40-59 (for chronic HBV/HCV) age groups. These are the age groups with the highest numbers of reported cases. **Gender analysis:** HBV and HCV coinfection was more frequent in male than in female cases. Although the gender-difference in coinfected cases was very slight, it was consistent for both infections. **Analysis by place of birth:** The coinfection of HBV and HCV was mostly prevalent in reported cases that were born outside of Canada, particularly in Asia and in Africa. An exception was for acute HCV, where the only coinfected case was born in Canada. **RF analysis:** Coinfection was most common in cases with IDU as a main RF for both diseases.

Frequency distributions of reported cases of HBV/HCV coinfection by age, gender, birthplace, and main risk factors is given in Figure 2.6 a-d. **Age analysis** of coinfected cases revealed that in the age-structure of all coinfected cases the 20-39 years old young people prevailed for acute HBV and were the only ones for acute HCV. For both chronic diseases the middle age group of 40-59 prevailed followed by the 20-39 year age group. The **gender** distribution showed that, as in all reported coinfection cases, males had the largest proportion for both diseases, with a 4-fold lead in comparison with females. **Birthplace analysis** of coinfected cases revealed that the vast majority of all coinfected cases in acute/chronic HBV were born in Asia. The second largest group was composed of the Africa-born population. In contrast, most of the coinfected acute/chronic HCV cases were born in Canada, with the Asia-born population in the second place. The distribution of **RFs** of coinfected cases revealed IDU as the most often reported main RF for all coinfected cases of acute/chronic HBV/HCV.

Table 2.1 Incidence (acute) and identification (chronic) rates of HBV and HCV cases at Ottawa site of EHSSS by age and gender, per 100,000 person-years (1999-2001 combined).[1]

		Acute HBV			Chronic HBV			Acute HCV			Chronic HCV		
		N	Inci-dence	95% CI	N	Reported rates	95% CI	N	Inci-dence	95% CI	N	Reported rates	95% CI
Age groups (yr)	0-19	2	0.3	[0.04, 1.24]	43	7.4	[5.3, 9.9]	8	1.4	[0.6, 2.7]	50	8.6	[6.4, 11.3]
	20-39	22	3.0	[1.9, 4.6]	446	61.6	[56.0, 67.4]	34	4.7	[3.3, 6.6]	618	85.3	[78.7, 92.2]
	40-59	9	1.3	[0.6, 2.5]	216	32.0	[27.9, 36.5]	8	1.2	[0.5, 2.3]	722	107.1	[99.4, 115.1]
	60+	0	-	-	70	19.8	[15.4, 25.0]	3	0.8	[0.2, 2.5]	111	31.4	[25.8, 37.8]
Gender	Male	26	2.3	[1.5, 3.3]	504	43.9	[40.2, 47.8]	39	3.4	[2.4, 4.6]	1031	89.9	[84.4, 95.4]
	Female	7	0.6	[0.2, 1.2]	271	22.8	[20.2, 25.6]	14	1.2	[0.6, 2.0]	470	39.6	[36.1, 43.3]
Total		33	1.4	[1.0, 2.0]	775	33.2	[30.9, 35.6]	53	2.3	[1.7, 3.0]	1501	64.3	[61.1, 67.6]

[1] Rates Formula = ∑Numbers of reported acute or chronic cases for 1999-2001 X 100,000person-years / ∑Population for 1999-2001.

Table 2.2 Numbers of reported and interviewed cases of acute and chronic HBV and HCV at the Ottawa site of the EHSSS year, October, 1998 - March, 2002.

Number of cases	Acute HBV		Chronic HBV		Acute HCV		Chronic HCV	
	Re-port	Interview (%)	Re-port	Interview (%)	Re-port	Interview (%)	Re-port	Interview (%)
1998	3	3 (100.0)	59	1 (1.7)	1	1 (100.0)	176	3 (3.9)
1999	13	12 (92.3)	209	26 (12.4)	11	10 (90.9)	580	301 (51.9)
2000	14	8 (57.1)	283	30 (10.6)	24	19 (79.2)	506	342 (67.6)
2001	6	3 (50.0)	283	42 (14.8)	18	16 (88.9)	415	259 (62.4)
2002	2	2 (100.0)	60	10 (16.7)	1	1 (100.0)	95	72 (75.8)
Total	38	28 (73.7)	894	109 (12.2)	55	47 (85.5)	1772	977 (38.2)

Table 2.3 Demographic characteristics of reported acute and chronic HBV and HCV cases at the Ottawa site of the EHSSS, all years combined (October, 1998 - March, 2002).

Demographic characteristics		Acute HBV (n=38)		Chronic HBV (n=894)		Acute HCV (n=55)		Chronic HCV (n=1772)	
		N	%	N	%	N	%	N	%
Age	0-19	2	5.3	49	5.5	8	14.5	54	3.0
	20-39	24	63.2	510	57.0	36	65.5	737	41.6
	40-59	10	26.3	258	28.9	8	14.5	847	47.8
	60+	2	5.3	77	8.6	3	5.45	134	7.6
Sex	Male	30	78.9	524	58.6	40	72.7	1215	68.6
	Female	8	21.1	370	41.4	15	27.3	557	31.4
Birth place	Africa	2	5.3	125	14.0	1	1.8	62	3.5
	Asia	6	15.8	611	68.3	1	1.8	114	6.4
	Canada	22	57.9	81	9.1	45	81.8	1185	66.9
	Other	8	21.1	77	8.6	8	14.5	411	23.2

Table 2.4 Interview rates: percentage of interviewed from all reported cases of acute/chronic HBV and HCV at Ottawa site of EHSSS distributed by age, gender, and birthplace (1998-2002 combined).[1]

Demographic characteristics		Acute HBV			Chronic HBV			Acute HCV			Chronic HCV		
		Reported	Interviewed	Response rate (%)	Reported	Interviewed	Response rate (%)	Reported	Interviewed	Response rate (%)	Reported	Interviewed	Response rate (%)
Age group (years)	0-19	2	1	50.0	49	6	13.0	8	8	100.0	54	22	40.7
	20-39	24	16	66.7	510	50	9.8	36	29	80.6	737	366	49.7
	40-59	10	9	**90.0**	258	39	15.1	8	7	87.5	847	528	**62.3**
	60+	2	2	**100.0**	77	14	18.2	3	3	100.0	134	61	45.5
Gender	Male	30	22	73.3	524	66	12.6	40	35	87.5	1215	652	53.7
	Female	8	6	75.5	310	43	13.9	15	12	80.0	557	325	58.3
Birth place	Canada	22	14	63.6	81	42	**51.6**	45	42	**93.3**	1185	752	**63.5**
	Others	16	14	**87.5**	813	67	8.2	10	5	50.0	587	225	38.3
Total		38	28	73.7	894	109	12.2	55	47	85.5	1772	977	55.1

[1] Interview rates highlighted show unbalanced representation of a demographic group.

Table 2.5 Interviewed acute/chronic HBV and HCV cases with known (RF) and unknown (URF) risk factors by age, gender, and birthplace (Ottawa site of EHSSS, 1998-2002 combined). [1, 2, 3]

Demographic characteristics		Acute HBV=28					Chronic HBV=109					Acute HCV=47					Chronic HCV=977				
		RF=14		URF=14			RF=82		URF=27			RF=38		URF=9			RF=936		URF=41		
		N	%	N	%	RR [4]	N	%	N	%	RR	N	%	N	%	RR[3]	N	%	N	%	RR
Age group	0-19	1	100.0	0	-		4	66.7	2	33.3	1	8	100.0	0	-		20	90.9	2	9.1	1
	20-39	8	50.0	8	50.0		36	72.0	14	28.0	0.8	25	86.2	4	13.8		356	97.3	10	2.7	0.3
	40-59	3	33.3	6	66.7		32	82.1	7	17.9	0.5	3	42.9	4	57.1		515	97.5	13	2.5	0.3
	60+	2	100.0	0	-		10	70.4	4	29.6	0.9	2	66.7	1	33.3		45	73.8	16	26.2	2.9
																					9.6
																					10.6
Gender	Male	11	50.0	11	50.0	1	52	78.8	14	21.2	1	31	88.6	4	11.4	1	628	96.3	24	3.7	1
	Female	3	50.0	3	50.0	1	30	69.8	13	30.2	1.4	7	58.3	5	41.7	**3.6**	308	94.8	17	5.2	1.4
Birthplace	Canada	11	78.6	3	21.4	1	38	90.5	4	9.5	1	35	83.3	7	16.7	1	741	98.5	11	1.5	1
	Others	3	21.4	11	78.6	**3.7**	44	65.7	23	34.3	**3.6**	3	60.0	2	40.0	2.4	195	86.7	30	13.3	**9.1**

[1] Bolded are the relative risks whose confidence intervals exclude 1.

[2] The RRs and their 95% confidence intervals were calculated using CIA software, version2.0.0, but only those CIs that excluded 1 are presented below.

60+ vs. 20-39	- inchronic HCV:	RR = 9.6 CI=[5.0, 32.9]
60+ vs. 40-59	- in chronic HCV:	RR = 10.6 CI=[5.9, 33.8]
Females	- in acute HCV:	RR = 3.6 CI=[1.2, 11.4]
Non-Canadian-born:	- in acute HBV:	RR = 3.7 CI=[1.3, 10.4]
	- in chronic HBV:	RR = 3.6 CI=[1.3, 9.7]
	- in chronic HCV:	RR = 9.1 CI=[4.6, 17.9]

[3] The numbers of unknown cases are presented as after reclassification of endemic cases (section 2.1)

[4] The RRs for age groups of both acute diseases where the numbers=0 were not calculated.

Table 2.6 a Distribution of main risk factors for interviewed acute/likely acute (within last 6 months) and chronic (lifetime) HBV cases at Ottawa site of the EHSSS, all years combined (October, 1998 -March, 2002).

Risk factors[1]	Acute HBV (n=28)	Chronic HBV (n=109)
	N (%)	N (%)
Injection drug use	5 (17.9)	13 (11.9)
Snorting	2 (7.1)	4 (3.7)
Blood transfusion	0 (0.0)	12 (11.0)
Blood product	0 (0.0)	3 (2.8)
Heterosexual partners ≥2	1 (3.6)	39 (35.8)
Men sex with men	4 (14.3)	2 (1.8)
Sex with carrier	2 (7.1)	2 (1.8)
Tattooing	0 (0.0)	1 (0.9)
Body piercing	0 (0.0)	11 (10.1)
Acupuncture	0 (0.0)	1 (0.9)
Blood contact	0 (0.0)	1 (0.9)
Hemodialysis	0 (0.0)	0 (0.0)
Carrier in family	0 (0.0)	6 (5.5)
Institutionalized	0 (0.0)	0 (0.0)
Hospitalization	1 (3.6)	7 (6.4)
Surgery	1 (3.6)	0 (0.0)
Transplant	0 (0.0)	0 (0.0)
Dental visit	1 (3.6)	5 (4.6)
Incarceration	0 (0.0)	0 (0.0)
Unknown	11 (39.3)	2 (1.8)
Total	28 (100.0)	109 (100.0)

[1] The main risk factors are listed here in HBV hierarchy (Appendix VI).

Table 2.6 b Distribution of main risk factors for interviewed acute/likely acute (within last 6 months) and chronic (lifetime) HCV cases at Ottawa site of the EHSSS, all years combined (October, 1998 -March, 2002).

Risk factors[2]	Acute HCV (n=47)	Chronic HCV (n=977)
	N (%)	N (%)
Injection drug use	33 (70.2)	499 (51.1)
Drug snorting	5 (10.6)	69 (7.1)
Blood contact	0 (0.0)	15 (1.5)
Blood transfusion	1 (2.1)	238 (24.4)
Blood product	0 (0.0)	12 (1.2)
Hemodialysis	1 (2.1)	3 (0.3)
Tattooing	2 (4.3)	19 (1.9)
Body piercing	0 (0.0)	37 (3.8)
Acupuncture	0 (0.0)	10 (1.0)
Organ Transplant	0 (0.0)	0 (0.0
Incarceration	1 (2.1)	4 (0.4)
Sex with hepatitis C carriers	0 (0.0)	3 (0.3)
Hepatitis C carrier in family	0 (0.0)	11 (1.1)
Institution associated	1 (2.1)	1 (0.1)
Hospitalization	1 (2.1)	32 (3.3)
History of surgery	1 (2.1)	1 (0.1)
History of dental visit	0 (0.0)	12 (1.2)
Unknown	1 (2.1)	11 (1.1)
Total	47 (100.0)	977 (100.0)

[2] The main risk factors are listed here in HCV hierarchy (Appendix VI).

Table 2.7 a Distribution (column %) of main risk factors for interviewed acute/chronic HBV and HCV cases at Ottawa site of the EHSSS by age, 1998-2002 combined.[1]

Risk factors	Acute HBV (n=28)				Chronic HBV (n=109)				Acute HCV (n=47)				Chronic HCV (n=977)			
	0-19	20-39	40-59	60+	0-19	20-39	40-59	60+	0-19	20-39	40-59	60+	0-19	20-39	40-59	60+
IDU	0	3 (18.8)	2 (22.2)	0	1 (16.7)	4 (8.0)	8 (20.5)	0	7 (87.5)	23 (79.3)	3 (42.9)	0	8 (36.4)	233(63.7)	256(48.5)	2 (3.3)
Snorting	1(100.0)	1 (6.3)	0	0	1 (16.7)	0	3 (7.7)	0	1 (12.5)	3 (10.3)	1 (14.3)	0	0	27 (7.4)	42 (8.0)	0
Blood transfusion	0	0	0	0	0	2 (4.0)	4 (10.3)	6 (42.9)	0	0	0	1 (33.3)	4 (18.2)	65 (17.8)	134 (25.4)	35 (57.4)
Blood product	0	0	0	0	0	0	3 (7.7)	0	0	0	0	0	3 (13.6)	2 (0.5)	6 (1.1)	1 (1.6)
Heterosexual partners≥2	0	1 (6.3)	0	0	1 (16.7)	23 (46.0)	11 (28.2)	4 (28.6)	0	0	0	0	0	0	0	0
Men sex with men	0	3 (18.8)	0	1 (50.0)	0	0	1 (2.6)	1 (7.1)	0	0	0	0	0	0	0	0
Sex with carrier	0	2 (12.5)	0	0	0	1 (2.0)	1 (2.6)	0	0	0	0	0	0	1 (0.3)	2 (0.4)	0
Tattooing	0	0	0	0	0	1 (2.0)	0	0	0	2 (6.9)	0	0	0	8 (2.2)	11 (2.1)	0
Body piercing	0	0	0	0	2 (33.3)	5 (10.0)	3 (7.7)	1 (7.1)	0	0	0	0	2 (9.1)	7 (1.9)	22 (4.2)	6 (9.8)
Acupuncture	0	0	0	0	0	0	1 (2.6)	0	0	0	0	0	0	2 (0.5)	4 (0.8)	4 (6.6)
Blood contact	0	0	0	0	0	0	0	1 (7.1)	0	0	0	0	0	1 (0.3)	13 (2.5)	1 (1.6)
Hemodialysis	0	0	0	0	0	0	0	0	0	0	0	1 (33.3)	0	1 (0.3)	1 (0.2)	1 (1.6)
Carrier in family	0	0	0	0	1 (16.7)	5 (10.0)	0	0	0	0	0	0	4 (18.2)	3 (0.8)	3 (0.6)	1 (1.6)
Institutionalized	0	0	0	0	0	0	0	0	0	0	1 (14.3)	0	0	0	1 (0.2)	0
Hospitalization	0	0	1 (11.1)	0	0	4 (8.0)	3 (7.7)	0	0	0	1 (14.3)	0	0	6 (1.6)	17 (3.2)	9 (14.8)
Surgery	0	0	1 (11.1)	0	0	0	0	0	0	0	0	0	0	0	1 (0.2)	0
Transplant	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Dental visit	0	0	0	1 (50.0)	0	4 (8.0)	0	1 (7.1)	0	0	0	1 (33.3)	1 (4.5)	5 (1.4)	6 (1.1)	0
Incarceration	0	0	0	0	0	0	0	0	0	1 (3.4)	0	0	0	1 (0.3)	3 (0.6)	0
Unknown	0	6 (37.5)	5 (55.6)	0	0	1 (2.0)	1 (2.6)	0	0	0	1 (14.3)	0	0	4 (1.1)	6 (1.1)	1 (1.6)
Total	1(100.0)	16(100.0)	9(100.0)	2(100.0)	6(100.0)	50(100.0)	39(100.0)	14(100.0)	8(100.0)	29(100.0)	7(100.0)	3(100.0)	22(100.0)	366(100.0)	528(100.0)	61(100.0)

[1] Risk differences for age groups were not calculated due to small numbers.

Table 2.7 b Distribution (column %) of main risk factors for interviewed acute/chronic HBV and HCV cases at the Ottawa site of the EHSSS by gender, 1998-2002 combined. [2]

Risk factors	Acute HBV (n=28)			Chronic HBV (n=109)			Acute HCV (n=47)			Chronic HCV (n=977)		
	Male	Female	RD	Male	Female	RD	Male	Female	RD	Male	Female	RD
IDU	4 (18.2)	1 (16.7)	-1.5	13 (19.7)	0	**-19.7**	24 (68.6)	9 (75.0)	6.4	383 (58.7)	116 (35.7)	**-23.1**
Snorting	2 (9.1)	0	-9.1	4 (6.1)	0	-6.1	4 (11.4)	1 (8.3)	-3.1	45 (6.9)	24 (7.4)	0.5
Blood transfusion	0	0	0.0	7 (10.6)	5 (11.6)	1.0	1 (2.9)	0	-2.9	128 (19.6)	110 (33.8)	**14.2**
Blood product	0	0	0.0	2 (3.0)	1 (2.3)	-0.7	0	0	0.0	9 (1.4)	3 (0.9)	-0.5
Heterosexual partners >2	1 (4.5)	0	-4.5	23 (34.8)	16 (37.2)	2.4	0	0	0.0	0	0	0.0
Men sex with men	4 (18.2)	0	-18.2	2 (3.0)	0	3.0	0	0	0.0	0	0	0.0
Sex with carrier	1 (4.5)	1 (16.7)	12.1	1 (1.5)	1 (2.3)	0.8	0	0	0.0	1 (0.2)	2 (0.6)	0.4
Tattooing	0	0	0.0	1 (1.5)	0	-1.5	2 (5.7)	0	5.7	14 (2.1)	5 (1.5)	-0.6
Body piercing	0	0	0.0	0	11 (25.6)	**25.6**	0	0	0.0	3 (0.5)	34 (10.5)	**10.0**
Acupuncture	0	0	0.0	0	1 (2.3)	2.3	0	0	0.0	9 (1.4)	1 (0.3)	-1.1
Blood contact	0	0	0.0	1 (1.5)	0	-1.5	0	0	0.0	6 (0.9)	9 (2.8)	**1.8**
Hemodialysis	0	0	0.0	0	0	0.0	1 (2.9)	0	-2.9	2 (0.3)	1 (0.3)	0.0
Carrier in family	0	0	0.0	4 (6.1)	2 (4.7)	-1.4	0	0	0.0	7 (1.1)	4 (1.2)	0.1
Institutionalized	0	0	0.0	0	0	0.0	1 (2.9)	0	-2.9	1 (0.2)	0	-0.2
Hospitalization	0	1 (16.7)	16.7	4 (6.1)	3 (7.0)	0.9	0	1 (8.3)	8.3	21 (3.2)	11 (3.4)	0.2
Surgery	1 (4.5)	0	-4.5	0	0	0.0	1 (2.9)	0	-2.9	1 (0.2)	0	-0.2
Transplant	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0
Dental visit	1 (4.5)	0	-4.5	4 (6.1)	1 (2.3)	-3.7	0	0	0.0	10 (1.5)	2 (0.6)	-0.9
Incarceration	0	0	0.0	0	0	0.0	1 (2.9)	0	-2.9	4 (0.6)	0	-0.6
Unknown	8 (36.4)	3 (50.0)	13.6	0	2 (4.7)	4.7	0	1 (8.3)	8.3	8 (1.2)	3 (0.9)	-0.3
Total	22 (100.0)	6 (100.0)	-	66 (100.0)	43 (100.0)	-	35 (100.0)	12 (100.0)	-	652 (100.0)	325 (100.0)	-

2

* Risk differences were calculated with males as a reference group, and those RDs whose CIs exclude 0 are presented in **bold**.

** 95% confidence intervals for all RDs were also calculated, but only those CIs that exclude 0 are presented here: For chronic HBV: IDU CI=[-30.8, -8.4] and Body piercing CI=[13.6, 40.2]; For chronic HCV: IDU CI=[-29.3, -16.5]; Blood transfusion CI=[8.3, 20.2]; Body piercing CI=[7.0, 13.8]; and Blood contact CI=[0.2, 4.3].

*** All calculations were done using CIA software, version2.0.0 (Altman D.G. et al. Statistics with confidence, BMJ Books, 2000).

Table 2.8 a Distribution (row %) of main risk factors for interviewed acute/chronic HBV and HCV cases at Ottawa site of EHSSS by age, 1998-2002 combined.

Risk factors	Acute HBV (n=28)				Chronic HBV (n=109)				Acute HCV (n=47)				Chronic HCV (n=977)			
	0-19	20-39	40-59	60+	0-19	20-39	40-59	60+	0-19	20-39	40-59	60+	0-19	20-39	40-59	60+
	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)
IDU	0	3 (60.0)	2 (40.0)	0	1 (7.7)	4 (30.8)	8 (61.5)	0	7 (21.2)	23(69.7)	3 (9.1)	0	8 (1.6)	233 (46.7)	256 (51.3)	2 (0.4)
Snorting	1 (50.0)	1 (50.0)	0	0	1 (25.0)	0	3 (75.0)	0	1 (20.0)	3 (60.0)	1 (20.0)	0	0	27 (39.1)	42 (60.9)	0
Blood transfusion	0	0	0	0	0	2 (16.7)	4 (33.3)	6 (50.0)	0	0	0	1(100.0)	4 (1.7)	65 (27.3)	134 (56.3)	35 (14.7)
Blood product	0	0	0	0	0	0	3(100.0)	0	0	0	0	0	3 (25.0)	2 (16.7)	6 50.0)	1 (8.3)
Heterosexual partner ≥2	0	1 (100.0)	0	0	1 (2.6)	23 (59.0)	11 (28.2)	4 (10.3)	0	0	0	0	0	0	0	0
Men sex with men	0	3 (75.0)	0	1 (25.0)	0	0	1 (50.0)	1 (50.0)	0	0	0	0	0	0	0	0
Sex with carrier	0	2 (100.0)	0	0	0	1 (50.0)	1 (50.0)	0	0	0	0	0	0	1 (33.3)	2 (66.7)	0
Tattooing	0	0	0	0	0	1(100.0)	0	0	0	2(100.0)	0	0	0	8 (42.1)	11 (57.9)	0
Body piercing	0	0	0	0	2 (18.2)	5 (45.5)	3 (27.3)	1 (9.1)	0	0	0	0	2 (5.4)	7 (18.9)	22 (59.5)	6 (16.2)
Acupuncture	0	0	0	0	0	0	1(100.0)	0	0	0	0	0	0	2 (20.0)	4 (40.0)	4 (40.0)
Blood contact	0	0	0	0	0	0	0	1(100.0)	0	0	0	0	0	1 (6.7)	13 (86.7)	1 (6.7)
Hemodialysis	0	0	0	0	0	0	0	0	0	0	0	1(100.0)	0	1 (33.3)	1 (33.3)	1 (33.3)
Carrier in family	0	0	0	0	1 (16.7)	5 (83.3)	0	0	0	0	0	0	4 (36.4)	3 (27.3)	3 (27.3)	1 (9.1)
Institutionalized	0	0	0	0	0	0	0	0	0	0	1(100.0)	0	0	0	1(100.0)	0
Hospitalization	0	0	1(100.0)	0	0	4 (57.1)	3 (42.9)	0	0	0	1(100.0)	0	0	6 (18.8)	17 (53.1)	9 (28.1)
Surgery	0	0	1(100.0)	0	0	0	0	0	0	0	0	0	0	0	1(100.0)	0
Transplant	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Dental visit	0	0	0	1(100.0)	0	4 (80.0)	0	1 (20.0)	0	0	0	1(100.0)	1 (8.3)	5 (41.7)	6 (50.0)	0
Incarceration	0	0	0	0	0	0	0	0	0	1(100.0)	0	0	0	1 (25.0)	3 (75.0)	0
Unknown	0	6 (54.5)	5 (45.5)	0	0	1 (50.0)	1 (50.0)	0	0	0	1(100.0)	0	0	4 (36.4)	6 (54.5)	1 (9.1)
Total	1 (3.6)	16 (57.1)	9 (32.1)	2 (7.1)	6 (5.5)	50 (45.9)	39 (35.8)	14 (12.8)	8 (17.0)	29(61.7)	7 (14.9)	3 (6.4)	22 (2.3)	366 (37.5)	528 (54.0)	61 (6.2)

Table 2.8 b Distribution (row %) of main risk factors for interviewed acute/chronic HBV and HCV cases at Ottawa site of the EHSSS by gender, 1998-2002 combined.

Risk factors	Acute HBV (n=28)		Chronic HBV (n=109)		Acute HCV (n=47)		Chronic HCV (n=977)	
	Male	Female	Male	Female	Male	Female	Male	Female
	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)
IDU	4 (80.0)	1 (20.0)	13 (100.0)	0	24 (72.7)	9 (27.3)	383 (76.8)	116 (23.2)
Snorting	2 (100.0)	0	4 (100.0)	0	4 (80.0)	1 (20.0)	45 (65.2)	24 (34.8)
Blood transfusion	0	0	7 (58.3)	5 (41.7)	1 (100.0)	0	128 (53.8)	110 (46.2)
Blood product	0	0	2 (66.7)	1 (33.3)	0	0	9 (75.0)	3 (25.0)
Heterosexual partners ≥2	1 (100.0)	0	23 (59.0)	16 (41.0)	0	0	0	0
Men sex with men	4 (100.0)	0	2 (100.0)	0	0	0	0	0
Sex with carrier	1 (50.0)	1 (50.0)	1 (50.0)	1 (50.0)	0	0	1 (33.3)	2 (66.7)
Tattooing	0	0	1 (100.0)	0	2 (100.0)	0	14 (73.7)	5 (26.3)
Body piercing	0	0	0	11 (100.0)	0	0	3 (8.1)	34 (91.9)
Acupuncture	0	0	0	1 (100.0)	0	0	9 (90.0)	1 (10.0)
Blood contact	0	0	1 (100.0)	0	0	0	6 (40.0)	9 (60.0)
Hemodialysis	0	0	0	0	1 (100.0)	0	2 (66.7)	1 (33.3)
Carrier in family	0	0	4 (66.7)	2 (33.3)	0	0	7 (63.6)	4 (36.4)
Institutionalized	0	0	0	0	1 (100.0)	0	1 (100.0)	0
Hospitalization	0	1 (100.0)	4 (57.1)	3 (42.9)	0	1 (100.0)	21 (65.6)	11 (34.4)
Surgery	1 (100.0)	0	0	0	1 (100.0)	0	1 (100.0)	0
Transplant	0	0	0	0	0	0	0	0
Dental visit	1 (100.0)	0	4 (80.0)	1 (20.0)	0	0	10 (83.3)	2 (16.7)
Incarceration	0	0	0	0	1 (100.0)	0	4 (100.0)	0
Unknown	8 (72.7)	3 (37.3)	0	2 (100.0)	0	1 (100.0)	8 (75.0)	3 (25.0)
Total	22 (78.6)	6 (31.4)	66 (60.6)	43 (39.4)	35 (74.5)	12 (35.5)	652 (64.0)	325 (36.0)

Table 2.9 Frequency distributions and prevalence proportions of all risk factors for interviewed acute (within last 6 months) and chronic (lifetime) HBV and HCV cases at Ottawa site of the EHSSS, all years combined (October, 1998 -March, 2002).

Risk factors	Acute HBV (n=28)			Chronic HBV (n=109)			Acute HCV (n=47)			Chronic HCV (n=977)		
	N	%[1]	%[2]	N	%[1]	%[2]	N	%[1]	%[2]	N	%[1]	%[2]
Injection drug use	5	11.4	17.9	13	2.8	11.9	33	67.3	70.2	584	9.9	59.8
Drug snorting	4	9.1	14.3	14	3.0	12.8	26	17.4	55.3	571	9.7	58.4
Blood transfusion	0	-	-	13	2.8	11.9	1	0.7	2.1	238	4.1	24.4
Blood product	0	-	-	4	0.9	3.7	0	-	-	48		4.9
Heterosexual partners ≥2	1	2.3	3.6	55	11.8	50.5	-[3]	-	-	-[3]	-	-
Men sex with men	7	15.9	25.0	9	1.9	8.3	-[3]	-	-	-[3]	-	-
Sex with HBV/HCVcarrier	3	6.8	10.7	11	2.4	10.1	17	11.4	36.2	153	2.6	15.7
Tattooing	0	-	-	12	2.6	11.0	5	3.4	10.5	450	7.7	46.1
Body piercing	1	2.3	3.6	34	7.3	31.2	4	2.7	8.5	371	6.3	38.0
Acupuncture	0	-	-	10	2.1	9.2	0	-	-	123	2.1	12.9
Blood contact	0	-	-	8	1.7	7.3	0	-	-	81	1.4	8.3
Hemodialysis	0	-	-	0	-	-	2	1.3	4.3	16	0.3	1.6
HBV/HCVcarrier in family	1	2.3	3.6	28	6.0	25.7	10	6.7	21.3	172	2.9	17.6
Institution associated	0	-	-	7	1.5	6.4	4	2.7	8.5	109	1.9	11.2
Hospitalization	1	2.3	3.6	76	16.2	69.7	26	17.4	55.3	852	14.5	87.2
Surgery	2	4.5	7.1	59	12.6	54.1	2	1.3	4.3	729	12.4	74.6
Transplant	0	-	-	0	-	-	0	-	-	10	0.2	1.0
Dental visit	7	15.9	25.0	101	21.6	92.7	6	4.0	12.8	935	15.9	95.7
Incarceration	1	2.3	3.6	12	2.6	11.0	12	8.1	25.5	418	7.1	42.8
Unknown	11	25.0	39.3	2	0.4	1.8	1	0.7	2.1	11	0.2	1.1
Total	44	100.0	-	468	100.0		149	100.0		5871	100.0	-

[1] Frequency distribution, or structure, of all RFs.

[2] Prevalence proportions of all RFs among all cases: add to >100% because most cases have several RFs.

[3] These risk factors are not listed in the RF hierarchy for HCV.

Table 2.10 a Associations between risk factors of interviewed cases at Ottawa site of the EHSSS, 1998-2002: ratios and kappa coefficients for acute HBV.

RISK FACTORS	NUMBER OF CASES											RATIO										KAPPA									
	SNORTDRU	HETEROSEXUAL	MSM	SEXHEPB	PIERCED	CARRIHEP	HOSPITAL	SURGERY	DENTAL	PRISON	Total RF	SNORTDRU	HETEROSEXUAL	MSM	SEXHEPB	PIERCED	CARRIHEP	HOSPITAL	SURGERY	DENTAL	PRISON	SNORTDRU	HETEROSEXUAL	MSM	SEXHEPB	PIERCED	CARRIHEP	HOSPITAL	SURGERY	DENTAL	PRISON
INJEDR	1		1			1				1	3	1.00	1.00	0.83	0.88	0.94	1.18	0.94	0.88	0.36	1.18	0.00	0.00	-0.17	-0.25	-0.14	**0.43**	-0.14	-0.25	-0.54	**0.43**
SNORTDRU			3		1				1		4		1.00	**1.33**	0.82	1.17	0.91	0.91	0.82	0.53	0.91		0.00	**0.33**	-0.29	**0.31**	-0.15	-0.15	-0.29	-0.42	-0.15
HETEROSEXUAL											0			1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00			0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
MSM				1	1				4	1	6				1.00	1.17	0.83	0.83	0.67	1.17	1.17				0.00	0.17	-0.17	-0.17	-0.33	0.17	0.17
SEXHEPB						1			2		2					0.96	1.18	0.96	0.92	**1.31**	0.96					-0.13	**0.63**	-0.13	-0.20	**0.25**	-0.13
PIERCED									1		1						0.98	0.98	0.96	1.16	0.98						-0.09	-0.09	-0.13	0.12	-0.09
CARRIHEP										1	1							0.98	0.96	0.77	1.18							-0.09	-0.13	-0.17	**1.00**
HOSPITAL								1			1								1.18	0.77	0.98								**0.63**	-0.17	-0.09
SURGERY									1		2									0.94	0.96									-0.05	-0.13
DENTAL											7										0.77										-0.17
PRISON											1																				
Total RF	4	0	6	2	1	1	1	2	7	1	12																				

*Criteria for ratios: ≥1.25 - moderate and ≥1.5 strong associations

**Criteria for kappa coefiicients: 0.20-0.40 - fair and >0.40 - moderate and better agreement

***95% CI for highlighted kappas: 1) K=0.43 CI=[-0.29; 1.15]; 2) K=0.43 CI=[-0.29; 1.15]; 3) K=0.33 CI=[-0.20; 0.87]; 4) K=0.31 CI=[-0.37; 0.99]; 5) K=0.62 CI=[-0.08; 1.33]; 6) K=0.25 CI=[-0.25; 0.75]; 7) K=1.00 CI=[1.00; 1.00]; 8) K=0.62 CI=[-0.08; 1.33].

****All the values for ratios/kappas with fair/moderate agreements between pairs of RFs are bolded, but only those whose 95% CIs did not include 0 are discussed in the text.

Table 2.10 b Associations between risk factors of interviewed cases at the Ottawa site of the EHSSS, 1998-2002: ratios and kappa coefficients for chronic HBV.

	NUMBER OF CASES																			RATIO																KAPPA																
RISK FACTORS	SNORTDRU	TRANSFU	BLODPRO	HETEROSEXUAL	NSEXWITHMEN	SEXHEPB	TATTOOED	PIERCED	ACUPUNCT	BLODCONT	CARRIHEP	INSTITUT	HOSPITAL	SURGERY	DENTAL	PRISON	Total	RF	SNORTDRU	TRANSFU	BLODPRO	HETEROSEXUAL	MSM	SEXHEPB	TATTOOED	PIERCED	ACUPUNCT	BLODCONT	CARRIHEP	INSTITUT	HOSPITAL	SURGERY	DENTAL	PRISON	SNORTDRU	TRANSFU	BLODPRO	HETEROSEXUAL	MSM	SEXHEPB	TATTOOED	PIERCED	ACUPUNCT	BLODCONT	CARRIHEP	INSTITUT	HOSPITAL	SURGERY	DENTAL	PRISON
INJEDRU	11	1		1		2	5	6	3	1	2	3	10	8	12	9	13	1.25	0.98	0.99	0.69	0.97	1.01	1.09	1.06	1.04	1.00	0.95	1.05	0.97	0.99	0.92	1.20	0.78	-0.07	-0.07	-0.25	-0.13	0.05	0.31	0.10	0.16	-0.01	-0.10	0.23	-0.01	-0.01	-0.01	0.68
SNORTDRU			1	1		2	5	6	2	1	4	5	13	12	13	8	14		0.95	1.01	0.66	0.96	1.01	1.09	1.05	1.01	1.00	1.01	1.10	1.13	1.16	0.93	1.17		-0.17	0.05	-0.27	-0.13	0.03	0.29	0.08	0.05	-0.02	0.01	0.42	0.05	0.11	-0.01	0.55
TRANSFU						3	1	2	2		3		11	10	11	1	13			0.99	0.64	0.97	1.04	0.98	0.92	1.02	0.97	0.98	0.98	1.04	1.09	0.79	0.98			-0.07	-0.28	-0.13	0.14	-0.05	-0.13	0.06	-0.12	-0.03	-0.11	0.02	0.06	-0.04	-0.05
BLOODPRO												1	3	2	3		4				0.89	0.99	0.99	0.99	0.96	0.99	0.99	0.97	1.02	0.98	0.97	0.74	0.99				-0.09	-0.06	-0.07	-0.07	-0.08	-0.06	-0.08	-0.06	0.14	-0.01	-0.02	-0.02	-0.07
HETEROSEXUAL					2	3	3	13	2	3	10	1	25	20	38	1	55					0.84	0.84	0.81	0.78	0.82	0.92	0.77	0.85	0.27	0.40	0.44	0.72					-0.12	-0.13	-0.15	-0.20	-0.14	-0.06	-0.20	-0.11	-0.88	-0.65	-0.75	-0.22
MSM						1					1		2	2	6		9						1.00	0.97	0.90	0.98	0.98	0.95	0.98	0.57	0.80	0.52	0.97						0.00	-0.12	-0.17	-0.11	-0.10	-0.10	-0.08	-0.15	-0.13	-0.06	-0.12
SEXHEPB							1	3	1		8	1	7	5	9	2	11							0.99	0.98	1.00	0.98	1.16	1.00	0.86	0.90	0.75	1.02							-0.04	-0.03	-0.02	-0.11	0.32	0.02	-0.05	-0.07	-0.04	0.06
TATTOOED								6	2	2	4	1	10	10	11	5	12								1.07	1.02	1.03	1.02	1.00	1.03	1.13	0.91	1.09								0.12	0.08	0.11	0.05	0.01	0.01	0.09	-0.02	0.33
PIERCED									3	5	7	3	25	19	30	5	31										0.99	1.08	0.95	1.02	1.01	0.97	1.00	1.04									-0.02	0.14	-0.07	0.04	0.01	-0.02	0.00	0.06
ACUPUNCT										1	5	1	9	8	10	2	10											1.00	1.07	1.01	1.08	1.09	1.05	1.02										0.02	0.15	0.03	0.03	0.06	0.01	0.08
BLODCONT											4	1	6	6	7	1	8												1.06	1.01	0.97	1.05	0.86	1.00											0.12	0.06	-0.01	0.03	-0.02	0.00
CARRIHEP												1	19	18	28	1	26													0.97	0.90	1.08	1.21	0.93												-0.06	-0.06	0.06	0.06	-0.15
INSTITUT													6	4	6	3	7														1.03	0.98	0.84	1.05													0.01	-0.01	-0.02	0.25
HOSPITAL														55	70	11	76															1.25	0.90	1.11															0.35	-0.35	0.04
SURGERY															59	7	60																1.03	0.97																0.05	-0.02
DENTAL																11	92																	0.91																	-0.02
PRISON																	12																																			
Total RF	14	13	4	55	9	11	12	31	10	8	26	7	76	60	92	12	95																																			

*Criteria for ratios: ≥1.25 - moderate and ≥1.5 strong associations

**Criteria for kappa coefficients: 0.20-0.40 - fair and >0.40 - moderate and better agreement

***95% CI for highlighted kappas: 1)K=0.78 CI=[0.60; 0.97]; 2)K=0.31 CI=[-0.01; 0.63]; 3) K=0.23 CI=[-0.15; 0.60]; 4) K=0.68 CI=[0.45; 0.91]; 5) K=0.29 CI=[-0.03; 0.61]; 6) K=0.42 CI=[0.10; 0.74]; 7) K=0.55 CI=[0.29; 0.82]; 8) K=0.32 CI=[0.07; 0.58]; 9) K=0.33 CI=[0.01; 0.66]; 10) K=0.35 CI=[0.14; 0.56].

****All the values for ratios/kappas with fair/moderate agreements between pairs of RFs are bolded, but only those whose 95% CIs did not include 0 are discussed in the text.

Table 2.10 c Associations between risk factors of interviewed cases at the Ottawa site of the EHSSS, 1998-2002: ratios and kappa coefficients for acute HCV.

