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Recommendations for the Public Health Response to Hepatitis C in Ontario

Provincial Infectious Diseases Advisory Committee on Communicable Diseases

July 2014

Public Health Ontario

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NOTE: This document is intended to provide guidance for public health practice. Public health units are encouraged to work with these recommendations in an effort to improve the public health response to hepatitis C.

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PIDAC also acknowledges the staff in Ontario's public health units who completed our hepatitis C information needs survey, and Dr. Liane MacDonald and a myriad of agencies for their input on the current document.

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Preamble

How and When to Use This Document

This document is primarily for the use of staff in Ontario public health units; it is intended to provide them with current recommendations for responding to hepatitis C.

These recommendations are meant to support public health staff in hepatitis C programs in accordance with the *Ontario Public Health Standards* and the *Sexual Health and Sexually Transmitted Infections Prevention and Control Protocol*.

This document is also intended for decision-makers who are responsible for program policies and resource allocations (e.g. medical officers of health, associate medical officers of health and program managers). It may also be of interest to other health care providers who work in the field.

This document was developed in consideration of the Ontario Hepatitis C Strategy, which was developed by the Ontario Hepatitis C Task Force and endorsed by the Ministry of Health and Long-Term Care. The Ontario Hepatitis C Strategy is based on information obtained during 13 community consultations held across Ontario with stakeholder representation, including Aboriginal health and social services, social service agencies, health care providers, correctional facilities and people living with/affected by the hepatitis C virus. The Ontario Hepatitis C Strategy builds on existing programs and supports new initiatives that focus on hepatitis C care and treatment in four key areas: enhanced services and supports; prevention; education and outreach; and better coordination.

FOR RECOMMENDATIONS IN THIS DOCUMENT:

Shall: Indicates mandatory recommendations based on legislated requirements or national standards (e.g., Canadian Standards Association).

Must: Indicates best practice (e.g., the standard of care based on current recommendations in the medical literature).

Should: Indicates a recommendation that is advised but not mandatory.

May: Indicates an advisory or optional statement.

Evidence for Recommendations

The recommendations in this document were developed by the Provincial Infectious Diseases Advisory Committee (PIDAC) Hepatitis C Working Group, based on a review of published and unpublished literature and on the expertise of the working group.

Assumptions and General Principles

Hepatitis C programs in Ontario operate within the legal framework provided by the *Health Protection and Promotion Act*. This recommendations document addresses public health practices within the existing legal framework.

Abbreviations

ALT	Alanine aminotransferase
aOR	Adjusted odds ratio
CDC	Centers for Disease Control and Prevention
CI	Confidence interval
HBV	Hepatitis B virus
HCV	Hepatitis C virus
HPPA	*Health Protection and Promotion Act*
HIV	Human immunodeficiency virus
IDU	Injection drug use
MSM	Men who have sex with men
NIH	National Institutes of Health
PHAC	Public Health Agency of Canada
PHU	Public health unit
RNA	Ribonucleic acid
STI	Sexually transmitted infection
USPSTF	United States Preventive Services Task Force
WHO	World Health Organization

Glossary of Terms

Term	Description
Adjusted odds ratio (aOR)	An odds ratio calculated when other potential confounders are controlled for in a multivariate statistical model.
Adjusted relative risk	A relative risk adjusted for confounding factors.
Alanine aminotransferase (ALT)	A liver enzyme used as a marker to screen for possible acute or chronic liver inflammation. This is a non-specific test; further testing is required to determine the presence of specific hepatitis infections or other liver diseases.
Case	A person who has been diagnosed with hepatitis C.
Case management	Appropriate counselling, testing and referral for treatment for those who are eligible and willing. It also includes contact tracing, as appropriate.
Contact	A person who has had significant or repeated direct or indirect blood-to-blood exposure to an individual who is newly or chronically infected with hepatitis C; this includes an infant born to an infected mother. Direct exposures (such as sharing injection equipment) carry the highest risk of transmission. Indirect exposures or exposures that may involve only minute quantities of blood (e.g. sexual contact or sharing personal-hygiene items) carry a much lower risk. Casual contact, such as shaking hands, speaking with or being in the same room with an infected person does not constitute exposure.
Contact tracing	The process of identifying relevant contacts of a person with an infectious disease. The purposes of contact tracing are to ensure that contacts are aware of their exposure, encourage contacts to be tested, and facilitate epidemiological investigation of disease clusters. For blood-borne infections (human immunodeficiency virus, hepatitis B and hepatitis C), contact tracing involves needle- and drug equipment–sharing contacts, transfusion recipients and those who may have been exposed to blood by other means, as well as those with relevant sexual exposures. In the case of hepatitis C, this refers to higher-risk sexual exposures involving possible blood contact (see Chapter 3, Modes of Transmission and Infection Risks).
Chronic case	A person infected with hepatitis C who does not clear the virus within six months.
Harm reduction	Public health policies, programs and practices intended to reduce the risk of negative consequences associated with specific behaviours. In this document, harm reduction focuses on strategies to decrease the risk of hepatitis C virus transmission.
Higher-risk sexual behaviour	Sexual practices that may cause bleeding or abrasions, resulting in blood-to-blood contact between participants. Examples may include unprotected anal intercourse, fisting, the use of sex toys, rough sex, unprotected sex between participants with open lesions from a sexually transmitted infection, sex during menstruation, or unprotected oral sex in the presence of open sores, abrasions or bleeding ulcers from smoking crack (“crack mouth”), etc. The risk of infection is also known to be increased among those infected with

Term	Description
	human immunodeficiency virus (HIV). The risk of heterosexual transmission in the absence of the above activities among people who are not infected with HIV is generally thought to be low.
HIV/HCV co-infection	The coexistence of human immunodeficiency virus and chronic hepatitis C infection in the same person.
Index case	The first person to be identified with an infection in a disease outbreak or cluster. The index case may or may not have infected others, but he or she represents a starting point for the process of contact tracing.
Newly acquired case	A person recently infected (within the previous 24 months).
Primary case	The person who introduces an infection into a group of people. The primary case may or may not be the index case. The primary case for a cluster of infections may never become apparent.
Safer inhalation (drug use) equipment	Pipes, straws etc. used for smoking or snorting drugs. For this document, the focus will be on equipment used for smoking drugs such as crack and methamphetamine: rubber mouthpieces, stems and brass screens. These are considered "safer" because they are less likely to cause cuts, burns or other injuries. Safer use also requires that each person has his/her own equipment and does not share. Alternative equipment, such as medicinal inhalers, car antennae, pop cans, metal pipes, Brillo pads for screens etc. are not considered safer, even if they are not shared, because of the injury risk they pose.
Safer injection drug use	The administration of injectable drugs in a way that substantially reduces the risk of transmission of human immunodeficiency virus (HIV), hepatitis B and hepatitis C. Safer injecting is possible only if hands remain clean. Injecting equipment (including mixing implements, water and filters) should never be shared, and hands touching the equipment should not be contaminated with blood. Reusing equipment that has been cleaned with bleach is not completely safe and not recommended, as both HIV and hepatitis C are known to have been transmitted despite bleaching.
Seroconversion	Development of an antibody response to an infectious agent, so that tests of serum that were previously negative are now positive.
Sustained virological response (SVR)	Undetectable levels of the virus six months after the cessation of hepatitis C therapy.
Trace-back period	The period prior to diagnosis for which a case is asked to identify contacts for contact tracing.
Unsafe injection drug use practices	Using previously used needles or other injection equipment (such as cookers, filters, water etc.) that may contain even minute quantities of blood. Sharing of any of these items is considered unsafe.

Executive Summary

Hepatitis C virus (HCV) causes chronic infection that is responsible for a significant burden of illness worldwide. In Ontario, it has been associated with the highest burden of any communicable disease. It is therefore essential that the public health response to hepatitis C be as effective as possible.

Hepatitis C is a blood-borne infection. It was once related to the receipt of blood or blood products, but since the introduction of blood donor screening, this source of infection has become extremely rare. The majority of new hepatitis C infections in Canada and other developed countries occur via the sharing injection equipment and other forms of direct or indirect blood-to-blood contact. Preventive measures aimed at minimizing unsterile injections (such as harm-reduction programs that distribute sterile needles and other injection equipment) have been successful in reducing the transmission of the human immunodeficiency virus (HIV), but have had less impact on hepatitis C. Nevertheless, they remain important components of the overall response to blood-borne infections.

In 2010, 4,512 new cases of hepatitis C were reported in Ontario. Reported cases are either newly acquired or chronic infections that were acquired in the past but have only recently been diagnosed. Modelled estimates suggest that the true incidence of new cases is increasing slightly. Modelling also suggests that in the absence of effective interventions, a large number of people will experience the sequelae of chronic hepatitis C in the coming years, including cirrhosis, liver failure, hepatocellular carcinoma and liver transplantation, as well as many hepatitis C-related deaths. It should be possible to significantly reduce these outcomes by ensuring effective treatment through screening, diagnosis, improved access to treatment initiation and well-managed therapy. New treatments have much higher success rates than older therapies.

For surveillance purposes, anyone reported as positive for hepatitis C antibodies is considered to be a case, since he or she has evidence of being infected at some point in the past. However, to effectively counsel cases, determine the need for treatment and prevent further transmission, those who are positive for HCV antibodies must also be tested to determine the presence of HCV RNA. At least 15 per cent of those who become infected with HCV will spontaneously clear the virus, becoming RNA-negative. These cases will remain antibody-positive but are no longer at risk for transmission and do not require treatment. They can become re-infected with further exposure to HCV, however, and need to be counselled accordingly. The best science to date suggests that cases who are RNA-negative following successful treatment remain antibody-positive but are not infectious; however, they are also at risk for re-infection if exposed again.