Risk Factor	NUMBER OF CASES													RATIO											KAPPA										
	SNORTDRU	TRANSFU	HEMODIAL	TATTOOED	PIERCED	PRISON	SEXHEPC	CARRIHEP	INSTITUT	HOSPITAL	SURGERY	DENTAL	Total RF	SNORTDRU	TRANSFU	HEMODIAL	TATTOOED	PIERCED	PRISON	SEXHEPC	CARRIHEP	INSTITUT	HOSPITAL	SURGERY	DENTAL	SNORTING	TRANSFU	HEMODIAL	TATTOOED	PIERCED	PRISON	SEXHEPC	CARRIHEP	INSTITUT	HOSPITAL	SURGERY	DENTAL
INJEDR	20		3	3	8	14	9	3	2		4	29	1.16	0.84	0.70	0.86	0.99	0.85	1.11	1.19	1.13	0.58	0.70	0.90	**0.21**	-0.05	-0.11	-0.06	0.00	-0.10	0.10	0.12	0.05	-0.20	-0.11	-0.04
SNORTDRU			3	4	7	9	6	1	2	1		24		0.91	0.83	0.98	1.20	0.93	0.81	0.96	0.88	0.77	0.96	0.51		-0.05	-0.11	-0.01	0.13	-0.06	-0.18	-0.03	-0.08	-0.16	-0.02	-0.34
TRANSFU									1			1			1.00	0.99	0.99	0.98	0.96	0.98	1.00	1.05	1.00	0.99			-0.04	-0.05	-0.04	-0.05	-0.05	-0.05	-0.04	**0.25**	-0.04	-0.05
HEMODIAL									2			2				0.98	0.99	0.95	0.91	0.96	0.99	1.11	0.99	0.98				-0.08	-0.08	-0.10	-0.10	-0.10	-0.07	**0.46**	-0.06	-0.09
TATTOOED				2	2	2	2	1	1		1	5					1.10	1.03	0.98	1.05	1.04	1.01	0.98	1.01					**0.37**	0.06	-0.03	0.11	0.17	0.04	-0.08	0.04
PIERCED					1	1	1					4						0.98	0.92	1.00	0.98	0.96	0.99	0.96						-0.04	-0.09	-0.01	-0.10	-0.14	-0.08	-0.14
PRISON						5	4			2	1	12							0.96	1.08	0.92	0.84	0.95	1.01							-0.04	0.11	-0.14	-0.27	-0.10	0.01
SEXHEPC							9	1	2	1	2	17								**1.45**	0.97	0.93	1.01	0.93								**0.50**	-0.04	-0.08	0.01	-0.08
CARRIHEP									1	1	1	10									0.94	0.95	1.04	0.95									-0.14	-0.09	0.09	-0.09
INSTITUT									2		1	3										1.10	0.99	1.04										**0.38**	-0.07	0.13
HOSPITAL										2	1	6											1.11	1.00											**0.46**	0.01
SURGERY												2												0.98												-0.09
DENTAL												6																								
Total	29	24	1	2	5	4	12	17	10	3	6	2	6	38																						

*Criteria for ratios: ≥1.25 - moderate and ≥1.5 strong associations

**Criteria for kappa coefiicients: 0.20-0.40 - fair and >0.40 - moderate and better agreement

***95% CI for highlighted kappas: 1) K=0.21 CI=[-0.14; 0.56]; 2) K=0.25 CI=[-0.36; 0.86]; 3) K=0.46 CI=[-0.05; 0.96]; 4) K=0.37 CI=[-0.14; 0.88]; 5) K=0.50 CI=[0.22; 0.79]; 6) K=0.38 CI=[-0.13; 0.89]; 7) K=0.46 CI=[-0.05; 0.96]

****All the values for ratios/kappas with fair/moderate agreements between pairs of RFs are bolded, but only those whose 95% CIs did not include 0 are discussed in the text.

Table 2.10 d Associations between risk factors of interviewed cases at Ottawa site of the EHSSS Surveillance, 1998-2002: ratios and kappa coefficients for chronic HCV.

RFS	SNORTDRU	BLODCONT	TRANSFU	BLOODPRO	HEMODIAL	TATTOOED	PIERCED	ACUPUNCT	ORGANTIS	PRISON	SEXHEPC	CARRIHEP	INSTITUT	HOSPITAL	SURGERY	DENTAL	Total	RF
INJEDR	276	27	54	6		279	162	54		179	93	45	27	476	388	492	586	
SNORTDRU	24	60	6	3	285	174	48		276	84	72	27	460	404	556	573		
BLODCONT		6			15	24	9		12	3	3	3	60	48	56	81		
TRANSFU			24	12	57	51	18	9	51	6	15	6	180	172	175	239		
BLOODPRO				12	3	15		9	3				44	40	44	49		
HEMODIAL					3	3		9					16	16	16	16		
TATTOOED						159	33		261	45	72	18	432	376	440	451		
PIERCED							36	3	126	66	63	24	316	188	356	372		
ACUPUNCT									30	15	6		96	92	100	123		
ORGANTIS													10	10	10	10		
PRISON										60	51	27	368	308	420	420		
SEXHEPC											84	9	124	92	144	154		
CARRIHEP												9	136	104	156	172		
INSTITUT													44	40	52	109		
HOSPITAL														616	796	855		
SURGERY															620	732		
DENTAL																935		
Total R	573	81	239	49	16	451	372	123	10	420	154	172	109	855	732	935	958	

RATIOS

RFS	SNORTDRU	BLODCONT	TRANSFU	BLOODPRO	HEMODIAL	TATTOOED	PIERCED	ACUPUNCT	ORGANTIS	PRISON	SEXHEPC	CARRIHEP	INSTITUT	HOSPITAL	SURGERY	DENTAL
SNORTDRU	0.70	0.88	0.57	0.87	0.95	1.01	0.71	0.89	0.97	0.67	0.99	0.71	0.80	0.83	0.78	0.72
BLODCONT		0.88	0.62	0.88	0.97	1.06	0.79	0.88	0.97	1.11	0.96	0.85	0.81	0.81	0.87	0.99
TRANSFU			0.96	0.99	1.00	0.91	0.97	1.00	1.00	0.91	0.97	0.97	0.98	0.85	0.90	0.54
BLOODPRO				1.03	1.02	0.77	0.84	0.96	1.02	0.79	0.90	0.91	0.94	0.77	0.94	0.53
HEMODIAL					1.02	0.92	0.99	0.98	1.02	0.93	0.98	0.98	0.99	1.00	1.02	0.89
TATTOOED						0.98	0.99	1.00	1.02	0.97	0.99	0.99	1.00	1.03	1.03	1.02
PIERCED							0.93	0.90	0.98	1.26	0.89	0.96	0.87	1.13	1.14	1.00
ACUPUNCT								0.96	1.00	0.85	1.02	0.99	0.93	0.92	0.54	0.96
ORGANTIS									1.00	0.91	0.99	0.95	0.96	0.86	0.99	0.71
PRISON										0.98	1.00	1.00	1.00	1.02	1.02	1.01
SEXHEPC											0.97	0.91	0.92	0.97	0.94	1.05
CARRIHEP												1.16	0.98	0.88	0.83	0.93
INSTITUT													0.97	0.85	0.83	0.87
HOSPITAL														0.43	0.69	0.14
SURGERY															0.89	0.91
DENTAL																0.74

KAPPA

RFS	SNORTDRU	BLODCONT	TRANSFU	BLOODPRO	HEMODIAL	TATTOOED	PIERCED	ACUPUNCT	ORGANTIS	PRISON	SEXHEPC	CARRIHEP	INSTITUT	HOSPITAL	SURGERY	DENTAL
SNORTDRU	-0.33	-0.08	-0.35	-0.08	-0.03	0.01	-0.26	-0.08	-0.02	-0.32	0.00	-0.22	-0.14	-0.24	-0.26	-0.42
BLODCONT		-0.09	-0.32	-0.08	-0.02	0.05	-0.19	-0.09	-0.02	0.10	-0.03	-0.11	-0.14	-0.25	-0.16	-0.02
TRANSFU			-0.10	-0.07	-0.03	-0.10	-0.04	-0.02	-0.02	-0.11	-0.10	-0.10	-0.07	-0.03	-0.04	-0.05
BLOODPRO				0.09	0.06	-0.24	-0.20	-0.08	0.05	-0.24	-0.21	-0.17	-0.14	-0.10	-0.04	-0.18
HEMODIAL					0.35	-0.09	-0.02	-0.08	0.29	-0.09	-0.08	-0.09	-0.08	0.00	0.01	-0.01
TATTOOED						-0.02	-0.02	-0.03	0.69	-0.03	-0.03	-0.03	-0.03	0.00	0.01	0.00
PIERCED							-0.07	-0.11	-0.02	0.27	-0.12	-0.04	-0.15	0.12	0.13	0.00
ACUPUNCT								-0.06	0.00	-0.16	0.03	-0.02	-0.09	-0.06	-0.36	-0.02
ORGANTIS									-0.02	-0.11	-0.04	-0.13	-0.14	-0.04	-0.01	-0.05
PRISON										-0.02	-0.02	-0.02	-0.02	0.00	0.01	0.00
SEXHEPC											-0.03	-0.11	-0.10	-0.03	-0.05	0.04
CARRIHEP												0.42	-0.07	-0.04	-0.08	-0.02
INSTITUT													-0.09	-0.05	-0.09	-0.03
HOSPITAL														-0.14	-0.13	-0.13
SURGERY															-0.27	-0.64
DENTAL																-0.79

*Criteria for ratios: ≥1.25 - moderate and ≥1.5 strong associations

**Criteria for kappa coefiicients: 0.20-0.40 - fair and ≥0.41 - moderate and better agreement

***95% CI for bolded kappas: HCV: 1) K=0.35 CI=[0.16; 0.55]; 2) K=0.29 CI=[0.08; 0.50]; 3) K=0.69 CI=[0.47; 0.90]; 4) K=0.27 CI=[0.20; 0.33]; 5) K=0.42 CI=[0.33; 0.50].

****All the values for ratios/kappas with fair/moderate agreements between pairs of RFs are bolded, but only those whose 95% CIs did not include 0 are discussed in the text.

Table 2.11 Number of risk factors per interviewed case at the Ottawa site of the EHSSS, 1998-2002 combined.

Number of risk factors	Acute HBV (n=28)		Chronic HBV (n=109)		Acute HCV (n=47)		Chronic HCV (n=977)	
	N	%	N	%	N	%	N	%
0 (URF)	11	39.3	2	1.8	1	2.1	11	1.1
1	5	17.6	3	2.8	7	14.8	1	0.1
2	7	35.7	4	3.7	18	38.3	176	18.0
3	2	7.1	20	18.3	11	23.4	218	22.3
4	2	7.1	33	14.7	6	12.8	247	25.3
5+	0	0.0	47	30.3	4	8.5	324	33.2
Average number per case	1.2	-	4.3	-	2.7	-	6.0	-

Table 2.12 Reported and coinfected cases of acute/chronic HBV and HCV by age, gender, birthplace, and main risk factors at the Ottawa site of the EHSSS all years combined (1998-2002).

Characteristics of reported And coinfected cases	Acute HBV			Chronic HBV			Acute HCV			Chronic HCV		
	Reported cases	Coinfected cases		Reported cases	Coinfected cases		Reported cases	Coinfected cases		Reported cases	Coinfected cases	
	N	N	%	N	N	%	N	N	%	N	N	%
Total number	38	5	13.2	894	24	2.7	55	1	1.8	1772	41	2.3
Age groups												
0-19	2	0	-	49	1	2.0	8	0	-	54	1	1.9
20-39	24	4	16.7	510	10	2.0	36	1	2.8	737	17	2.3
40-59	10	1	10.0	258	12	4.7	8	0	-	847	21	2.5
60+	2	0	-	77	1	1.3	3	0	-	134	2	1.5
Gender												
Male	30	4	13.3	524	20	3.8	40	1	2.5	1215	32	2.6
Female	8	1	12.5	370	4	1.1	15	0	-	557	9	1.6
Birth place												
Africa	2	1	50.0	125	3	2.4	1	0	-	62	6	9.7
Asia	6	3	50.0	611	19	3.1	1	0	-	114	12	10.5
Canada	22	1	9.1	81	1	1.2	45	1	2.2	1185	19	1.6
Other	8	0	-	77	1	1.3	8	0	0	411	4	1.0
Main Risk Factors (interviewed cases)												
IDU	5	2	40.0	13	7	53.8	33	1	3.1	501	11	22.2
Blood transfusion	0	0	-	12	1	8.3	1	0	0.0	196	5	3.7
Heterosexual parteners>2	1	0	0.0	39	1	2.5	0	0	-	0	0	-
HepC carrier in family	0	0	-	6	0	0.0	0	0	-	11	1	9.1
Hospitalization	1	0	0.0	7	0	0.0	1	0	0.0	32	2	6.3

Figure 2.1 Quarterly numbers of reported cases of acute and chronic HBV and HCV at the Ottawa site of the Enhanced Surveillance in logarithmic scale (October, 1998 - March, 2002).

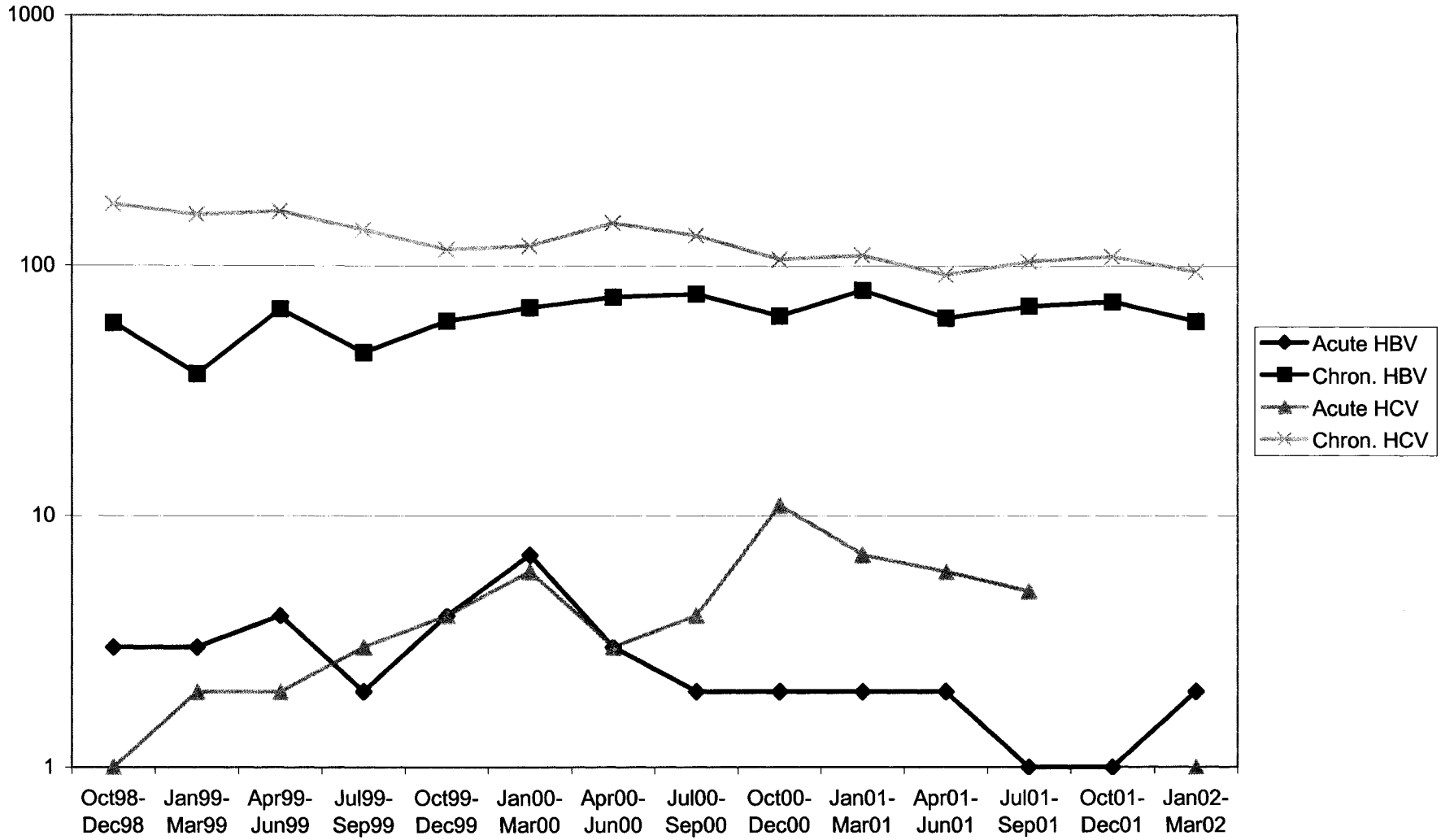


Figure 2.2 Incidence (acute) and identification (chronic) rates of HBV and HCV cases at the Ottawa site of the EHSSS per 100,000 person-years,1999-2001 (Logarithmic scale).

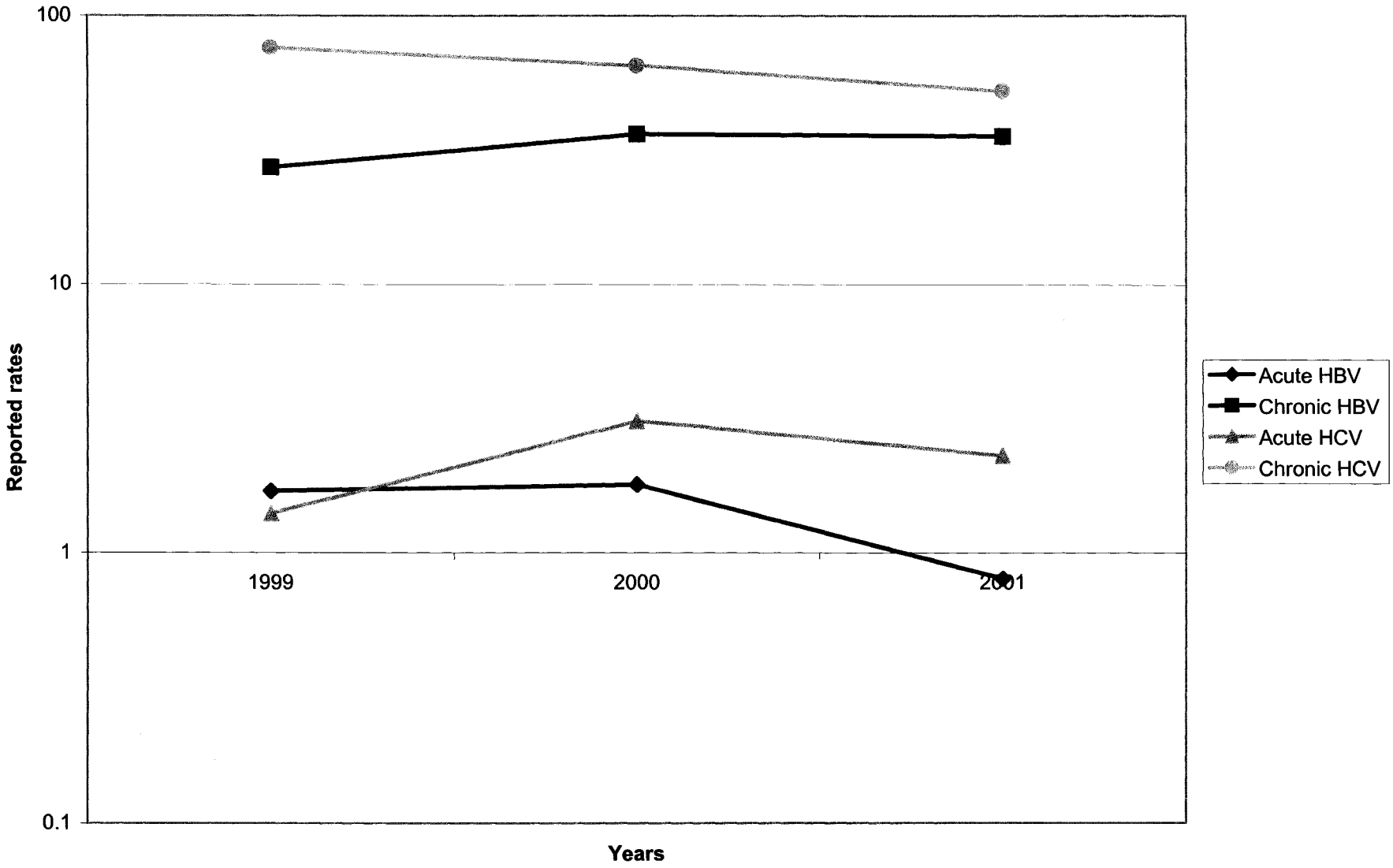


Figure 2.3 a Time trends in age characteristics of reported HBV/HCV cases, 1999-2001.

i. Acute and chronic HBV

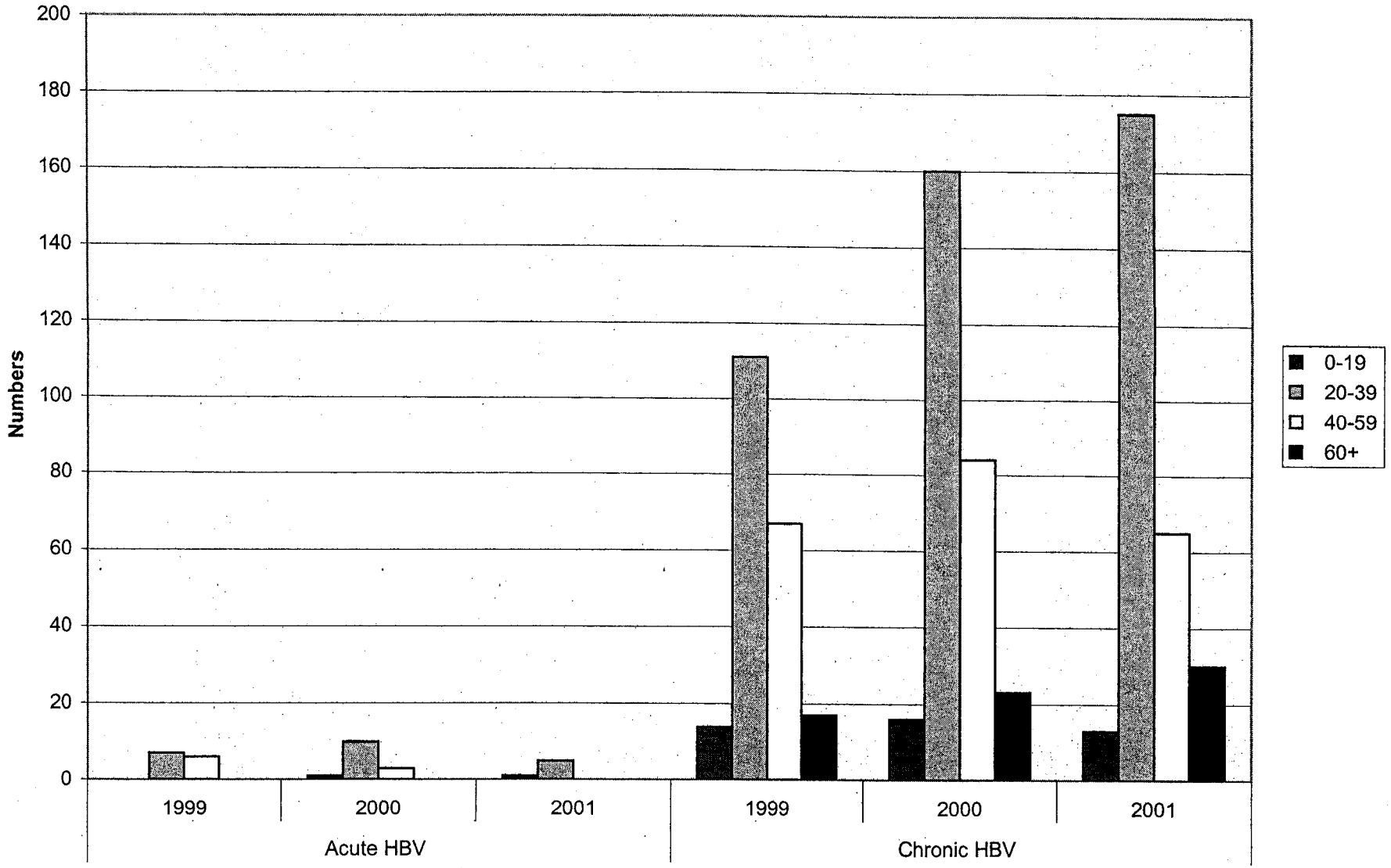


Figure 2.3 a Time trends in age characteristics of reported HBV/HCV cases, 1999-2001.

ii. Acute and chronic HCV

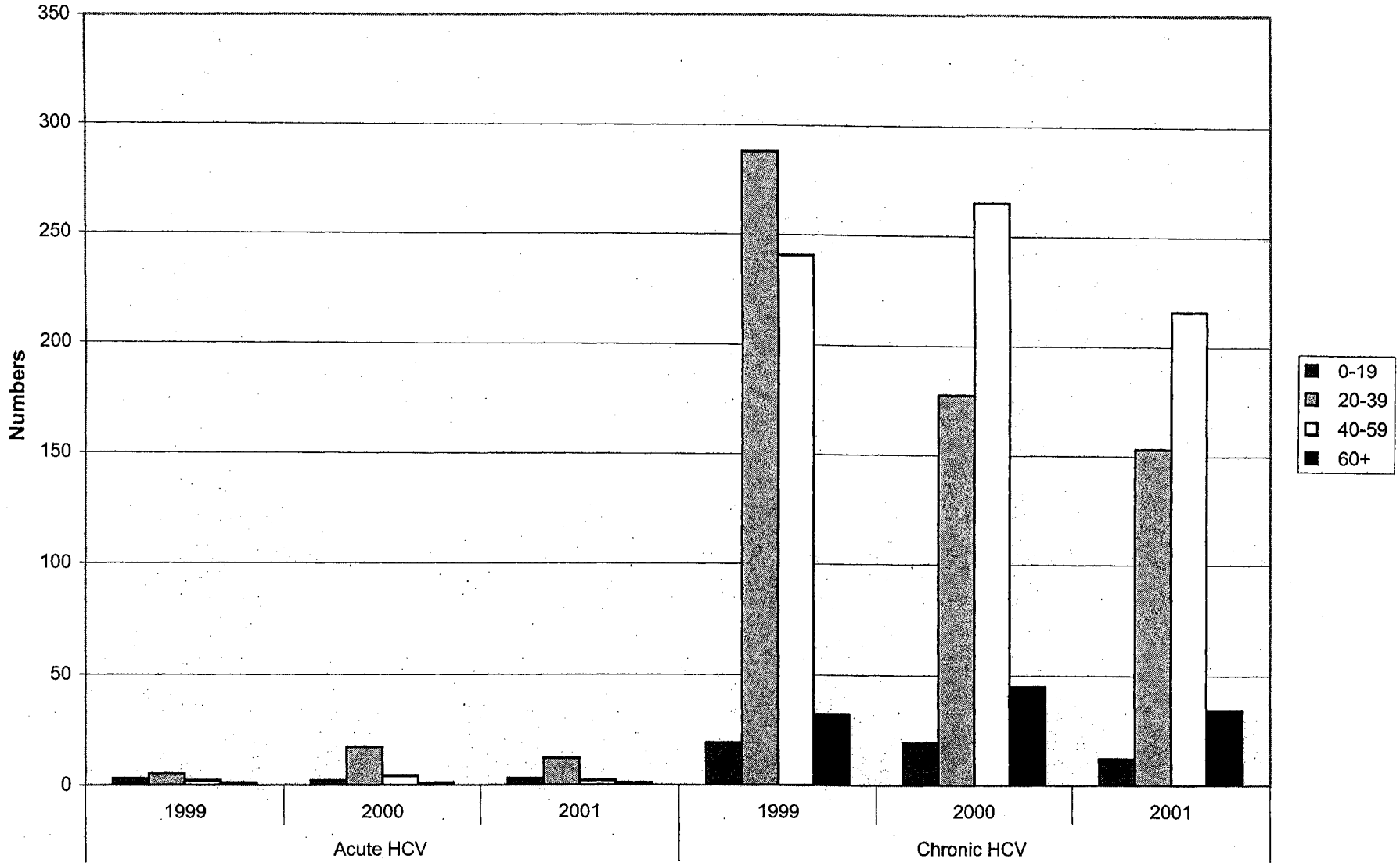


Figure 2.3 b Time trends in gender characteristics of reported HBV/HCV cases, 1999-2001.

i. Acute and chronic HBV

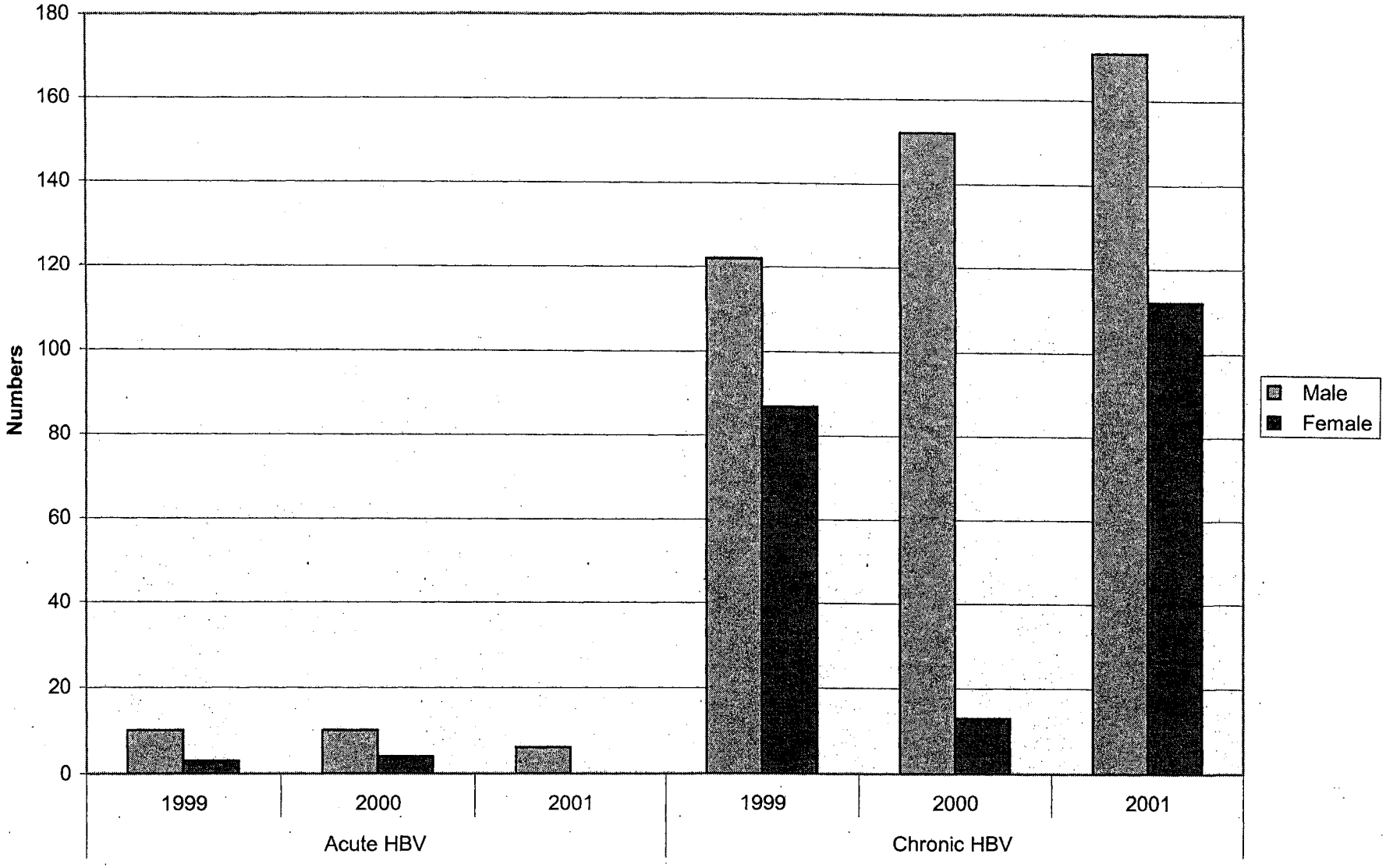


Figure 2.3 b Time trends in gender characteristics of reported HBV/HCV cases, 1999-2001 (cont-d).
ii. Acute and chronic HCV

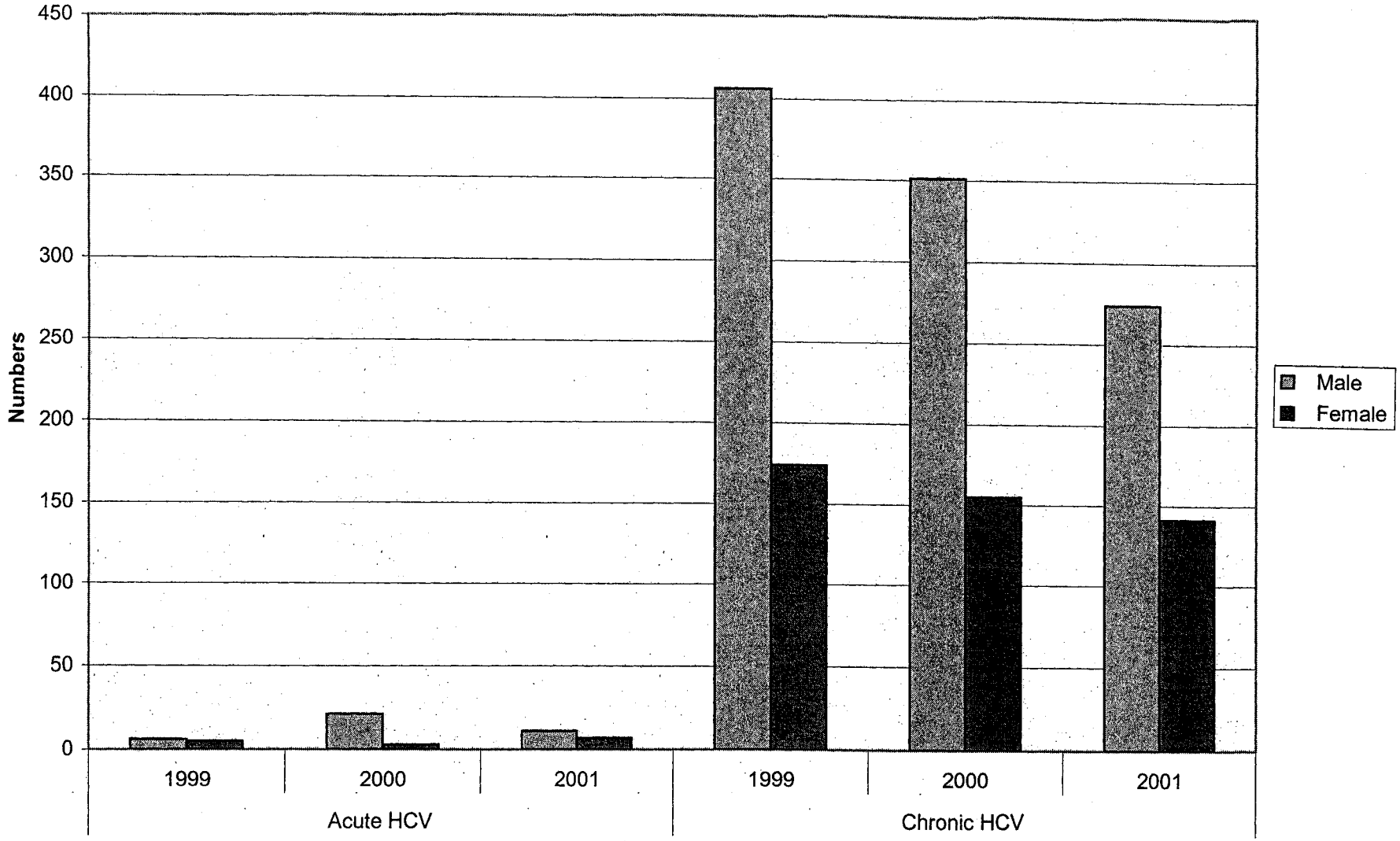


Figure 2.3 c Time trends in birthplace characteristics of reported HBV and HCV cases, 1999-2001.
i. Acute and chronic HBV

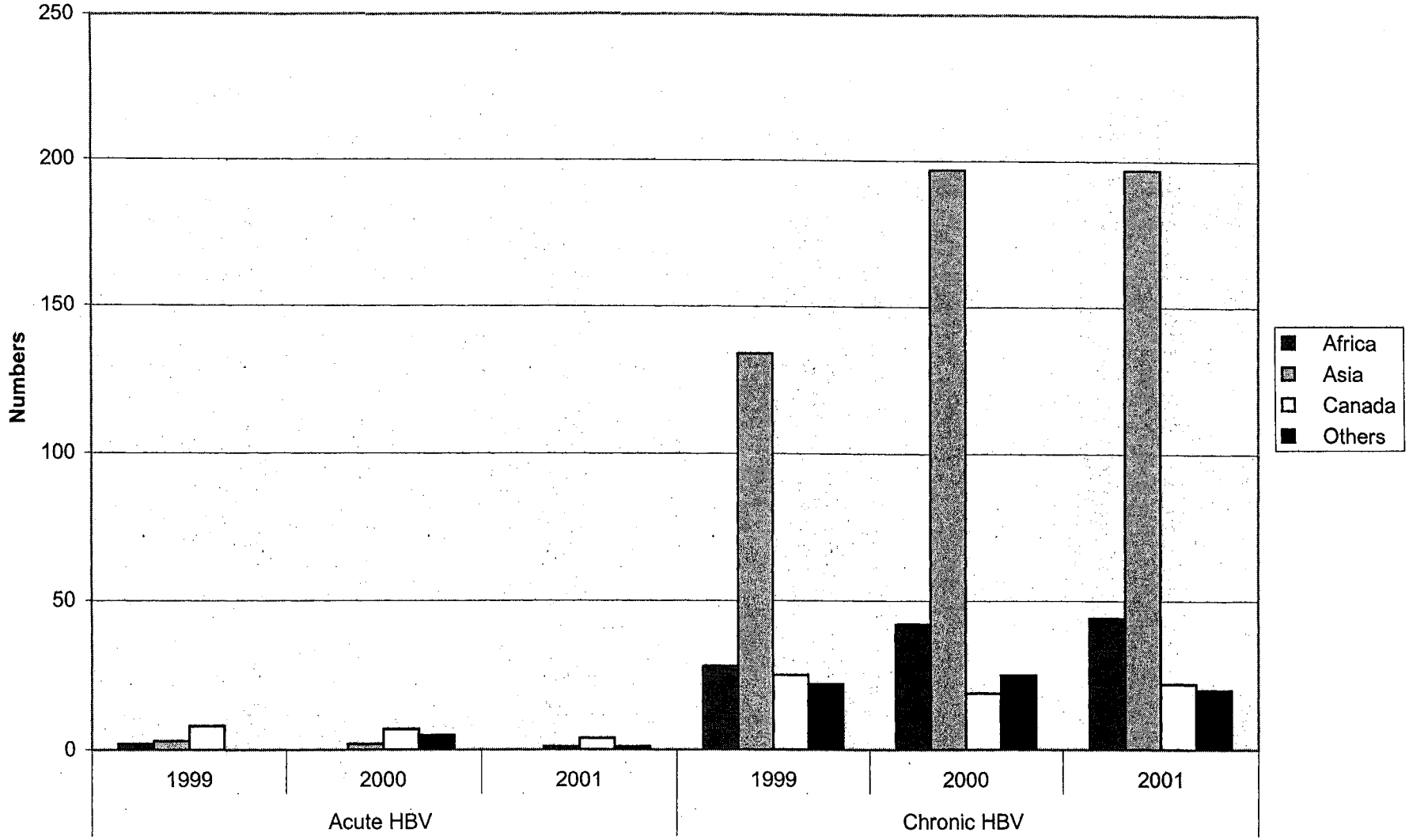


Figure 2.3 c Time trends in birthplace characteristics of reported HBV and HCV cases, 1999-2001 (cont-d).
ii. Acute and chronic HCV

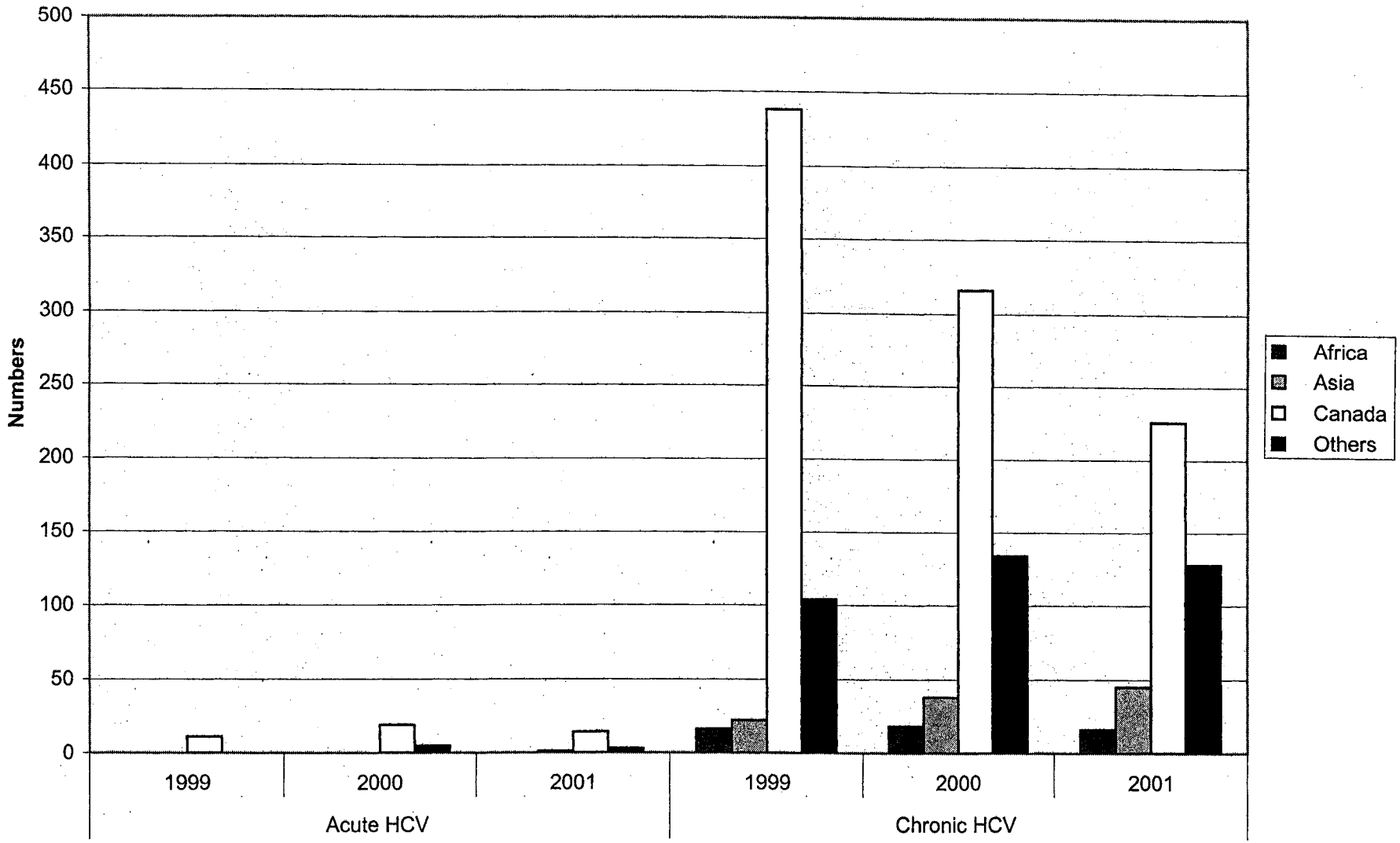


Figure 2.4a Time-trends in prevalence proportions of risk factors for acute HBV cases

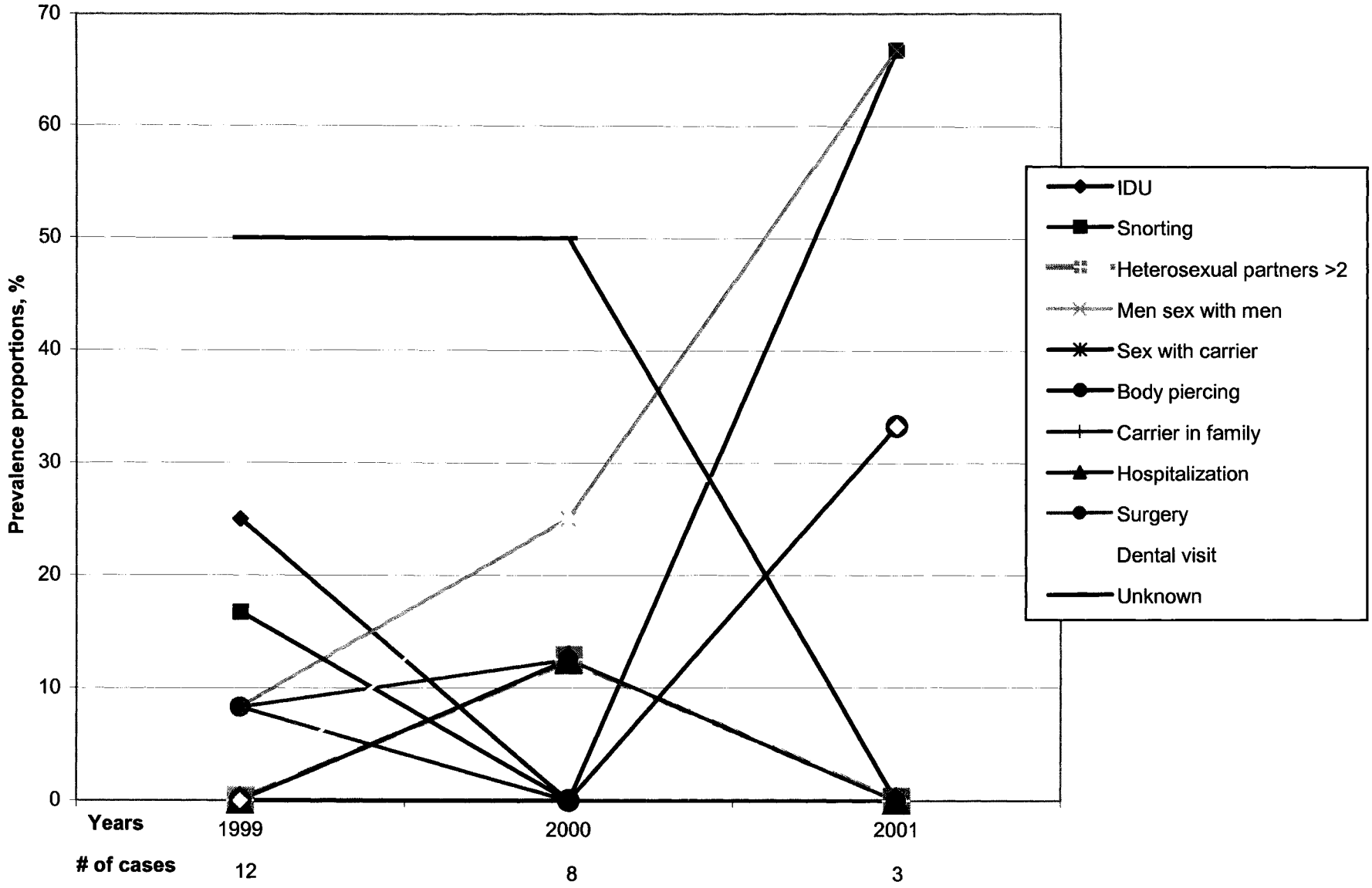


Figure 2.4b Time-trends in prevalence proportions of risk factors for acute HCV cases

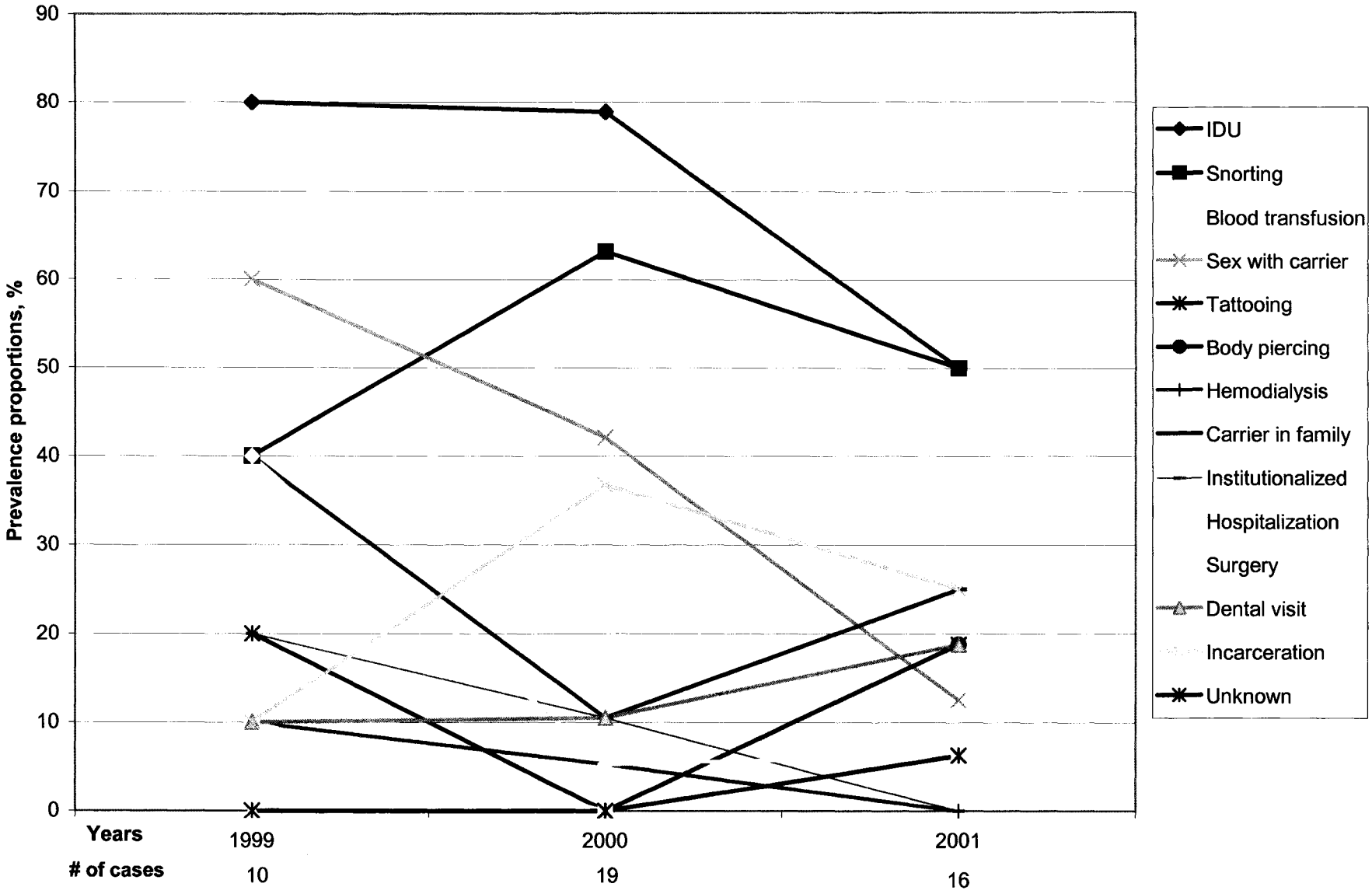
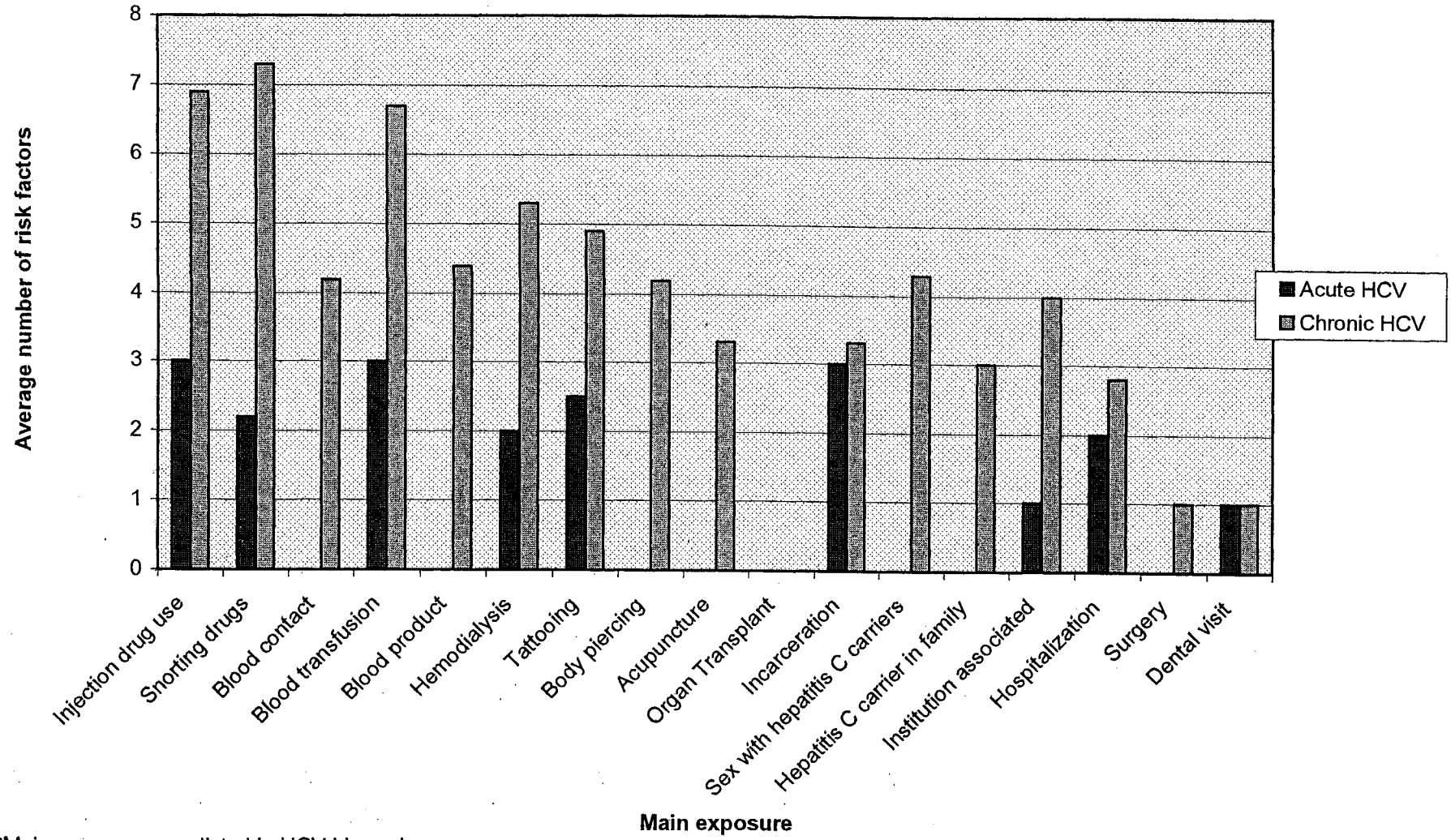
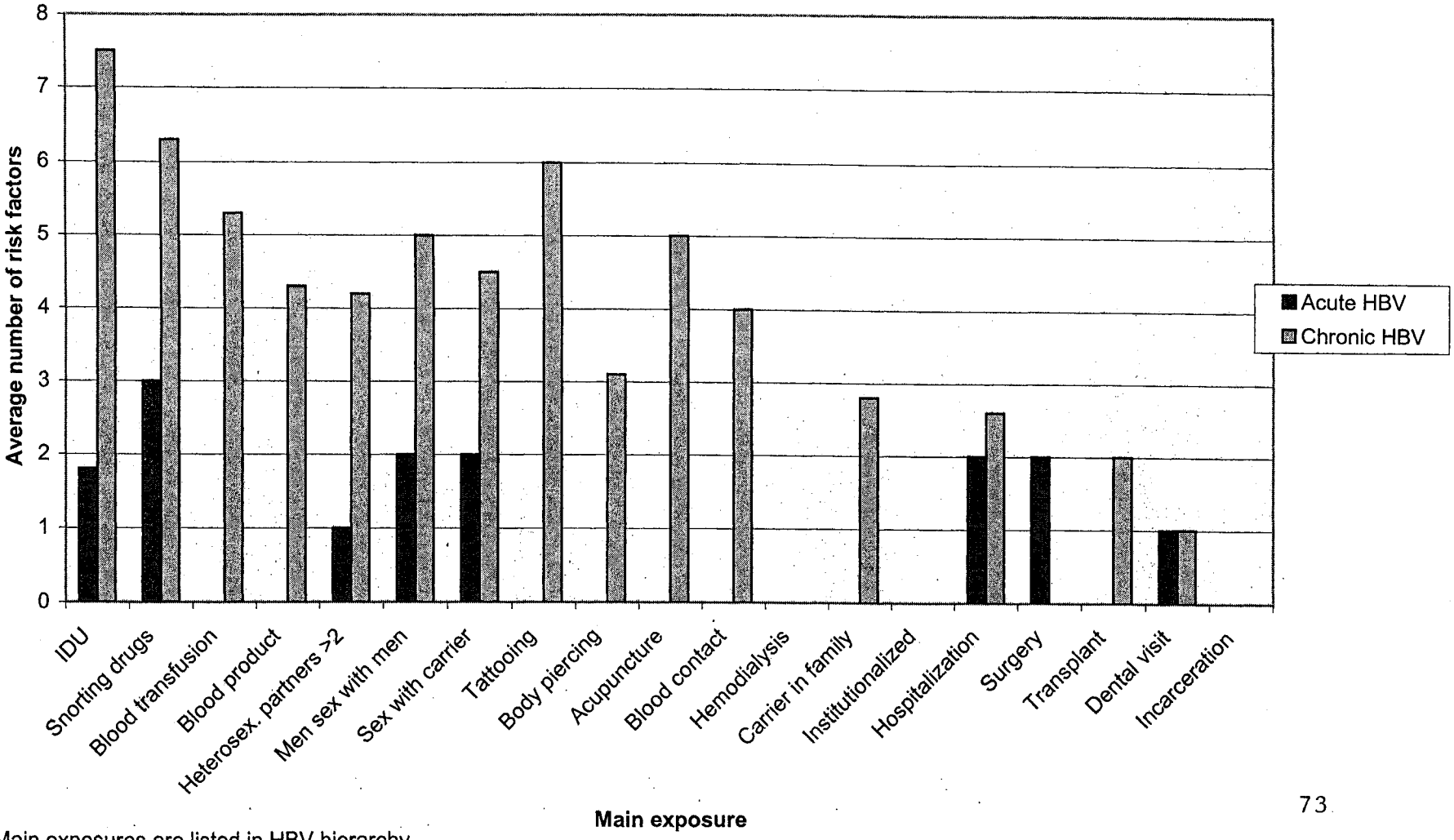


Figure 2.5 b Average total number of risk factors for acute/chronic HCV by main exposure*, 1998-2002 combined.



*Main exposures are listed in HCV hierarchy.

Figure 2.5 a Average total number of risk factors for acute/chronic HBV by main exposure*, 1998-2002 combined.



*Main exposures are listed in HBV hierarchy

Figure 2.6 a Distribution of reported cases of HBV/HCV coinfection by age, 1998-2002.

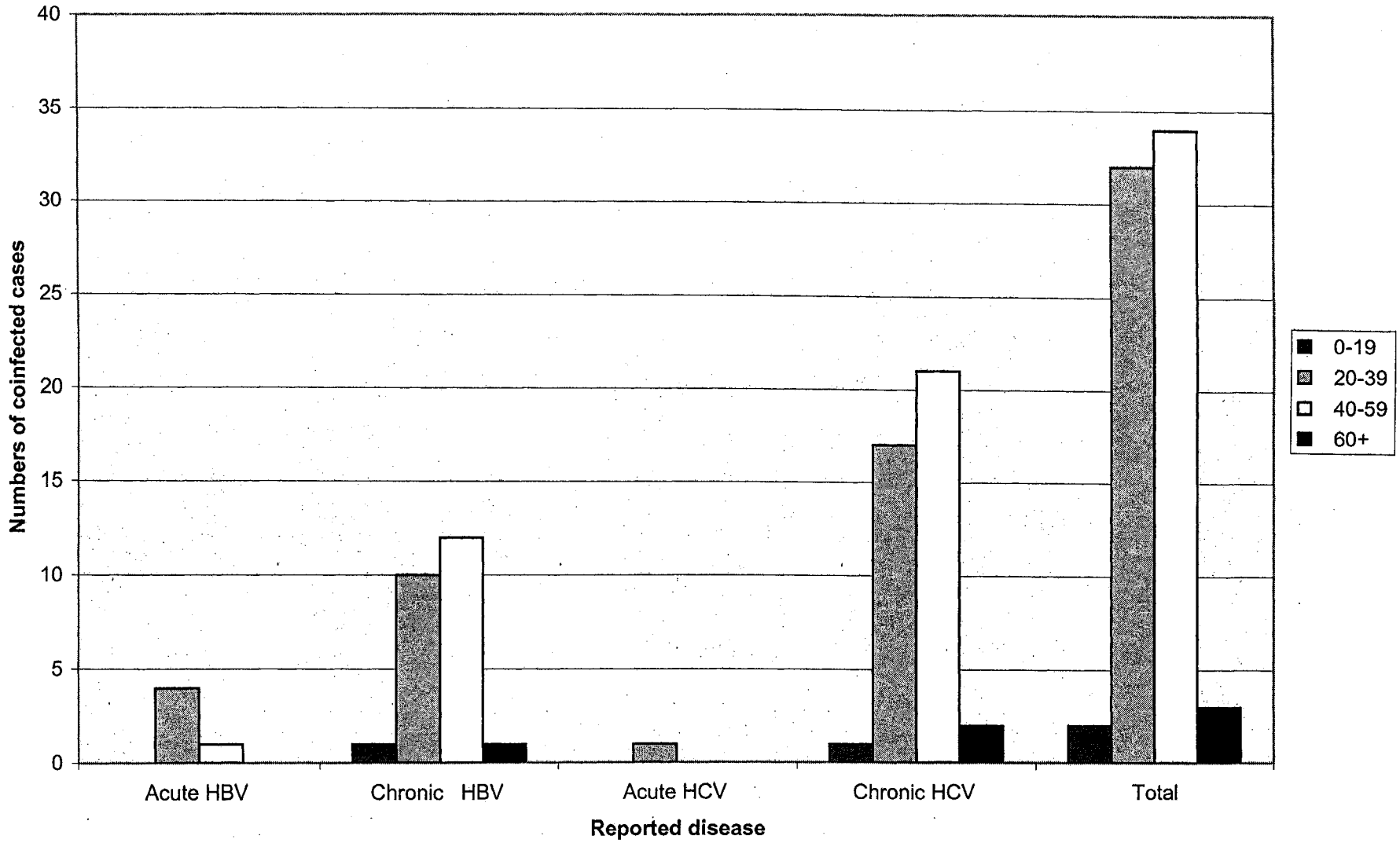


Figure 2.6 b Distribution of reported cases of HBV/HCV coinfection by gender, 1998-2002.

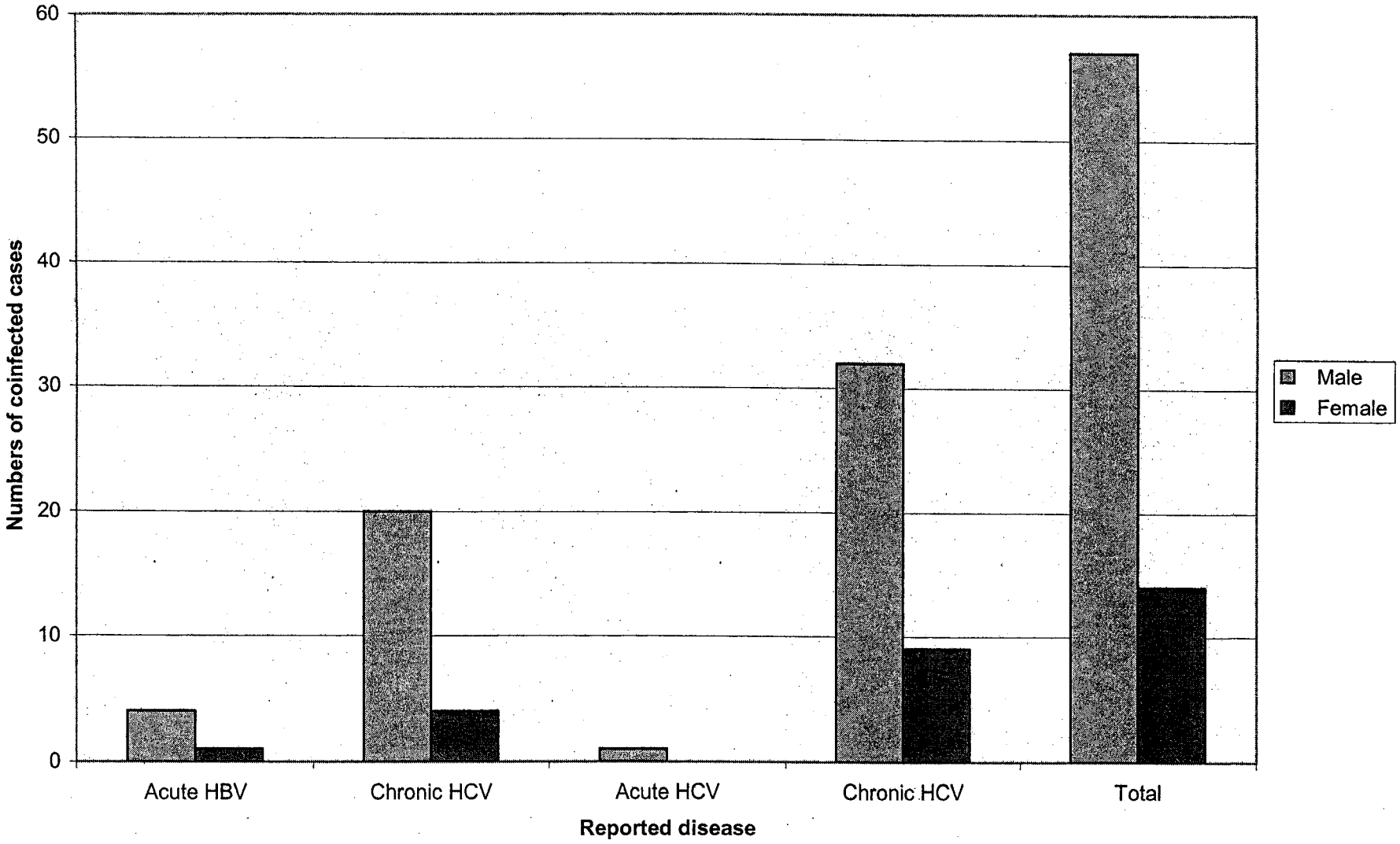


Figure 2.6 c Distribution of reported cases of HBV/HCV coinfection by birthplace, 1998-2002.

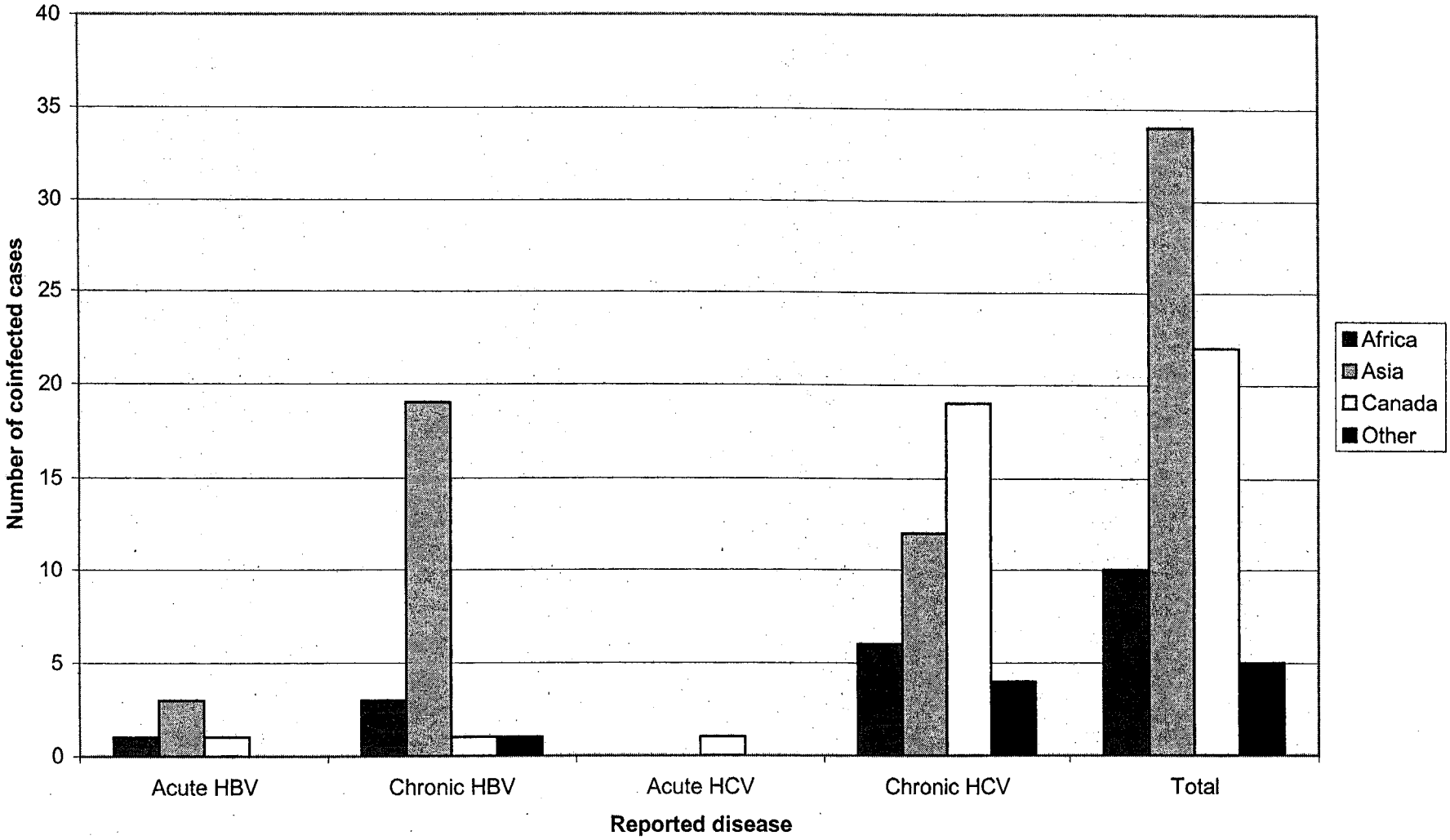
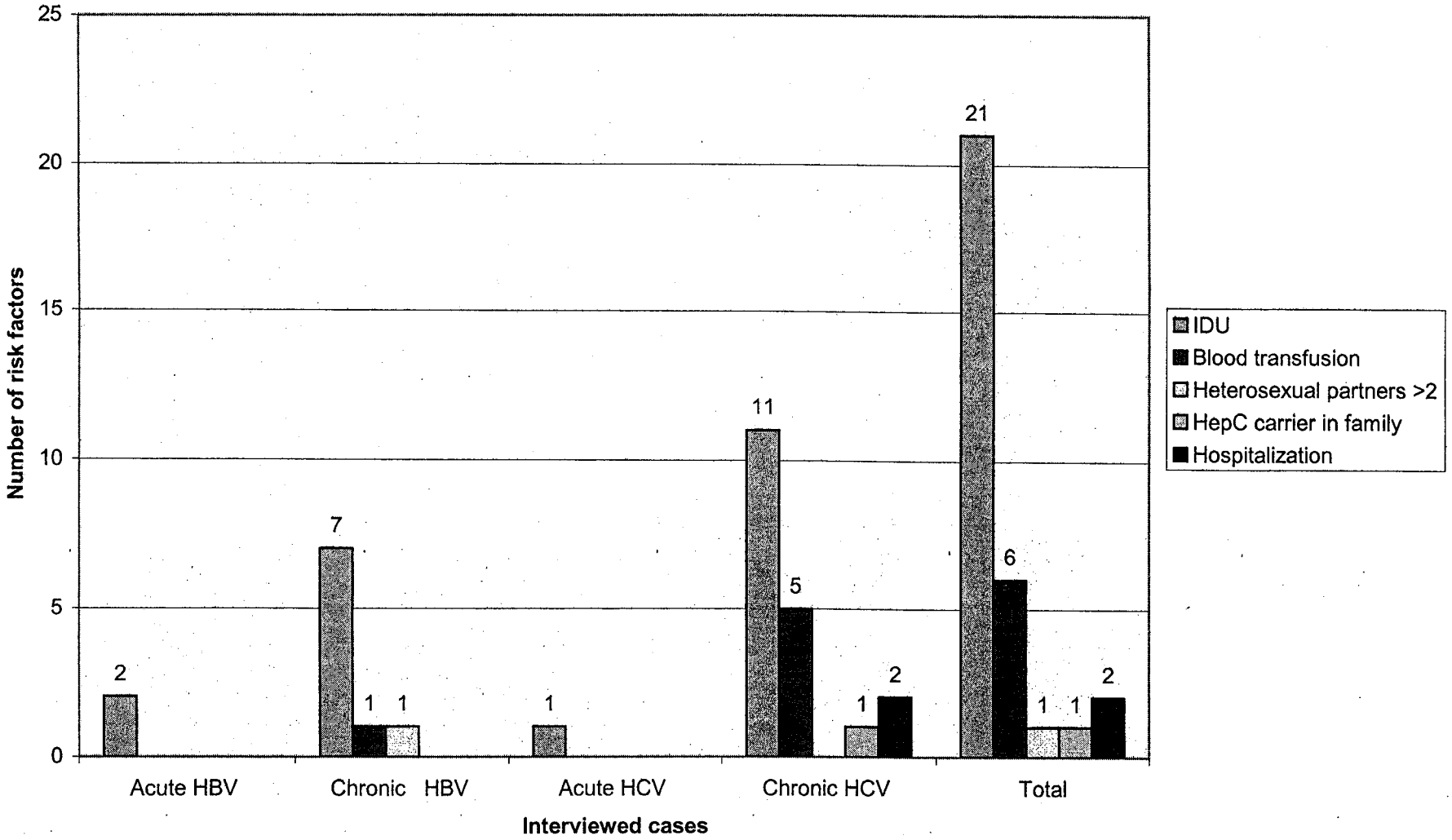


Figure 2.6 d Distribution of main risk factors for interviewed cases of HBV/HCV coinfection, 1998-2002.



3. EXPLORATORY STUDY OF HEPATITIS B AND HEPATITIS C CASES WITH UNKNOWN RISK FACTORS AT THE OTTAWA SITE OF THE ENHANCED SURVEILLANCE (1998-2002)

3.1 Review of Literature on Risk Factors for Hepatitis B and Hepatitis C

Substantial numbers of cases had no RF detected by the Enhanced Surveillance. These cases were the focus of the Exploratory Study. The aim of this literature review was to analyse the current literature regarding the modes of transmission for hepatitis B and hepatitis C and its global prevalence in different groups of people. It was anticipated that the literature review would help to guide development of the Exploratory Study and to elaborate its questionnaire aimed on unveiling potential new risk factors.

3.1.1 Literature search strategies

The literature search and evaluation was based on the following strategy and principles:

1) The literature review was intended to produce a comprehensive summary of HBV/HCV published associations and RFs rather than a formal systematic evaluation of the quality of evidence. Since the literature is very vast, it was more realistic to look at review articles.
2) The usual logistical approach to the hierarchy of the literature evaluation such as first considering major cohort-prospective, cohort-historical, and case-control studies might not be the best option for this thesis. Those types of studies mostly investigate well-known risk factors, whereas the purpose of the thesis is to further explore unknown risk factors. It is less likely to get information about new possible risk factors from the traditional publications listed above. In contrast, case reports or expert opinions may be more valuable categories of the literature search to be considered as an alternative to the traditional approach. A study of review articles was deemed to be the most efficient approach to capturing this literature.

3) Although a number of Canadian sources got captured in the literature review, it was not believed necessary to limit the search to Canadian sources, since Canada belongs to the same North-American region with overall low endemicity of HBV/HCV, as the United States. Therefore, it was expected that transmission modes, contamination mechanisms, and structure of risk factors for HBV/HCV in Canada would be quite similar to those in USA, from where the most of research and publications on the topic are originated.
4) It should also be noted that the largest Canadian source on HBV/HCV epidemiology is the current National Enhanced Surveillance System, discussed in chapters 2 and 3 of this thesis.

Thus, a review of the literature on the epidemiology of hepatitis B and hepatitis C from 1991 to 2001 using computerised bibliographic databases, including Medline (via Current PubMed), Embase, a number of websites, and the Viral Hepatitis e-Newsletter of the Blood-borne Pathogens Division of Health Canada, as well as a review of official and grey publications/reports on HBV and HCV by Canadian and international governments and agencies was done.

A search of Medline and other electronic databases mentioned above was done using the following major MESH headings: 1) "hepatitis B", 2)"hepatitis C", 3) "risk factors", 4) "transmission". The search was limited to the following: 1) publication types of "review articles"; 2) English language articles or abstracts; 3) articles published during 1991-2001.

Similar search strategies were used for selecting the appropriate articles from the electronic newsletter of the Blood-borne Pathogens Division of Health Canada. Entering the terms "HBV", "HCV", "hepatitis B", "hepatitis C", "risk factor", "mode of transmission" into popular Internet search engines such as Microsoft Network (MSN), Infoseek, Yahoo, Goodies etc., yielded hundreds of matches. The information contained on these Web sites varied from

highly technical and accurate epidemiological and genetic information about HBV and HCV to information about unusual and untested remedies that are quite unknown to many in the scientific community. Only materials closely related to HBV/HCV risk factors were considered.

The results of the literature search on prevalence of anti-HCV in health care professionals, sexual partners, high sexual risk groups, and in intravenous drug users of different geographical regions were consolidated into three tables that will be presented at the end of this chapter. The tables are organised by alphabetical order of countries in which the studies were done.

3.1.2 HBV modes of transmission and risk factors

Hepatitis B virus infection is a global health problem. HBV is transmissible though several routes (23, 42, 63, 64): percutaneous (IDU, exposures to contaminated blood or bodily fluids); sexual (heterosexual or male homosexual activities; vertical (from mother to infant); and horizontal (among children and household contacts).

IDU and high-risk heterosexual activities are the major risk factors associated with HBV transmission in Canada (65-67). Increasing years of sexual activity, multiple sexual partners and sex with HBeAg-positive carriers were associated with an elevated risk (2). Homosexual activities, tattooing and body piercing, having an HBsAg carrier in the family, and a history of blood transfusion also increase the risk of HBV infection among Canadians (40, 65, 68).