Hepatitis C–infected cases are often at increased risk for other blood-borne infections, such as HIV and hepatitis B, and may also be at risk for sexually transmitted infections because of lifestyle factors. Technical difficulties and data-sharing barriers must be resolved to ensure effective surveillance of co-infections for case management and other program purposes.

Since many cases with chronic hepatitis C can be asymptomatic for years and remain unaware of their infection, screening is required to identify these individuals. Public health providers should offer or encourage/facilitate screening for those at risk as a result of the following:

- Previous or current unsafe injection drug use practices
- Sharing of intranasal or inhalation equipment
- Receipt of blood, blood products or organs prior to 1990
- Receipt of a tattoo or piercing in a setting where the equipment may not have been sterile
- Sharing items that may become contaminated with blood of a hepatitis C–infected person (e.g. razors, nail clippers or toothbrushes)

- Infection with HIV or hepatitis B
- High-risk sexual behaviour (i.e. involving potential for blood-to-blood contact) with a hepatitis C case or a current or former injection drug user
- Blood-to-blood contact with a person who has hepatitis C, including infants born to mothers with hepatitis C
- Immigration from high-prevalence countries

It is also reasonable to suggest that those at significant ongoing risk be tested at least annually. The United States Centers for Disease Control and Prevention has recommended general population screening for adults in the 1945–1965 birth cohort. However, the estimated prevalence of undiagnosed hepatitis C in Canada is substantially lower than in the United States; the appropriateness of this approach for Canada cannot be assumed, but it should be assessed.

Public health units have a key role to play in the investigation and management of newly reported hepatitis C cases. As part of the initial investigation, all clients should be encouraged to undergo RNA testing (if it has not already been done) to determine whether they have active infection or have cleared the virus (spontaneously or through treatment). Cases infected within the preceding two years are the highest priority for follow-up because of the greater opportunity to identify sources of infection and prevent transmission to others. Public health providers should endeavour to find new infections by taking histories and working with the public health laboratory. For newly acquired infections in particular, detailed inquiries should be made about possible exposures, and further investigations should be undertaken if appropriate. Cases should be educated about how to avoid transmission to others, and known contacts who may have had blood-to-blood exposure during the period of infection should be informed and offered testing. Cases should also be assessed for drug and alcohol use and offered counselling, referrals and harm-reduction measures as appropriate. Other needs—including housing, social support, mental health care etc.—should also be assessed and appropriate referrals offered. Where services are unavailable or unable to meet clients' needs, public health can advocate for service improvements.

There is also a role for public health, in partnership with local corrections authorities and others, to help to ensure the availability of hepatitis C education, counselling, testing and support for inmates in their jurisdiction. Public health should also work to ensure that inmates being paroled or released to the community have information and referrals related to harm-reduction programs, hepatitis C treatment services and other available supports.

There is some evidence to suggest that Aboriginal people have a higher prevalence of hepatitis C, and public health units should seek to ensure effective access to harm-reduction and treatment programs, including appropriate coordination and continuity with federal on-reserve care for Aboriginal people who live off-reserve.

There is also evidence that street-involved youth are at increased risk for hepatitis C infection. Public health units should assess the availability of services to ensure youth have access to hepatitis C counselling, testing, harm-reduction services and referrals for care and treatment.

Public health units should ensure the provision of appropriate immunization for hepatitis A and B to those who meet the criteria for publicly funded vaccines under Ontario's Publicly Funded Immunization Schedules, including all cases of hepatitis C. Immunizations are to be provided in accordance with the Canadian Immunization Guide; please refer to this guide for further information about immunizing individuals with a chronic infection.

Recommendations

SURVEILLANCE AND TESTING (CHAPTER 4)

Ministry of Health and Long-Term Care, Public Health Ontario and Local Public Health Units

4.1 Public health units, Public Health Ontario and the Ministry of Health and Long-Term Care should use surveillance data to examine the epidemiology of newly acquired hepatitis C infections and human immunodeficiency virus (HIV)/hepatitis C virus (HCV) co-infections; they should use this information to identify possible clusters that require immediate investigation, as well as to identify the need for further prevention measures tailored to the risk factors being reported.

Ministry of Health and Long-Term Care and Public Health Ontario

4.2 Public Health Ontario and the Ministry of Health and Long-Term Care should work towards making both positive and negative hepatitis C ribonucleic acid (RNA) laboratory results reportable to public health (when these are available after a positive antibody result) for surveillance and, where appropriate, case and contact management.

4.3 Public Health Ontario and the Ministry of Health and Long-Term Care should divide the surveillance case definition for hepatitis C into more specific ones for newly acquired and chronic cases.

Ministry of Health and Long-Term Care

4.4 The Ministry of Health and Long-Term Care should use surveillance data to plan and evaluate hepatitis C control in Ontario.

Public Health Ontario

4.5 Laboratories undertaking HCV antibody testing should include with each positive test result a recommendation to clinicians to conduct follow-up RNA testing. They should facilitate this by providing a testing form and information.

Local Public Health Units

4.6 All hepatitis C cases may benefit from (and should have access to) treatment. Where resources are sufficient, follow-up of all newly reported cases (with collection of risk-factor information) should be undertaken, whether cases are newly acquired or chronic. Where resources are limited, priority should be given to active follow-up of newly acquired cases (those infected within the preceding two years).

4.7 Positive RNA tests after sustained virological response to treatment should be investigated as possible re-infection.

4.8 Public health units and the Public Health Laboratory should work together to improve the identification of newly acquired hepatitis C infections by matching HCV-antibody–positive tests with previous negative tests.

4.9 People infected with HIV or hepatitis B should be strongly encouraged to undergo testing for hepatitis C, and vice versa. If not already immunized for hepatitis A and hepatitis B, people with hepatitis C should be encouraged to be appropriately immunized for these, unless contraindicated or unnecessary (i.e. already known to be immune to or infected with hepatitis B).

4.10 People who are severely immunocompromised but are potentially chronically infected based on exposures that put them at risk for hepatitis C should have RNA testing, even if antibody testing is negative.

SCREENING (CHAPTER 5)

Public Health Ontario

5.1 Research is recommended to determine whether the recent recommendation from the United States Centers for Disease Control and Prevention about birth cohort screening is applicable in Canada.

Local Public Health Units

5.2 Public health units should offer or facilitate access to hepatitis C screening for people at increased risk of infection (see list in Chapter 5).

5.3 Public health units should make specific efforts to offer or facilitate hepatitis C screening to all people at increased risk because of current or former sharing of injection drug use equipment or drug inhalation equipment. Screening may be offered through street outreach and partnership with community agencies or services offering harm-reduction programs.

5.4 Public health units should facilitate access to primary care follow-up for those found to be infected, either on-site at harm-reduction programs or via referral.

5.5 As an essential part of screening, patients must be provided with pre- and post-test counselling about hepatitis C (see Appendix H) so that they understand the reasons for testing and the implications of the results and can provide informed consent. Those who test positive must be given education, the means to prevent transmission to others, information about the availability of treatment, and referral to follow-up care.

5.6 People with ongoing risk of exposure to the hepatitis C virus should be offered counselling and support services to reduce risk behaviour (see Chapters 6 and 7), advised of methods to prevent transmission to others in the event that they do become infected, and encouraged to undergo testing at least annually for hepatitis C.

HARM REDUCTION (CHAPTER 6)

Local Public Health Units

6.1 Public health units should ensure access to harm-reduction programs for injection drug users, including distribution of sterile needles/syringes and drug and injection preparation equipment as supplied by the Ontario Harm Reduction Distribution Program: sterile water in single-use vials, sterile cookers, new filters, sterile alcohol swabs, ascorbic acid and new tourniquets. Harm-reduction programs should not place arbitrary limits on numbers of needles or other supplies provided; instead, they should provide supplies according to client need. Clients should not be required to return needles to obtain new ones, but they should be encouraged to do so; given sharps disposal containers; and offered counselling on safe disposal of needles, syringes and other injection drug use equipment. Clients should be specifically educated about the risks of sharing needles, syringes and other drug and injection preparation equipment (such as spoons/cookers, filters, water, swabs and tourniquets) at the time these materials are distributed, and they should be educated about the appropriate use of the equipment.

6.2 Public health units should seek to involve people who are currently using or have previously used drugs (frequently referred to as *peers*) to participate in the planning, delivery and evaluation of harm-reduction programs to enhance service relevance and credibility for program users and to develop trust in the community that uses drugs.

6.3 Public health units should incorporate harm-reduction measures in their programming (such as distribution of safer inhalation equipment) for smokers of illegal drugs, particularly crack and methamphetamine.

6.4 Clients with a history of illicit drug use and/or imprisonment should be counselled about their risks and offered testing for HCV, hepatitis B and HIV.

CASE MANAGEMENT (CHAPTER 7)

Local Public Health Units

7.1 Hepatitis C cases should be investigated to determine the reason for the test (whether the case or the physician suggested testing and for what reason); potential sources/risks for infection (see below); and co-infections with HIV, hepatitis B or other sexually transmitted infections. Testing for RNA should be recommended if not already completed.

7.2 Hepatitis C cases should be offered counselling and testing for HIV and hepatitis B virus. They should also be assessed for their risk of bacterial sexually transmitted infections and offered testing as appropriate. All hepatitis C cases qualify for publicly funded hepatitis A and hepatitis B vaccinations and should be offered appropriate vaccination, either by public health units or via their health care provider.

7.3 Among women, pregnancy status should be determined; specific treatment recommendations exist for pregnant women. Pregnant women should be advised to notify their health care provider about their infection and discuss treatment options. They should be educated about testing of their infant to determine infection status. Testing for hepatitis C RNA in infants should take place on two occasions: between the ages of two and six months and again at 18 to 24 months; HCV antibody should be included with the 18–24-month test. HCV-positive infants should be referred to a pediatrician.