Coinfection of HBV and other viruses. Coinfection of HBV with other bloodborne pathogens, such as HCV, hepatitis D and HIB, may affect the natural history and clinical severity of HBV infection. HBV-HCV coinfection among IDU seems to increase the severity of chronic HBV infection outcomes, especially the risk of hepatocellular carcinoma (69). One study

reported that chronic HBV and HCV infection increased the risk by a factor of 28.8 and 31.2, respectively, and that coinfection of HBV-HCV increased the risk by a factor of 42.9 [70].

3.1.3 HCV modes of transmission and risk factors

HCV is transmitted primarily by exposure to infected blood. However, in up to 50% of cases no recognizable transmission factor/route can be identified [71]. Therefore, a number of other routes of transmission such as sexual or household exposure to an infected contact are postulated but not widely accepted. This is because conflicting data have emerged regarding the presence of HCV in body fluids other than blood. Some authors have found total absence of the virus in sperm, saliva, vaginal secretions and other body fluids [71]. However, others have documented the presence of HCV-specific antigens in semen of infected individuals [72, 73].

Commonly accepted risk factors for HCV infection include intravenous drug abuse, haemodialysis, transfusion of blood products, tattooing, high sexual behaviour, exposure to healthcare and organ transplants from HCV-positive donors and use of blood-contaminated straws for cocaine snorting [74, 75].

As far back as 1981, two separate American studies showed that there was increased risk of acquiring post-transfusion non-A, non-B infection (PTH-NANB) following blood transfusion if the donors have elevated ALT levels [76-78].

Furthermore, the exclusion of blood donors with antibodies to the hepatitis B core antigen was found to prevent another 20-30% of the PTH-NANB, though this was not confirmed by other European studies [78-80]. The screening of donors for ALT and anti-HBc for prevention of PTH-NANB was termed surrogate testing.

Before 1986, the incidence of post-transfusion HCV was reported to be 5% to 13%. This declined to between 1.5% and 9% from 1986 to 1990 [81-87]. Since 1990, when anti-HCV screening of blood donors became mandatory, the incidence of post-transfusion HCV declined to <1%, but was not completely eliminated. This is because the first generation ELISA may not become positive for months after infection with HCV, and seronegative HCV carriers were responsible for 10-15% of HCV transmission [88]. It has been also suggested that HCV can down-regulate the pace of replication in order to escape viral clearance by the host immune system, yet can still exist in a low replicative state within hepatocytes, which in part is responsible for the high degree of viral persistence in HCV infection [88].

Recipients of blood and blood products. The incidence of acquiring post –transfusion HCV infection is directly related to the number and amount of blood products received [89-91]. Therefore, haemophilics have a very high incidence of HCV infection (46%-90%) [92-94]. Similarly patients receiving >100 000 U of cryoprecipitate per year compared with those receiving <100 000 U have a significantly higher chance of becoming infected (76% versus 46%) [94].

Although viricidal procedures for blood products such as heat treatment, pasteurization and solvent-detergent treatment have nearly totally eliminated the risk of HCV transmission, they nonetheless do not guarantee complete security [94-96]. This is because a number of incidents of HCV transmission via intravenous immunoglobulin preparations [95,97-99]. However, a recent Dutch study [100], failed to show any seroconversion amongst 57 patients who received clotting products between 1989 and 1993 following viricidal treatment.

In children receiving multiple blood transfusions for thalassemia, the prevalence of HCV infection varies from 55% to 83% [89-101].

Other nosocomial routes of transmission. There is increased prevalence of HCV infections amongst certain groups of patients, which include: 1) long-term cancer survivors (20%); 2) bone marrow transplant recipients (29%); 3) renal dialysis patients (15-20%); 4) renal transplant patients – which is directly related to the frequency and duration of haemodialysis received prior to their transplant [11, 91, 102-110].

The prevalence of HCV infection differs greatly between different countries and even between different dialysis centers in the same country. The highest has been reported from Brazil (82%) and the lowest from Europe (4%). There is a direct correlation between the duration of dialysis and number of blood transfusions received and the incidence of acquiring HCV [111].

Other possible mechanisms of transmission include sharing dialysis machines between HCV positive and negative patients [112, 113] and nosocomial transmission by the dialysis staff [114-117]. It is clear from various studies that rigorously applied universal infection precautions during dialysis by the staff significantly decrease the nosocomial transmission of HCV infections [111, 115, 116, 118, 119]. The nosocomial transmission has also been documented from a cardiac surgeon (to 5 patients), via anaesthetic tubing, and via syringes for intravenous catheter flushing [120-122].

Risk to health care professionals. Healthcare professionals dealing with blood and blood products are at a greater risk of contracting HCV via needle stick injury. High-risk groups include surgeons, obstetricians, haemodialysis nurses/technicians, oral surgeons, emergency department workers and intensive care workers (Table 3.1). The risk factors include: 1) the type of needle, that is hollow versus solid, the first being worse; 2) the frequency of occupational blood contacts; 3) the type of patients, that is acute infection versus chronic carriers, the first being worse; and 4) high prevalence of HCV among patients.

The risk of acquiring HCV infection following a single needle stick injury with contaminated blood is low, as determined by anti-HCV seroconversion using the second generation assay and PCR [123-125].

Three European studies [126-128] failed to show any HCV seroconversion in healthcare workers following anti-HCV positive needle prick injuries, with at least 10 months of follow-up. In contrast, two Japanese prospective studies revealed a seroconversion rate of 3.3% and 5.6% amongst 90 and 56 healthcare workers, respectively, following needle-stick injury [129, 130]. Use of blunt needles, use of double gloving in high-risk patients, use of protective goggles and passing of sharp instruments via a tray rather than directly are important precautionary measures in minimizing iatrogenic transmission of HCV. It is clear from the various studies that the risk of occupational HCV transmission does exist and preventive measures as outlined above are currently the mainstay of healthcare workers against HCV infection.

Household (intrafamilial) transmission. There is some evidence that intrafamilial spread of HCV also occurs, as seropositivity for anti-HCV is 5-10 fold higher in individuals living with an HCV-positive patient compared with the general population. A number of studies [131-137], totaling 335 patients, found the prevalence of HCV infection in household nonsexual contacts to be between 0% and 11%, with an average of 3.6%. Children are less affected than spouses. The nonsexual household transmission of HCV is speculative and includes sharing of instruments of personal hygiene such as toothbrushes, dental appliances, razors, nail-grooming equipment, etc. The low rates of transmission may be due to low serum titer of virus in HCV carriers [15]. However, no conclusive data exist as to the threshold concentration of HCV required to transmit infection [11].

Sexual transmission in families. The prevalence of anti-HCV among the sexual and household contacts of chronic hepatitis C patients ranges between 0% to 11.3% and is quite controversial (Table 3.2). Caporaso et al. [138] published one of the largest studies, evaluating the intrafamilial spread of HCV among 1370 household contacts of 585 HCV positive subjects (index cases). By using third generation ELISA and PCR techniques they found the incidence of anti-HCV to be 5.6% in spouses and 3.2% in other relatives. After adjusting for various confounders, the study failed to show any correlation between spouses vs. other relatives and length of marriage and acquiring HCV infection. The authors concluded that sexual transmission does not seem to play a role in the intrafamilial spread of HCV infection.

In contrast to this study, Guadagnino et al [139] showed that spouses who had been married to the index cases longer than 20 years had a 7.5-fold higher risk of HCV seropositivity than those married less than 20 years. They concluded that sexual contact plays an independent role in the spread of HCV infection in the family setting.

A study from Japan [140] found spouses with anti-HCV positive partners to be twice as likely to have anti-HCV as spouses with anti-HCV negative partners. However, 50% of the couples presented discordant HCV genotypes. The authors concluded that the clustering of HCV infection among specific couples within this endemic population may not be attributable to heterosexual transmission.

In contrast, a study from Taiwan [141] showed a direct correlation with the duration of marriage (>20 years vs. <20 years) and with duration of actual exposure to the index patients, but not with serum HCV titers. The infected couples had more frequent sexual contacts and more commonly shared toothbrushes than those with uninfected spouses. The authors concluded that spouses of patients with chronic hepatitis C have a higher risk of acquiring HCV, which

increases with longer marriage and duration of exposure, and that they should be educated about how to avoid contracting HCV infection from their spouses.

One study showed a higher prevalence of anti-HCV in female partners of positive males, but not vice versa [142]. As the data are so conflicting, some experts believe that in long-standing monogamous relationships no modification in sexual practices is required except during menstruation and if one of the partners has overt genital ulceration. In other situations safe sex practices may help prevent the transmission of HCV.

Sexual transmission in high risk groups. Sexual transmission of HCV occurs, but infrequently. The prevalence of HCV infection is higher amongst heterosexual individuals attending sexually transmitted diseases clinics, male homosexuals, prostitutes and partners of intravenous drug abusers.

There seems to be a positive correlation with the overall number of sexual partners, not using a condom, receptive anal intercourse, sexual activity involving trauma, history of other sexually transmitted diseases and those coinfected with HIV [137, 142-145].

Perinatal or vertical or mother-to-child transmission. Perinatal transmission of HCV infection occurs between 0 and 15% of cases [111]. There remains a debate as to the exact role of this route of HCV spread [146]. Vertical transmission from mother to child has been reported in a number of studies [147-156] on the basis of asymptomatic biochemical abnormalities of liver function tests, in particular ALT and transient anti-HCV seropositivity using either ELISA or PCR, in the majority of infants born to mothers with HCV infection.

Persistence of anti-HCV has been noted with HIV coinfection suggesting a facilitatory role of HIV in HCV transmission [147, 148, 150, 153, 157]. RT-PCR has confirmed vertical transmission of HCV infection, but has also generated contradictory data when mother-infant

pairs were evaluated. Some studies have shown no detectable anti-HCV in infants despite detectable anti-HCV in mothers [158-162], whereas others have shown the prevalence of anti-HCV to be between 5% and 80% [150, 152, 156, 163-169]. There is a positive correlation between HCV-RNA titer in the mother and subsequent development of HCV infection in children [166, 167, 170, 171]. Furthermore, acute HCV infection during pregnancy even in the absence of HIV carries an increased risk of vertical transmission [157, 163, 170].

What remains controversial is the route and timing of HCV transmission. It seems logical to think that selective vertical transmission of certain subsets of HCV variants either "in utero" or in the immediate postnatal period is a possibility [172]. A study from Taiwan showed that elective cesarean sections were associated with lower microtransfusion from mother to fetus than spontaneous vaginal delivery or emergency cesarean sections [167, 173].

In the light of the current knowledge, no effective way of preventing transmission of HCV infection from mother to child exists. Similarly, transmission of HCV by breast milk has been suggested but never proved [149, 174-175]. It has been suggested that there might be some correlation between the duration of breastfeeding by an HCV-RNA positive mother and the acquiring of HCV infection by the baby.

Intravenous drug users (IDU). Intravenous drug abusers not only have the highest prevalence of HCV infection but also constitute a potential reservoir of HCV in the community. The prevalence varies between 31% to as high as 98% in different parts of the world (Table 3.3). The prevalence of HCV infection increases proportionally with the duration of intravenous drug abuse [176-178].

Other risk factors include male gender, being older, sex trade worker, risky sexual behaviour, multiple sexual partners, needle sharing and history of being in prison [176, 178-182].

Oral drug abusers, when compared with IDU, were found to have far lower incidence of HCV infections in 2 studies, from New Zealand (4% vs. 73%) and Taiwan (5.4% vs. 53%) [179].

Conclusion. Better understanding of the mode of spread of the disease will assist in minimizing HCV spread globally. The overall burden on the society both financially and socially to support and manage individuals with HCV is a time bomb waiting to explode unless urgent measures are undertaken to 1) develop a strategy to inform and educate the lay public and press regarding this disease such as HCV awareness programs; 2) set up clinical information systems to monitor trends, occurrence and effectiveness of intervention programs; 3) identify the route of spread for sporadic cases of HCV, which account for almost 50% of cases; 4) develop inexpensive sensitive and specific tests for detection of HCV infection at an early stage; 5) make available these diagnostic tests universally and in particular for the poor countries where HCV is reaching epidemic proportions; and 6) expedite the efforts to develop a vaccine. This process depends upon better identification of RFs.

3.1.4 Possible risk factors

Based on the literature review on HBV and HCV the following list of "Possible risk factors for HBV and HCV" was developed to be used in constructing an open-ended questionnaire for the Exploratory Study (Appendix IV). The list contains 3 broad groups and numerous subgroups of potential risk factors, where only less investigated and not well-known RFs are presented (recognised RFs are mostly excluded from this list since they were well represented in the Enhanced Surveillance questionnaire).

I. **Exposure to blood and body fluids,** including:

   a) Occupational exposure or hazards

- Firefighters
- Paramedics
- Police
- Military (war soldiers or peacekeepers)
- Acupuncture specialists
- Security guards
- Prison workers
- Contact sports: boxing, wrestling, hockey etc.
- Shelter workers
- Laboratory technicians: medical devices etc.
- Hair dressers
- Barbers
- Tailors
- Construction workers
- Glass installers
- Carpenters
- Auto mechanics
- Millwrights
- Veterinarians
- Prostitutes
- Hotel/motel housekeeping
- Personal care workers
- Any employment other than medical/dental/ and listed above that might possibly be a cause of an accidental needle-sticks, nicks, cuts, wounds, burns etc.

b) Behavioral/Cultural/Ceremonial

- A special behaviour related to drug use
- Sexual contacts: consensual (if the partner have never been screened for HBV or HCV, non-consensual (abuse, rape), sado-masochistic sex
- Fighting (bloodfighting particularly)
- Blood letting: blood sister, blood brother, Sun Dance ritual in some First Nations communities, a cure for high blood pressure in developing countries
- Circumcisions
- Sharing the attributes of personal hygiene and common equipment such as crack pipes, cigarettes, tooth brushes, razors, and so on.

II. Medical treatment and procedures

a) Neonatal blood microtransfusions (e.g., erythrocyte transfusions in infants as a treatment for poor weight gain or simply to maintain a given haemoglobin concentration – a common practice in Italy in 1960s and 70s)

b) Spring-loaded finger stick device for sampling capillary blood (in diabetic patients)

c) Jet injections (in weight reduction clinics)

d) Obstetrical delivery

e) Intubation (anesthesia)

f) Gastro-intestinal endoscopy

g) Chelation therapy

h) Electrolysis

i) Electro-shock therapy

j) Immunization/vaccination

k) RH Ig injection (during pregnancy)

l) Gynecological procedures

m) Bronchoscopy

n) Plasmapheresis

o) Laser treatment

p) EEG

q) Alternative treatments (acupuncture)

r) Hospitalization/institutionalization

III. Other

a) General public

- Accidental needlestick
- Car accidents
- Giving first aid
- Volunteer in firefighting
- Aesthetics (nicks and cuts at cosmetic saloons, barbershops, hairdressers etc.)

b) Other countries (such as endemic, developing, war torn countries etc.)

- Have been living in other counties, as above
- Have been travelling to other countries, as above
- Medical/dental care or immunizations given in another country, as above

c) Comorbid illnesses/Immunocompromised

- HIV
- Cancer
- Diabetes
- Any liver disease
- Any skin disease (psoriasis etc.) and other disorders of immune system.

3.2 Methods and Procedures of the Exploratory Study

3.2.1 Design

The Exploratory Study of HBV and HCV cases with unknown risk factors identified at the Ottawa site was designed as a pilot study of targeted surveillance performed in addition to the continuing Enhanced Hepatitis Strain Surveillance System (Schema 1.3, Appendices III and IV). The Study was designed and conducted with two arms: 1) Retrospective – reviewing past cases of the Enhanced Surveillance with URF from October, 1998 to March, 2001 and 2) Prospective - a parallel arm to capture new current cases with URF from April, 2001 to March, 2002 and to interview them in parallel with conducting the Enhanced Surveillance.

3.2.2 Population/Eligibility criteria

3.2.2.1 Study population

The study population was recruited from all acute and chronic HBV and HCV cases with unknown risk factors identified by the Enhanced Surveillance at the Ottawa site during October, 1998 – March, 2002, that met the eligibility criteria. The availability of cases was influenced by the selection strategy adopted by the Enhanced Surveillance (please see section 2.1.3).

Study setting: Public Health Branch, City of Ottawa; **Coordinating Centers:** Blood-borne Pathogens Division, Centre for Infectious Disease Prevention and Control, Population and Public Health Branch, Health Canada and Department of Epidemiology and Community Medicine of the University of Ottawa.

3.2.2.2 Eligibility criteria

Inclusion criteria:

- **Case definition.** Persons with clinical diagnosis of hepatitis B or hepatitis C by physicians, or identification of hepatitis C or B infections by laboratories, with no known risk factors identified at the Enhanced Surveillance
- Availability to be reached
- Consent to participate in the study

Exclusion criteria:

- Inability to communicate in English
- Major mental disorder with cognitive impairment
- Inability to provide an informed consent with the Study Protocol and the absence of a person with power of attorney

3.2.3 Sample size

Initially, only the cases classified by the Enhanced Surveillance team as cases with unknown risk factors were included into the study population. Therefore, the initial sample size of the Study consisted of 23 retrospective cases accumulated over 2.5 years of conducting the Enhanced Surveillance (October, 1998 – March 2001).

At the time of conducting the Exploratory Study, so-called "endemic" cases were reclassified as having "unknown risk factors" (URF), which increased the sample size. The justification for the reclassification was as follows. A number of cases previously classified by the team of the Enhanced Surveillance as "endemic" had no any risk factor identified except that they were born in countries with endemic HBV and HCV. The definition of "endemic" did not contain any information of epidemiological importance with respect to the modes of transmission and/or risk factors for contracting the contagious disease. After a number of consultations with

virologists/field epidemiologists/family physicians, it was decided to reclassify "endemic" cases as cases with URF, making them eligible for recruitment into the Exploratory Study.

The prospective phase of the Study used this revised definition. The eventual sample size of the study was 91. The details on sample size numbers are given in Appendix V.

3.2.4 Data collection/Interviewing

3.2.4.1 Data collection tools – the Exploratory Study questionnaire

A semi-structured open-ended questionnaire designed to capture unknown risk factors (URF) was used for the Exploratory Study (Appendix IV). In the questionnaire, risk factors were considered in the following major groups:

I. Exposure to blood and body fluids (occupational exposure and behavioral/ cultural/ceremonial hazards);
II. Medical treatment and procedures;
III. Other (general public accidents, originating in or visiting other countries such as endemic, developing, war-torn countries, and comorbid illnesses/immunocompromised).

3.2.4.2 Data collection procedures – telephone interviewing

The questionnaire was administered through telephone interviews by an MSc student (the author) or by a Public Health Nurse of the City of Ottawa (the site investigator for the Enhanced Surveillance) and took on average about 20 minutes.

The interviewer told the informed that he/she (or his/her children) was recently found to have viral hepatitis B and/or hepatitis C infections and was reported as a case with no known risk factors for the disease identified. In order to investigate and possibly identify unknown risk

factors, an Exploratory Study was to be conducted with a number of additional open-ended questions that would take some 15 to 20 minutes to answer. Then, the interviewee was asked whether that was an appropriate time to talk. If the answer was "Yes", the consent form was read to the interviewee over the phone and the interview proceeded. Otherwise, the interviewer would call back later, at a mutually convenient time, to conduct the interview.

The telephone number of the Coordinator of the Enhanced Surveillance at the Blood-Borne Pathogens Division (BBPD) of Health Canada was provided to the interviewees in case they wished to confirm the identity of the interviewer or had questions to ask.

3.2.5 Data analysis

Analysis of the Exploratory Study paralleled that of the Enhanced Surveillance (please see section 2.1.5) in calculating prevalence proportions (calculated as % among all cases) and frequency distributions (calculated as % among all RFs), but with emphasis on potential new risk factors that were not evaluated in the EHSSS study. Thus, if we arrange the data as in Schema 3.1, we focussed attention on cells "a" and (especially) "c", since no explanation was available to explain the disease in the latter case.

Schema 3.1 Recognised and potential new RFs for hepatitis

		Potential New RFs*	
		Yes	No
Recognised RFs**	Yes	a	b
	No	c	d

*Previously not known risk factors identified only at Exploratory Study.
** Known risk factors not identified at Enhanced Surveillance.

The following software was used to collect and analyse the data: Microsoft Access and Microsoft Excel, versions 7.0, as a database and data analysis tool.

3.2.6 Ethical considerations

Ethics approval was obtained for the Exploratory Study from Ethics Review Boards of both the Population and Public Health Branch, Health Canada (in August, 2001) and the Public Health Branch of the City of Ottawa (October, 2001), since the Study was designed as a pilot to the Enhanced Surveillance System, which was a joint investigation between Health Canada and the City of Ottawa.

The following ethical, data management and security considerations were ensured for the study. All information, including history of risk factors and test results, was entered into this study using a code, e.g. "case 1" or case "213". Collected data were gathered in a strictly confidential manner and no names were used in the database of the study. Information containing personal data was kept confidential, as required by Provincial legislation, at the site of the investigation (i.e., at the Public Health Branch of the City of Ottawa).

The electronic database from completed questionnaires was stored in a secure building (# 6 building) at the BBPD, PPHB, Health Canada and was password-protected. Access to the collected information was granted only to the Study Investigators located at the BBPD, PPHB, Health Canada and at the Public Health Branch of the City of Ottawa. The Enhanced Surveillance System Coordinator ensured the security and appropriate management of the electronic database.

3.3 Results of the Exploratory Study

3.3.1 Overall numbers of acute/chronic HBV and HCV cases

As we see in Table 3.4 for the analysis of the overall numbers of the Exploratory Study population, the 91 cases were fairly evenly distributed between HBV and HCV. Three quarters

of the cases were recruited in the prospective stage of the study, which commenced on April 1, 2001. Most of the HBV and HCV cases were chronic, although with a much bigger absolute and relative excess for HCV.

By the response status (Table 3.5), the highest rates of eligibility and consent were found in chronic HBV and the lowest in acute HBV patients. For HCV infection, the rates were similarly high for both acute and chronic cases. As a result, we had a good overall response rate of about 90 interviewed cases. The reasons for failure to interview were fairly evenly distributed among inability to locate the cases (usually because no information about their residence was available), difficulty to communicate and refusal to participate.

3.3.2 Demographic characteristics of interviewed acute/chronic HBV and HCV cases

The detailed demographic analysis of the Exploratory Study population (Table 3.6, a-b) revealed the following patterns.

Age analysis. The distribution of interviewed cases for both infections showed that the largest groups were from either the young or the middle-aged population between 20 and 59 years of age. The numbers in age group 30-39 were particularly high. The only exception was for chronic HCV, where the largest concentration of cases was in the elderly population of 60+.

Gender analysis. Most interviewed cases in the Exploratory Study (as in the Enhanced Surveillance) were men, with a greater excess in acute than in chronic HBV. The only exception comprised the cases of acute HCV, where the patients were mostly female.

Place of birth. The largest groups of interviewed HBV cases were born in Asian countries and in Europe, whereas the largest groups of HCV population were born in Canada and in Europe. The high proportion of Canada-born population in acute HCV might be explained by

the larger number of HCV cases selected for investigation at the stage of conducting the Enhanced Surveillance. (See Appendix VII for specific country information.)

3.3.3 Epidemiologic characteristics of acute/chronic HBV and HCV cases

This section presents the epidemiologic characteristics of acute/chronic HBV and HCV cases, provided in Tables 3.7 – 3.10 and in Figures 3.1 – 3.3.

3.3.3.1 Prevalence proportions and frequency distributions of recognised and potential new risk factors for HBV/HCV cases

First, the definition for the terminology of Recognised and Potential new risk factors. All risk factors identified in the Exploratory Study were grouped into two major categories: 1) Recognised Risk Factors - known risk factors that had been already revealed among other cases at the stage of the Enhanced Surveillance, but somehow failed to be identified among cases later recruited into the Exploratory Study; 2) Potential New Risk Factors - new, previously not known or sought during EHSSS, risk factors that have been exclusively revealed and identified during the Exploratory Study. Of course, these can only be *potential* RFs until they have been confirmed by analytical studies.

Based on the totals given in Table 3.7 a-b, it was found that potential new risk factors comprised about 70% of all RFs revealed by the Exploratory Study for acute HBV cases, whereas recognised RFs prevailed in chronic HBV cases – about 62%. In contrast, recognised RFs predominated for both acute and chronic HCV infection, especially for chronic cases (53% vs. 59%). Nevertheless, it is significant that 70%, 38%, 47%, and 40% of all RFs for acute and

chronic HBV and HCV (respectively) revealed during the Exploratory Study were previously unknown and were exclusively identified at this stage.

The distributions of all RFs for acute/chronic HBV and HCV cases were tabulated to show detailed categories of recognised risk factors, first, and potential new risk factors, second. For the acute process, just the last 6 months' events were considered relevant as possible exposures to the viruses, whereas for chronic disease, all lifetime events were counted as having potential to be an RF.

Analysis of **prevalence proportions** of individual RFs, whether recognised or potential new, is given in Table 3.7 a-b. For acute HBV, the most prevalent RF was other work related (cases in high-risk occupations), followed by sexual modes of transmission, medical procedures, vaccination against HBV and so on. For chronic HBV, the prevalent RFs were medical procedures, followed by dental visits, hospitalisation, and surgery. Based on the total numbers of cases and of all RFs, it was estimated that on average there were twice as many RFs per case for chronic HBV as for acute HBV. The analysis of prevalence proportions of all RFs for HCV cases showed that health care work related and sex with hepatitis C carrier were on the top of the list for acute HCV. In contrast to acute HBV, where drug use (whether injection or snorting) was not reported as a mode of transmission, for acute HCV it was present as a risk factor in half of all cases. The majority of chronic HCV cases had hospitalisation, dental visit, and surgery as their top RFs. The average number of RFs per case in acute HCV was comparable with that in chronic HCV and chronic HBV, and much higher than in acute HBV.

3.3.3.2 Numbers and characteristics of acute/chronic HBV and HCV cases with potential new risk factors

The **relationship between recognised and potential new risk factors** identified by the Exploratory Study is presented in Table 3.8 a-b. For acute HBV, 81.8% of cases had been identified as having potential new risk factors, including 63.6% (the vast majority) *only* with potential new risk factors (!). Among 3 cases with recognised RFs just one had no potential RF. For chronic HBV, 80.8% of cases had been identified with potential new risk factors, including 38.5% only with potential RFs. Thus, 18.2% (or one) of all acute and 42.3% (or 11) of all chronic HBV cases had risk factors that should have been identified at the stage of the Enhanced Surveillance. In acute and chronic HCV, the relationships between potential new and recognised risk factors were quite similar, with about 75% of cases identified as having potential new RFs, including over 35% exclusively with potential RFs, and only two cases of no potential new RF in acute HCV, but only one with no RF at all. Thus, 37.5% (or 3) of all acute and 40.0% (or 14) of all chronic HCV cases had risk factors that should have been found at the Enhanced Surveillance stage. This proportion for acute HCV is twice as large as for acute HBV.

Tables with detailed description of acute/chronic HBV and HCV cases with potential new RFs as well as demographic analysis of cases with exclusively potential new ("c"-cell) and both potential new and recognised ("a"-cell) RFs are presented in Appendices VIII and IX.

The **distribution of potential new RFs** is presented in Figures 3.1 a-b. For acute HBV, the largest proportions belonged to other work related, followed by medical procedures, frequent nicks/cuts/burns, vaccination against HBV, and sex with prostitute. In chronic HBV, medical procedures predominated among all potential new RFs. The comparison of potential new risk factor distributions for HBV revealed the following similarity: medical procedures and other work-related categories were among the most frequent modes of transmission for both acute and chronic diseases, with much smaller proportions for the latter. On the other hand, there were also

differences such as that circumcision - second most frequent potential RF for chronic HBV (12%) was completely absent from the RF distribution of acute disease (of course, very few people are circumcised as adults).

The most common potential new RFs for acute HCV cases (Figure 3.1 b, i) were health care work related, medical procedures and immunocompromised, the last two of which held their positions as the most frequent RFs in chronic HCV. Surprisingly and in contrast to acute HCV, the health care work related category was in the last place in the distribution of RFs in chronic HCV. The comparison of HCV distributions revealed that medical procedures (first for chronic and second for acute) and immunocompromised (second for both) were the most frequent reasons for contracting the infection for both acute and chronic diseases.

3.3.3.3 Distribution and comparison of risk factor groups for acute/chronic HBV and HCV cases

In Table 3.9, all RFs from both categories of recognised and potential new RFs were combined into major RF groups, in order to reveal the most common modes for transmission of HBV and HCV infections in the community. All RFs identified by the Exploratory Study were combined into 10 RF groups with similar modes of transmission of the diseases. The high susceptibility host group included cases with immunocompromising diseases such as cancer, diabetes, AIDS, and so on. The last group of other RFs included those RFs that did not have a clear route of transmission of infection, such as blood contact, accidents/wars, and comorbid diseases other than immunocompromising (e.g., sexually transmitted diseases, mental illness).

Calculated frequency distributions of major risk factor groups for acute/chronic HBV and HCV infections are presented in Figures 3.2 a-b. For acute HBV, the largest RF groups were

health care acquired and sexual mode of transmission (at nearly one third of all RF groups each), work-related group of RFs, other subcutaneous interventions, and exposure to high prevalence environment. For chronic HBV, again the groups of health care acquired RFs and sexual mode of transmission had the largest proportions, but the first was almost twice as large and the second was only half as large as for acute HBV. The third largest RF group was other subcutaneous. Drug use was absent from both HBV distributions (apparently, it was all picked up by EHSSS), and there were no URFs in chronic HBV cases, and only one URF in acute HBV. As is clear from the table, health care acquired and sexual transmission were the most frequent groups of RFs for both acute/chronic HBV cases of the Exploratory Study population.

The distribution of RF groups for acute HCV cases (Figure 3.2 b, i), shows that the largest proportion belonged to sexual transmission, which according to the world literature is quite controversial and occurs in only 5%-8% of infected cases (Table 3.2). The group of health care acquired, drug use, and work-related RFs were next in the descending list of group RFs. As in acute HBV, here also there was a case with URF. For chronic HCV, as in acute/chronic HBV, the health care acquired group of RFs was the largest and comprised half of all RFs, but sexual transmission comprised only 1/10 of all RFs; as in chronic HBV, there were no cases with URF.

Thus, as for acute and chronic HBV, for acute and chronic HCV also the sexual mode of transmission (!) and health care acquired infections were the most frequently reported groups of risk factors in this selected group of patients.

Table 3.1 Prevalence of anti-HCV in healthcare professionals of different geographical locations.

Ref.#	Authors	Year	Location	Type of subjects	Number tested	Positive %
183.	Frider et al.	1994	Argentina	Healthcare workers	439	2.7
184.	Jadoul et al.	1994	Belgium	Dialysis nurses	120	4.1
185.	Vanderborght et al.	1995	Brazil	Healthcare workers	242	2.7
186.	Germanaud	1994	France	Healthcare workers	430	0.9
187.	Schlipkoter et al.	1992	Germany	Dialysis staff	121	1.6
188.	Jochen et al.	1992	Germany	Hospital staff	1033	0.6
189.	Ribero et al.	1991	Italy	Dentists	526	6.3
190.	Campello et al.	1992	Italy	Healthcare workers	407	1.2
191.	Petrosillo et al.	1995	Italy	Healthcare workers	5813	2
192.	Nakashima et al.	1993	Japan	Hospital staff & acupuncturist	1077	1
193.	Fujiyama et al.	1995	Japan	Dialysis staff	216	2.3
194.	Rehman et al.	1996	Pakistan	Healthcare workers	95	4
195.	Mujeeb et al.	1998	Pakistan	Operating room personnel	104	4.4
196.	Soni et al.	1993	South Africa	Healthcare workers	212	0
197.	Struve et al.	1994	Sweden	Healthcare staff	880	0.7
198.	Liaw et al.	1991	Taiwan	Hospital administrative staff	123	0.8
199.	Oge et al.	1998	Turkey	Urologist	24	12.5
200.	Mortimer et al.	1989	UK	Healthcare workers	100	0
201.	Herbert et al.	1992	UK	Dentist	94	0
126.	Zuckerman et al.	1994	UK	Healthcare workers	1053	0.3
202.	Neal et al.	1997	UK	Healthcare workers	1949	0.2
203.	Lodi et al.	1997	UK	Dental healthcare workers	167	1.2
125.	Klein et al.	1991	USA	Dentists	456	1.8
204.	Abb J.	1991	USA	Healthcare workers	1018	0.6
205.	Shapiro et al.	1992	USA	Orthopaedic surgeons	3262	0.8
206.	Cooper et al.	1992	USA	Hospital staff	243	1.6
207.	Thomas et al.	1993	USA	Teaching hospital healthcare personnel	943	0.7
208.	Polish et al.	1993	USA	Community hospital healthcare personnel	1677	1.4

209.	Niu et al.	1993	USA	Dialysis staff	142	1.4
210.	Forseter et al.	1993	USA	Dialysis nurses	51	1.9
211.	Gerberding	1994	USA	Hospital care providers	976	1.4
212.	Goietz et al.	1995	USA	Liver transplantation personnel	57	5.3
213.	Panlilio et al.	1995	USA	Hospital surgeons in moderate to high AIDS areas	770	0.9
214.	Tokars et al.	1998	USA	Dialysis staff	54194	2

Table 3.2. Prevalence of anti-HCV in sexual partners of HCV cases in different geographical locations.

	Authors	Year	Location	Number tested	Positive %
215.	Davis et al.	1996	Australia	19	0
216.	Koho et al.	1991	Finland	30	3.3
217.	Meisel et al.	1995	Germany	94	0
218.	Brettler et al.	1992	International	106	2.7
219.	Power et al.	1995	Ireland	393	0.5
220.	Scotto et al.	1996	Italy	83	8.4
138.	Caporaso et al.	1998	Italy	11379	5.6
139.	Guadagnino et al.	1998	Italy	267	11.3
221.	Akahane et al.	1994	Japan	154	27
222.	Koda et al.	1996	Japan	121	7.4
223.	Mauser-Bunschoten et al.	1995	Netherlands	75	0
224.	Win et al.	1994	Scotland	75	5.3
225	Diage et al.	1996	Spain	394	7.6
141.	Kao et al.	1996	Taiwan	100	17
226.	Saltoglu et al.	1998	Turkey	38	7.8
227.	Gordon et al.	1992	UK	42	4.7

Table 3.3. Prevalence of anti-HCV in the intravenous drug users of different geographical locations.

Ref #	Authors	Years	Locations	Number tested	Positive %
177	Bell et al.	1990	Australia	172	84
228	Crofts et al.	1993	Australia	303	68
229	Crofts et al.	1997	Australia	1741	66.7
230	Van Beek et al.	1998	Australia	1078	75.6 (<20years)
231	Chang et al.	1999	China	899	67.2
232	Smyth et al.	1998	Dublin	733	61.8
181	Stark et al.	1995	Germany	405	83
233	Stark et al.	1996	Germany	324	94
234	Van den Hoek et al.	1990	Holland	304	74
235	Van Amejden	1995	Holland	305	65
236	Galeazzi et al.	1995	Italy	227	75
182	Guadagnino et al.	1995	Italy	146	68
237	Woodfield et al.	1993	New Zealand	110	73
238	Robinson et al.	1995	New Zealand	92	77
239	Kemp et al.	1998	New Zealand	241	64.7
240	Hagan et al.	1999	North America	2462	85.7
241	Bolumar et al.	1996	Spain	1056	85.5
242	Santana Rodriguez et al.	1998	Spain	122	87.6
176	Lamden et al.	1998	UK	773	67
243	Garfein et al.	1998	USA	229	37.6

Table 3.4 Numbers of eligible HBV and HCV cases for the Exploratory Study by the stage of recruitment (% of column totals).

Stages of the Exploratory Study	HBV cases (N=41)				HCV cases (N=50)				Total number of cases (N=91)	
	Acute		Chronic		Acute		Chronic			
	N	%	N	%	N	%	N	%	N	%
Retrospective	11	78.6	2	7.4	4	44.4	6	14.6	23	25.3
Prospective	3	21.4	25	92.6	5	55.6	35	85.4	68	74.7
Total	14	34.1 of 41	27	65.9 of 41	9	18.0 of 50	41	82.0 of 50	91	100.0

Table 3.5 Distribution of Exploratory Study population by response status.

Status	HBV cases (N=41)				HCV cases (N=50)				Total number of cases (N=91)	
	Acute		Chronic		Acute		Chronic			
	N	%	N	%	N	%	N	%	N	%
Interviewed	11	78.6	26	96.3	8	88.9	35	85.4	80	87.9
Refused	1	7.1	0	-	0	-	2	4.9	3	3.3
Unable to locate	1	7.1	0	-	1	11.1	3	7.3	5	5.5
Language problem	1	7.1	1	3.7	0	-	1	2.4	3	3.3
Total eligible	14	100.0	27	100.0	9	100.0	41	100.0	91	100.0

Table 3.6 a Distribution of all interviewed HBV cases of the Exploratory Study by demographic characteristics of age, gender, and birthplace.

Characteristics		Acute HBV (N=11)		Chronic HBV (N=26)	
		N	%	N	%
Age groups	0 - 19	0	-	2	7.7
	20-29	3	27.3	6	23.1
	30-39	4	36.4	8	30.8
	40-59	4	36.4	6	23.1
	60+	0	-	4	15.4
Gender	Male	8	72.7	14	53.8
	Female	3	27.3	12	46.2
Ethnic origin (country of birth[1])	Africa	2	18.2	4	15.4
	Asia	3	27.3	8	30.8
	Carribean	1	9.1	2	7.7
	Europe	3	27.3	4	15.4
	Middle East	0	-	4	15.4
	Canada	2	18.2	4	15.4

[1] For details on particular countries of birth included in these regions, please refer to Table A9 a in Appendices.

Table 3.6 b Distribution of interviewed cases of HCV of the Exploratory Study by demographic characteristics of age, gender, and birthplace.

Characteristics		Acute HCV (N=8)		Chronic HCV (N=35)	
		N	%	N	%
Age groups	0 - 19	0	-	0	-
	20-29	1	12.5	2	5.7
	30-39	2	25.0	6	17.1
	40-59	4	50.0	11	31.4
	60+	1	12.5	16	45.7
Gender	Male	3	37.5	20	57.1
	Female	5	62.5	15	42.9
Ethnic origin (country of birth[1])	Africa	1	12.5	8	22.9
	Asia	0	-	6	17.1
	Carribean	0	-	3	8.6
	Europe	1	12.5	7	20.0
	Middle East	0	-	2	5.7
	Canada	6	75.0	9	25.7

[1] For details on particular countries of birth included in these regions, please refer to Table A9 b in Appendices.

Table 3.7 a Prevalence proportions of all risk factors for acute (exposure during last 6 months) and chronic (lifetime exposure) HBV cases of the Exploratory Study.

	Risk factors	Acute HBV cases		Chronic HBV cases	
		N	% of all cases (n=11)	N	% of all cases (n=26)
Recognized Risk Factors	Injection drug use	0	-	0	-
	Drug snorting	0	-	0	-
	Blood transfusion	1	9.1	4	15.4
	Blood product	0	-	1	3.8
	Heterosexual partners ≥ 2	2	18.2	5	19.2
	Men sex with men	0	-	3	11.5
	Sex with hepatitis B carriers	2	18.2	4	15.4
	Tattooing	0	-	1	3.8
	Body piercing	0	-	5	19.2
	Acupuncture	0	-	1	3.8
	Blood contact	0	-	2	7.7
	Hemodialysis	0	-	0	-
	Hepatitis B carrier in family	0	-	6	23.1
	Institution associated	0	-	0	-
	Hospitalization	1	9.1	12	46.2
	Surgery	0	-	9	34.6
	Organ transplant	1	9.1	0	-
	Dental visit	0	-	15	57.7
	Incarceration	0	-	0	-
	Total	7	-	68	-

Potential New Risk Factors	Medical procedures: I/M & I/V injections for parenteral treatment, vaccinations etc.	2	18.2	17	65.4
	Blood donation in endemic zones or developing countries	0	-	2	7.7
	Vaccination against HBV	2	18.2	0	-
	Sex with potential carrier (partner vaccinated vs. HBV)	1	9.1	0	-
	Sex with prostitute	2	18.2	0	-
	Sado-masochistic sex	0	-	1	3.8
	Health care work related	0	-	3	11.5
	Other work related (high risk occupations)	4	36.4	3	11.5
	Frequent nicks, cuts, burns etc.	2	18.2	1	3.8
	Cultural/Ceremonial/Rituals	0	-	1	3.8
	Circumcision	0	-	5	19.2
	Aesthetics (cut by barber & hairdresser, artificial acrylic nails, manicure, pedicure etc.)	0	-	3	11.5
	Good Samaritan	0	-	1	3.8
	Accidents, fights, wars etc.	0	-	1	3.8
	Travel/living in endemic zones	1	9.1	1	3.8
	Visitors from endemic zones	1	9.1	0	-
	Immunocompromised	1	9.1	2	7.7
	Comorbid diseases	0	-	1	3.8
	Total	16	-	42	-
Unknown Risk Factors		1	9.1	0	-
Total		24	Average 2.1 RF/case	110	Average 4.2 RF/case

Table 3.7 b Prevalence proportions of all risk factors for acute (exposure during last 6 months) and chronic (lifetime exposure) HCV cases of the Exploratory Study.

	Risk factors	Acute HCV cases		Chronic HCV cases	
		N	% of all cases (n=8)	N	% of all cases (n=35)
Recognized Risk Factors	Injection drug use	2	25.0	0	-
	Drug snorting	2	25.0	1	2.9
	Blood contact	1	12.5	2	5.7
	Blood transfusion	0	-	7	20.0
	Blood product	0	-	3	8.6
	Hemodialysis	0	-	0	-
	Tattooing	2	25.0	1	2.9
	Body piercing	0	-	7	20.0
	Acupuncture	0	-	6	17.1
	Organ transplant	0	-	0	-
	Incarceration	2	25.0	1	2.9
	Sex with hepatitis C carriers	3	37.5	8	25.7
	Hepatitis C carrier in family	2	25.0	5	14.3
	Institution associated	0	-	0	-
	Hospitalization	1	12.5	21	60.0
	Surgery	1	12.5	19	54.3
	Dental visit	1	12.5	20	57.1
	Total	17	-	101	-

Potential New Risk Factors	Medical procedures: I/M&I/V injections for parenteral treatment, vaccinations etc.	2	25.0	10	28.6
	Blood donation in endemic zones or developing countries	0	-	5	14.3
	Sex with multiple partners	1	12.5	4	11.4
	Sex with prostitute	1	12.5	2	5.7
	Sex with IDU	1	12.5	2	5.7
	Sado-masochistic sex	1	12.5	0	-
	Health care work related	3	37.5	1	2.9
	Other work related (high risk occupations)	1	12.5	7	20.0
	Frequent nicks, cuts, burns etc	1	12.5	3	8.6
	Cultural/Ceremonial/Rituals	0	-	6	17.1
	Circumcision	0	-	6	17.1
	Aesthetics (cut by barber & hairdresser, artificial acrylic nails, manicure, pedicure etc.)	0	-	0	-
	Good Samaritan	0	-	3	8.6
	Accidents, fights, wars etc.	1	12.5	0	-
	Travel/living in endemic zones	0	-	7	20.0
	Visitors from endemic zones	0	-	0	-
	Immunocompromised	2	25.0	8	22.9
	Comorbid diseases	1	12.5	5	14.3
	Total	15	-	69	-
Unknown		1	12.5	0	-
Total		33	Average 4.0 RF/ case	170	Average 4.8 RF/ case

Table 3.8 a Numbers of HBV cases of the Exploratory Study with recognized and potential new risk factors, 1998-2002.

Risk factors identified by the Exploratory Study		Potential New Risk Factors[1]					
		Acute HBV			Chronic HBV		
		Yes	No	Total	Yes	No	Total
Recognized Risk Factors[2]	Yes	2	1	3	11	5	16
	No	7	1	8	10	0	10
Total		9	2	11	21	5	26

Table 3.8 b Numbers of HCV cases of the Exploratory Study with recognised and potential new risk factors, 1998-2002.

		Potential New Risk Factors[1]					
		Acute HCV			Chronic HCV		
		Yes	No	Total	Yes	No	Total
Recognized Risk Factors[2]	Yes	3	1	4	14	9	23
	No	3	1	4	12	0	12
Total		6	2	8	26	9	35

1 Previously not known risk factors identified only at Exploratory Study

2 Known risk factors not identified at Enhanced Surveillance

Table 3.9 Risk factor groups for acute/chronic HBV and HCV cases of the Exploratory Study.

Risk Factor Groups	Risk Factors
Drug use	▸ Injection ▸ Snorting
Health care acquired	▸ Blood transfusion ▸ Medical procedures ▸ HBV vaccination ▸ Organ transplant ▸ Hospitalization ▸ Surgery ▸ Dental visits and procedures
Other subcutaneous	▸ Tattooing ▸ Body piercing ▸ Acupuncture ▸ Frequent nicks and cuts ▸ Aesthetics
Sexual transmission	▸ Multiple partners ▸ Men sex with men ▸ Sex with carrier ▸ Sex with a prostitute ▸ Sado-masochistic sex ▸ Sex with injection drug user
Work related	▸ Health care work related ▸ Other work related
Cultural/Behavioural	▸ Circumcision ▸ Good Samaritan ▸ Blood letting, blood brothers/sisters
High prevalence environment	▸ Carrier in family ▸ Incarceration (prison) ▸ Traveling/living in endemic zones ▸ Visitors from endemic zones
High susceptibility host	▸ Immunocompromised
Other RFs	▸ Blood contacts ▸ Accidents and wars ▸ Comorbid diseases

Figure 3.1 a Distribution of potential new risk factors for HBV.
i. Acute HBV

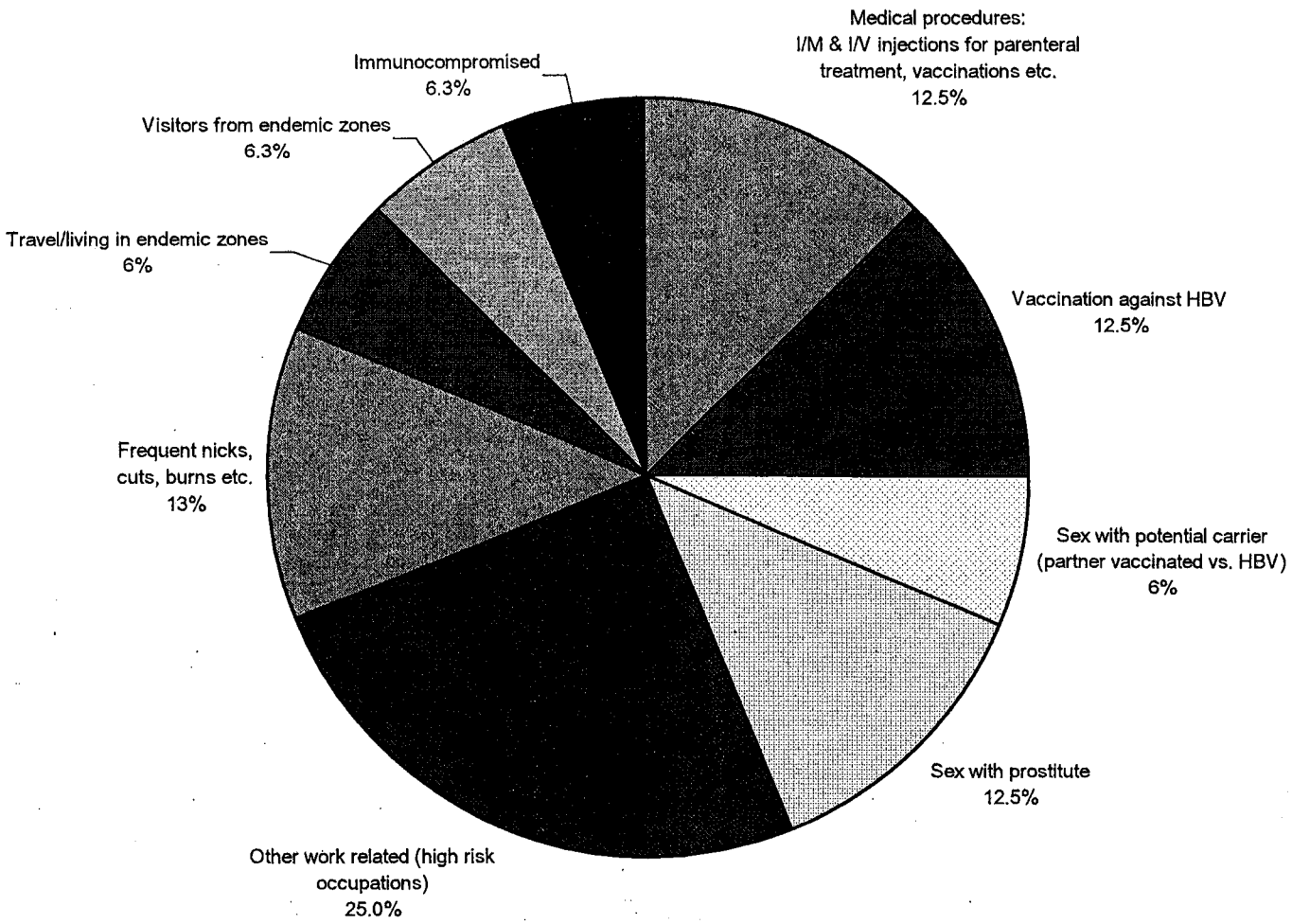


Figure 3.1 a Distribution of potential new risk factors for HBV (cont-d).
ii. Chronic HBV

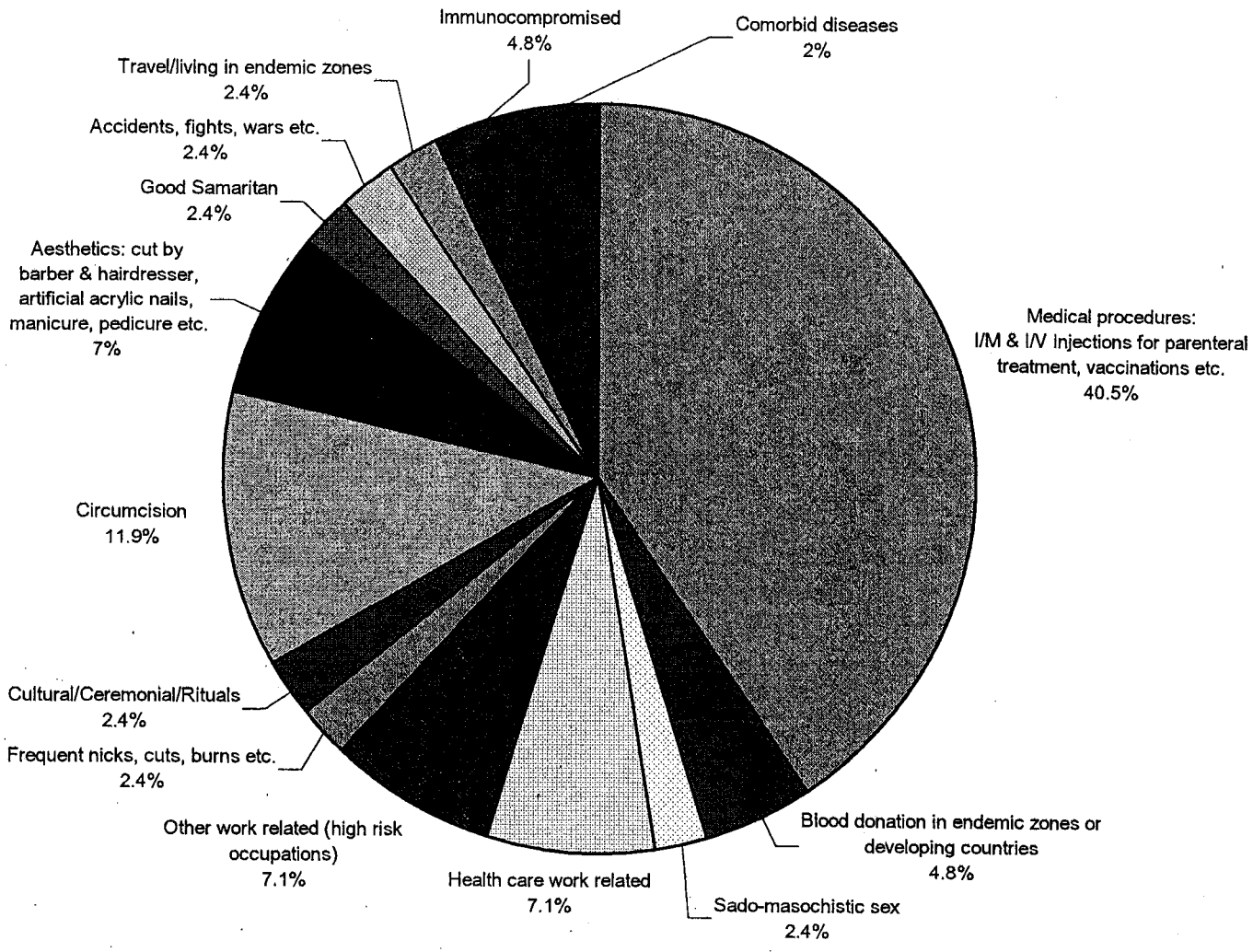


Figure 3.1 b Distribution of potential new risk factors for HCV.
i. Acute HCV

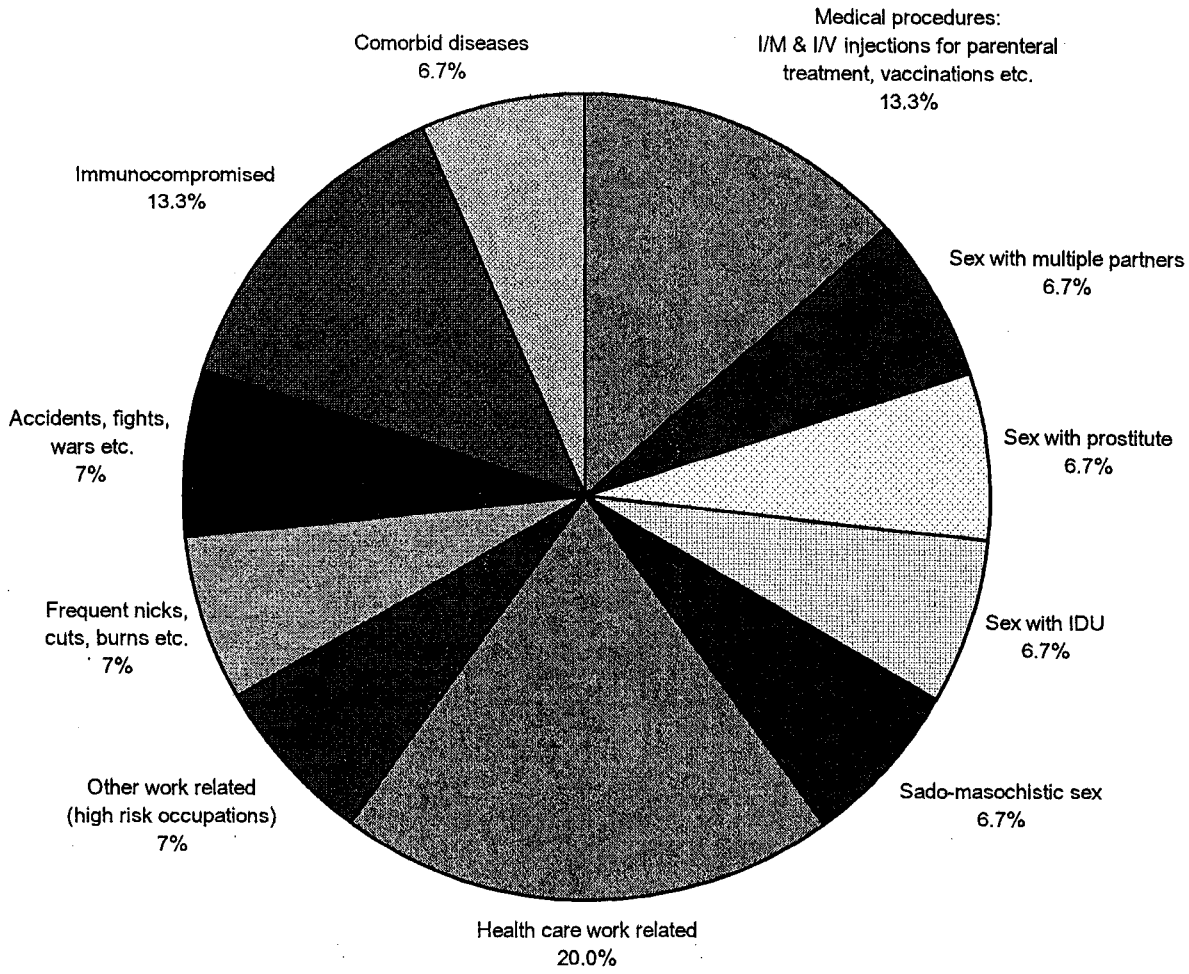


Figure 3.1 b Distribution of potential new risk factors for HCV (cont-d).
ii. Chronic HCV

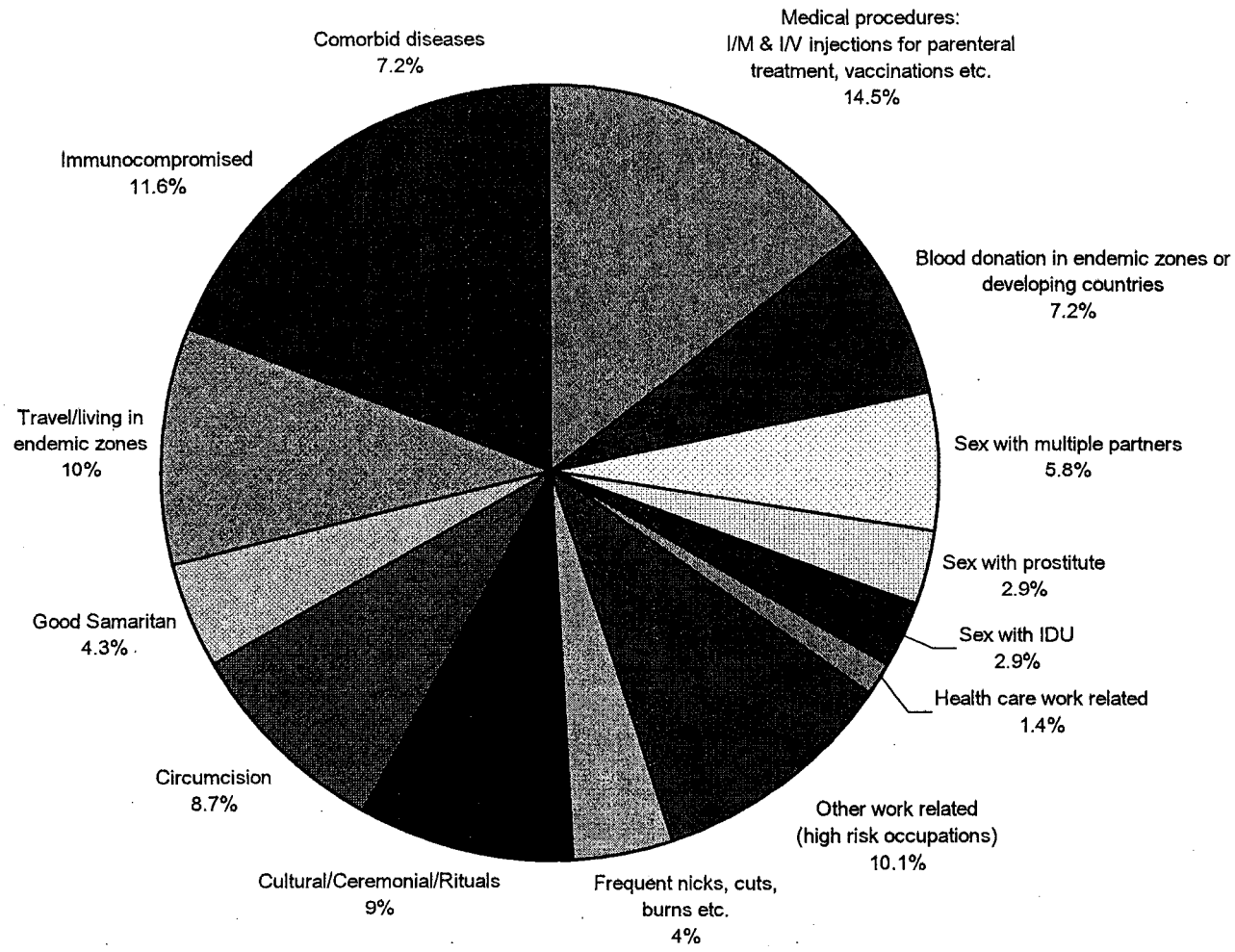


Figure 3.2 a Distribution of risk factor groups for HBV.
i. Acute HBV

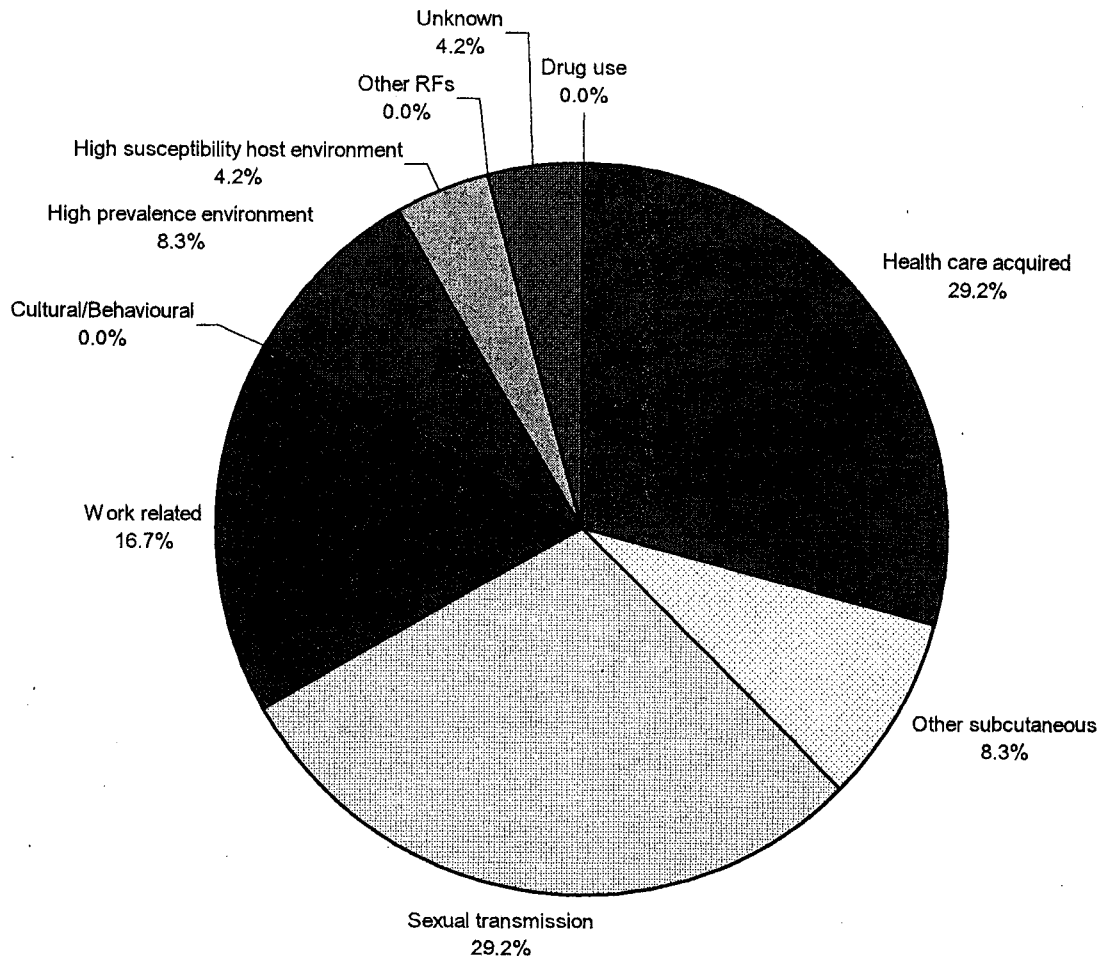


Figure 3.2 a Distribution of risk factor groups for HBV (cont-d).
ii. Chronic HBV

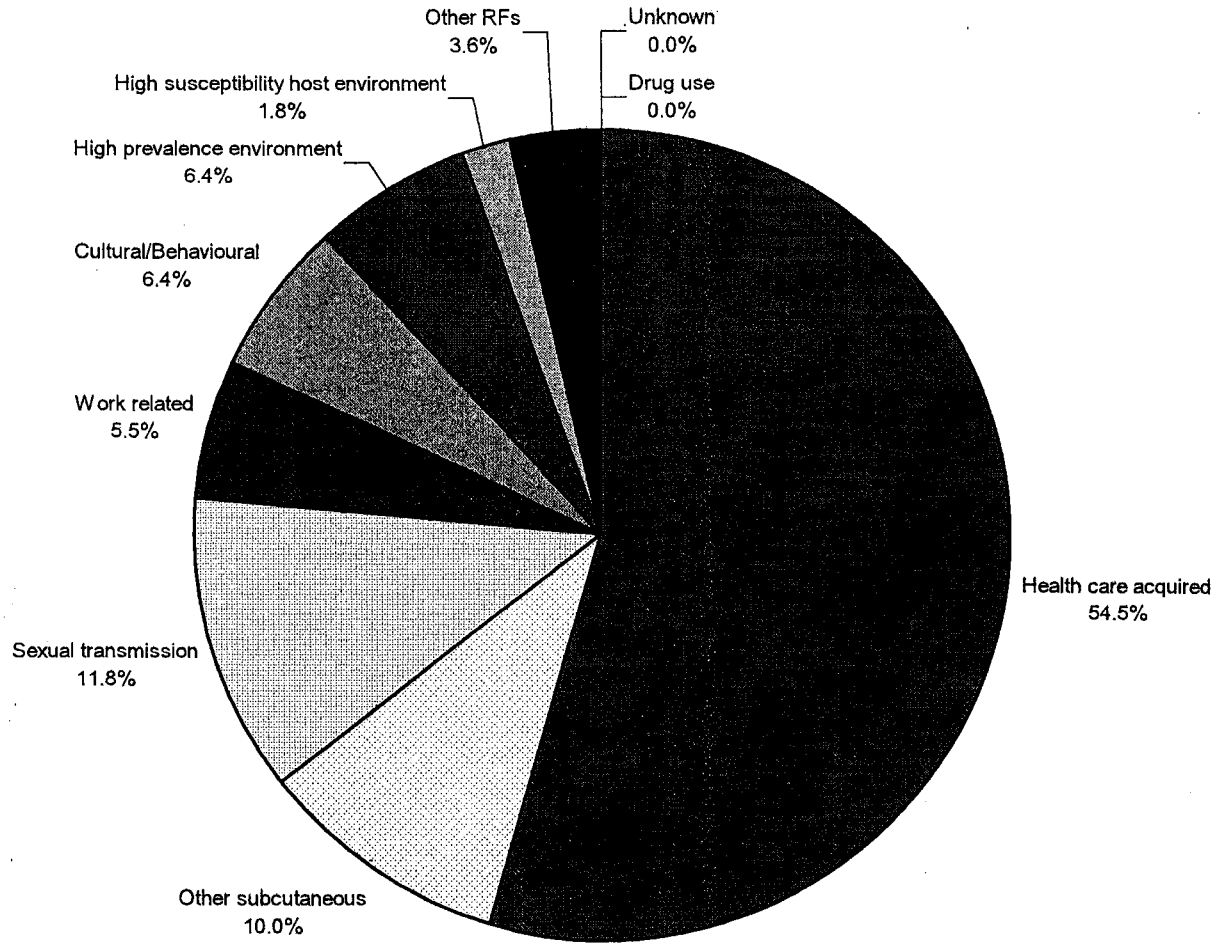


Figure 3.2 b Distribution of risk factor groups for HCV.
i. Acute HCV

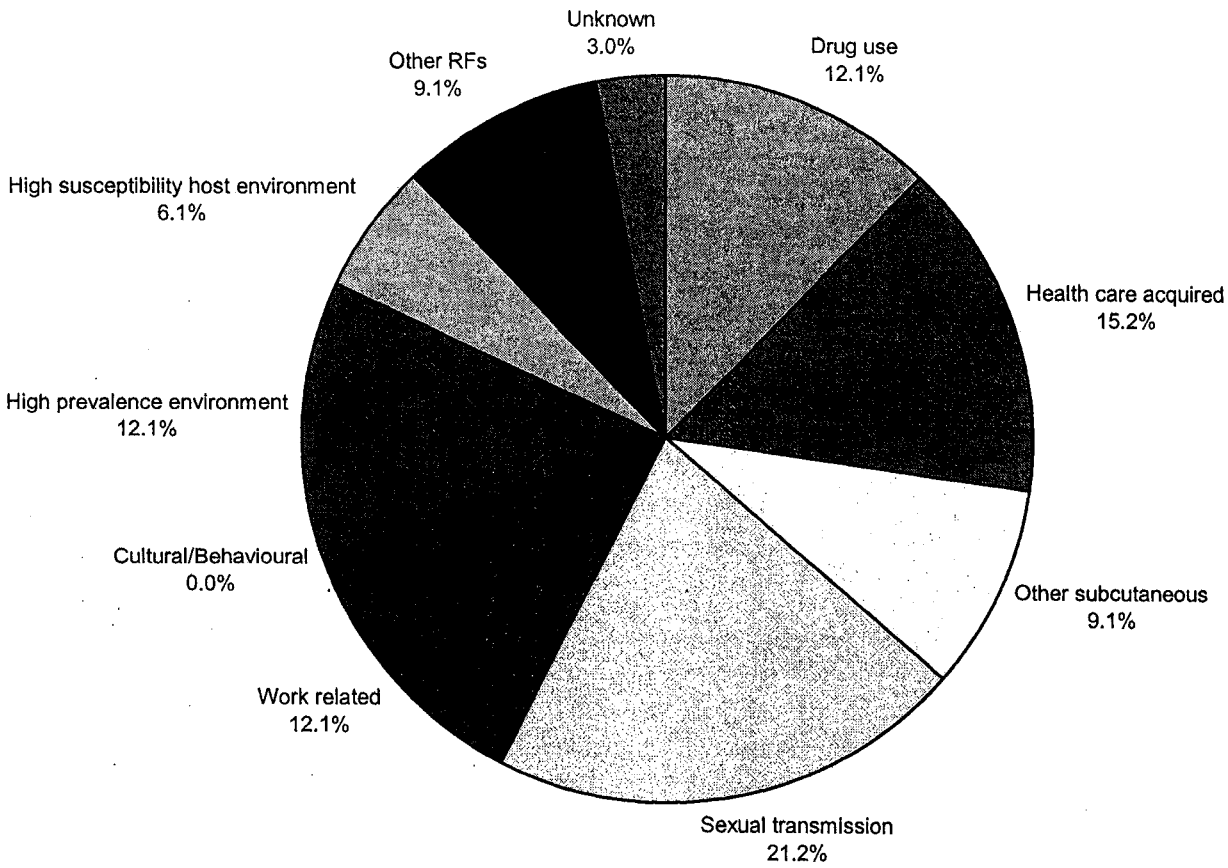
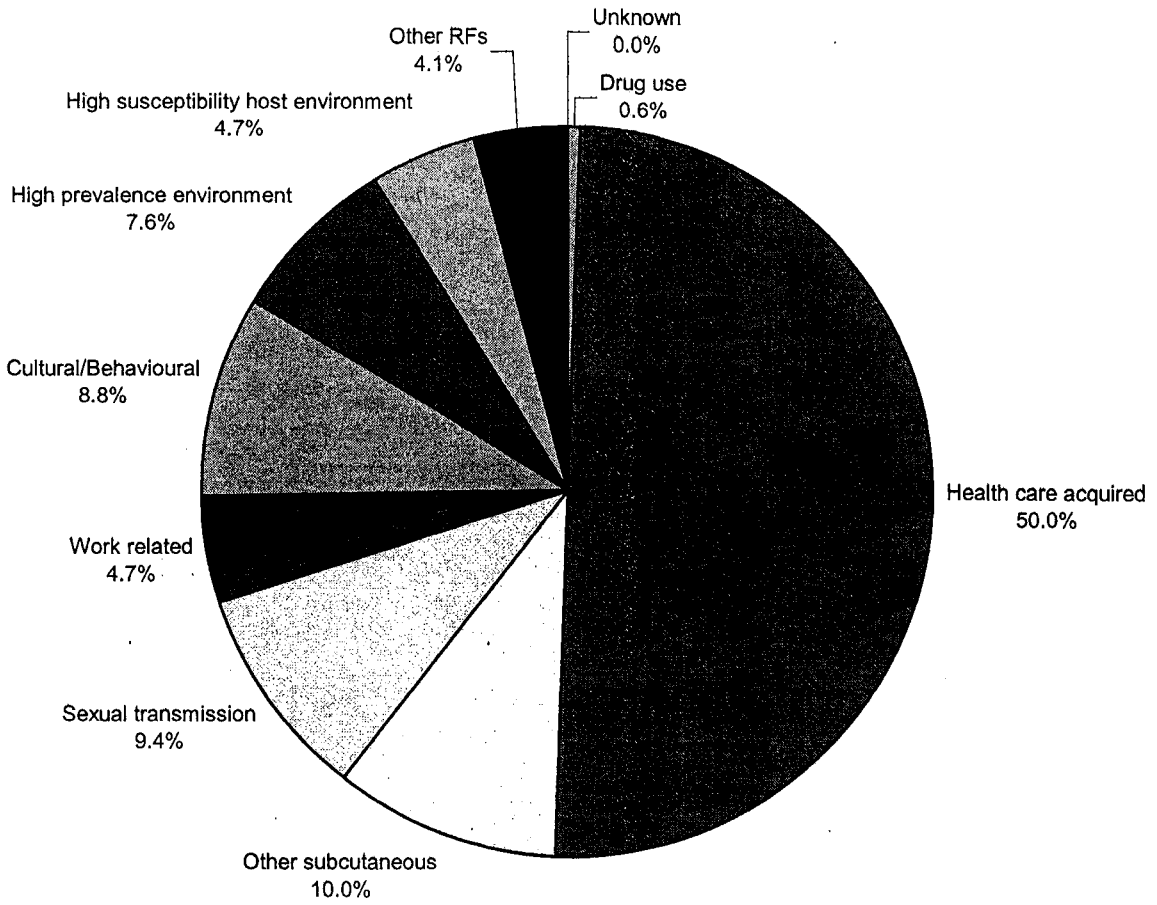


Figure 3.2 b Distribution of risk factor groups for HCV (cont-d).
ii. Chronic HCV



4. DISCUSSION AND CONCLUSIONS

4.1 Summary and Discussion of Findings

4.1.1 Findings of the Enhanced Surveillance

The Discussion chapter begins with interpretation of overall numbers, time trends, and population-based rates of reported cases of acute and chronic HBV and HCV.

Overall numbers and time trends. Based on the time-trends analysis, it is clear that occurrence of both acute and chronic diseases is consistent with the epidemiology of viral infection in general. Starting in October 1999, there was a parallelism in numbers and in time-trends of chronic HBV and chronic HCV (the latter being higher), which could be an indicator of a similar routes of transmission and in risk factor profiles of these infections. The slightly higher numbers in HCV than in HBV could be justified by the following:. 1) it is a relatively new, less known infection, with less investigated and quite controversial modes of transmission (for acute cases); 2) the phenomenon of prevalence pool when cases are accumulated during the years and then revealed more often at the beginning of surveillance (for chronic cases). The second would also explain the peak of chronic HCV in the first quarter of the Enhanced Surveillance: the cases had accumulated in the community prior to year 1992, when screening test for HCV was first introduced. Moreover, a gradual decline in chronic HCV can be regarded as an exhaustion of the prevalence pool with a 72% absolute drop from the initial number of cases that started in 1999, i.e., a year after launching the Enhanced Surveillance.

The prevalence pool phenomenon does not explain the gradually increasing numbers of chronic HBV. The latter could be due to immigration from high endemic zones such as Asia/Africa into Canada, particularly into Ottawa. So far, we have no available data for years 1999-2001 that could answer the question and could shed a light on this puzzle.

Population-based rates. We understand that three data-points cannot adequately reflect the long-term patterns in incidence and identification rates of HBV/HCV in Ottawa. Of course, it would be more informative to have a longer perspective, but these were the only data in our possession, and we decided to cautiously analyse and present them in the thesis. More marked decline in population-based rates of acute HBV through years in comparison with HCV may be explained by more effective anti-HBV prevention measures in the community. Patterns in identification rates of chronic diseases (increase in HBV and decrease in HCV) are the same as in overall numbers and are explained above. In general, given that the population did not change substantially over the 3.5 years of observation, the population-based rates show similar patterns as the raw numbers of cases.

As we have observed in the analysis of population-based rates, significantly higher incidence and reported rate of HCV than HBV is explained by HCV being relatively newer infection, whose routes of transmission are less understood and whose RFs are less known. There is no vaccination for HCV at all, whereas for several years Canadians have been offered largely available vaccination against HBV, particularly a publicly funded universal immunization of children and routine screening of pregnant women. Benefit of immunization and screening is supported by lower incidence of HBV in comparison with HCV, particularly in children and teenagers (5-fold) and in female population (2-fold).

For both diseases, the highest incidence (acute) and identification rate (chronic) were in males and in young/middle aged population (20-59 years), the latter being the economically most productive group of the population. It makes the tangible burden of viral hepatitis on health care system and on the society even more overwhelming due to increased indirect costs on top of expenses on treatment, medication, hospitalisation, immunization. All that emphasizes an urgent importance of elaborating new and improving existing preventive measures against HBV/HCV.

Recruitment. The significant difference in the interview rates between acute and chronic diseases was not a random result but the outcome of the sampling strategy adopted by the Enhanced Surveillance team, with a priority focus on interviewing the acute cases first, as of more importance for public health (please see the details in the section 2.1.3). Slightly higher rates for acute HCV than for acute HBV are also justified by the sampling strategy focussed on HCV cases first, as a comparatively new and less known infection. No plausible explanation though could be found for a significant drop in interview rates of acute HBV in the years 2000 and 2001, unless there may have been difficulties in locating cases and a language barrier. The lowest rates in the first year of the enhanced surveillance are quite understandable since at the beginning of establishing the system some time was needed to develop working relationships between central and provincial laboratories, public health services, as well as to improve the telephone interviewing technique of investigators.

Demographic characteristics. The analysis of demographic characteristics of reported cases revealed a quite interesting pattern with some similarities in trends for both HBV and HCV. The majority of patients were in 20-39 and 40-59 age groups. Gender description categorically indicates the males as the predominant population contracting the diseases, with a big relative difference in numbers in comparison with females (over 3-fold in acute HBV and HCV and over 2-fold in chronic HCV). The only deviation from this pattern was for chronic HBV, where the difference in proportion of men and women was less drastic (58.6% vs. 41.4%).

Explanation of the age-gender characteristics of infected cases could be found in subsequent analysis of risk factors, which showed a number of prevalent risk factors that characterise young people's and, particularly, young men's risky behavior more than women's (for example, IDU, snorting, tattooing, incarceration, multiple sexual contacts and so on). The

smaller male-female gap in chronic HBV may reflect body piercing as one of the top RFs for chronic HBV since it is believed that women are more involved in that activity.