7.4 History of receiving blood, tissue or organs should be determined to define possible eligibility for compensation. History of donating blood, tissue or organs should be assessed to determine possible requirements for follow-up with recipients. Donation history can also be used to establish timing of prior negative hepatitis C screening to help determine approximate time of infection.

7.5 Education/counselling of cases should be ensured. This should include information about the availability and location of harm-reduction services, if appropriate. Individual public health units will determine how much of this counselling they do and how much clinicians will do. Table 9, Appendix H and the Primary Care Management of Chronic Hepatitis C Professional Desk Reference 2009 can be useful for clinicians who may not have experience counselling hepatitis C cases.

7.6 To the extent possible, determine whether reported cases are newly infected (within the preceding two years), and if they are, what their risk factors are and whether they may be associated with other cases (i.e. a cluster or outbreak).

7.7 Current identifiable contacts considered at increased risk for infection (such as known sharing of drug use equipment or higher-risk sexual behaviour involving blood-to-blood contact) should be offered hepatitis C testing. Because of the low risk of sexual transmission in the absence of blood-to-blood contact, routine public health contact tracing of low-risk sexual partners is not recommended; it is not an effective use of resources.

7.8 Where there is indication of a cluster of cases, public health units should conduct an investigation appropriate to the circumstances and consider outreach to specific contacts to encourage testing and provide counselling and prevention.

PUBLIC EDUCATION AND SOCIAL MARKETING (CHAPTER 8)

Ministry of Health and Long-Term Care and Local Public Health Units

8.1 The Ministry of Health and Long-Term Care and local public health units should partner to identify means of educating the public about harm reduction and drug use, with the goal of increasing acceptance and reducing stigma and discrimination.

8.2 The Ministry of Health and Long-Term Care and local public health units should partner with the Ministry of Education and local school boards to identify and address gaps in education in secondary schools about blood-borne infections, including HIV, hepatitis B and hepatitis C, with attention paid to ensuring understanding of the differences and similarities between these viruses, as well as the availability and role of prevention and treatment for each.

Local Public Health Units

8.3 Public health units should advocate for measures such as improved access to low-cost housing, healthy food and income support as part of improving the health of people living with hepatitis C and increasing their chances of successfully undergoing treatment.

SPECIFIC POPULATIONS (CHAPTER 9)

Ministry of Health and Long-Term Care

9.1 The Ministry of Health and Long-Term Care should attempt to collect data on hepatitis C prevalence, incidence, risk factors and sequelae specific to Aboriginal people (including the rates and causes of morbidity and mortality from chronic liver disease) to assist in the development of appropriate public health programming.

9.2 The Ministry of Health and Long-Term Care should work to create policies that address the social determinants of health to better meet the needs of subpopulations at increased risk for hepatitis C.

Local Public Health Units

9.3 Corrections authorities have primary responsibility for the health of inmates. Public health units with correctional facilities, jails or detention centres in their jurisdiction should determine the availability of hepatitis C education, counselling, testing, support and other resources, and help corrections authorities deliver appropriate services where feasible. They should also work with local corrections authorities to help them ensure that inmates being paroled or released into the community are provided with information about and referrals to needle-exchange programs, other harm-reduction programs and other available support services.

9.4 Public health units should seek to ensure effective access to harm-reduction and treatment programs, including appropriate coordination and continuity with federal on-reserve care for Aboriginal people with hepatitis C who are living off-reserve in their jurisdiction.

9.5 Public health units should assess the need for and availability of services for street-involved youth in their jurisdiction; ensure access to hepatitis C counselling, testing and harm-reduction services; and facilitate access to care and treatment for those infected with hepatitis C.

9.6 Public health units should work with drug-treatment services in their jurisdiction to ensure access to hepatitis C counselling, testing, care, treatment and support for clients in drug treatment, including methadone maintenance or detoxification facilities. This should include providing information about the availability and location of harm-reduction services and ensuring provision of hepatitis A and B vaccines as indicated.

9.7 Public health units that offer clinical services and hepatitis C counselling and testing may offer counselling and testing to newcomers to Canada who are from highly endemic countries if they have not already been tested, and deliver culturally appropriate counselling and follow-up. Public health units should encourage primary care providers to offer hepatitis C counselling and testing to newcomers to Canada.

9.8 Public health units should offer or facilitate hepatitis C counselling and testing to men who have sex with men who are HIV-positive. Counselling should include discussing the high rates of co-infection with hepatitis C and HIV, the higher risk of sexual transmission of hepatitis C to contacts of those who are co-infected, safer sex practices and harm-reduction approaches, as indicated.

Methods

This document was developed using multiple evidence sources, including the review and evaluation of evidence from both published and grey literature, as well as expert opinion. Expert opinion took the form of information and documentation about methods used by experienced public health practitioners and information obtained from infectious disease experts.

Survey: Hepatitis C Information Needs of Ontario Public Health Staff

The Hepatitis C Working Group sought to ensure the relevance of this document conducting a brief online survey distributed to all Ontario public health units (PHUs). The survey instrument is provided in Appendix A.

Literature Review

To determine the nature and scope of the evidence to be sought from the published and unpublished literature, the Hepatitis C Working Group identified a series of key subject areas related to hepatitis C case and contact management for which evidence was needed. Multiple literature search strategies were developed to address these questions (see Appendix B). The searches were run in various databases, including Ovid MEDLINE, Embase, PsycINFO, EBSCOhost CINAHL Plus, Academic Search Premier, and in some cases SocINDEX. Each database was searched using database-specific controlled vocabulary, but all searches were supplemented by keyword queries to increase the article recall. Searches covered the years 1950 to 2011, although in a few cases literature up to May 2012 was included. Only English-language abstracts were reviewed.

For selected topics, the working group also undertook searches of grey literature sources: that is, unpublished sources considered to be relevant and reliable were included as part of the literature review. These were limited primarily to government publications from the United Kingdom (U.K.), United States, Canada and Australia. Grey literature was retrieved from Google using synonyms for topic categories, including counselling, testing, best practice guidelines, harm reduction, screening, management and education. For the search on street-involved youth and access to health care, the following strategy was applied: "(street-involved youth OR homeless youth) (public health OR community health)". Similarly, the grey literature search on hepatitis C testing and counselling was retrieved using the following search terms: "Hepatitis C test* counsel*". Jurisdictional scans were also conducted.

Abstracts of identified published studies were reviewed for relevance, and full reviews were conducted for selected articles. Relevance was based on whether the study addressed the question being considered and whether the sociocultural setting and health care system in relation to the search question was sufficiently similar to Canada's.

Resource limitations did not allow the working group to conduct full systematic reviews. Whenever possible, published systematic reviews or other high-quality reviews were used, instead of undertaking a full separate review of primary literature. Where a systematic or other high-quality review was identified, it was supplemented as necessary with studies done since its publication or studies addressing gaps or limitations. Where no reviews were available, the most relevant studies were considered, summarized in table form, and assessed for individual strength. These studies were assessed for methodological rigour using criteria similar to those published by the National Institute for Health and Clinical Excellence public health guidance methods used in the U.K.[1] Where relevant, the strength of individual studies is presented using the same approach as the National Institute for Health and Clinical Excellence documents for guidance in public health[1]: ++, +, or – ratings of internal validity according to the degree of potential for the results to be affected by biases (with "++" having the lowest potential for bias and "–" having the highest potential for bias), and the same ranking

system for external validity based on the likelihood that the findings can be applied in other settings—in this case, Ontario to assess generalizability.

The evidence was summarized and presented at Hepatitis C Working Group meetings. Discussion and feedback were incorporated into the relevant chapters, and recommendations were determined by consensus. The evidence and other considerations behind the recommendations are discussed in some detail to help readers understand the basis for each recommendation.

1. Control of Hepatitis C: Overview

Hepatitis C is of major public health importance in Ontario and worldwide. In Ontario, it is associated with the highest burden of any communicable disease.[2] It is a flavivirus, and six different genotypes have been identified so far. Genotypes 1 to 3 have been found worldwide, and are the main genotypes found in Canada, with genotype 1 predominating. Testing to determine genotype is important, since the effectiveness and length of treatment differ for each. With the evolution of new treatments, genotyping may become less necesssary.

There is currently no vaccine available to prevent hepatitis C; instead, preventing infection relies on preventing exposures and behaviours linked to transmission. Hepatitis C can be successfully treated, but because of the high cost, serious side effects and relatively prolonged duration of interferon and ribavirin therapy, it is often delayed until there is evidence of liver damage and the benefits of treatment are likely to outweigh the harms. Newer treatments are emerging that have fewer side effects, but they are also very costly. The feasibility of cure means that communicability can be ended with treatment, rendering early treatment desirable from a public health perspective. There is also reason to believe that cure rates are higher in those who are treated early (i.e. during acute infection), with sustained virological response rates of 80 to 98 per cent.[3-6] Still, these impressive rates must take into consideration the fact that at least 15 per cent or more of newly infected people will clear the virus without treatment. It is suggested that treatment be delayed for 8 to 12 weeks after acute hepatitis onset to allow for spontaneous clearing of the virus. Those who have not spontaneously cleared the virus by then will not likely do so without treatment.[7]

In Ontario, the *Health Protection and Promotion Act* (HPPA) is the legislation under which diseases of public health importance are designated as reportable, investigated and treated.[8] Hepatitis C is a reportable and communicable disease under the HPPA. The HPPA requires the reporting of diagnosed infections of reportable diseases to local medical officers of health. Reporting of hepatitis C infections allows public health agencies to monitor the disease in the community and tailor prevention and intervention programs to reduce the risk of infection and transmission.

The goal of public health communicable disease programs is two-fold: to prevent harm to the infected individual and his/her potentially infected contacts, and to control the spread of communicable disease at the population level. Disease surveillance and individual case management are primary public health functions. However, to achieve population-level control of hepatitis C, local PHUs must develop and deliver diverse programming aimed at the individual, the population and the health care system. For example, because a high proportion of prevalent and new cases of hepatitis C are related to illicit drug use, related harm-reduction programs have become common. Population-level strategies that may be applicable include education, particularly of young people; social marketing campaigns (e.g. to promote voluntary counselling and testing for those at risk); screening programs; and behaviour change programs targeting higher-risk population groups, including outreach and support delivered by peers.

A majority of those infected with hepatitis C are asymptomatic for many years. Asymptomatic infected people who do not routinely seek medical care and are not named as contacts may be identified if they have access to screening programs. Screening implies that a health care provider recommends testing to a person who does not request it or exhibit symptoms of the disease. This requires that providers be aware of hepatitis C and who is at risk, and be willing and able to discuss it with their patients and encourage those at risk to be tested. Screening can be carried out in primary care settings, as well as in health service settings that may see a higher-risk clientele, such as needle-exchange programs; methadone maintenance and other drug-treatment programs; correctional facilities; and services for street youth. Key issues for screening programs are how to access hard-to-reach people who are at increased risk of being infected; how to assess the balance of risks and

benefits of screening for healthy asymptomatic individuals; how to ensure adequate resources to address the needs of chronically infected people identified through screening; and how to initiate and maintain participation in effectively managed treatment programs that can successfully eliminate infection so that cases do not pose a risk to others.

Detecting cases can also be promoted by educating the public and/or higher-risk groups to encourage testing, combined with ready access to voluntary counselling and testing. The effectiveness of voluntary counselling and testing depends on the degree to which cases accurately perceive themselves to be at risk—particularly if they are asymptomatic—and the degree to which they are willing to be diagnosed and treated. Fear of stigma and discrimination, concern about disclosure to others, denial and lack of perceived benefit can all prevent people at risk from seeking testing.

For local PHUs to engage effectively in hepatitis C case management and support behaviour change in cases and contacts, staff require training and quality-assurance measures. Particularly important are training in counselling skills; understanding of diversity and cultural norms; training in harm reduction and understanding of drug use and mental health issues; and opportunities for continuing education and upgrading of knowledge and skills.

While the focus of this document is primarily on public health practices such as case management, other levels of intervention are necessary and important. Hepatitis C is a difficult disease to control, because the underlying determinants behind most new infections are related to larger social problems such as poverty; stigma; addiction and mental health; the illicit nature of non-prescription drug use; alcoholism; homelessness; imprisonment; and other related issues. The multifaceted nature and broad scope of the social determinants of hepatitis C infection mean that public health alone cannot control hepatitis C. Current prevention programs tend to be compartmentalized and may fail to address, in an integrated manner, the needs of people who have multiple risks and whose needs extend beyond health care to include issues such as adequate housing, adequate income and opportunities for social inclusion and support.

The range of interventions likely to be needed to control hepatitis C cuts across government departments and levels of government. In this document, we have limited ourselves to recommendations for hepatitis C control by provincial and local public health authorities, while at the same time recognizing that the problem is too large to be addressed by public health alone. Public health practitioners may need to advocate for policies and programs that are beyond the scope of individual PHUs. It may also be important to expand the resources of local PHUs to allow them to provide needed services, such as more extensive harm-reduction and behaviour-change interventions and more effective outreach programs.

2. Epidemiology of Hepatitis C in Ontario

KEY POINTS

- There were 4,512 new reports of cases of hepatitis C in Ontario in 2010. With a few exceptions, the main temporal trend has been a relatively steady decline in reported cases since a peak in 1996.
- Males account for approximately 62 per cent of newly reported cases.
- The average age of newly reported cases is increasing. In the mid-1990s, most newly reported cases were aged 30 to 49. In 2010, the most newly reported cases were aged 50 to 59.
- Newly reported cases are a combination of newly acquired cases and cases that may have been infected decades ago. True incidence and prevalence are not measured at the population level; they must be estimated from epidemiological models.
- Estimates of true (versus reported) incidence and prevalence based on epidemiological models suggest that hepatitis C prevalence is decreasing slightly, while incidence is increasing slightly.
- Current or former unsafe injection drug use practices account for 54 per cent of prevalent cases and 81 per cent of incident cases.
- The estimated prevalence of hepatitis C in Ontario in 2010 was 0.84 per cent, but there is considerable variability across public health units.
- The public health units with the highest estimated incidence and prevalence based on modelling are Kingston, Frontenac and Lennox & Addington; Thunder Bay District; Timiskaming; Algoma; and Chatham-Kent. The public health units with the lowest estimated incidence and prevalence based on modelling are Huron County; Perth District; York Region; Halton Region; and Wellington-Dufferin-Guelph (table 4).
- The public health units with the greatest relative increases in hepatitis C prevalence since 2007 are Chatham-Kent, Porcupine, Lambton and Hamilton. The public health units with the greatest relative declines are Renfrew, Halton Region, Haliburton-Kawartha-Pine Ridge, York Region, Niagara Region and Toronto.

Incidence and Prevalence

Surveillance of hepatitis C is complicated by several factors that make it difficult to accurately determine current incidence and prevalence in Ontario. First, three terms should be defined: *incidence, prevalence* and *reported incidence*. *Incidence* is the actual number of new cases that occur in a given time period, usually one year. *Prevalence* is the number of people living with chronic hepatitis C infection at a given time. *Reported annual incidence* is the number of people who test positive for hepatitis C antibody and are reported to PHUs in a given year.

True incidence and prevalence are unknown, but they differ from reported incidence for several reasons. It is estimated that approximately one-third of those infected with hepatitis C have never been tested and are unaware of their infection,[9] leading to an underestimation of incidence and prevalence when based on

reported cases. Cases that are reported may have been infected decades ago but only diagnosed recently; reported incidence may better reflect current testing intensity rather than current transmission patterns. At the same time, there are factors that may inflate reported incidence and prevalence. For example, the current case definition for hepatitis C requires only a positive antibody test, which indicates only that a person has been exposed to the hepatitis C virus (HCV) and has mounted an immune response to it. Many individuals who have received positive antibody tests have not had confirmatory nucleic acid testing to detect the ongoing presence of HCV. Studies have shown that anywhere from 15 to 50 per cent (averaging approximately 20 per cent) of antibody-positive people will have cleared the virus spontaneously and should not be counted as prevalent cases. While this may lead to an overestimate of prevalence, it may also lead to an underestimate of incidence, since a person may acquire and clear the virus several times if exposure is ongoing. For the reasons noted above, true incidence and prevalence must be estimated using epidemiological models.

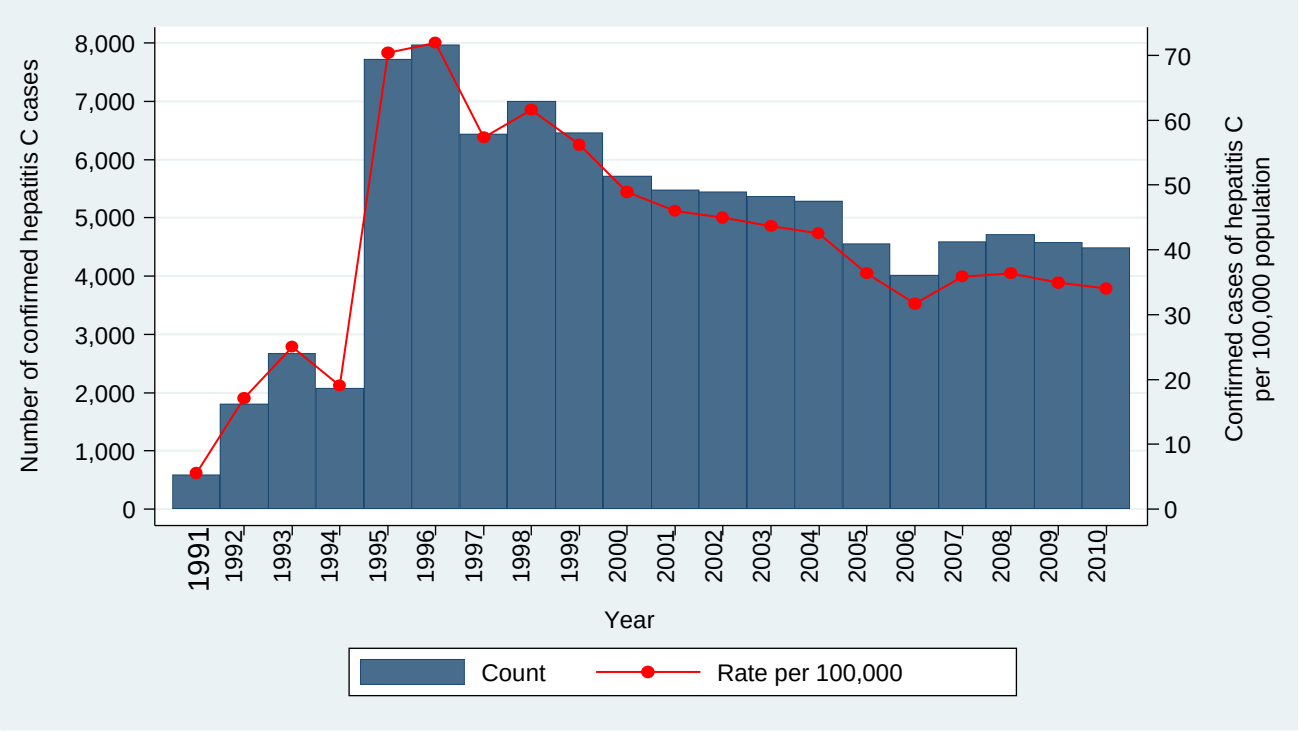
There are two main sources of data used in epidemiological modelling of hepatitis C prevalence and incidence in Ontario. The first is reported incidence data from the Ontario public health system (laboratories and PHUs), and the second is data from research studies of groups at increased risk. The latter can provide a source of information about the extent of testing coverage of higher-risk groups, indicating the extent to which they are included in the laboratory testing data, as well as estimates of hepatitis C prevalence. Most research studies have used antibody testing only, and are therefore subject to the same overestimation problem mentioned above. Modelling methods such as those reported by Dr. Robert Remis include an estimate of the rate of spontaneous clearance of the virus, thereby taking this into account when considering the prevalence of chronic infection and sequelae.[10]