Canadian-born cases were predominant in both acute diseases and in chronic HCV, which might partly be due to the selection priorities, with prevailing Canadian-born population in acute/chronic HCV (sections 2.1.3 and 2.2.2.2). However, we can not argue whether it is a true reflection of hepatitis C epidemiology in the community or not, since there are no other national surveillance data available for hepatitis C to compare with. Nevertheless, we are quite confident in the results for chronic HBV with prevailing immigrant population, since it is not due to sampling (3-fold less response rate speaks in favour of that). It is also supported by national data, with about 9-fold increased RR in prevalence of HBV and over 3-fold increased RR in HBeAg+ for the immigrant (particularly, Asian and Indochinese) in comparison with the Canadian-born population (see section 1.2.2).

Based on the above, some may wonder whether we should take HBV titres on immigrants and **immunise** if not already immune. Although a compulsory immunisation of one or other group of population may be an attractive idea, we do not think that the immunisation of not immune immigrants would be an effective measure to prevent the spread of the infection in the community, for the following reasons. Once on Canadian land, they should be treated with same as Canada-born Canadians, in respect to everything including immunisation. If there is no mandatory immunisation against HBV in Canada in general, then no Canadian (whether born in or out of Canada) should be immunised unless they belong to the high-risk population such as:

- residents and staff of institutions for the developmentally challenged;
- males having sexual contact with other males;
- others with multiple sexual partners or with a recent history of a sexually transmitted disease;

- injection drug users;
- hemophiliacs and others receiving repeated infusions of blood or blood products;
- hemodialysis patients (40 μg of vaccine antigen per dose should be used);
- staff and inmates of long-term correctional facilities;
- household and sexual contacts of acute HBV cases and HBV carriers;
- populations or communities in which HBV is highly endemic;
- children < 7 years of age whose families have immigrated to Canada from areas where there is a high prevalence of hepatitis B and who may be exposed to HBV carriers through their extended families;
- travelers to hepatitis B endemic areas;
- children in child care settings in which there is an HBV infected child.

In order to anticipate and prevent any spread of the HBV infection, it would be meaningful to recommend quarantining new immigrants from the endemic zones who are HBV-negative, having in mind that they might be infected but in the incubation period.

The **time-trends in demographic characteristics** of cases confirmed the patterns uncovered in the total numbers. Over time, variations in birth-place were characterized by an increase in the Asia-Africa-born population and near-stability in the Canada-born population, which again could be related to increased immigration from countries with high endemicity of HBV and HCV.

Epidemiologic characteristics.

Comparison of URF/RF frequency distributions by age/gender/birthplace among all interviewed in the EHSSS cases confirmed the **first hypothesis** that the cases with URFs and known RFs differ by their demographic characteristics. The increased risk of having URFs in

oldest group of population for chronic HCV might be explained by state of mental health, particularly, by difficulty to recollect. There is no plausible explanation for increased risk in females for acute HCV, though. The significant increased risk of having URFs for non-Canadian born cases emphasises a possibly poor knowledge and education of that particular population about the viral hepatitis and about the routes by which it gets transmitted in their native countries.

The discussion of the primary task of this thesis, i.e., the epidemiologic characteristics of viral hepatitis B and viral hepatitis C, begins with analysing the **main risk factors**, since it was more informative in terms of characterising the profile of actual RFs. The most prevalent main RFs were IDU, MSM for acute HBV, multiple heterosexual partners, blood transfusion and body piercing for chronic HBV, IDU and drug snorting for acute HCV, and IDU and blood transfusion for chronic HCV. The much bigger proportion of cases with URFs in acute HBV vs. chronic HBV might partly be explained by differences in the time span for risk identification, which is much larger for chronic cases (lifetime vs. the last 6 months). The higher URF in earlier years of the Enhanced Surveillance might be explained by interviewer skill bias, since the most cases with URF occurred in the first years of launching the surveillance system.

Since hepatitis B, hepatitis C, and HIV are spread via similar routes, patients often have evidence of infection with viral hepatitis and HIV agents, especially those who are injection drug users. However, only about 10% of HIV-positive subjects are chronic carriers of hepatitis B [244, 245], whereas hepatitis C infection occurs in HIV-positive patients with a frequency between 50-90% that is due to the specifics of hepatitis C virus [246-252].

The results of the **second hypothesis** testing confirmed expected differences in the **age/gender distribution of risk factors (column %)**. It is plausible that IDU, snorting, body piercing were more frequent main RFs in the youngest age range, justified by the fact that youth

usually tends to experiment and gets first acquainted to risky behaviour more often than people from older age groups. The same logistics applies for explanation of tattooing as one of frequently occurred exposure in the young adults for acute HCV cases. As the same age is associated with beginning of an active sexual life, the sexual mode of transmission was added on top of the list of prevailing RFs for acute and chronic HBV. Further in life (40-59), we saw blood transfusion joining the list of the RFs. Then, among 60+ cases we observed dental exposure prominent for both acute diseases. Should we infer here that the older population has other concomitant or comorbid conditions/illnesses that could have immunocompromised them and made them more vulnerable to contamination from dental interventions? It might be a plausible conclusion since some sources [253-259] indicate immune system compromise by a number of illnesses (such as cancer, diabetes, thyroid and some other) as a predisposition for contracting an infectious disease, including viral hepatitis. Or it might be that they have just lived more years, which provided more opportunities for going to the dentist, or a combination of both.

The risk factor structure of cases by gender in comparison with by age analysis did not reveal much except more exposure to body piercing in females and more snorting in males, as anticipated. The age differences are a more important distinguishing indicator of risky behaviour, which tends to be a crucial factor for contracting viral hepatitis, than gender differences. We did not analyse the distribution of RFs by birthplace since no significant results were expected due to small numbers on one hand, and strong presence of the selection bias in that demographic category on the other.

Having said the above, we have to remember that just a very few confidence intervals of the described differences excluded the null value, and only in gender characteristics, and none of them in acute diseases. Therefore, we have to regard these age/gender differences in RF distribution with a great caution.

The analysis of **risk factor distribution by age and gender within demographic groups (row %)** revealed no surprising patterns although any new pattern unveiled could have been argued as not significant or not valid due to very small numbers, especially, in acute HBV/HCV. Population in a socially active and curious age (teenagers and younger people) is more exposed to such risk factors as drug use, snorting, tattooing/body piercing and so on, which could mean they tend to be more involved in a risky behaviour that is less- or unacceptable for the society. In contrast, the risk factor pattern in middle-aged and older population showed their excessive exposure to health care hazards such as having blood transfusions, hospitalisations, dental visits and so on.

The fact that male cases are prevailing in almost each main risk factor has a valid explanation for the most of RFs except for dental visits and hospitalisation, where one would expect an equal distribution of male and female cases. It might be that some male cases tended to conceal their other, apparently "taboo", exposures (such as homosexual contacts, paid sex, drug use) by highlighting just the dental visits. A dominant majority of female cases with body piercing and blood contacts was also justifiable since more women have, at least, their ears pierced. Also, more women are thought to have contact with blood through nicks/cuts at home or at workplace, such as in health care where most nurses are female.

Less valuable, but interesting information about overall burden of risk factors in the community was revealed from investigation of **all RFs**. In the discussion of these risk factors, the presence of MSM, IDU and snorting on the top of the list of risk factors for acute HBV is consistent with the surveillance results elsewhere, but the second place occupied by dental visits as a risk factor for acute HBV is outstanding, since it is very rarely mentioned in the world literature. For both chronic disease, there are no major surprises, as dental visits, hospitalisation, surgery were the most frequent risk factors occurring during a lifetime timeframe. Other results

that fall outside the widely accepted RFs for acute HCV were hospitalisation as the third prevalent risk factor as well as sex with carrier/carrier in family. They look quite surprising appearing in the same company as the commonly known IDU, snorting, incarceration, tattooing, blood transfusion and others.

The comparison within parallel stages of diseases (i.e., between acute HBV and acute HCV and between chronic HBV and chronic HCV) showed that drug use (whether injection or snorting) was among most frequently reported risk factors for both acute infections, whereas dental, hospitalisation, and surgery were the most frequent RFs for both chronic infections. Both results are plausible considering the time frame in the definition of risk factors as the last 6 months for acute disease and lifetime for chronic disease. During life-time the vast majority of the general population has at least once undergone some type of medical/health care intervention.

In regards to dental visits as one of leading RFs, we have to be very cautious since it is based on all RF analysis, whereas in the ranking of main RFs dental visits appear at the bottom of the RF hierarchy due to large exposure of general population to that RF, but much small probability of acquiring the infection through that route.

The frequency distributions of individual categories of risk factors repeated the picture that we had seen in the analysis of prevalence proportions for both diseases. When combined, the groups of URF, sexual transmission, medical/health care acquired, and drug use were the most prevalent for acute HBV and (in reverse order) for acute HCV; medical/health care acquired and sexual transmission for chronic HBV and medical/health care group for chronic HCV. These findings are mostly consistent with published literature, except for our finding of the group of sexual transmission as one of the most common risk factors for acute HCV. The very high percentage of URFs among all risk factors for acute HBV also raises some questions, including

the possibility that the selection strategy adopted by the Enhanced Surveillance team led the interviewer to be less vigorous in investigating the HBV cases.

As we saw the results of **third hypothesis** testing about **associations between risk factors and their clustering**, all pairs of RFs that had moderately high ratios also had a moderate or better kappa coefficients, but only few pairs of RFs with greater kappas had coexisting greater ratios. All 95% confidence intervals for the largest values of kappa coefficients in both acute infections included zero, except for the perfect agreement between carrier in family/incarceration (in acute HBV) and for the moderate/better agreement between sex with HCV carrier/carrier in family for acute HCV. Actually, non-significant results of kappas for acute diseases were expected, since observed numbers of paired risk factors were particularly small for both acute diseases. On the other hand, all the highest chance-corrected ratios as a statistically significant index of moderate or better concordance that were found between pairs of RFs also could have been expected as the most plausible and logically justified clusters. The results are quite useful in not only validation of existing clusters of RFs, but also in evaluation of their strength. They are also very interesting from the public health point of view since almost all pairs of RFs in high agreement originated from the following major routes in transmission of communicable diseases in the population: 1) high-risk behaviour (drug users-prisoners-sex with carrier-carrier in family and so on) and 2) health care acquired (hospitalisation-surgery-hemodialysis-organ transplant and so on). In the main, the analysis of associations between RFs was consistent for both diseases with just two outstanding results that might raise interesting questions, both in acute HBV: 1) a perfect agreement between hepatitis B carrier in family and incarceration that despite its statistical significance should be considered with a caution since it was based on a single observation; 2) a fair agreement between sex with HBV carrier/dental visits (R=1.31, K=0.25) but whose confidence interval included zero (CI_k=[-0.25; 0.75]). Thus,

the results of kappa statistics supported our third hypothesis that there are associations between RFs and that the RFs tend to cluster. The wide confidence intervals for acute infections reflect the small sample size.

More numerous **RFs per case** for chronic in comparison with acute disease (for both HBV/HCV) are justified by the time frame for collecting RF information included into their definitions: 6 months exposures for acute and lifetime exposures for chronic disease. A larger proportion of cases with multiple (≥5) RFs per case in HCV than in HBV can be explained by the natural history of hepatitis C virus and subsequently by a larger spectrum of potential RFs.

An interesting case description and risk profile for both diseases can be drawn from **average number of all RFs by main exposure**. Cases whose main RFs were IDU, snorting drugs, blood transfusion, tattooing, sexual transmission or incarceration had a higher number of total RFs on average, which indicates that patients with those main RFs had a tendency to more risky behaviour.

The prevalence of **combined HBV/HCV** infections in Canada is unknown. Elsewhere the prevalence ranges between 3.4-18.3% in series of patients with hepatitis C [260-262]. Various studies have demonstrated that the outcome of combined infection is more severe than infection with either virus alone [263-264]. In most patients one infection predominates, while the other is dormant. If it is an HBV-dominant disease, the HBV DNA is detectable while the HCV RNA is not, and vice versa. Very occasionally both diseases may be active. Unfortunately, the Enhanced Surveillance data are limited, and we can not be sure with any degree of certainty whether HBV or HCV infection was acute in our coinfected cases.

The **frequency distributions of coinfected cases** of the Enhanced Surveillance by demographic and epidemiologic characteristics showed that coinfection was most common in the male 40+ aged population, those born in Asia and Canada, and those with IDU and blood

transfusion. This is consistent with the fact that both risk factors are common reasons for contracting both infections. On the other hand, the **prevalence proportions of coinfected cases** among all reported showed that coinfection was most common in males of 20 to 39 years of age, those born in Asia or Africa, and whose with IDU as the main risk factor. It is explained by the fact that youth and mostly men are more prone to experimenting with different things including drugs, while being born in countries with high endemicity of both HBV and HCV makes them more susceptible to coinfection. Summarizing the above, coinfection with HBV and HCV was most common in males of 20 to 39 years of age born in Asia or Africa with IDU as a main RF.

4.1.2 Findings of the Exploratory Study

Recruitment. Three quarters of the cases were recruited in the prospective stage of the study, and most of them were chronic cases for both HBV and HCV, although with a much bigger absolute and relative excess for HCV. That can be explained by the previously mentioned (in the chapter 2.1.3) selection strategy of the Enhanced Surveillance (for HCV) and by the reclassification of the endemic cases (most of whom were chronic HBV) into cases with unknown risk factors (for HBV).

A very high overall interview rate of about 90% from all eligible in the Exploratory Study cases was a result of high consent (refusal rate only 3.3%) and high compliance. In fact, we observed that patients were concerned with their disease and eager to find out a risk factor that might have exposed them to contracting the viral infection. Therefore, there were not any major reasons for failing to interview the cases except a very few fairly evenly distributed cases without information about place of residence or with difficulty to communicate in English or French. Actually, during the interviews, the language clause of the eligibility criteria stated in the Exploratory Protocol got altered since I had a couple cases interviewed in Russian as well.

Demographic characteristics. In **age** distribution of the Exploratory Study cases there was a similar pattern of patients being either from the young (20-39) or from the middle-aged (40-59) population, with the highest numbers in 30-39-year old people, which was comparable with the age distribution of hepatitis B and C patients in the general population. The only exception of chronic HCV, with cases being mostly 60+, could again be explained by the residue of the prevalence pool phenomenon. Since HCV was more recently discovered, surveillance for it has been possible for a shorter time, and there was a longer time available for a prevalence pool to develop and to age.

As a reflection of the **gender** distribution of viral hepatitis in the general population and in accordance with the Enhanced Surveillance results, the most prevalent gender in the Exploratory Study population was male. The excess of female patients in the acute HCV does not agree with the general gender-distribution concept mentioned above.

The fact that in distribution of cases by **birthplace** Canadian-born prevailed in the HCV population whereas the Asian-born and European-born were the largest groups in HBV, can also be explained by the selection strategy of the Enhanced Surveillance team (2.1.3, pages 24-25).

Epidemiologic characteristics. We begin by looking at the results of distributions as well as relationships between recognised and potential new RFs for HBV and HCV cases.

As was mentioned in the "Results of the Exploratory Study" chapter, for analysis of epidemiologic characteristics of cases we differentiated risk factors into two groups of **"Recognised" and "Potential new" RFs**, and a considerable part of all risk factors in both diseases (from 38% to 70%) comprised potential new RFs. Also the overwhelming majority of cases in both HBV and HCV reported some kind of potential new risk factor (including most of acute HBV cases *only* with potential new risk factors (!)). Simultaneously, 1/5-1/3 all cases in both diseases had well known RFs that should have been identified at the stage of the EHSSS.

It is significant that such substantial proportions of all risk factors for acute/chronic HBV/HCV, respectively (or at least over one third of all risk factors for both diseases) were previously unknown and were exclusively identified by the Exploratory Study. On the other hand, it is also important to acknowledge that some of RFs identified by the Exploratory Study could have been revealed earlier, by the Enhanced Surveillance, and in that case they would not have been eligible for recruitment into the Exploratory Study. Nevertheless, it worth mentioning that having the cases with recognised RFs included in the Exploratory Study brought a special flavour into its results, since it proved that potential new risk factors were present not only in cases with URF, but also in cases with well known RF identified at the stage of the Enhanced Surveillance. Therefore, it might be appropriate to conclude that the new approach to interviewing the patients and the open-ended structure of the Exploratory Study questionnaire appeared to be more successful in conducting the Exploratory Study than the data collection tools and procedures of the Enhanced Surveillance.

Since the vast majority of cases with previously unknown risk factors who were interviewed in the Exploratory Study had at least one potential new risk factor reported, it might be appropriate to state that the Exploratory Study served its purpose and achieved the objective of revealing potential new risk factors for HBV and HCV viral infections.

Analysis of **prevalence proportions** of RFs revealed quite interesting results. It is a new and surprising phenomenon to see other work related as the leading (!) risk factor in contracting HBV infection, since it had not been cited in any previous publication on HBV risk factors. We could see the well known category of health care workers as a major high-risk occupations group for contracting hepatitis B viral infection, but not the new category of other work related that was investigated in the Exploratory Study. Moreover, a new category of medical procedures (including intra-muscular and intra-venous injections for parenteral treatment, vaccinations and

so on) appeared to be a very important risk factor for contracting HBV infection (most prevalent category in chronic disease and second most prevalent category in acute disease). This applied mostly to patients born outside Canada, in counties with high HBV endemicity. Also a new revelation was the presence of vaccination against HBV and frequent nicks and cuts as one of the more prevalent risk factors among acute HBV cases. Furthermore, although we agreed with the world literature on sexual modes of transmission as one of the most important routes of contracting HBV (in the Exploratory Study, having over two heterosexual partners and sex with hepatitis B carrier tied for second among of risk factors), we also revealed a completely new individual category of having sex with prostitute (!) as a potential new risk factor within the group of sexual risk factors. The presence of dental visits, hospitalisation, and surgery as a risk factor in over 1/3 of chronic HBV cases is quite logical since the lifetime timeframe in the definition of chronic disease makes it very likely for a person (correlated with age, of course) to have at least one visit to a dentist, one hospitalisation or one surgery during life.

Quite interesting and controversial were the results on prevalence proportions of HCV cases of the Exploratory Study: over 1/3 of acute cases had health care work related and sex with hepatitis C carrier and 1/4 of acute cases had exposure to medical procedures, immunocompromised and so on as a risk factor, whereas over 1/2 of chronic cases had hospitalisation, dental visit, surgery and 1/4 chronic cases had medical procedures, sex with hepatitis C carriers, immunocompromised, blood transfusion, body piercing and travelling/living in endemic zones as a risk factor.

In the world literature, the sexual mode of transmission for viral hepatitis C is quite controversial and, according to different sources, it varies from 3% to 8%. In contrast, in the Exploratory Study we ended up with sex with a hepatitis C carrier as one of the most prevalent risk factors (!) for HCV cases with initially unknown RFs (tied for most prevalent in acute and

tied for second most prevalent in chronic HCV cases). Another controversy in the Exploratory Study results was that hepatitis C carrier in family tied for second most prevalent risk factor in acute HCV cases. Next in the list of discoveries of the Exploratory Study were that medical procedures and immunocompromised were important risk factors for HCV cases, with 25% prevalence and being the second in descending order for both acute and chronic disease, as well as travelling/living in endemic zones as a risk factor for chronic HCV cases.

Parallel comparison between acute and chronic diseases showed the following similarities and differences. As in HBV, in HCV also the potential new category of medical procedures appeared as one of the most prevalent risk factors among both acute and chronic cases. Similarly, the finding that hospitalisation, dental visit, and surgery were the most prevalent risk factors for both chronic HBV and HCV has a quite simple, logical explanation (please see above). Sexual mode of transmission in general and sex with virus carrier in particular appeared to be an important mode of transmission not only for HBV (already confirmed by world scientists), but also for contracting HCV infection. In contrast to acute HBV, where drug use (whether injection or snorting), was not reported as a risk factor at all, for acute HCV it was present as a risk factor in a quarter of all cases (or in second ordinal place). Other risk factors that appeared noticeably only in HCV cases were individual categories of immunocompromised, tattooing, incarceration, blood transfusion, body piercing, and travelling/living in endemic zones. The absence of drug use from both HBV distributions has a logical explanation in that all cases with IDU and snorting were previously identified at the stage of the Enhanced Surveillance and, therefore, did not appear in population of the Exploratory Study (the same explanation may apply to other recognised RFs that were under-represented in the Exploratory Study).

Twice as many **RFs per case** were found in chronic HBV as in acute HBV in the Exploratory Study, as in the EHSSS as well, and as was expected. It is anticipated for chronic

cases to have more numerous risk factors on average than for acute cases, since the timeframe in definition of risk factors for chronic disease is extended to lifetime from the last six months of the acute disease timeframe. This pattern was not repeated in the results for HCV cases, where there were on average 4.0 risk factors per case for acute HCV and 4.8 risk factors per case for chronic HCV. One of explanations for the almost 2-fold difference in average numbers of risk factors per case between acute HBV and acute HCV might be the possibility that patients with hepatitis C infection tend to have more risky behaviour than patients with HBV. Also, HCV is newer, so lifetime exposure is shorter than for HBV.

As is clear from the demographic characteristics of cases, the predominating proportions of medical procedures, circumcisions, and travelling/living in endemic zones as risk factors in both HBV and HCV could be explained by majority of cases being born outside of Canada (90% on average), particularly, in countries with high HBV/HCV endemicity such as Africa, Asia, and Eastern Europe (over 75% of cases). In those countries there always existed a shortage of disposable needles and syringes, and medical instruments and appliances did not get properly sterilized. The presence of a quite considerable proportion of cases with circumcision and/or cultural/ceremonial as a risk factor is explained by numerous patients born in countries where there are many cultural ceremonies and rituals, particularly, circumcisions, blood letting, blood brothers/sisters and so on. While health care work related is a well-known category of risk factors, other work related is a new finding of the Exploratory Study, together with frequent nicks/cuts/burns and immunocompromised for both HBV/HCV, aesthetics for HBV, and comorbid disease and sex with multiple partners for HCV.

At the end of the Exploratory Study there were no URF in chronic HBV and chronic HCV, and only 1 case in acute HBV and acute HCV, which indicates the exhaustive nature of

the study methods and procedures in investigating the cases with URF, and proves the feasibility and confirms the usefulness of the Exploratory Study.

4.2 Strengths and Limitations

4.2.1. Strengths

I. Strengths of the Enhanced Surveillance were:

1. A population based study.
2. A detailed investigation of risk factor epidemiology across Ottawa.

II. Strengths of the Exploratory Study were:

1. High recruitment and consent rates of the Exploratory Study that proved its feasibility.
2. Thorough elaborated open-ended questionnaire that was based on the list of possible risk factors derived from a review of literature and that helped to identify the recognised RFs missed by the Enhanced Surveillance as well the potential new risk factors.

4.2.2 Limitations

1. **Bias** in this work could have originated from factors affecting both surveillance in general and this enhanced surveillance in particular, as well as from features of the Exploratory Study, and they can be combined in two large groups.

I. Selection bias including:

a) Reporting bias at the stage of the surveillance that is typical for any surveillance. For example, correctness and completeness of identification and reporting of cases to the OHU by physicians' office, as well as reporting to NDRS by the health unit;

b) Ability to contact the cases for interviewing;

c) Selection bias that was very specific for this particular surveillance and was described in the Methods of the Chapter 2 might have resulted in differential interview rates. In spite of the obvious selection bias, the structure of interviewed in the Enhanced Surveillance cases appeared to be representative with respect to gender and age, except that those over 40 years old (in acute HBV) and 40-59 years old (in chronic HCV) populations are over-represented in the selection. The structure of selected cases by birthplace completely reflected the priority that was given to interviewing Canadian-born population with the sole exception of acute HBV cases, where the non Canadian-born population prevailed. Although the latter might seem like a deviation from the announced selection strategy, it could be explained as follows: 1) ranked selection strategy where acute state of the disease had a priority over birthplace in choosing the cases for interview; 2) reclassification of endemic cases where the cases born in endemic areas and initially considered as having known RFs were reclassified into URFs; 3) possibly, more availability of non-Canadian-born cases over Canadian-born in acute HBV to be reached and interviewed (eg., not yet employed). Also, take into consideration relatively small numbers in general.

Thus, the selection bias should not have affected the results of the analysis except in 40+ in acute HBV, 40-59 years old in chronic HCV, and non-Canadian-born in all categories of both infections except acute HBV. Therefore, a comparison between cases with unknown and known RFs might be valid in some extent. It made plausible a preliminary cautious testing of hypotheses (URF/RF comparison and RF-distribution by demographic characteristics and tendency of RFs to cluster).

II. Information bias including:

a) Recall bias, particularly for cases that were interviewed at launching the Enhanced Surveillance. Although the recall bias would have more affected the results for chronic cases since they were asked about lifetime RFs, it is also relevant for risk factor epidemiology of acute cases (last 6 months);

b) Misclassification errors in diagnosis for acute and chronic conditions, particularly for hepatitis C, might have affected, to a small extent, the validity of the risk factor epidemiology. It could bias the interview results since the cases would have been asked for different exposures by nature and intensity, depending on the disease: the last 6 months exposures for acute and lifetime exposures for chronic cases;

c) Unwillingness of interviewees to disclose the information, particularly when it concerned such sensitive issues as drug use, sexual practices, cultural habits.

2. Limitations of the Enhanced Surveillance:

a) A biased case selection strategy adopted by the team of EHSSS. Bias may have been introduced into the results of risk factor investigation because not all cases were interviewed for risk factor information. Most of the chronic hepatitis B cases who were not interviewed were likely to be immigrants from endemic areas. For the acute hepatitis B and acute hepatitis C group, the patients who were not interviewed could be at a higher risk of HBV or HCV infection. For example, injection drug users or persons with risky sexual behaviours may not have been interviewed because of their lack of permanent address and tendency to migrate from one place to another. Therefore, the percentage of IDU and that of risky behaviours among the acute cases identified may be underestimated;

b) Imperfections in diagnosis and in case definitions for acute and chronic cases, particularly for HCV;

c) Limited scope of the Enhanced Surveillance questionnaire that allowed it to miss a number of well known and recognised RFs, identified later at the stage of the Exploratory Study.

3. **Exploratory Study** limitations were inherited from the EHSSS, such as:
   a) Selection bias as noted in the points 1 and 2 of these Limitations;
   b) Limitations imposed by telephone interviewing and lack of qualitative analysis;
   c) Inability to conduct a case-control study (no comparison group).

   The "Potential new RFs" identified by the Exploratory study must be viewed as very preliminary.

4.3 Conclusions

1. Population-based rates of HBV and of HCV revealed the following:
   a) For both diseases, the highest incidence (acute) and identification (chronic) rates were found in males and in the economically most productive group of society such as young/middle aged population of 20-59;
   b) The youngest age group and females had much lower rates of HBV than of HCV (5-fold and 2-fold, respectively), probably due to publicly funded universal immunisation of children and routine screening of pregnant women for HBV.
2. Risk of having URF was significantly higher in oldest population (chronic HCV) and in immigrants (both diseases).
3. The most prevalent main RFs among the enhanced surveillance population were:
   a) IDU, MSM for acute HBV and IDU, drug snorting for acute HCV;
   b) Multiple heterosexual partners, blood transfusion, body piercing for chronic HBV and blood transfusion for chronic HCV.

4. The main RFs differed by age and gender (the results should be regarded with a great caution due to a lack of statistical significance in most of them):
    a) The most frequent RFs were IDU/snorting/body piercing in the youngest age range, sexual transmission/tattooing in young adults, blood transfusion in middle ages, and dental visits in older population;
    b) The most prevalent RF was body piercing in females and snorting in males.
5. A number of RFs were found to be in high concordance and tended to cluster, mostly originating from the following major routes of transmission in the population: 1) high-risk behaviour (drug use-prison, sex with carrier-carrier in family and so on) and 2) health care acquired (hospitalisation-surgery, hemodialysis-organ transplant and so on).
6. Average number of all RFs per case is much higher in HCV than in HBV, and is twice as high in acute diseases as in chronic diseases.
7. Average number of all RFs by main exposure revealed that cases with certain main RFs (such as IDU, snorting, blood transfusion, tattooing, sexual contact, and incarceration) were more likely to have numerous RFs and, therefore can serve as an indicator of a risky behaviour.
8. Coinfection with HBV and HCV was most common in males of 20 to 39 years of age, those born in Asia or Africa and those with IDU as a main RF.
9. Some of the cases with unknown risk factors included in the Exploratory Study could have been identified as having one or another of known risk factor at the stage of the Enhanced Surveillance. EHSSS has the potential to identify known RFs that it is currently missing.
10. In contrast to publications in the world literature, the sexual mode of transmission and health care acquired appeared to be important routes of transmission for hepatitis C virus, in both the EHSSS and the Exploratory Study.

11. The Exploratory Study revealed a number (18) of potential new risk factors, some of which (such as medical procedures, other than healthcare work related, frequent nicks/cuts/burns, immunocompromised, circumcisions, cultural/ceremonial rituals, travelling/living in endemic zones and so on) were quite prevalent among cases with initially unknown risk factors. These potential RFs deserve further study, using analytical designs.

4.4 Recommendations/Implications

1. a) The potential new risk factors revealed by the Exploratory Study should be incorporated into the EHSSS questionnaires, preferably after their confirmation by further analytical studies. [Some of the potential new risk factors such as comorbid diseases (STD), cultural/ceremonial rituals (blood letting, circumcision, Sun dance), living/travelling in endemic zones and some other are already considered in the new versions of the EHSSS questionnaires.];

   b) To have the open-ended questions from the Exploratory Study questionnaire incorporated into the Enhanced Surveillance questionnaire since this may uncover yet more RFs and should considerably reduce the number of cases with no risk factor reported.

2. In order to efficiently reveal the recognised, or well-known, risk factors in the Enhanced Surveillance System, the following measures should be taken (and have already been done through the EHSSS Coordinators seminars and through the Ottawa Regional Hepatitis C Working Group during 2001-2002):

   a) For widely known RFs: to develop better interviewing skills to completely use the capacities of the Enhanced Surveillance questionnaires and to organise educational programs to publicise recognised risk factors for HBV and HCV infections among healthcare workers and the Ottawa population at high risk;

b) For confirmed RFs that are not known to the large public: to conduct surveys to study public awareness about the HBV/HCV risk factors and high-risk populations.

3. Consider recommending to quarantine the immigrants, who are coming from countries with high endemicity of HBV or HCV and who are not immune yet.

4.5 Implementation Efforts to Date

1. The results of the Enhanced Surveillance analysis at the Ottawa site and the results of the literature review were reported and discussed at the Enhanced Surveillance Coordinators' seminar at the 1st Canadian Conference on Hepatitis C in May, 2001.
2. The design, data collection and results of the Exploratory Study were repeatedly reported, discussed and well received at the Enhanced Surveillance Investigators' meetings in May, 2001 and in September, 2002, as well as at the Ottawa Regional Hepatitis C Working Group in September, 2001 and in November, 2002.
3. The data and the results of this thesis in its all parts (Enhanced Surveillance at the Ottawa site, review of literature on HBV and HCV epidemiology, and the Exploratory Study) were used in numerous presentations and publications on the topic at the Blood-borne Pathogens Division of Health Canada.

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Appendix I

ENHANCED SURVEILLANCE FOR NEWLY IDENTIFIED HBV AND HCV INFECTIONS

PROTOCOL

It is part of the mandate of the provincial public health services and the Laboratory Centre for Disease Control (LCDC) at Health Canada to track the incidence and risk factors for the viral hepatitis including B and C. Data concerning these hepatitis collected in the National Notifiable Diseases Registry System cannot be used for such tracking. Hence, to fulfill this mandate, it is necessary to explore other methods of data collection; one method is through more focussed collection of data in narrower geographic areas, by committed public health jurisdictions, to specifically meet these surveillance needs.

The primary aim of this surveillance is to have collection of data that will ensure that, among cases of these hepatitis reported to the cooperating public health jurisdiction, newly acquired cases and remotely acquired cases are identified and a specific set of data related to these cases is obtained and transmitted to provincial/territorial epidemiologists and LCDC. The data from this surveillance will have local, provincial/territorial and national application.

This surveillance will be carried out by cooperating public health units.

TRIGGERING EVENT

Clinical diagnosis of hepatitis C or B by physicians, or identification of hepatitis C or B infections by laboratories is the triggering event for this enhanced surveillance.

OPERATIONAL PROCEDURE

The person in charge of this surveillance in the health unit will be required to inform every physician and all private and public health laboratories in the jurisdiction of this enhanced surveillance.

All physicians will be informed that a follow-up test for anti-HCV three months after onset is recommended for cases who are not diagnosed as hepatitis A or B or C but have symptoms of hepatitis.

The person in charge of this surveillance in the health unit will be required to contact all private and public health laboratories in the jurisdiction at least once a

week to ask for newly identified hepatitis C and B cases, their laboratory test results and other related information or feedbacks.

The person in charge of this surveillance in the health unit should maintain a list of all hepatitis B cases identified and a list of all hepatitis C cases identified and keep track of the status of investigation of each case.

The person in charge of this surveillance in the health unit will be required to contact physicians of all newly identified hepatitis B and C cases to inquire about clinical and laboratory data, including symptoms and results of laboratory tests indicated below in the Case Definition.

The person in charge of this surveillance in the health unit will be required to conduct interview of every newly identified hepatitis B (except for those remotely acquired hepatitis B cases who are first-generation immigrants from an area of high endemic, i.e. South East Asia and Africa) or hepatitis C cases for epidemiologic data and for confirmation of any changes in the general information items.

The person in charge of this surveillance in the health unit will make necessary effort to complete the investigation of each case and enter the data into the prescribed EpiInfo database files within a period of two months following identification of the case.

CASE DEFINITION

I. Acute/Newly Acquired HBV and HCV Infections

Clinical Case Definition: An acute illness with: discrete onset of symptoms[1]; and jaundice or elevated serum aminotransferase levels.

Laboratory Criteria for Diagnosis:

HBV: serum aminotransferase levels > 2.5 times the upper limit of normal

and
HBsAg positive **or** IgM anti-HBc positive
(if done)
and
IgM anti-HAV negative (if done)

[1]e.g. nausea, malaise, fatigue, dark urine, loss of appetite.

HCV: serum aminotransferase levels > 2.5 times the upper limit of normal
and
IgM anti-HAV negative
and
IgM anti-HBc negative (if done) or HBsAg negative
and
anti-HCV positive (confirmed by a supplemental test) or seroconversion[2].

Confirmed Case: a case that meets the clinical case definition and is laboratory confirmed.

II. Unconfirmed/Remotely Acquired HBV and HCV Infections

HBV: does not meet the above definition for confirmed case
but
has any laboratory evidence of current HBV infection (e.g. HBsAg positive)

HCV: does not meet the above definition for confirmed case
but
has any laboratory evidence of current HCV infection (e.g. confirmed anti-HCV positive)

III. Mixed Infections

a case acutely infected with HBV but chronically infected with HCV (no seroconversion) is regarded as HBV;

a case acutely infected with HCV but not acutely infected with HBV is regarded as HCV;

a case acutely infected with both HCV (seroconversion) and HBV is regarded as HBV and HCV;

for each case of mixed infections stated above, two separate questionnaires, one for HBV and one for HCV should be filled out.

DATA COLLECTION

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[2]seroconversion here refers to anti-HCV negative in the first test but anti-HCV positive in the follow-up test 3 months or later after the first test.

The two questionnaires attached, one for hepatitis B cases and the other for hepatitis C cases, are to be used for data collection through communication with physicians and interview of each of the newly identified hepatitis B or C cases.

The completed questionnaires will be transferred to the Community Acquired Bloodborne Infections (CABBI Section), Laboratory Centre for Disease Control (LCDC) in an electronic format to be incorporated into a national database. Initial data collection may be carried out by paper questionnaires and then transferred to the electronic format. The data to be transferred to LCDC shall not contain names or other personal identifiers through which individual patients can be identified.

I. From Physicians and laboratories

For both hepatitis B and hepatitis C virus infections

For all hepatitis C or B cases identified by physicians or laboratories, a questionnaire will be filled out and efforts shall be made to eliminate any duplications.

General information and clinical and laboratory data about each patient will be sought from physicians. The person in charge of this surveillance in the health unit will make sure each item of the questionnaires will be entered and checked for accuracy.

In summary, the following information about each case will be collected from physicians:

A. General information: patient file number, name, gender, date of birth, country of birth, and telephone numbers.

B. Clinical data: all symptoms (including nausea, malaise, fatigue, loss of appetite or dark urine) the patient had/has, date of the first symptom(s), with or without jaundice and date when jaundice was first noticed.

C. Laboratory test results:

1. serum aminotransferase level and date of the test;

2. specific tests for hepatitis C and B (and A) including HBsAg, IgM anti-HBc, IgM anti-HAV, and anti-HCV and dates of those tests;

It is recommended that all HBsAg positive patients be tested for anti-HCV as mixed infections are not uncommon.

3. a follow-up test for anti-HCV: for symptomatic hepatitis cases who are negative for HAV and HBV and HCV laboratory tests at the onset, a follow-up

test for anti-HCV three months or later after the first anti-HCV test is requested to detect seroconversion.

D. Hospitalization data: the patient was/is hospitalized or not and date if hospitalized, and the outcome of the illness (death or survival).

E. Address and telephone/fax numbers of the physician herself or himself for further inquiry.

II. From Patients

Interviewing procedures

Informed consent is to be sought before case interview according to relevant provincial legislation and regulation. The interviewers will first introduce themselves to the interviewees, read the consent form to them over the telephone to ask for their consent, and then conduct the interview over the telephone by asking questions according to the described questionnaires. If it is required by the provincial legislation or regulation, a written informed consent should be obtained for children from their parent or guardian by visiting the parent or guardian or by mail. Every identified hepatitis B or hepatitis C case, or the parent/guardian in the case of a child, will be interviewed to complete the questionnaire.

Introduction

The interviewers shall introduce themselves, for example, as the following: "This is First-name Last-name from the X Health Department. You (your child was) were recently examined for viral hepatitis infections and your (your child's) name was reported to us as needed for public health surveillance purposes. To better understand the occurrence of hepatitis B and hepatitis C infections in Canada and to prevent these important diseases, we need to ask you some questions about your (your child's) infection and it will take approximately 20 minutes. Is this an appropriate time to talk to you or shall I call you later?" If the answer is yes, the consent form will be read to the interviewee over the phone and the interview will proceed as indicated above. Otherwise, the interviewer will call back later to conduct the interview.

Consent form

A suggested consent form is attached in Appendix D but each cooperating health unit must make sure of the appropriateness of using this suggested consent form and modify it as necessary according to relevant provincial regulation or legislation.

The consent form, as decided by each participating cooperating health unit, will be read to the interviewee over the phone and a consent will be obtained verbally by telephone. If it is required by the provincial legislation or regulation, a written informed consent

should be obtained for children from their parent or guardian. The telephone number of the health department will be provided to the interviewee in case he or she wishes to confirm the identity of the interviewer or has questions to ask.

Questionnaire for hepatitis B virus infections

Obtain general information and data about the risk factors indicated in the questionnaire for "Enhanced Surveillance for newly identified Hepatitis B Virus Infections" (Appendix B).

Questionnaire for hepatitis C virus infections

Obtain general information and data about the risk factors indicated in the questionnaire for "Enhanced Surveillance for newly identified Hepatitis C Virus Infections" (Appendix C).

III. Regarding Public Health Response to Cases

Different jurisdictions may have different policies for public health response. The questions in the questionnaires do not represent a standard or recommendation. These items are for surveillance purposes only.