Reported Incidence

In 2010, the Ontario Ministry of Health and Long-Term Care was notified of 4,512 cases of hepatitis C, a rate of 34 cases per 100,000 population. Figure 1 provides an examination of the numbers of cases per 100,000 population reported in Ontario since mandatory reporting of hepatitis C testing came into effect in 1991. This shows a pattern of exponentially increasing numbers of positive tests in the early years, reflecting the uptake of testing among the many chronic cases that had accumulated in the population over previous decades, including people who had been infected through blood transfusion prior to the availability of blood donor testing in 1990. A number of federal and provincial compensation programs in the 1990s and into the early 2000s also stimulated additional testing to provide proof of infection or confirm tests done in the early 1990s (owing to the relatively low specificity of early tests).

Since a peak in 1996, the rate of newly reported cases has declined. Ongoing reported incidence continues to represent a combination of chronically and newly infected cases identified via a combination of screening of people at increased risk and presentation of chronic cases to health care providers, who are identifying liver abnormalities and testing for hepatitis C as part of the clinical investigation. Some debate exists about the apparent decline in reported cases in Ontario in 2005 and 2006. It is not clear whether this represented a true decline and subsequent rebound in hepatitis C incidence, or whether there were errors in the surveillance data for that period. We know that a major transition occurred in 2005 and 2006 as Ontario PHUs moved, on a staggered schedule, from the old Reportable Disease Information System (RDIS) to the new Integrated Public Health Information System. At this time, there is no satisfactory explanation; data for those years should be interpreted with caution.

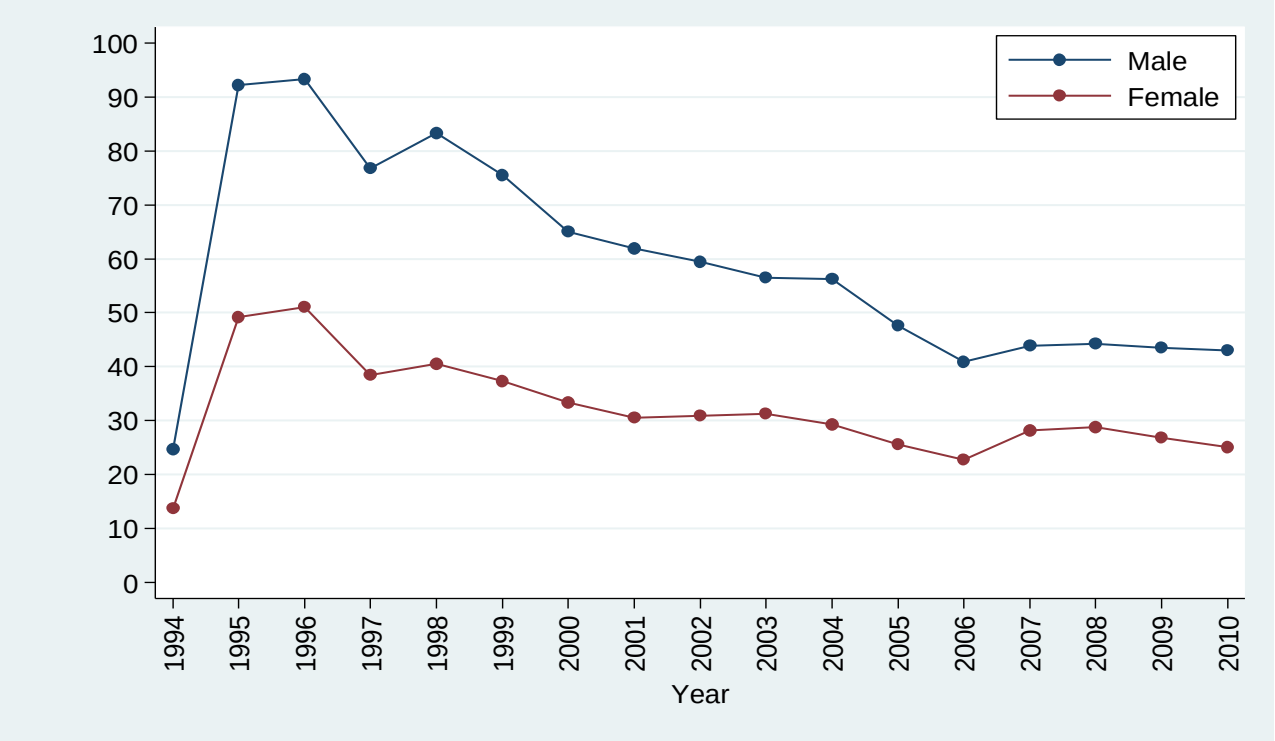
Figure 1: Confirmed reported cases of hepatitis C in Ontario, 1991–2010



Source: Ontario Ministry of Health and Long-Term Care, integrated Public Health Information System database, extracted by Public Health Ontario (05/12/2011). These data are subject to change due to data cleaning initiatives and removal of duplicates.

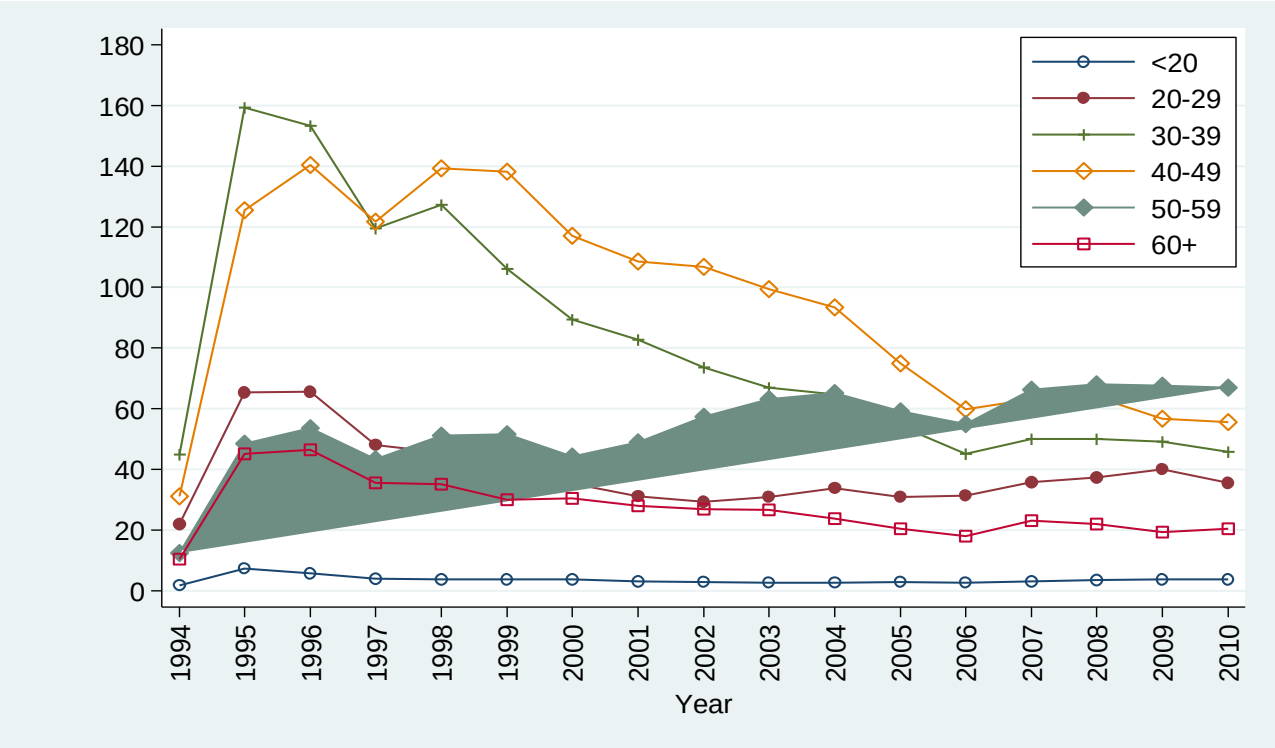
Figure 2 identifies rates of confirmed hepatitis C cases per 100,000 population by sex since 1994, and Figure 3 provides the same information by age group. The significantly higher rates seen among males may relate at least in part to the general finding that approximately two-thirds of injection drug users in North America are male. In countries where a significant proportion of hepatitis C appears to arise from infected transfusions and other medical care with contaminated equipment, the prevalence of hepatitis C rises with age. In Ontario, the highest proportion of confirmed cases appears to be fairly consistent in 40- to 49-year-olds. The pattern of increasing prevalence in the 20s, 30s and 40s is consistent with duration of unsafe injection drug use (IDU) practices as a major risk factor, but is complicated by the likelihood that many are being tested only in their 40s and 50s after the onset of serious liver disease symptoms. The pattern of lower rates of confirmed cases in people over age 60 is compatible with unsafe IDU practices as a major risk factor, since both untreated IDU and untreated hepatitis C may contribute to early morbidity and mortality, and relatively few cases will reach their 60s without being identified.

Figure 2: Confirmed cases of hepatitis C by sex for Ontario, 1994–2010



Source: Ontario Ministry of Health and Long-Term Care, integrated Public Health Information System database, extracted by Public Health Ontario (05/12/2011). These data are subject to change due to data cleaning initiatives and removal of duplicates.

Figure 3: Confirmed cases of hepatitis C by age group for Ontario, 1994–2010



Source: Ontario Ministry of Health and Long-Term Care, integrated Public Health Information System database, extracted by Public Health Ontario (05/12/2011). These data are subject to change due to data cleaning initiatives and removal of duplicates.

As indicated in Table 1 and Map 1, there is wide variation in reported incidence of hepatitis C in Ontario PHUs. The highest rates are in Kingston, Frontenac and Lennox & Addington and Thunder Bay District. This variability is likely related to the presence of higher-risk populations in certain PHUs. For example, the Kingston area is the site of nine federal and provincial correctional facilities, and hepatitis C cases identified therein are counted for statistical purposes as part of the Kingston, Frontenac and Lennox & Addington PHU. Approximately 50 per cent of cases attributed to Kingston, Frontenac and Lennox & Addington are identified in the correctional system (personal communication, van Dijk A, 2012). In contrast, Thunder Bay has the second-highest reported incidence in Ontario, and almost all cases are community-based. Thunder Bay is thought to have a disproportionately large IDU population.

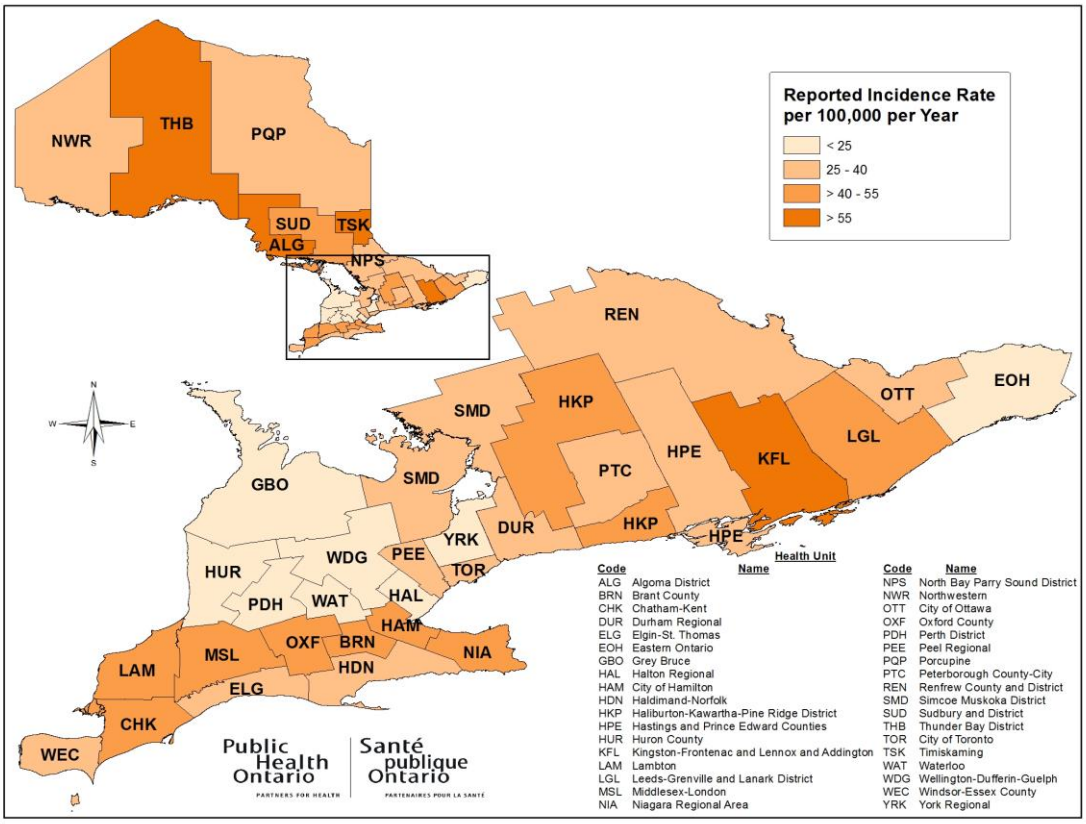
Table 1: Reported incidence of confirmed Hepatitis C cases in Ontario by Public Health Unit, 2008–2010

Public Health Unit	Reported Cases			Average Rate per 100,000 2008–2010
	2008	2009	2010	
Kingston, Frontenac and Lennox & Addington	188	194	195	99.3
Thunder Bay District	155	121	136	87.6
Algoma	86	64	69	61.3
Timiskaming	14	27	18	56.3
Middlesex-London	236	248	240	53.5
Niagara Region	228	196	208	47.6
Sudbury and District	84	99	98	46.8
Haliburton, Kawartha, Pine Ridge District	79	87	62	42.9
Brant County	58	60	60	42.8
Leeds, Grenville and Lanark District	67	77	70	42.4
Oxford County	40	46	49	42.1
Chatham-Kent	24	43	70	41.3
Lambton	38	45	80	41.1
City of Hamilton	214	215	221	40.9
Elgin-St. Thomas	38	30	38	39.3
Windsor-Essex County	173	153	131	37.7
Toronto	1069	959	941	37.1
North Bay Parry Sound District	41	45	48	35.3
Simcoe Muskoka District	171	173	185	34.4
Haldimand-Norfolk	35	44	33	33.6
Porcupine	19	33	32	31.9
Peterborough County-City	39	52	40	31.5

Public Health Unit	Reported Cases			Average Rate per 100,000 2008–2010
	2008	2009	2010	
Ottawa	273	306	226	30.6
Durham Region	203	175	179	30.4
Hastings and Prince Edward Counties	55	43	49	30.1
Peel	398	396	371	29.8
Renfrew County and District	36	28	27	29.5
Northwestern	15	27	28	28.5
Eastern Ontario	41	47	58	24.5
Region of Waterloo	119	114	144	24.4
Halton Region	127	107	102	22.9
Grey Bruce	42	29	41	22.9
Wellington-Dufferin-Guelph	68	63	52	22.5
York Region	239	227	193	21.8
Perth District	7	16	10	14.3
Huron County	11	2	8	11.5
Ontario Total	**4,730**	**4,591**	**4,512**	**35.4**

Source: Ontario Ministry of Health and Long-Term Care, integrated Public Health Information System database, extracted by Public Health Ontario (05/12/2011). These data are subject to change due to data cleaning initiatives and removal of duplicates.

Map 1: Reported incidence rate of confirmed hepatitis C cases in Ontario by public health unit, 2010



Source: Data from Table 1.

Modelled Incidence and Prevalence

Epidemiological modelling has been used to estimate true hepatitis C incidence and prevalence by exposure category, sex, age, PHU and stage of disease. Modelling has also estimated hepatitis C-related morbidity, including trends in serious sequelae.[10]

Tables 2 and 3 provide estimates of true incidence and prevalence of hepatitis C in Ontario for 2007 to 2011 (personal communication, Remis R, 2012). These estimates indicate that in 2011, 54 per cent of cases were attributed to current or former unsafe IDU practices; 5 per cent to transfusion; 5 per cent to hemophilia; and 36 per cent to other causes, including unsafe tattooing, unsafe non-injection drug use, unreported unsafe IDU practices, and transfusions and other medical exposures outside Canada by people who have immigrated to Ontario. The modelled true incidence of newly infected cases in Ontario in 2011 was estimated at 3,591, with 2,893 (81 per cent) of these cases in people who inject drugs. Overall, these models estimate that the prevalence of hepatitis C may be declining slightly, while incidence may be increasing slightly.

Table 2: Modelled true incidence of hepatitis C in Ontario by sex and exposure category, 2007–2011

Sex	Exposure Category	Year				
		2007	2008	2009	2010	2011
Male	IDU	1,893	1,911	1,929	1,946	1,964
	Ex-IDU	0	0	0	0	0
	Blood products	4	5	5	5	6
	Other	353	355	357	360	362
	Total	**2,250**	**2,271**	**2,291**	**2,311**	**2,332**
Female	IDU	898	906	914	921	929
	Ex-IDU	0	0	0	0	0
	Blood products	0	0	0	0	0
	Other	321	323	326	328	330
	Total	**1,219**	**1,229**	**1,239**	**1,249**	**1,259**
Both sexes	IDU	2,791	2,817	2,842	2,868	2,893
	Ex-IDU	0	0	0	0	0
	Blood products	5	5	5	6	6
	Other	674	678	683	687	692
	Total	**3,470**	**3,500**	**3,530**	**3,561**	**3,591**

IDU, injection drug use.
Counts rounded to nearest integer. Columns may not sum to their totals due to rounding.
Source: Dr. Robert Remis, Ontario HIV Epidemiology Monitoring Unit (OHEMU).

It is important to note that although modelling predicts five or six incident blood product transmitted cases per year based on possible transmission from window period cases who may donate blood or blood products and test negative, in reality there has not been a reported case of blood product transmission of hepatitis C in Canada since 1997. HCV-antibody donor testing was implemented by Canadian Blood Services and Hema Quebec in 1990, with improved second- and third-generation assays in 1992 and 1996. The addition of HCV nucleic acid testing in 1999 has further reduced the window period.