Appendix II

ENHANCED SURVEILLANCE FOR NEWLY IDENTIFIED HEPATITIS B VIRUS INFECTIONS
(Laboratory Centre for Disease Control, March 2000)

Please fill out this questionnaire by recording the answer in the space provided or circling one of the choices listed for each question.

I. IDENTIFICATION

Administrator ID Code _____ Health Unit ID Code _____
Health Unit Name _____

Unique ID Number of the Patient _____

This case was identified to the health department by (please circle a number)
1. physician 2. laboratory
3. infection control practitioner 4. patient himself or herself
5. other means

II. DEMOGRAPHIC DATA

Gender: Female Male Date of Birth (dd/mm/yyyy) ____/____/_____

Country of Birth _____

if born outside of Canada, year came to Canada (yyyy) _____

if born in Canada, what ethnic origin does this patient consider himself or herself to be?
1. patient doesn't want to answer
2. Aboriginal 3. Afro-American 4. Asian
5. Caucasian 6. Other 7. Unknown

III. CLINICAL & LABORATORY DATA

a. Did the patient have any symptoms of hepatitis (e.g. nausea, malaise, fatigue, loss of appetite or dark urine)? Yes No Unknown

if yes, date of first symptom (dd/mm/yyyy) ____/____/_____
source of data (please circle a number): 1. physician 2. laboratory
did the patient have nausea? Yes No Unknown
did the patient have malaise? Yes No Unknown

did the patient have fatigue? Yes No Unknown
did the patient have loss of appetite? Yes No Unknown
did the patient have dark urine? Yes No Unknown

b. Did the patient have jaundice? Yes No Unknown
if yes, date when jaundice was first noticed (dd/mm/yyyy) ____/____/_____

c. Laboratory Test Results:

Was the patient tested for serum aminotransferase level (ALT/AST)?
Yes No Unknown

if yes, date of the test (dd/mm/yyyy) ____/____/_____
peak ALT value _____ peak AST value _____

was the ALT/AST level higher than 2.5 times the upper limit of the normal level?
Yes No Unknown

Did the patient have any positive laboratory test result to support the specific diagnosis of hepatitis B? Yes No Not Done Unknown

HBsAg:
Positive Negative Not Done Unknown
if done, date (dd/mm/yyyy) ____/____/_____

IgM anti-HBc:
Positive Negative Not Done Unknown
if done, date (dd/mm/yyyy) ____/____/_____

IgM anti-HAV:
Positive Negative Not Done Unknown
if done, date (dd/mm/yyyy) ____/____/_____

anti-HCV:
Positive Negative Not Done Unknown
if done, date (dd/mm/yyyy) ____/____/_____

Had this person been tested for hepatitis B previously?
Yes No Unknown

if yes,
HBsAg:
Positive Negative Not Done Unknown
if done, date (dd/mm/yyyy) ____/____/_____

anti-HBs:
Positive Negative Not Done Unknown
if done, date (dd/mm/yyyy) ____/____/_____

anti-HBc:
Positive Negative Not Done Unknown
if done, date (dd/mm/yyyy) ____/____/_____

d. Source of all the above laboratory data:
1. physician 2. laboratory
3. patient 4. other means

e. Physician's Diagnosis for this patient:
1. Acute hepatitis B 2. Chronic hepatitis B 3. Unknown

if yes for chronic hepatitis B, what was the diagnosis for chronic liver disease?
1. Cirrhosis 2. Hepatocellular Carcinoma
3. Unknown 4. Others

the source of the physician's diagnosis:
1. Physician 2. laboratory
3. nurse 4. patient
5. other means

Hospitalization Information

f. Was the patient hospitalized for the hepatitis B illness?
Yes No Unknown
if yes, date (dd/mm/yyyy) ____/____/_____

g. Did the patient die as a result of the hepatitis B illness?
Yes No Unknown

Does this case meet the definition of a confirmed acute/newly acquired case?
Yes No Unknown

Is this case also infected by hepatitis C virus?
Yes No Unknown
if yes,
the unique identification number on the hepatitis C questionnaire for this case _____

IV. EPIDEMIOLOGIC DATA (case interview)

Please state reason if the patient cannot be interviewed (please circle a number):
0. interviewed 1. refused 2. unable to locate

3. died 4. non-case
5. first generation of immigrants from endemic areas
6. language barrier 7. others

(If the answer to the above question is ***not*** "interviewed", go to Section VIII in the end)

(if the case **does** meet the definition of a confirmed acute/newly acquired case or if it is **not certain** that the case meets the definition of a confirmed acute/newly acquired case, go to the Section below)

(if the case does ***not*** meet the definition of a confirmed acute/newly acquired case, go to Section V below)

In the SIX months prior to your present illness (**SIX months** before the date indicated in a, b, c or f, whichever was earlier),

- Reference date used (dd/mm/yyyy) ___/___/_____

1. Did you inject any drug not prescribed by a physician, e.g. street drugs, steroids?
   Yes No Unknown
   if yes,
   did you share needle, syringe or other material used for injecting (e.g. cooker, cotton) with others? Yes No Unknown
   how many partners did you share with (1, 2, ...)? ___ (99=unknown)
   how many years (in total) have you injected drugs ____ (99=unknown)?

2. Did you snort any drug not prescribed by a physician, e.g. cocaine?
   Yes No Unknown
   if yes, did you share straw or other material used for snorting with others?
   Yes No Unknown
3. Did you receive a blood transfusion? Yes No Unknown

   if yes, how many times (1, 2, ...)? ___ (99=unknown)

4. Did you receive an injection of a blood product, e.g. albumin, immune globulin, clotting factor? Yes No Unknown

   if yes, how many times (1, 2, ...)? ___ (99=unknown)

5. How many partners of the opposite sex have you had intercourse with in the six months prior to the present illness (0, 1, 2,...)? ___ (99=unknown)

6. For both men and women, how many partners of the same sex have you had intercourse with in the six months prior to the present illness (0, 1, 2,...)? ___ (99=unknown)

7. Did you have sexual contact (vaginal, anal or oral intercourse) with a person who had hepatitis B or was a carrier of hepatitis B virus in this period?
Yes No Unknown

8. Did you have sexual contact (vaginal, anal or oral intercourse) with a person who is/was an injection drug user ?
Yes No Unknown

8. Have you been diagnosed with bacterial sexual transmitted disease(s) (STDs such as genital chlamydia, gonorrhea and syphilis) by physician(s) ?
Yes No Unknown

8. Do you use condoms during sexual contact (vaginal, anal or oral) ?
1. Always 2. Frequently 3. Occasionally
4. Never 5. Unknown 6. Not applicable

11. Have you been tattooed in this period? Yes No Unknown

if yes, how many times (1, 2, ...)? ___ (99=unknown)

12. Have you had any part of your body pierced in this period?
Yes No Unknown
if yes, how many times (1, 2, ...)? ___ (99=unknown)

13. Have you had acupuncture treatment in this period?
Yes No Unknown
if yes, how many times (1, 2, ...)? ___ (99=unknown)

14. Were you employed in a medical or dental field involving contact with human blood or body fluids? Yes No Unknown

if yes, what was your job? _____

degree of blood contact: Occasionally Weekly Daily

15. Did you have hemodialysis? Yes No Unknown
16. Was there anyone in your family/household who had hepatitis B or was a carrier of hepatitis B virus? Yes No Unknown

if yes, relation of that person to you:
mother father partner brother/sister child others

17. Were you associated with an institution for the developmentally disabled (not including group homes)? Yes No Unknown

if yes,
were you a resident in the institution? Yes No Unknown

were you an employee in the institution? Yes No Unknown
Were you a household contact of a resident or employee?
Yes No Unknown

18. Were you hospitalized in the six months prior to the present illness?
Yes No Unknown

19 Did you have surgery in this period? Yes No Unknown
if yes, how many times (1, 2, ...)? ___ (99=unknown)

20. Have you received an organ/tissue transplant (including skin and bone grafts)?
Yes No Unknown

21. Did you have any dental visit in this period?
Yes No Unknown
if yes, how many visits (1, 2, ...)? ___ (99=unknown)

22. Were you incarcerated in prison? Yes No Unknown

23. Specify the possible reason(s) for your acute hepatitis B infection if you have not identified any of the potential reasons provided above:
_____
_____

24. Were you a blood donor in the recent six months?
Yes No Unknown
if yes, when: date (dd/mm/yyyy) ____/____/_____
where: province _____
city _____

V. EXTENDED HISTORY OF POTENTIAL EXPOSURE TO HEPATITIS B VIRUS

S1. Did the patient ***ever*** inject any drug not prescribed by a physician, e.g. street drugs, steroids?
Yes No Unknown

S2. Did the patient ***ever*** snort any drug not prescribed by a physician, e.g. cocaine?
Yes No Unknown

S3. Did the patient ***ever*** receive a blood transfusion?
Yes No Unknown
if yes, date of transfusion (please circle a number):
1. before 1990 2. in or after 1990 3. in both periods

S4. Did the patient ***ever*** receive an injection of a blood product, e.g. albumin, immune globulin, clotting factor? Yes No Unknown

S5. How many partners of the opposite sex has the patient ***ever*** had intercourse with (0, 1, 2, ...)? ___ (99=unknown)

S6. For both men and women, how many partners of the same sex has the patient ***ever*** had intercourse with (0, 1, 2,...)? ___ (99=unknown)

S7. Did the patient ***ever*** have sexual contact (vaginal, anal or oral intercourse) with a person who had hepatitis B or was a carrier of hepatitis B virus?
Yes No Unknown

S8. Did you ***ever*** have sexual contact (vaginal, anal or oral) with a person who was an injection drug user ?
Yes No Unknown

S9 Has this patient ***ever*** been diagnosed with bacterial sexual transmitted diseases (STDs such as genital chlamydia, gonorrhea and syphilis) by physician(s) ?
Yes No Unknown

S10. Do you ***ever*** use condoms during sexual contact (vaginal, anal or oral) ?
1. Always 2. Frequently 3. Occasionally
4. Never 5. Unknown 6. Not applicable

S11. Has the patient ***ever*** been tattooed? Yes No Unknown

S12. Has the patient ***ever*** had any part of his/her body pierced?
Yes No Unknown

S13. Has the patient ***ever*** had acupuncture treatment?
Yes No Unknown

S14. Was the patient ***ever*** employed in a medical or dental field involving contact with human blood or body fluids? Yes No Unknown

S15. Did the patient ***ever*** have hemodialysis?
Yes No Unknown

S16. Was there ***ever*** anyone in the patient's family/household who had hepatitis B or was a carrier of hepatitis B virus? Yes No Unknown

if yes, relation of that family member to this patient:
mother father partner brother/sister child others

S17. Was the patient ***ever*** associated with an institution for the developmentally disabled (not including group homes)? Yes No Unknown

S18. Was the patient ***ever*** hospitalized prior to the present illness?
Yes No Unknown

S19. Did the patient ***ever*** have surgery? Yes No Unknown

S20. Has the patient ***ever*** received an organ/tissue transplant (including skin and bone grafts)?
Yes No Unknown

S21. Did the patient ***ever*** have any dental visit?
Yes No Unknown

S22. Was the patient ***ever*** incarcerated in prison?
Yes No Unknown

S23. Was the mother of this patient ***ever*** diagnosed with HBV or unknown hepatitis before the birth of this patient ?

S24. Specify the possible reason(s) for your hepatitis B infection if you have not identified any of the potential reasons provided above:

_____

_____

S25. What was the risk factor that was believed to have most likely caused the transmission of the virus to this patient (S1, S2,..., S24, SS for others and S0 for unknown)? ___

S26. Have you ***ever*** been a blood donor ? Yes No Unknown
if yes, when: date (dd/mm/yyyy) ____/____/_____
where: province _____
city _____

VI. HISTORY OF HEPATITIS B VACCINATION:

Did you ***ever*** receive vaccination for hepatitis B?
Yes No Unknown if yes,
what year did you receive the vaccine (yyyy)? _____

did you receive all three doses of vaccine? Yes No Unknown
if no, how many doses did you receive (1, 2)? __

VII. PUBLIC HEALTH RESPONSE TO THIS CASE:

a. Is contact tracing done? Yes No Not Applicable

b. Was contact given HBIg (hepatitis B immunoglobulin)?
Yes No Not Applicable

c. Is contact immunization done? Yes No Not Applicable
d. Is sexual partner(s) notified? Yes No Not Applicable
e. Is this patient an infant born to an infected mother?
Yes No Unknown
if yes,
did the infant receive recommended prophylaxis (HBIg and vaccine) for hepatitis B in the postnatal period? Yes No Unknown
if did, number of vaccine doses received (1, 2, 3): ___

f. Is this patient the mother of a neonate or an infant?
Yes No Unknown
if yes,
did the neonate or infant receive recommended prophylaxis (HBIg and vaccine) for hepatitis B in the postnatal period? Yes No Unknown
if did, number of vaccine doses received (1, 2, 3): ___

g. Is this patient pregnant? Yes No Unknown
if yes,
is the patient informed of the recommended postnatal prophylaxis (HBIg and vaccine) for hepatitis B? Yes No Unknown

h. If this patient received or gave blood/blood products, is the information about this patient provided to the Canadian Blood Services or HemaQuebec?
Yes No Not Applicable

Interview conducted through: Visit Phone Letter

VIII. Form completed by _____

Date (dd/mm/yyyy) ____/____/_____

ENHANCED SURVEILLANCE FOR NEWLY IDENTIFIED HEPATITIS C VIRUS INFECTIONS
(Laboratory Centre for Disease Control, March 2000)

Please fill out this questionnaire by recording the answer in the space provided or circling one of the choices listed for each question.

I. IDENTIFICATION

Administrator ID Code _____ Health Unit ID Code _____
Health Unit Name _____

Unique ID Number of the Patient _____

This case was identified to the health department by (please circle a number)
1. physician 2. laboratory
3. infection control practitioner 4. patient himself or herself
5. other means

II. DEMOGRAPHIC DATA

Gender: Female Male Date of Birth (dd/mm/yyyy) ____/____/_____

Country of Birth _____

if born outside of Canada, year came to Canada (yyyy) _____

if born in Canada, what ethnic origin does this patient consider himself or herself to be?
1. patient doesn't want to answer
2. Aboriginal 3. Afro-American 4. Asian
5. Caucasian 6. Other 7. Unknown

III. CLINICAL & LABORATORY DATA

a. Did the patient have any symptoms of hepatitis (e.g. nausea, malaise, fatigue, loss of appetite or dark urine)? Yes No Unknown

if yes, date of first symptom (dd/mm/yyyy) ____/____/_____
source of data (please circle a number): 1. physician 2. laboratory

did the patient have nausea? Yes No Unknown

did the patient have malaise? Yes No Unknown
did the patient have fatigue? Yes No Unknown
did the patient have loss of appetite? Yes No Unknown
did the patient have dark urine? Yes No Unknown

b. Did the patient have jaundice? Yes No Unknown
if yes, date when jaundice was first noticed (dd/mm/yyyy) ____/____/_____

c. Laboratory Test Results:

Was the patient tested for serum aminotransferase level (ALT/AST)?
Yes No Unknown

if yes, date of the test (dd/mm/yyyy) ____/____/_____
peak ALT value _____ peak AST value _____

Was the ALT/AST level higher than 2.5 times the upper limit of the normal level?
Yes No Unknown

Did the patient have any positive laboratory test result to support the specific diagnosis of hepatitis C? Yes No Not Done Unknown

anti-HCV antibody test:
Positive Negative Not Done Unknown
if done, date (dd/mm/yyyy) ____/____/_____
initial method _____
confirmed by a supplemental test:
Yes No Unknown
if yes, name of the test _____

Hepatitis C virus RNA PCR test:
Positive Negative Not Done Unknown
If done, date (dd/mm/yyyy) ____/_____/_____

HBsAg:
Positive Negative Not Done Unknown
if done, date (dd/mm/yyyy) ____/____/_____

IgM anti-HBc:
Positive Negative Not Done Unknown
if done, date (dd/mm/yyyy) ____/____/_____

IgM anti-HAV:
Positive Negative Not Done Unknown
if done, date (dd/mm/yyyy) ____/____/_____

Had this person been tested for hepatitis C previously?
Yes No Unknown

if yes,
anti-HCV antibody test result:
Positive Negative Not Done Unknown
if done, date (dd/mm/yyyy) ____/____/_____

d. Source of all the above laboratory data (please circle a number):
1. physician 2. laboratory
3. patient 4. other means

e. Physician's Diagnosis for this patient:
1. Acute hepatitis C 2. Chronic hepatitis C 3. Unknown

if yes for chronic hepatitis C, what was the diagnosis for chronic liver disease?
1. Cirrhosis 2. Hepatocellular Carcinoma
3. Unknown 4. Others

the source of the physician's diagnosis:
1. Physician 2. laboratory
3. nurse 4. patient
5. other means

Hospitalization Information

f. Was the patient hospitalized for the hepatitis C illness?
Yes No Unknown
if yes, date (dd/mm/yyyy) ____/____/_____

g. Did the patient die as a result of the hepatitis C illness?
Yes No Unknown

Does this case meet the definition of a confirmed acute hepatitis C case?
Yes No Unknown

Is this case also infected by hepatitis B virus?
Yes No Unknown
if yes,
the unique identification number on the hepatitis B questionnaire for this case _____

IV. EPIDEMIOLOGIC DATA (case interview)

Please state reason if the patient cannot be interviewed (please circle a number):

0. interviewed 1. refused 2. unable to locate
3. died 4. non-case
5. first generation of immigrants from endemic areas
6. language barrier 7. others

(If the answer to the above question is ***not*** "interviewed", go to Section VII in the end)

(if the case **does** meet the definition of a confirmed acute/newly acquired case or if it is **not certain** that the case meets the definition of a confirmed acute/newly acquired case, go to the Section below)

(if the case does ***not*** meet the definition of a confirmed acute case, go to Section V below)

In the SIX months prior to your present illness (**SIX months** before the date indicated in a, b, c or f, whichever was earlier),

- Reference date used (dd/mm/yyyy) ____/____/_____

1. Did you inject any drug not prescribed by a physician, e.g. street drugs, steroids?
   Yes No Unknown if yes,
   did you share needle, syringe or other material used for injecting (e.g. cooker, cotton) with others? Yes No Unknown
   how many partners did you share with (1, 2, ...)? ___ (99=unknown)
   how many years (in total) have you injected drugs? ____ (99=unknown)

2. Did you snort any drug not prescribed by a physician, e.g. cocaine?
   Yes No Unknown
   if yes, did you share straw or other material used for snorting with others?
   Yes No Unknown
3. Were you employed in a medical or dental field involving contact with human blood or body fluids? Yes No Unknown

   if yes,
   what was your job _____
   degree of blood contact: Occasionally Weekly Daily

4. Did you receive a blood transfusion? Yes No Unknown
   if yes, how many times (1, 2, ...)? ____ (99=unknown)

5. Did you receive an injection of a blood product, e.g. albumin, immune globulin, clotting factor? Yes No Unknown
   if yes, how many times (1, 2, ...)? ____ (99=unknown)

6. Did you have hemodialysis? Yes No Unknown
7. Have you been tattooed in this period?
   Yes No Unknown

if yes, how many times (1, 2, ...)? ____ (99=unknown)

8. Have you had any part of your body pierced in this period?
Yes No Unknown
if yes, how many times (1, 2, ...)? ____ (99=unknown)

9. Have you had acupuncture treatment in this period?
Yes No Unknown
if yes, how many times (1, 2, ...)? ____ (99=unknown)

10. Have you received an organ/tissue transplant (including skin and bone grafts)?
Yes No Unknown

11. Were you incarcerated in prison? Yes No Unknown

12. Did you have sexual contact (vaginal, anal or oral intercourse) with a person who had hepatitis C or was a carrier of hepatitis C virus in this period?
Yes No Unknown

12. Did you have sexual contact (vaginal, anal or oral intercourse) with a person who is/was an injection drug user ?
Yes No Unknown

12. How many partners of the opposite sex have you had intercourse with in the six months prior to the present illness (0, 1, 2,...)? ___ (99=unknown)

12. For both men and women, how many partners of the same sex have you had intercourse with in the six months prior to the present illness (0, 1, 2,...)? ___ (99=unknown)

12. Have you been diagnosed with bacterial sexual transmitted disease(s) (STDs such as genital chlamydia, gonorrhea and syphilis) by physician(s) ?
Yes No Unknown

12. Do you use condoms during sexual contact (vaginal, anal or oral) ?
1. Always 2. Frequently 3. Occasionally
4. Never 5. Unknown 6. Not applicable

18. Was there anyone in your family/household who had hepatitis C or was a carrier of hepatitis C virus? Yes No Unknown

if yes, relation of that person to you:
mother father partner brother/sister child others

19. Were you associated with an institution for the developmentally disabled (not including group homes)? Yes No Unknown

if yes,
were you a resident in the institution? Yes No Unknown
were you an employee in the institution? Yes No Unknown
Were you a household contact of a resident or employee?

Yes No Unknown

20. Were you hospitalized in the six months prior to the present illness?
Yes No Unknown

21. Did you have surgery in this period? Yes No Unknown
if yes, how many times (1, 2, ...)? ____ (99=unknown)

22. Did you have any dental visit in this period?
Yes No Unknown
if yes, how many visits (1, 2, ...)? ____ (99=unknown)

23. Specify the possible reason(s) for your acute hepatitis C infection if you have not identify any of the potential reasons provided above:
_____
_____

24. Were you a blood donor in the recent six months?
Yes No Unknown
if yes, when: date (dd/mm/yyyy) ____/____/_____
where: province _____
city _____

V. EXTENDED HISTORY OF POTENTIAL EXPOSURE TO HEPATITIS C VIRUS

S1. Did the patient ***ever*** inject any drug not prescribed by a physician, e.g. street drugs, steroids?
Yes No Unknown

S2. Did the patient ***ever*** snort any drug not prescribed by a physician, e.g. cocaine?
Yes No Unknown

S3. Was the patient ***ever*** employed in a medical or dental field involving contact with human blood or body fluids? Yes No Unknown

S4. Did the patient ***ever*** receive a blood transfusion?
Yes No Unknown

if yes, date of transfusion (please circle a number):
1. before 1990 2. in or after 1990 3. in both periods

S5. Did the patient ***ever*** receive an injection of a blood product, e.g. albumin, immune globulin, clotting factor?
Yes No Unknown

S6. Did the patient ***ever*** have hemodialysis?
Yes No Unknown

S7. Has the patient ***ever*** been tattooed? Yes No Unknown

S8. Has the patient ***ever*** had any part of his/her body pierced?
Yes No Unknown

S9. Has the patient ***ever*** had acupuncture treatment?
Yes No Unknown

S10. Has the patient ***ever*** received an organ/tissue transplant (including skin and bone grafts)?
Yes No Unknown

S11. Was the patient ***ever*** incarcerated in prison?
Yes No Unknown

S12. Did the patient ***ever*** have sexual contact (vaginal, anal or oral intercourse) with a person who had hepatitis C or was a carrier of hepatitis C virus?
Yes No Unknown

S13. Did you ***ever*** have sexual contact (vaginal, anal or oral) with a person who was an injection drug user ?
Yes No Unknown

S14. How many partners of the opposite sex has the patient ***ever*** had intercourse with (0, 1, 2, ...)? ___ (99=unknown)

S15. For both men and women, how many partners of the same sex has the patient ***ever*** had intercourse with (0, 1, 2,...)? ___ (99=unknown)

S16. Has this patient ***ever*** been diagnosed with bacterial sexual transmitted diseases (STDs such as genital chlamydia, gonorrhea and syphilis) by physician(s) ?
Yes No Unknown

S17. Do you ***ever*** use condoms during sexual contact (vaginal, anal or oral) ?
1. Always 2. Frequently 3. Occasionally
4. Never 5. Unknown 6. Not applicable

S18. Was there ***ever*** anyone in the patient's family/household who had hepatitis C or was a carrier of hepatitis C virus? Yes No Unknown

if yes, relation of that family member to this patient:
mother father partner brother/sister child others

S19. Was the patient ***ever*** associated with an institution for the developmentally disabled (not including group homes)? Yes No Unknown

S20. Was the patient ***ever*** hospitalized prior to the present illness?
Yes No Unknown

S21. Did the patient ***ever*** have surgery? Yes No Unknown

S22. Did the patient ***ever*** have any dental visit?
Yes No Unknown

S23. Was the mother of this patient ***ever*** diagnosed with HCV or unknown hepatitis before the birth of this patient ?

S24. Specify the possible reason(s) for your hepatitis C infection if you have not identified any of the potential reasons provided above:

_____

_____

S25. What was the risk factor that was believed to have most likely caused the transmission of the virus to this patient (S0 for unknown, S1, S2,..., S24, SS for others)? ____

S26. Have you ***ever*** been a blood donor ? Yes No Unknown
if yes, when: date (dd/mm/yyyy) ____/____/_____
where: province _____
city _____

VI. PUBLIC HEALTH RESPONSE TO THIS CASE:

a. Is contact tracing done? Yes No Not Applicable

a. Is sexual partner(s) notified? Yes No Not Applicable

a. Is this patient an infant born to an infected mother ?
Yes No Unknown

if yes, at what age (in month) was the patient diagnosed with HCV infection ?
_____months (99 = unknown)

a. Is this patient the mother of a neonate or an infant?
Yes No Unknown

if yes, is the neonate or the infant being followed up by physicians or public health nurses?
Yes No Unknown

a. Is this patient pregnant ?
Yes No Unknown

If yes, did the patient receive consultative care regarding the risk of vertical transmission ?
Yes No Unknown

f. If this patient received or gave blood/blood products, is the information about this patient provided to the Canadian Blood Services or HemaQuebec?

Yes No Not Applicable

Interview conducted through: Visit Phone Letter

VII. Form completed by _____

Date (dd/mm/yyyy) ____/____/_____

Appendix III

AN EXPLORATORY STUDY TO FURTHER EXAMINE ACUTE AND CHRONIC HEPATITIS B AND HEPATITIS C CASES WITH UNKNOWN AND WEAK RISK FACTORS

(Based on the Results of the Enhanced Surveillance for Newly Identified HBV and HCV Infections at the Ottawa Site)

RESEARCH PROTOCOL

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Dr G. Wells***
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Coordinating Centers:

- *Blood-borne Pathogens Division, Center for Infectious Disease Prevention and Control, Population and Public Health Branch, Health Canada
- **Public Health Branch, City of Ottawa
- ***Department of Epidemiology and Community Medicine of the University of Ottawa

THE OVERALL AIM OF THE STUDY

The purpose of this study is to describe and evaluate the epidemiology of viral hepatitis B and viral hepatitis C in Ottawa during 1998-2001 that would help in attempts to develop effective measures for their prevention in the community. This study will be conducted in addition to the continuing Enhanced Surveillance Program (Appendix 1).

The study will contain two parts:

1) Analysis of the epidemiological trends of viral hepatitis B and viral hepatitis C infections in Ottawa and evaluation of the risk factor profiles based on the enhanced surveillance for newly identified HBV and HCV infections at the Ottawa site (Appendix 1).

2) Investigation and possible identification of unknown and weak-evidence-based risk factors for acute and chronic hepatitis B and hepatitis C viral infections by designing and conducting an exploratory study in collaboration with the Public Health Branch of City of Ottawa.

BACKGROUND

Definition. Hepatitis B and hepatitis C are viral infections of the liver caused by the Hepatitis B virus (HBV) and Hepatitis C virus (HCV), respectively. The virus is spread by direct exposure to the blood, blood products or body fluids (such as semen, saliva etc.) of those infected with the viruses. Symptoms include loss of appetite, nausea and vomiting, abdominal pain, extreme fatigue, and jaundice.

Epidemiology

Prevalence and Incidence Data. HBV and HCV infections are a major challenge and an important public health concern in the contemporary world [1]. According to WHO data, the prevalence of these infections in the world is very high. About 1/3 (2 billion people) around the world population have serologic evidence of being exposed to HBV, of which more than 350 million suffer from chronic infection. Although the published numbers for HCV are much smaller due to the lack of screening programs and incomplete data reporting, they are very alarming also (Table 1).

Table 1. Prevalence of HCV in the world (Source: WHO website).

HCV	Total population, mln	HCV prevalence, %	Infected population,mln	No data available (# of countries)
Total	5 811	3.1	169.7	57

According to the Centre for Disease Control and Prevention (CDC) data, an estimated 3.9 million (or 1.8%) Americans have been infected with HCV.

In Canada, it is estimated that over 100,000 people are infected with HBV [20] and about 240,000 - with HCV [18]. Examination of the rates of HBV and HCV infections in Canada over the last 12 years (Figure 2) shows that reported incidence rates for HBV have decreased slightly (probably, due to vaccination strategies), but identification rates for HCV have increased very sharply. (However, the later figures may include many newly reported chronic cases).

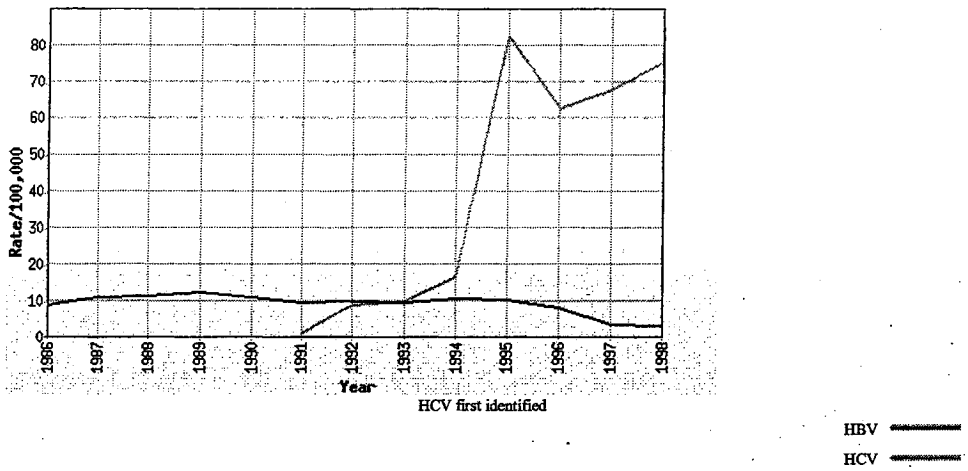


Figure 1. Incidence of HBV and identification rates for HCV over time for both sexes and all ages combined Canada, 1986-1998 (Source: Health Canada).

The examination of the spread of HBV and HCV infections in provinces and territories reveals that HBV is highest in North West Territories and HCV highest in British Columbia (Please, see the maps in Appendix 4).

Mortality. As a leading cause of chronic liver disease and hepatocellular carcinoma, and because of the magnitude of the infection worldwide, HCV and HBV have important implications on public health [2-5]. For instance, chronic liver disease is the tenth leading cause of death among adults in the United States, and accounts for approximately 25,000 deaths annually, or approximately 1% of all deaths. Population-based studies indicate that 40% of chronic liver disease is HCV-related, resulting in an estimated 8,000–10,000 deaths each year.

According to Statistics Canada, 2,030 deaths, accounting for 0.9% of all deaths in that year, occurred from chronic liver diseases that is 3.2 times as high as deaths attributable to HIV.

Table 2. Age-standardised mortality rates from chronic liver diseases and HIV (Source: Statistics Canada).

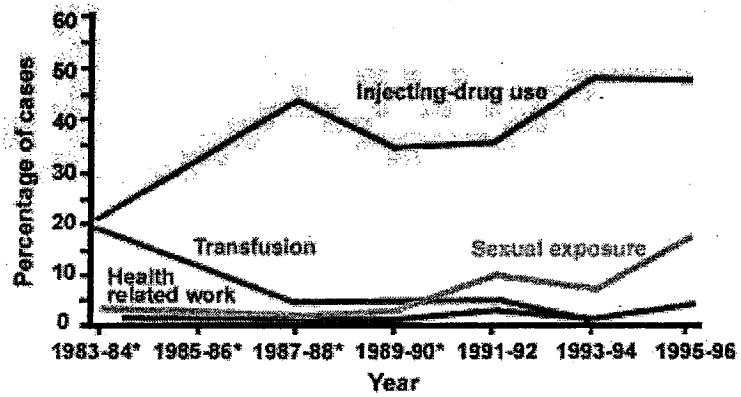
Causes of Death	1997				
	Number	%	Total	Males	Females
			Rate*		
All causes	215,669	100.0	658.7	844.0	521.6
Chronic liver diseases and cirrhosis**	**2,030**	**0.9**	**6.4**	**8.9**	**4.2**
HIV infection	626	0.3	2.0	3.6	0.5

*Age-standardized mortality rate per 100,000 populations.

** Please note that chronic liver disease and cirrhosis may have causes other than HBV or HCV (e.g., alcohol-related cirrhosis etc.)

Risk factors. The epidemiology of HBV and HCV infections in developed countries has changed. Former main source of HCV infection, transfusion of contaminated blood and/or blood products (before 1992), but now injection-drug use accounts for the majority of new infections [2,6,7]. For instance, the trends of the well-established groups of risk factors responsible for acute hepatitis C over the time are reflected in Figure 2 (Source CDC, USA).

Figure 1. Reported cases of acute hepatitis C by selected risk factors - United States, 1983-1996



On the other hand, Alter MJ et al. (1999, USA) found that the factors with the strongest independent associations with HCV infection among persons 17 to 59 years old are: 1) illegal drug use (ever used cocaine or marijuana-smoking 100 or more times); 2) high-risk sexual behaviour (an early age at first intercourse or 50 or more lifetime sexual partners) in the absence of illegal drug use; 3) marital status (divorced or separated); 4) income (below poverty level); and 5) the number of years of education (12 and fewer) [27].

Risk factors associated with HBV and HCV infections in Canada have been studied by Tepper [22], Gully [23], Roy E. et al. [24], and Delage G. et al [25]. For HBV, they are: injection drug use, multiple sex partners, sexual contact with hepatitis carriers, high risk homosexual activity of men, and possibly tattooing and body piercing. For HCV, the risk factors are injection drug use, history of blood transfusion or receipt of blood products prior to 1992, and sexual contact with an infected drug user. Occupational blood exposure, history of surgery and hospitalisation/ institutionalisation (including prisons) may be related to an increased risk of acquiring HCV in Canada [23, 25].

According to the majority of the world literature, between 19-50% of adults with acute hepatitis (HBV and, possibly, HCV) infection in low-endemic countries have been recorded to have an unknown risk factor for their infection [8-19]. In some of the studies, poorly defined transmission routes (for example, needlestick injuries, organ transplantation, renal hemodialysis, non-sterile tattooing/body pursing, contact with contaminated surfaces, and having visited a foreign country) were also recorded [28].

Enhanced Surveillance for Newly Identified HBV and HCV Infections

To monitor the incidence and risk factors associated with acute hepatitis B and hepatitis C, the enhanced surveillance system was established in 4 regions in October 1998 covering approximately 3,2 million people. As of August 2000, the enhanced surveillance has expanded to include 6 sites: Ottawa (ON), Calgary and Edmonton (AB), Vancouver (BC), Winnipeg (NWT), and New Brunswick. It is performed as a part of the mandate of the Blood-borne Pathogens Division (BBPD) and National Microbiology Laboratory (NML) of Health Canada (Please, see the Protocol in Appendix 1). Relevant demographic, clinical, laboratory and potential risk factor data are collected using pre-defined questionnaires (Appendices 2 and 3). One of the major concerns revealed by the enhanced surveillance is that a relatively significant percentage of cases with unknown risk factors - about 21% of all interviewed with acute HCV and 27% with acute HBV, - did not report any known risk factors (Oct 1998- Dec 1999). These data are quite consistent with what is reported elsewhere. On the other hand, the analysis of the year 2000 data reveals a significant drop in the proportional weight of cases with unknown risk factors to approximately 3% for both infections combined but slightly higher for HBV (Appendix 5). For now, it is unclear as to whether the observed decline is a true reflection of the proportions of cases with URF or is an outlier. More likely the latter as our previous data with much higher proportional weight of the cases with URF are consistent with what is reported elsewhere in the world.

Conclusion

Thus, to follow the epidemiological trends and to comprehensively explain the numbers and the features of risk factors for HBV and HCV seem to be imperative issues for public health in Canada. Reducing the burden of HCV and HBV infections and their related disease requires implementation of primary prevention activities to reduce the risk of contracting HBV and HCV infections and secondary prevention activities to reduce the risk for liver and other chronic diseases in infected persons. Therefore, a serious and thorough analysis of risk factors for viral hepatitis based on the results of the mentioned above enhanced surveillance of acute and chronic HBV and HCV cases is an imperative requirement. The first step will be designing and conducting an exploratory study in order to explore and identify the structure and context of URF. That will potentially allow elaborating and applying effective measures for prevention of HBV and HCV infections in the community.

OBJECTIVES

The Primary Objective

To thoroughly investigate, describe and evaluate cases of viral hepatitis B and viral hepatitis C infections with unknown (URF) and "weak" risk factors (WRF) identified at the Ottawa site of the enhanced surveillance during 1998-2001.

Secondary Objectives

1. To determine the number and proportion as well as detailed social-demographic, behavioral, and cultural characteristics of HBV/HCV cases with known, unknown and "weak" risk factors identified at the Ottawa site of the enhanced surveillance during 1998-2001 through quantitative analysis.

2. To interpret the results of the enhanced surveillance database analysis within context of harm reduction services offered in Ottawa with elaboration of recommendations for improvements and provision of support for well-targeted intervention in the community (if warranted).

3. To design and conduct an exploratory study of identifying URF and further examining WRF for HCV and HBV transmission cases captured by the enhanced surveillance at the Ottawa site in 2001.

4. To propose modification to the enhanced surveillance questionnaire based on the results of the exploratory study as an appropriate tool for comprehensively identifying risk factors for HCV and HBV infection cases captured by the enhanced surveillance.

RESEARCH DESIGN AND METHODS

I. Database Analysis of all Interviewed HBV and HCV Cases Revealed by the Enhanced Surveillance at the Ottawa Site During 1998-2001

Population
All the interviewed cases at the Ottawa site during 1998-2001 among the study population of the Enhanced Surveillance Program (Appendix 1). N = [758 (Oct1998-2000) + new cases (2001)] (see Total of Interviewed in Table 1 of Appendix 6).

Eligibility criteria: 1) clinical diagnosis of hepatitis B or hepatitis C by physicians, or identification of hepatitis C or B infections by laboratories; 2) availability to be reached; and 3) consent to be interviewed.

Data Collection Tools
- A universal questionnaire for both acute and chronic HCV and HBV used in the Enhanced Surveillance Program for data collection, interviewing, and identifying each new consenting case of HBV and HCV infections at all sites including Ottawa (Appendices 2 and 3).
- The questionnaire is administered through telephone interviews by the Ottawa site investigator, Ms. Darlene Poliquin

Methods and Data Analysis
- Descriptive epidemiology and detailed quantitative analysis of all risk factors (including URF and WRF) for all the cases of HBV and HCV infections based on the enhanced surveillance data at the Ottawa site during 1998-2001 (cross-tabulation, charts, figures, proportions, social and demographic characteristics etc.)
- During the analysis, to differentiate between Canadian and Foreign born cases and analyze them separately due to the fact that the site investigators are asked to more focus on recruiting for interviews the Canadian-born cases and, therefore, "interview" rates among them are much higher.

II. An Exploratory Study of HBV and HCV Cases URF and WRF Identified At the Ottawa Site of the Enhanced Surveillance During Oct1998-2001

The Exploratory Study will include Retrospective (1998-2000) and Prospective (2001) components and use semi-structured open-ended interviews. It will be conducted as a supplement to the continuing Enhanced Surveillance Program (Appendix 1).