Table 3: Modelled true prevalence of hepatitis C in Ontario by sex and exposure category, 2007–2011

Sex	Exposure Category	Year				
		2007	2008	2009	2010	2011
Male	IDU	14,606	14,622	14,639	14,656	14,672
	Ex-IDU	25,048	25,106	25,165	25,223	25,281
	Blood products	6,307	6,045	5,784	5,523	5,261
	Other	19,961	20,154	20,348	20,541	20,734
	Total	**65,921**	**65,928**	**65,935**	**65,942**	**65,949**
Female	IDU	7,026	7,035	7,043	7,051	7,060
	Ex-IDU	12,205	12,255	12,304	12,354	12,404
	Blood products	6,090	5,795	5,499	5,204	4,908
	Other	18,475	18,657	18,839	19,020	19,202
	Total	**43,796**	**43,741**	**43,685**	**43,629**	**43,574**
Both sexes	IDU	21,632	21,657	21,682	21,707	21,732
	Ex-IDU	37,253	37,361	37,469	37,577	37,685
	Blood products	12,397	11,840	11,283	10,726	10,170
	Other	38,436	38,811	39,186	39,561	39,937
	Total	**109,717**	**109,669**	**109,620**	**109,572**	**109,523**

IDU, injection drug use.
Counts rounded to nearest integer. Columns may not sum to their totals due to rounding.
Source: Dr. Robert Remis, Ontario HIV Epidemiology Monitoring Unit (OHEMU).

Using these modelled estimates of true incidence and prevalence, we estimated the true incidence and prevalence of hepatitis C in each Ontario PHU for each year for 2007 to 2010 by multiplying the total modelled incidence and prevalence for Ontario by the proportion of reported incidence reported in each PHU. Since annual reported incidence at the PHU level is subject to year-to-year fluctuations, we then fit Poisson regression models to each PHU's reported incidence from 2007 to 2010 to estimate the 2010 true incidence rate and prevalence proportion. These modelled annual incident and prevalent cases, as well as the 2010 incidence rates and prevalence proportions by PHU, are given in Tables 4 and 5. Map 2 depicts the modelled prevalence of hepatitis C by Ontario PHU for 2010. Figure 4 shows the trend in the PHU-specific prevalence proportions from 2007 to 2010. PHUs with a statistically significant trend in their prevalence proportions are shown in Table 6.

Table 4: Modelled estimates of hepatitis C incidence in Ontario by Public Health Unit, 2007–2011

Public Health Unit	Modelled Number of Incident Cases				Estimated Incidence Rate per 100,000
	2007	2008	2009	2010	2010
Kingston, Frontenac and Lennox & Addington	171	139	149	154	75.6
Thunder Bay District	102	115	93	107	66.2
Timiskaming	12	10	21	14	49.0
Algoma	44	64	49	54	46.7
Chatham-Kent	25	18	33	55	44.8
Middlesex-London	155	175	191	189	43.2
Lambton	41	28	35	63	39.1
Sudbury and District	68	62	76	77	38.6
Oxford County	29	30	35	39	36.0
Leeds, Grenville and Lanark District	42	50	59	55	35.2
Niagara Region	184	169	151	164	35.1
City of Hamilton	119	158	165	174	34.2
Brant County	44	43	46	47	33.9
Elgin-St. Thomas	19	28	23	30	32.7
Porcupine	15	14	25	25	30.5
Haliburton, Kawartha, Pine Ridge District	74	58	67	49	29.6
North Bay Parry Sound District	35	30	35	38	28.8
Windsor-Essex County	93	128	118	103	28.3
Simcoe Muskoka District	117	127	133	146	28.2
Toronto	796	791	737	743	27.4
Northwestern	18	11	21	22	26.2
Haldimand-Norfolk	29	26	34	26	25.7
Peterborough County-City	37	29	40	32	24.3
Durham Region	129	150	135	141	23.1
Ottawa	177	202	235	178	23.1
Peel	295	295	304	293	22.5
Hastings and Prince Edward Counties	43	41	33	39	22.0
Eastern Ontario	43	30	36	46	20.5
Renfrew County and District	32	27	22	21	19.6
Region of Waterloo	111	88	88	114	19.5
Grey Bruce	29	31	22	32	17.7
Wellington-Dufferin-Guelph	48	50	48	41	16.0
Halton Region	105	94	82	81	15.7
York Region	173	177	175	152	15.6
Perth District	10	5	12	8	11.8
Huron County	7	8	2	6	7.6
Ontario Total	**3,470**	**3,500**	**3,530**	**3,561**	**27.2**

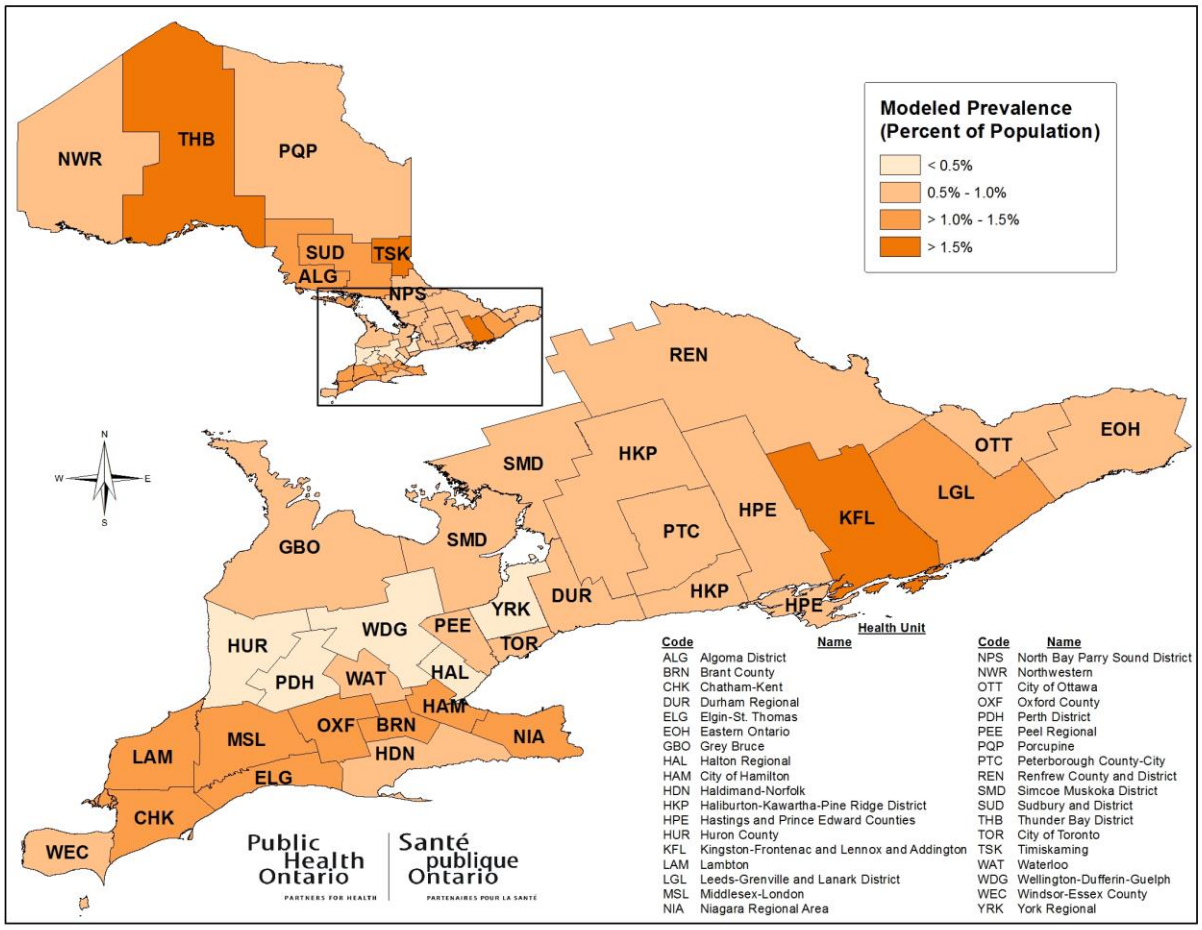
Health unit modelled incidence counts may not sum to the Ontario total due to rounding.
Source: Dr. Robert Remis, Ontario HIV Epidemiology Monitoring Unit (OHEMU), provided the modelled annual Ontario incidence totals. Distribution of incident cases among health units was based on reported incidence from Table 1.

Table 5: Modelled estimates of hepatitis C prevalence in Ontario by Public Health Unit, 2007–2010

Public Health Unit	Estimated Number of Prevalent Cases				Estimated Prevalence per 100 2010
	2007	2008	2009	2010	
Kingston, Frontenac and Lennox & Addington	5,419	4,359	4,632	4,735	2.33
Thunder Bay District	3,233	3,594	2,889	3,303	2.04
Timiskaming	380	325	645	437	1.51
Algoma	1,402	1,994	1,528	1,676	1.44
Chatham-Kent	784	556	1,027	1,700	1.38
Middlesex-London	4,896	5,472	5,922	5,828	1.33
Lambton	1,307	881	1,074	1,943	1.20
Sudbury and District	2,163	1,948	2,364	2,380	1.19
Oxford County	927	927	1,098	1,190	1.11
Leeds, Grenville and Lanark District	1,331	1,553	1,839	1,700	1.08
Niagara Region	5,823	5,286	4,680	5,051	1.08
City of Hamilton	3,755	4,962	5,134	5,367	1.05
Brant County	1,379	1,345	1,433	1,457	1.04
Elgin-St. Thomas	594	881	716	923	1.01
Porcupine	475	441	788	777	0.94
Haliburton, Kawartha, Pine Ridge District	2,353	1,832	2,077	1,506	0.91
North Bay Parry Sound District	1,117	951	1,074	1,166	0.89
Windsor-Essex County	2,947	4,011	3,653	3,181	0.87
Simcoe Muskoka District	3,684	3,965	4,131	4,493	0.87
Toronto	25,171	24,786	22,898	22,852	0.84
Northwestern	570	348	645	680	0.81
Haldimand-Norfolk	927	812	1,051	801	0.79
Peterborough County-City	1,165	904	1,242	971	0.75
Durham Region	4,064	4,707	4,179	4,347	0.71
Ottawa	5,586	6,330	7,306	5,488	0.71
Peel	9,317	9,228	9,455	9,010	0.69
Hastings and Prince Edward Counties	1,355	1,275	1,027	1,190	0.68
Eastern Ontario	1,355	951	1,122	1,409	0.63
Renfrew County and District	998	835	669	656	0.60
Region of Waterloo	3,494	2,759	2,722	3,497	0.60
Grey Bruce	903	974	692	996	0.55
Wellington-Dufferin-Guelph	1,521	1,577	1,504	1,263	0.49
Halton Region	3,328	2,945	2,555	2,477	0.48
York Region	5,467	5,541	5,420	4,687	0.48
Perth District	309	162	382	243	0.36
Huron County	214	255	48	194	0.23
Ontario Total	**109,717**	**109,669**	**109,620**	**109,572**	**0.84**