Study Population

- **Retrospective:** The study population will be recruited from all acute and chronic HBV and HCV cases with URF that have already been identified by the enhanced surveillance at the Ottawa site during Oct 1998–2000 and meet the eligibility criteria. N = 21 (see Table 1 in Appendix 6).
- **Prospective:** The study population will be recruited from all the persons with acute and chronic HCV and HBV cases with URF and WRF that will be identified by the enhanced surveillance at the Ottawa site during 2001-2002 fiscal year and who meet the eligibility criteria.

Eligibility Criteria

Case definitions

- Persons with clinical diagnosis of hepatitis B or hepatitis C by physicians, or identification of hepatitis C or B infections by laboratories (please, see the "Case Definitions" on the page 2 of the Protocol in Appendix 1.) as the triggering event for the enhanced surveillance, with no known or only "weak-evidence-based" risk factors identified.
- **Unknown risk factors, or URF**, are identified as cases with no known risk factors revealed from those listed in the enhanced surveillance questionnaires (Appendices 2 and 3).
- **The "weak", or "weak-evidence-based" risk factors, or WRF** are identified as:
  - Qualitatively - cases whose strongest risk factor is supported only by anecdotal case report or case-series studies, in other words the factors supported by "weak-evidence", or "not well-established" risk factors.
  - Quantitatively - ranking of mutually exclusive risk factors (in absence of well-established factors) will be done based on the enhanced surveillance data of the year 2000 for all the cases combined (Appendix 5).

Inclusion criteria

All those cases of HBV and HCV with URF or WRF that have already been identified at the Ottawa site of the enhanced surveillance, meet the case definitions and who could be reached and agreed to participate.

Exclusion criteria

- Major cognitive (mental) disorder
- Lack of consent

Data Collection Tools

- A semi-structured open-ended questionnaire, elaborated to further investigate the HBV and HCV cases with unknown and "weak" modes of transmission captured by the enhanced surveillance, will be used for the Exploratory Study (Appendix 7). According to the list of "Possible Risk Factors for HCV and HBV" (Attachment 1 to the Appendix 7), all risk factors in the questionnaire are considered in the following major groups and subgroups:

- Collected data will be gathered in a strictly confidential manner and no names will be used in the database of the study.
- The Enhanced Surveillance Program Coordinator will ensure the security and appropriate management of the data maintained in the electronic database.
- As required by Provincial legislation, the information consisting of personal data will be confidentially kept at the Site of the investigation, i.e., at the Public Health Branch of the City of Ottawa.
- When publishing the results or presenting them at scientific meetings, the information provided by all participants will be shown in aggregate form, so, that no individual participant could ever be identified.

Dissemination of Information

- On a regular basis, the site of the investigation (i.e., the Public Health Branch of the City of Ottawa) will be provided with interim and final reports outlining the results of the Study.
- The results of the Study will be made available to the study participants as well.

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Do you have any questions? Yes No

Do you agree to answer these questions about risk factors?

Yes No

*[If no]:** May I ask you what's holding you back from participating: Any particular circumstance or concern that I might clarify for you?

Yes No

[If no]: Thank you and take care *[end of the conversation]*.

[If yes: Please specify and carry on according to circumstances]:

_____

_____

_____

_____

_____

_____

_____

_____

_____

_____

[If yes]: We can do it on the phone now. Is this is an appropriate time to talk to you?

Yes No

[If no]: When would be a convenient time to call you back?

_____

Specify the date/time

Thank you and take care *[end of the conversation]*.

[If yes]: Now, when I've read you the Consent form and got your agreement to participate in the study, we can proceed with the interview over the phone. Let's begin."

[A note for the interviewer: Please refer to the List of Possible Risk Factors while asking specific questions and/or clarifying details.]"

* All instructions in brackets [] and in *Italic* fonts are directed to the interviewers.

1. What kind of medical treatments, tests, or procedures could you have had done prior to your diagnosis with hepatitis B or C that we haven't discussed in our first interview? I am thinking of finger prick tests, EEG, tests where they may have had to stick an instrument into your body, laser treatments, special shots or vaccinations, those kind of things. [*If a woman*: "Have you had special shots when you were pregnant because your baby's blood type is different from your blood type?"].

What kind?	Where		When	How often
	In Canada	Other country (please specify)		
1.				
2.				
3.				
4.				
5.				

2. Back in the 70s, in Ottawa there was a clinic where they paid you to donate part of your blood. They called it plasmapheresis. They would pass your blood through a machine, take the part that they needed and give your blood back to you. Did you ever take part in this?

   Yes No Don't know/can't recall

3. Have you ever undergone any kind of treatment, procedures, or alternative therapies that involved the use of needles or breaking the skin?

   Yes No Don't know/can't recall

   [If yes, please fill out the table below]:

What kind?	Where		When	How often
	In Canada	Other country (please specify)		
1.				
2.				
3.				
4.				
5.				

4. Have you ever undergone any other kind of treatment that might possibly have given you the infection?

Yes No Don't know/can't recall

[If yes, please fill out the table below]:

What kind?	Where		When	How often
	In Canada	In other country (please specify)		
1.				
2.				
3.				
4.				
5.				

5. Have you ever had any other illnesses that would weaken your body as a whole?

Yes No Don't know/can't recall

[If yes, please fill out the table below]:

What	When (year or a period of time)
1.	
2.	
3.	
4.	
5.	

6. Have you ever had any kind of skin conditions (such as eczema or psoriasis)?

Yes No Don't know/can't recall

[If yes, please fill out the table below]:

What	When (year or a period of time)
1.	
2.	
3.	
4.	
5.	

7. Have you ever visited any esthetic places and had electrolysis done, manicures, pedicures, waxing, hair cuts where they use the close shaver?

Yes No Don't know/can't recall

[If yes: Please specify by filling out the table below]

What	How often	Where		When
		At professionals	At home/other (specify)	
Electrolysis				
Manicures				
Pedicures				
Waxing				
Hair cuts				
Other (please specify) 1.				
2.				
3.				

8. Have you ever had done: body piercing? Yes No
tattoos? Yes No
tongue splitting (or lizard tongue)? Yes No

[If yes: Please fill out the table below]

What	Where			When	How many
	Authorized place	Street/ home	Other (please specify: jail etc.)		
Body piercing					
Tattoos					
Lizard tongue					
Other (please specify)					
1.					
2.					
3.					

9. *[Ask these questions for all jobs starting with the most recent]*

What type of work do you do?	Where do you work?	What do you particularly do in your work? (brief description)	How long have you been working there?	When was it? (Dates)
1.				
2.				
3.				
4.				
5.				

10. Have you ever worked in a job where you would get nicks, cuts, burns etc.?

Yes No Don't know/can't recall

[If yes: Please fill out the table below]

What was it?	What kind of a job is/was it?	When was it?
1. Nicks		
2. Cuts		
3. Burns		
Other (please specify): 1.		
2.		
3.		

11. Have you ever or are currently involved in kind of activities (such as sports, hobbies etc.) where you may be apt to get nicks, cuts, burns etc.?

Yes No Don't know/can't recall

[If yes]: Please specify

What	Where	When	How often
1.			
2.			
3.			
4.			
5.			

12. Do you tend to get nicks, cuts, burns, etc. in everyday life?

Yes No Don't know/can't recall

[If yes]: Please specify _____

13. Have you ever been a volunteer firefighter, giver of first aid, etc.?

Yes No Don't know/can't recall

[If yes: Please fill out the table below]

What kind of help did you provide?	When?	For how long?	How often?	Do you remember if during that time:		
				you had a contact with blood/body fluids	cut yourself	got burns
Firefighter						
First aid						
Other (specify): 1.						
2.						
3.						

14. Have you ever acted as a Good Samaritan and come to the help of someone in an accident?

Yes No Don't know/can't recall

[If yes: Please fill out the tables below]

What kind of help did you provide?	When	Where		How often
		In Canada	Other (specify)	
1.				
2.				
3.				
4.				
5.				

Do you remember if during that helping time:	Yes	No	Don't know/ can't recall
You had a contact with blood/body fluids			
Cut yourself			
Got burns			
Other (specify): 1.			
2.			
3.			

15. Were you ever involved in a fight where there was cuts and blood involved?

Yes No Don't know/can't recall

[If yes]: Please specify

What	When	Where		How often
		In Canada	Other (specify)	

16. Have you ever had an accidental needlestick from a hypodermic needle?

Yes No Don't know/can't recall

[If yes]: Please specify

What	When	Where		How often
		In Canada	Other (specify)	

17. Have you ever shared personal articles such as toothbrushes, crack pipes, razors, combs/hairbrushes?

Yes No Don't know/can't recall

[If yes]: Please specify

What	Where	When	How often
1.			
2.			
3.			
4.			
5.			

Was it someone you knew well?

Yes No Don't know/can't recall

Could that person have had Hepatitis B or C?

Yes No Don't know/can't recall

18. Have you ever lived outside of Canada even for a short time?

Yes No Don't know/can't recall

[If yes]: Please specify

Where	When	How long
1.		
2.		
3.		
4.		
5.		

Were any medical or dental procedures done at that time?

Yes No Don't know/can't recall

[If yes]: Please specify

What	Where	When	How often
1.			
2.			
3.			
4.			
5.			

19. Have you ever traveled outside of Canada?

Yes No Don't know/can't recall

[If yes]: Please specify

Where	When	How long
1.		
2.		
3.		
4.		
5.		

Did you have a medical or dental procedure done?

Yes No Don't know/can't recall

[If yes]: Please specify

What	Where	When
1.		
2.		
3.		
4.		
5.		

Now, I will be getting into some questions that may seem to be a little more personal. I'll be also asking about cultural, ceremonial, and sexual behavior as well as about history of physical violence and/or abuse that you might have experienced. These questions specifically relate to how hepatitis is known to spread. If you do not wish to answer any of these questions once they are read, you do not have to do so.

20. In certain cultures, there are home treatments, rituals or ceremonies *[e.g., a Sun Dance ceremony among aboriginals etc.]* that involve cutting the skin, bleeding, burning, that sort of thing. Or as a child some kids got involved with being blood brothers/sisters. Has any of these things ever happened to you?

Yes No Don't know/can't recall

[If yes]: Please specify

What	When	Where
1.		
2.		
3.		
4.		
5.		

21. *[For males - to ask directly;*

For females - to situate the question (such as "In some cultures,...")]:

Are you circumcised? Yes No Don't know/can't recall

[If yes, please specify]:

The country where it was done		The setting		When (how old were you)
In Canada	Other (specify)	In health care facilities (specify: e.g., hospital etc.)	Elsewhere (please, specify)	

22. Can you think of any other ways in your personal life that you might have been infected (such as anal sex, oral sex, etc.)? _____

_____

_____

_____

_____

_____

_____

_____

_____

_____

_____

_____

Specify

23. *[A note for the interviewers: This is a very sensitive question. With this question we might need to be prepared to have floodgates opened: Some people may never have disclosed rape or abuse in the past but by the question being asked now, they may choose to disclose about this painful topic. We have prepared a referral lists and distress center phone ## should such happen: Please see the Attachment 1.]*

This is the last question but it may be a sensitive topic. I am looking at instances where sex may have been forced and/or rough where there may have been blood involved through cuts and tears.

The sex that you have had, was it always with your consent or not ?

Were you ever involved with S&M activities? Yes No Don't know/ can't recall

[If yes]: If you don't mind, please explain what kind of S&M activities were those?

_____
_____
_____
_____
_____
_____
_____
_____
_____
_____
_____
_____

Specify

Have you ever traded sex for money, drugs, shelter, etc.?

Yes No Don't know/can't recall

[If yes]: How often? _____

Specify

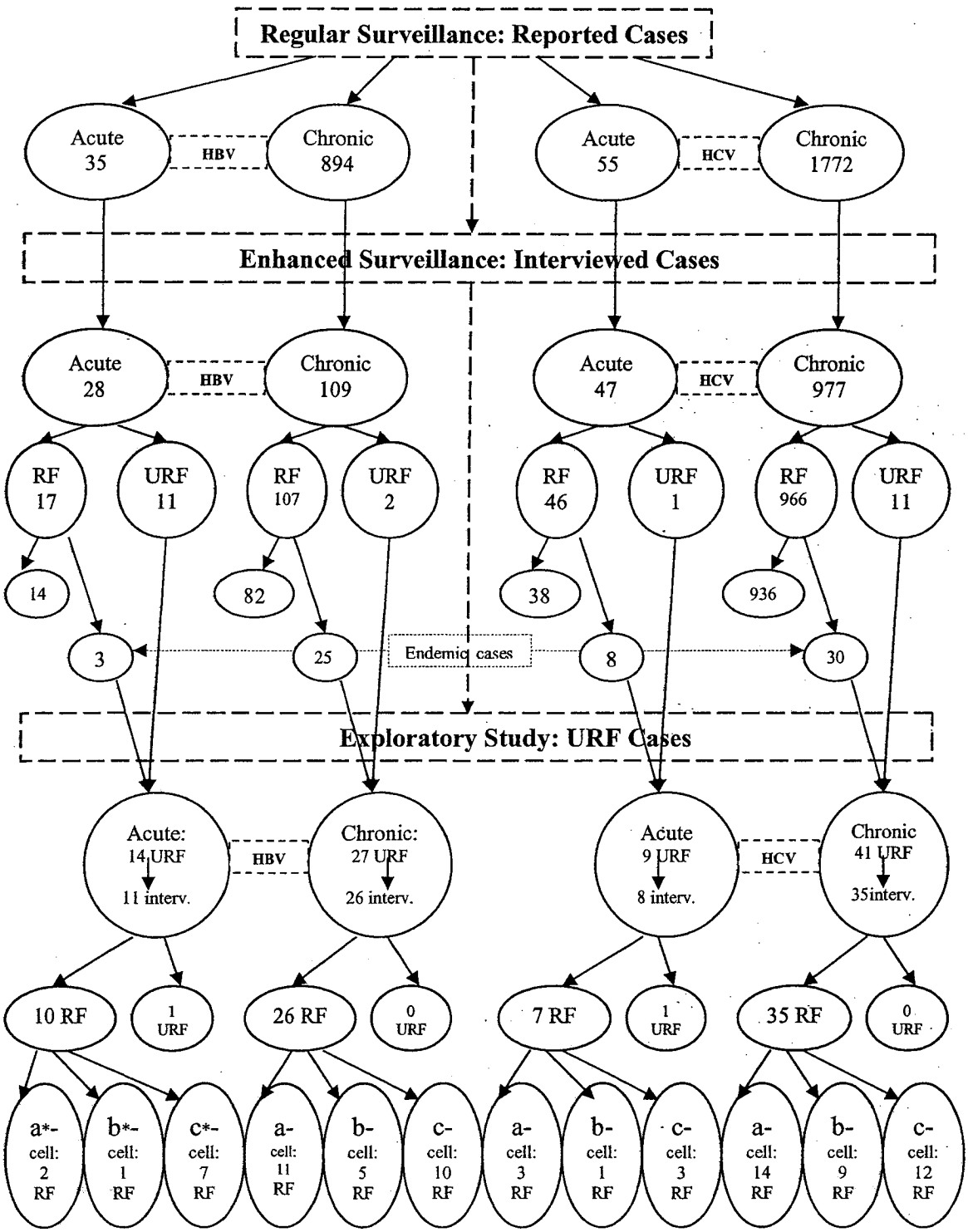
That's it for the questions.

Do you have any questions for me while you have me on the phone?

Thank you very much for your time. Take care.

Appendix V

Schema of numbers of reported/interviewed cases and known/unknown risk factors in Enhanced Surveillance and Exploratory Study



* a-cell = Recognised RFs + Possibly new RFs; b-cell = Recognised RFs only; c-cell = Possibly new RFs only.

Appendix VI

```
/************************** *
Enhanced Surveillance * *
for Newly Identified *
* HBV Data analysis *
*Risk Factor Ranking *
**************************/
```

Algorithm for risk factor ranking

to create mutually exclusive risk factors for acute HBV infection patients

```
if injedrug='Y'
  then acutehbv='injection drug use';
if snortdru='Y' and injedrug ne 'Y'
  then acutehbv='drug snorting';
if transfu='Y' and injedrug ne 'Y' and snortdru ne 'Y'
  then acutehbv='Blood transfusion';
if bloodpro='Y' and injedrug ne 'Y' and snortdru ne 'Y' and transfu ne 'Y'
  then acutehbv='Blood product';
if hesexual='yes multiple' and injedrug ne 'Y' and snortdru ne 'Y'
 and transfu ne 'Y' and blood pro ne 'Y'
  then acutehbv='Heterosexual';
if samesexu='yes MSM' and injedrug ne 'Y' and snortdru ne 'Y'
 and transfu ne 'Y' and bloodpro ne 'Y' and hesexual ne 'yes multiple'
  then acutehbv='MSM';
if sexhepb='Y' and injedrug ne 'Y' and snortdru ne 'Y'
 and transfu ne 'Y' and blood pro ne 'Y' and hesexual ne 'yes multiple'
 and samesexu ne 'yes MSM'
  then acutehbv='Sex with Hep B carrier';
if tattooed='Y' and injedrug ne 'Y' and snortdru ne 'Y'
 and transfu ne 'Y' and bloodpro ne 'Y' and hesexual ne 'yes multiple'
 and samesexu ne 'yes MSM' and sexhepb ne 'Y'
  then acutehbv='T attooing';
if pierced='Y' and injedrug ne 'Y' and snortdru ne 'Y'
  and transfu ne 'Y' and blood pro ne 'Y' and hesexual ne 'yes multiple'
  and samesexu ne 'yes MSM' and sexhepb ne 'Y' and tattooed ne 'Y'
  then acutehbv='piercing';
if acupunct='Y' and injedrug ne 'Y' and snortdru ne 'Y'
  and transfu ne 'Y' and blood pro ne 'Y' and hesexual ne 'yes multiple'
  and samesexu ne 'yes MSM' and sexhepb ne 'Y' and tattooed ne 'Y'
  and pierced ne 'Y'
   then acutehbv='Acupuncture';
if blodcont='Y' and injedrug ne 'Y' and snortdru ne 'Y'
  and transfu ne 'Y' and bloodpro ne 'Y' and hesexual ne 'yes multiple'
  and samesexu ne 'yes MSM' and sexhepb ne 'Y' and tattooed ne 'Y'
 and pierced ne 'Y' and acupunct ne 'Y'
   then acutehbv='Blood contact';
if hemodial='Y' and injedrug ne 'Y' and snortdru ne 'Y'
  and transfu ne 'Y' and bloodpro ne 'Y' and hesexual ne 'yes multiple'
  and samesexu ne 'yes MSM' and sexhepb ne 'Y' and tattooed ne 'Y'
  and pierced ne 'Y' and acupunct ne 'Y' and blodcont ne 'Y'
   then acutehbv='Haematolysis';
if carrihep='Y' and injedrug ne 'Y' and snortdru ne 'Y'
  and transfu ne 'Y' and blood pro ne 'Y' and hesexual ne 'yes multiple'
  and samesexu ne 'yes MSM' and sexhepb ne 'Y' and tattooed ne 'Y'
  and pierced ne 'Y' and acupunct ne 'Y' and blodcont ne 'Y'
  and hemodial ne 'Y'
   then acutehbv='Hep B in family';
```

```
if institut='Y' and injedrug ne 'Y' and snortdru ne 'Y'
  and transfu ne 'Y' and bloodpro ne 'Y' and hesexual ne 'yes multiple'
  and samesexu ne 'yes MSM' and sexhepb ne 'Y' and tattooed ne 'Y'
  and pierced ne 'Y' and acupunct ne 'Y' and blodcont ne 'Y'
  and hemodial ne 'Y' and carrihep ne 'Y'
   then acutehbv='institution';
if hospital='Y' and injedrug ne 'Y' and snortdru ne 'Y'
  and transfu ne 'Y' and blood pro ne 'Y' and hesexual ne 'yes
  multiple' and samesexu ne 'yes MSM' and sexhepb ne 'Y' and
  tattooed ne 'Y' and pierced ne 'Y' and acupunct ne 'Y' and blodcont
  ne 'Y'
  and hemodial ne 'Y' and carrihep ne 'Y' and institut ne 'Y'
   then acutehbv='Hospitalization';
if surgery='Y' and injedrug ne 'Y' and snortdru ne 'Y'
  and transfu ne 'Y' and blood pro ne 'Y' and hesexual ne 'yes
  multiple' and samesexu ne 'yes MSM' and sexhepb ne 'Y' and
  tattooed ne 'Y' and pierced ne 'Y' and acupunct ne 'Y' and blodcont
  ne 'Y'
  and hemodial ne 'Y' and carrihep ne 'Y' and institut ne 'Y'
  and hospital ne 'Y'
   then acutehbv='surgery';
if organtis='Y' and injedrug ne 'Y' and snortdru ne 'Y'
  and transfu ne 'Y' and bloodpro ne 'Y' and hesexual ne 'yes multiple'
  and samesexu ne 'yes MSM' and sexhepb ne 'Y' and tattooed ne 'Y'
  and pierced ne 'Y' and acupunct ne 'Y' and blodcont ne 'Y'
  and hemodial ne 'Y' and carrihep ne 'Y' and institut ne 'Y'
  and hospital ne 'Y' and surgery ne 'Y'
   then acutehbv='organ transplant';
if dental='Y' and injedrug ne 'Y' and snortdru ne 'Y'
  and transfu ne 'Y' and blood pro ne 'Y' and hesexual ne 'yes
  multiple' and samesexu ne 'yes MSM' and sexhepb ne 'Y' and
  tattooed ne 'Y' and pierced ne 'Y' and acupunct ne 'Y' and blodcont
  ne 'Y'
  and hemodial ne 'Y' and carrihep ne 'Y' and institut ne 'Y'
  and hospital ne 'Y' and surgery ne 'Y' and organtis ne 'Y'
   then acutehbv='Dental visit';
if prison='Y' and injedrug ne 'Y' and snortdru ne 'Y'
  and transfu ne 'Y' and blood pro ne 'Y' and hesexual ne 'yes
  multiple' and samesexu ne 'yes MSM' and sexhepb ne 'Y' and
  tattooed ne 'Y' and pierced ne 'Y' and acupunct ne 'Y' and blodcont
  ne 'Y'
  and hemodial ne 'Y' and carrihep ne 'Y' and institut ne 'Y'
  and hospital ne 'Y' and surgery ne 'Y' and organtis ne 'Y'
  and dental ne 'Y'
   then acutehbv='prison';
if prison ne 'Y' and injedrug ne 'Y' and snortdru ne 'Y'
  and transfu ne 'Y' and blood pro ne 'Y' and hesexual ne 'yes
  multiple' and samesexu ne 'yes MSM' and sexhepb ne 'Y' and
  tattooed ne 'Y' and pierced ne 'Y' and acupunct ne 'Y' and blodcont
  ne 'Y'
  and hemodial ne 'Y' and carrihep ne 'Y' and institut ne 'Y'
  and hospital ne 'Y' and surgery ne 'Y' and organtis ne 'Y'
  and dental ne 'Y'
   then acutehbv='unknown'.
```

Appendix VII

Table of distribution of cases of the Exploratory Study by country of birth:

1) Acute and chronic HBV

Country of Birth		Acute HBV		Chronic HBV	
		N	%	N	%
Africa	Burundi	0		1	
	Djibouti	1		0	
	Kenya	0		1	
	Somali	1		0	
	Tanzania	0		1	
	Zaire	0		1	
	Total	2	18.2	4	15.4
Asia	China	0		1	
	India	1		0	
	Malaysia	0		1	
	Philippines	1		2	
	Vietnam	1		4	
	Total	3	27.3	8	30.8
Carribean	Haiti	1		2	
	Jamaica	0		0	
	Total	1	9.1	2	11.1
Europe	Bulgaria	0		1	
	Italy	0		1	
	Netherlands	1		0	
	Romania	0		1	
	Russia	1		1	
	Spain	1		0	
	Total	3	27.3	4	15.4
Middle East	Egypt	-		0	
	Iran	-		2	
	Iraq	-		2	
	Total	0	-	4	15.4
Canada		2	18.2	4	15.4
Total		11	100.0	26	100.0

2) Acute and chronic HCV.

Country of Birth		Acute HCV		Chronic HCV	
		N	%	N	%
Africa	Burundi	1		0	
	Congo	0		2	
	Rwanda	0		3	
	Somali	0		1	
	Tanzania	0		1	
	Zaire	0		1	
	Total	1	12.5	8	22.9
Asia	Bangladesh	-	-	1	
	Burma	-	-	1	
	China	-	-	0	
	India	-	-	0	
	Taiwan	-	-	1	
	Vietnam	-	-	3	
	Total	0	0	6	17.1
Carribean	Haiti	-	-	1	
	Jamaica	-	-	1	
	Martinique	-	-	1	
	Total	0	0	3	8.6
Europe	UK	1		0	
	(England)	0		1	
	Germany	0		2	
	Italy	0		4	
	Russia	1	12.5	7	20
	Total				
Middle East	Egypt	0	0	1	
	Kuwait			1	
	Total			2	5.7
Canada		6	75	9	25.7
Total		8	100	35	100

Appendix VIII
Table of characteristics of acute/chronic HBV and HCV cases with potential new risk factors identified at the Exploratory Study

1) Acute and chronic HBV

N	Age	Sex	Country of birth & Immigration date	Risk factors identified at Exploratory Study	
				1. Potential new risk factors	2. Recognized risk factors
Acute HBV cases					
1 c	52	F	India; May 1999	Medical procedure (cortisone injections) in rural India	None
2 c	46	M	Canada	Sex with prostitute in December, 1998 (broken condom)	None
3 c	32	F	Djibouti; Aug.1998	Medical procedure (Mantoux test in December, 1998)	None
4 c	33	M	Canada	Sexual partner previously vaccinated against HBV; Other work related (computer technician in Alert Military Base[1] in July-September, 1999)	None
5 c	35	M	Philippines; 1993	HBV vaccination in 1999 (for work purpose); Other work related & Frequent nicks & cuts (waste disposal truck driver)	None
6 c	56	M	Netherlands; As a child	Travel to endemic zone (South Africa, 9 months ago[2]); Other work related (correctional services)	None

1 There is a relatively high prevalence of HBV in the Alert Base because of closeness of aboriginal population, and as a computer technician he is exposed to nicks and cuts.

2 Usually, the cut off point for HBV infection is 6 months, but in some cases it can be extended to until 9-12 months.

7 c	21	M	Somali; 1995	Other work related & Frequent nicks and cuts (assembly job at JDS Uniphase in December, 2000 - August, 2001); Visitors from endemic zone (Saudi Arabia, in October, 2000)	None
8 a	49	M	Spain; 1975	Vaccination with HBV dormant cells due to immune suppression; Immunocompromised (anaemia)	Blood transfusion & Organ transplant (bone marrow) & Hospitalization in Ottawa, 1998
9 a	22	M	Russia; December, 1998	Sex with prostitute (in Russia)	Sex with multiple partners & Sex with carrier in fall, 1998
Chronic HBV cases					
1 c	24	F	Haiti; 1993	Health care work related (nurse in Haiti)	None
2 c	56	M	Bulgaria; 1990	Medical procedures (vaccinations and blood tests in Bulgaria); Blood contact & Car accident in Iraq in 1980s	None
3 c	37	M	Iran; 1989	Medical procedures (tests, vaccinations, I/M penicillin) & Circumcision in Iran; Good Samaritan (help to a fight victim in Iran, in mid 1980s)	None
4 c	20	F	Zaire; 1994	Medical procedures (vaccinations in Zaire)	None
5 c	40	M	Iran; 1994	Medical procedures (vaccinations) & Circumcision (at home) in Iran	None
6 c	33	F	Vietnam; 1987	Medical procedures (vaccinations & therapeutic abortion in Vietnam)	None
7 c	50	M	China; 1964	Blood donation in Hong Kong; Living in endemic zones (in Hong Kong & in Guatemala, in 1998)	None

8 c	25	M	Kenya; 1999	Medical procedures (blood tests/ vaccinations) & Circumcision in Kenya; Health care work related (paramedic-St-John's Ambulance); Other work related (construction in Kenya); Aesthetics (cut by a barber & a hairdresser in Kenya)	None
9 c	46	M	Philippines; 2000	Medical procedures (vaccinations) & Blood donation in Philippines; Comorbid disease (STD[3])	None
10 c	38	M	Philippines; 1990	Sexual (men sex with men with sado-masochistic elements)	None
11 a	23	M	Russia; 2000	Medical procedures (vaccinations and blood tests in Russia)	Sex with multiple partners (4); Dental surgery (extraction)
12 a	68	M	Italy; 1995	Medical procedures (vaccinations, blood tests in Italy)	Hospitalization & Surgery (hernia at Ottawa Civic 20 years ago); Dental (surgery, dentures)
13 a	26	F	Malaysia; 1998	Medical procedures (vaccination in Malaysia)	Hospitalization & Blood transfusion (for tubal pregnancy in June, 2000); Dental cleaning
14 a	38	M	Burundi; 1991	Health care work related (nurse in Burundi and health aid for developmentally disabled in Canada); Frequent nicks and cuts (with knives/ razors); Circumcision in Burundi	Acupuncture; Dental (root canal, extraction) in Burundi and in Canada

[3] History of sexually transmitted disease (STD) is an indicator of irregular sexual life and multiple sexual partners, and is interpreted here as a potential sexual exposure.

15 a	31	F	Haiti; 1974	Medical procedures (vaccinations in Haiti)	Sex with multiple partners (5); Body piercing (at home); Hospitalization & Surgery (in Canada, in 1997); Dental surgery
16 a	55	M	Tanzania; 1985	Cultural/Ceremonial (cutting with blades & knives); Circumcision in Tanzania; Immunocompromised (HCV+)	Blood transfusion; Hospitalization; Dental surgery & cleaning
17 a	68	F	Canada	Aesthetics (cut by a hairdresser); Other work related (hospital laundry room, in Ottawa)	Blood transfusion (in 1956, 1963); Sex with carrier & Carrier in family (husband); Body piercing (ears); Hospitalization; Surgery; Dental (extraction, deep cleaning, dentures,)
18 a	72	M	Canada	Other work related (housekeeping in hospital laundry, in Ottawa)	Homosexual contact (men sex with men, 20-30 years ago); Sex with carrier & Carrier in family (wife); Hospitalizations & Surgeries (tonsilectomy, hernia, kidney stone in 1992); Dental (surgery, root canal, dentures)
19 a	49	F	Canada	Aesthetics (cut by a hairdresser, artificial acrylic nails in January, 2001); Immunocompromised (diabetes for 15 years, on insulin for 11 years)	Body piercing (ears); Hospitalizations & Surgeries (hernia, hysterectomy in 1978, 1985); Dental (oral surgery, root canal, tooth extraction)

20 a	39	M	Vietnam; 1993	Medical procedures (vaccinations and blood tests in Vietnam)	Sex with carrier & Carrier in family (wife)
21 a	36	F	Vietnam; 1996	Medical procedures (vaccinations and blood tests in Vietnam)	Sex with carrier & Carrier in family (husband); Dental (root canal, extraction)

2) Acute and chronic HCV.

N	Age	Sex	Country of birth & Immigration date	Risk factors identified at the Exploratory Study	
				1. Potential new risk factors	2. Recognized risk factors
Acute HCV cases					
1 c	52	F	Canada	Medical procedure (IV injections for cellulitis at Queensway Carleton Hospital, Bradson HomeCare & Riverside Urgent Care in July 2001); Other work related (5 years as an administrative assistant in Director's office in prison); Immunocompromised (breast cancer in March, 2000)	None
2 c	31	M	Canada	Sex with prostitute; Sado-masochistic sex; Comorbid disease (STD[1])	None
3 c	62	F	Burundi; October, 2001	Ethnic wars in Rwanda/Burundi	None
4 a	42	F	Canada	Health care worker	IDU (shared equipment); Snorting

[1] History of sexually transmitted disease (STD) is an indicator of irregular sexual life and multiple sexual partners, and is interpreted here as a potential sexual exposure.

5 a	50	F	England; 1953	Medical procedure (breast biopsy); Health care worker (mental health outreach); Frequent nicks and cuts; Sex with multiple partners (5); Immunocomrpomised (breast cancer)	IDU (shared equipment, Feb-Oct 2000); Sex with carrier (Feb-Oct 2000); Carrier in family (partner)
6 a	46	F	Canada	Sex with IDU; Other work related (in catering at Nortel)	Snorting; Tattoos (November, 2000); Sex with carrier (husband)
Chronic HCV cases					
1 c	47	M	Egypt; 1994	Blood donation & Circumcision (in Egypt); Living and working in endemic zones (in Eastern Berlin in 1983 & in Beijing in 1989-1993; a diplomat)	None
2 c	54	M	Congo; 1988	Medical procedure & Cultural/ Ceremonial (razor blades) & Circumcision in Congo; Living in endemic zone (Italy); Comorbid (STD)	None
3 c	41	F	Canada	Sex with IDU (partner); Comorbid disease (STD)	None
4 c	52	M	Canada	Good Samaritan (first aid to a stubbed victim); Other work related (satellite dish installer); Frequent nicks and cuts	None
5 c	31	F	Rwanda; May, 2001	Blood donation & Cultural/Ceremonial (razor blades) in Rwanda; Comorbid disease (STD)	None
6 c	47	M	Canada	Sex with an IDU; Comorbid disease (mental illness[2])	None

[2] Persons suffering from a mental illness might be more exposed to nicks, cuts, burns and to accidental injuries in general.

7 c	29	M	Jamaica; 1996	Frequent nicks and cuts (needle/lancet finger pricks in Jamaica); Other work related (cleaner in an office building); Travel to England (in June 2000); Immunocompromised (Sickle cell anaemia)	None
8 c	56	F	Rwanda; July, 2000	Medical procedures (vaccinations, blood tests, hypodermic needles) in Rwanda	None
9 c	36	M	Rwanda; August, 2001	Cultural rituals & Circumcision & Sex with prostitutes in Rwanda; Other work related (airline pilot[3]); Immunocompromised (HIV+)	None
10 c	32	M	Bangladesh ; 1990	Medical procedures (vaccination, blood tests) & Circumcision in Bangladesh	None
11 c	49	F	Haiti; 1970	Medical procedures (vaccinations) in Haiti; Health care worker (RNA, health care aid for agency)	None
12 c	42	M	Vietnam; 1980	Medical procedures (vaccinations) & Circumcision in Vietnam	None
13 a	51	M	Canada	Sex with multiple partners[4] (200); Other work related (water purification for City of Ottawa); Circumcision in Canada; Good Samaritan (helped in car accidents and home fire in Canada); Travel into endemic zones (Eastern Europe, Asia, Carribean)	Hospitalization; Surgery (tonsilectomy as a child); Dental (surgery, root canal, cleaning)

[3] The occupation of an airline pilot involves frequent travel into endemic zones as well as assumes potential sexual exposure due to irregular sexual life.

[4] Since the sexual exposure is not considered as a major mode of transmission for HCV infection in contrast to HBV infection, the history of multiple sexual partners wasn't defined as a risk factor for HCV infection at the stage of the Enhanced Surveillance as it was done for HBV infection. Therefore, in the results of the Exploratory Study, the category of multiple sexual partners is classified as a potentially new risk factor.

14 a	31	M	Russia; October, 1999	Medical procedures (vaccinations and blood tests) in Russia	Hospitalization, Surgery & Blood transfusion (for gun shot wound in early 90s); Dental surgery; all in Russia
15 a	68	M	Martinique; 1969	Immunocompromised (Sickle cell anemia) & Comorbid disease (STD)	Hospitalization & Surgery in Quebec (in 1969); Dental (surgery, extractions, dentures etc.)
16 a	46	F	Canada	Other work related (First Aid in Loblaw's); Frequent cuts and nicks; Immunocompromised (diabetes)	Body piercing; Acupuncture; Hospitalization; Surgery (back, gallbladder etc.); Dental surgery
17 a	77	M	Germany; 1960	Ceremonial (blood letting) & Other work related (technician in construction) in Germany	Blood transfusion; Hospitalization; Surgery; Dental (extractions, root canals, dentures)
18 a	48	F	Taiwan; 1988	Medical procedures (vaccinations in Taiwan); Work related (kindergarten aid in Taiwan); Good Samaritan (first aid to a bleeding person in Taiwan); Living in Japan	Hospitalization & Surgery in Taiwan; Dental surgery in Canada
19 a	49	M	Canada	Medical procedures (plasmapheresis)	Blood product; Acupuncture; Hospitalization; Surgery; Dental surgery

20 a	50	F	Canada	Multiple sexual partners (12); Immunocompromised (diabetes & cancer)	Hospitalization; Surgery (cholecystectomy and partial hysterectomy in 1970-s); Dental (extraction, root canal, cleaning)
21 a	72	F	Italy; 1956	Medical procedures (radio-isotope treatment for thyroid in Canada, in 1996); Immunocompromised (type II diabetes & thyroid)	Hospitalization & Blood transfusion for miscarriage in Italy, in early 50s.
22 a	55	M	Tanzania; 1982	Blood donation & Cultural/ Ceremonial (use of razor blades in family) in Tanzania; Multiple sexual partners (10); Living in UK (1 year); Immunocompromised (HBV+)	Hospitalization and Surgery in Tanzania; Dental visits (extraction, cleaning) in Canada.)
23 a	72	F	Congo; 1980	Cultural/Ceremonial (cutting with blades & knives) in Congo	Blood transfusion; Hospitalization; Dental surgery, dentures
24 a	60	M	Zaire; 1996	Medical procedures (vaccinations) & Blood donation in Zaire; Living in Belgium for several years; Immunocompromised (prostate cancer)	Acupuncture; Hospitalization; Surgery (prostate biopsy in 2001)
25 a	38	M	Russia; 1995	Medical procedures (vaccinations and blood tests) & Sex with multiple partners (5) in Russia	Acupuncture; Dental surgery in Russia & root canal in Canada
26 a	35	M	Burma; 1998	Sex with IDU; Blood donation in Burma	Snorting; Tattoo; Prison in Thailand

Appendix IX

Table of distribution of demographic characteristics of "c" and "a"-cell cases for acute/chronic HBV and HCV patients with potential new risk factors identified by the Exploratory Study.

Demographic characteristics		Acute HBV		Chronic HBV		Acute HCV		Chronic HCV	
		"c"-cell	"a"-cell	"c"-cell	"a"-cell	"c"-cell	"a"-cell	"c"-cell	"a"-cell
		N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)
Age	0 - 19	-	-	-	-	-	-	-	-
	20-39	4 (57.1)	1 (50.0)	6 (0.6)	6 (54.5)	1 (33.3)	-	4 (33.3)	3 (25.0)
	40-59	3 (42.9)	1 (50.0)	4 (0.4)	2 (18.2)	1 (33.3)	3 (100.0)	8 (66.7)	6 (42.9)
	60+	-	-	-	3 (27.3)	1 (33.3)	-	-	5 (35.7)
Gender	Male	5 (71.4)	2 (100.0)	7 (0.7)	6 (54.5)	1 (33.3)	-	8 (66.7)	9 (64.3)
	Female	2 (28.6)	-	3 (0.3)	5 (45.5)	2 (66.7)	3 (100.0)	4 (33.3)	5 (35.7)
Birth place	Africa	2 (28.6)	-	2 (0.2)	2 (18.2)	1 (33.3)	-	5 (41.7)	4 (28.6)
	Asia	2 (28.6)	-	4 (0.4)	3 (27.3)	-	-	2 (16.7)	1 (7.1)
	Canada	2 (28.6)	-	-	3 (27.3)	2 (66.7)	2 (66.7)	3 (25.0)	4 (28.6)
	Carib-bean	-		1 (0.1)	1 (9.1)	-	-	2 (16.7)	1 (7.1)
	Europe	1 (14.3)	2 (100.0)	1 (0.1)	2 (18.2)	-	1 (33.3)	-	4 (28.6)
	Middle East	-	-	2 (0.2)	-	-	-	-	-
Total		7	2	10	11	3	3	12	14