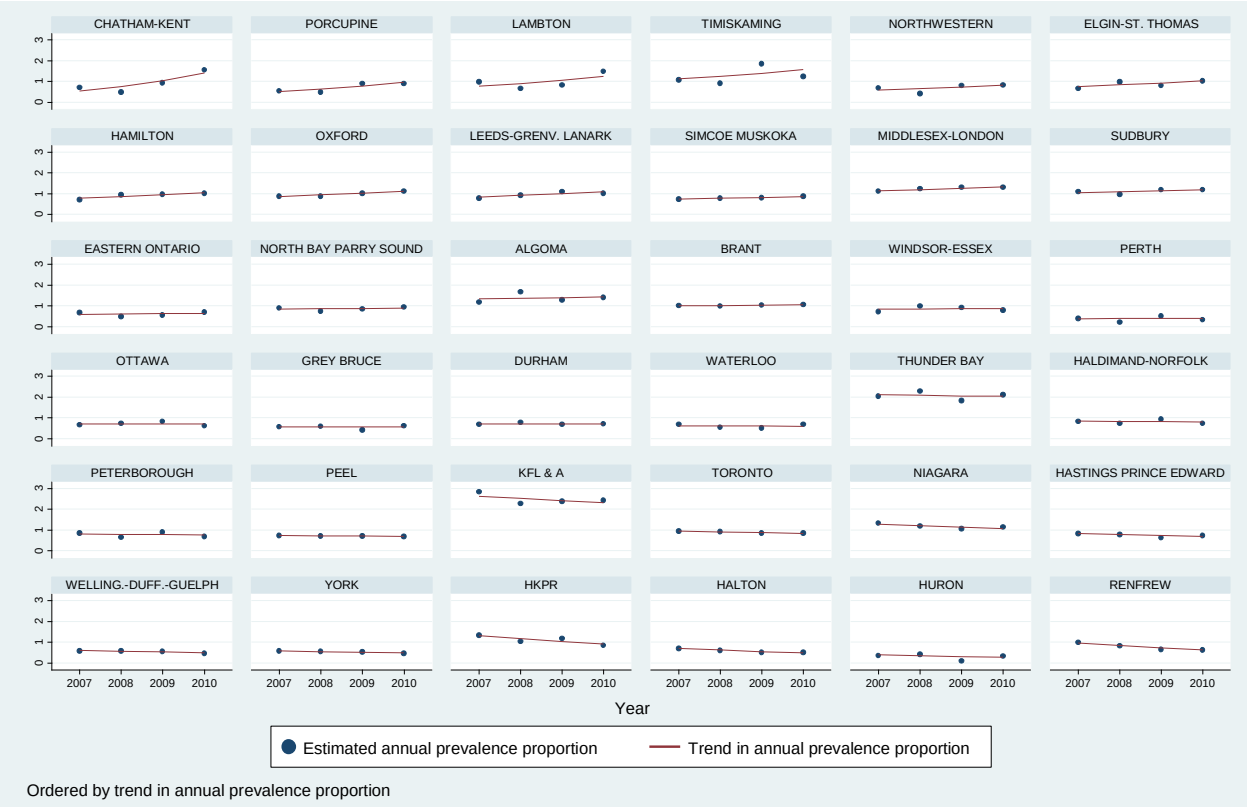
Health unit-specific estimated prevalence counts may not sum to the Ontario total due to rounding.
Source: Dr. Robert Remis, Ontario HIV Epidemiology Monitoring Unit (OHEMU), provided the modelled annual Ontario prevalence totals. Distribution of prevalent cases among health units was based on reported incidence from Table 1.

Map 2: Modelled estimates of hepatitis C prevalence in Ontario by public health unit, 2010



Source: Data from Table 5.

Figure 4: Modelled estimates with trend lines of the percentage of the population infected with hepatitis C by Ontario public health unit, 2007–2010



Source: Data from Table 5.

Table 6: Estimated annual relative change in modelled hepatitis C prevalence among Heath Public Health Units with statistically significant changes 2007–2010

Public Health Unit	Estimated Annual Change in Hepatitis C Prevalence	p-value
Chatham-Kent	+38%	<0.0001
Porcupine	+22%	0.0229
Lambton	+16%	0.0123
City of Hamilton	+10%	0.0039
Toronto	−5%	0.0002
Niagara Region	−6%	0.0295
York Region	−7%	0.0124
Haliburton, Kawartha, Pine Ridge District	−12%	0.0100
Halton Region	−12%	0.0015
Renfrew County and District	−15%	0.0395

Positive values indicate increasing prevalence; negative values indicate decreasing prevalence.
Source: Dr. Robert Remis, Ontario HIV Epidemiology Monitoring Unit (OHEMU).

Prevalent HIV/HCV Co-infections

Models have also been used to estimate the prevalence of human immunodeficiency virus (HIV)/HCV co-infected people in Ontario in 2006 (Table 7). Injection drug users constitute the largest single risk category.

Table 7: Modelled numbers of prevalent HIV/HCV co-infections in Ontarion in 2006

Risk Factor	Estimated Number
Injection drug use	1,606
Men who have sex with men	658
Men who have sex with men/injection drug use	584
Hemophilia	114
Other heterosexual	97
Immigrant from country with high HIV prevalence	63
Transfusion	3
Total	**3,124**

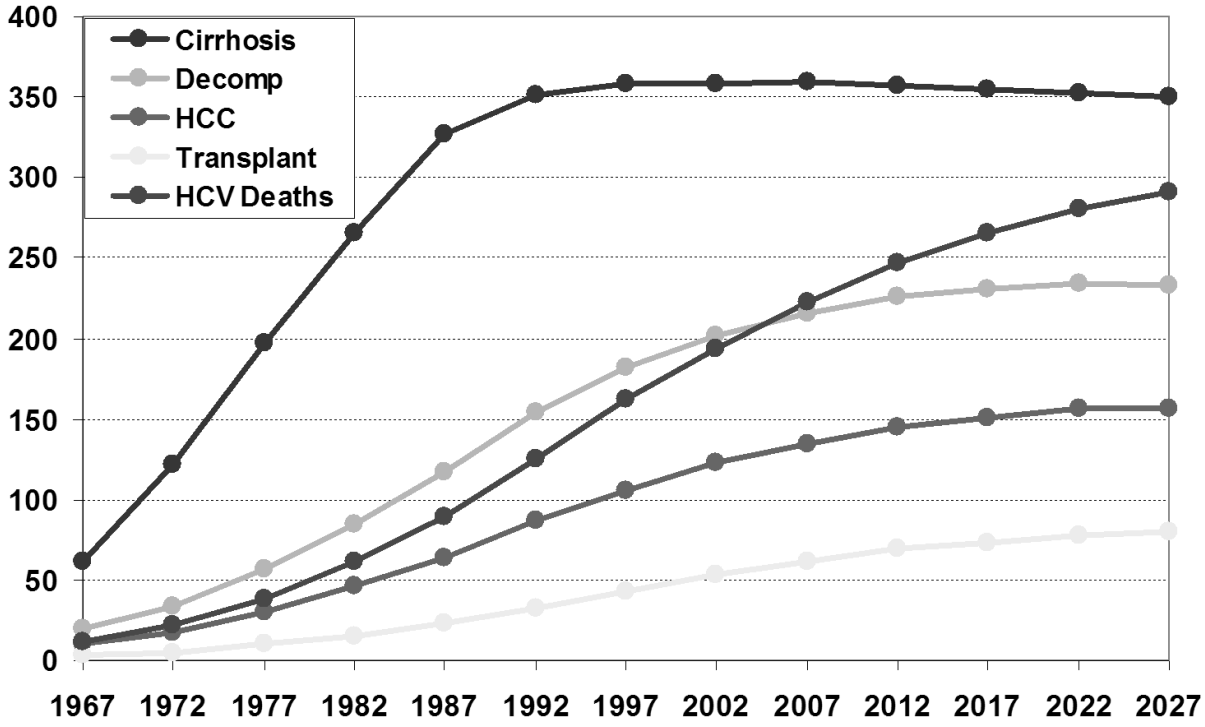
The modelled number of risk-factor–specific co-infections may not sum to the total due to rounding.
Source: Dr. Robert Remis, Ontario HIV Epidemiology Monitoring Unit (OHEMU).

Based on these models, it is estimated that in Ontario in 2006, 2.8 per cent of HCV-infected people also had HIV, and 11.9 per cent of HIV-infected people also had hepatitis C. This document addresses HIV/HCV co-infection from the perspective of hepatitis C prevention and control; prevention of sexual transmission of HIV and public health HIV case management are addressed in the document *Best Practices for Case Management and Contract Tracing for Reportable Sexually Transmitted Infections*.[11]

Sequelae of Untreated Chronic Hepatitis C Infection

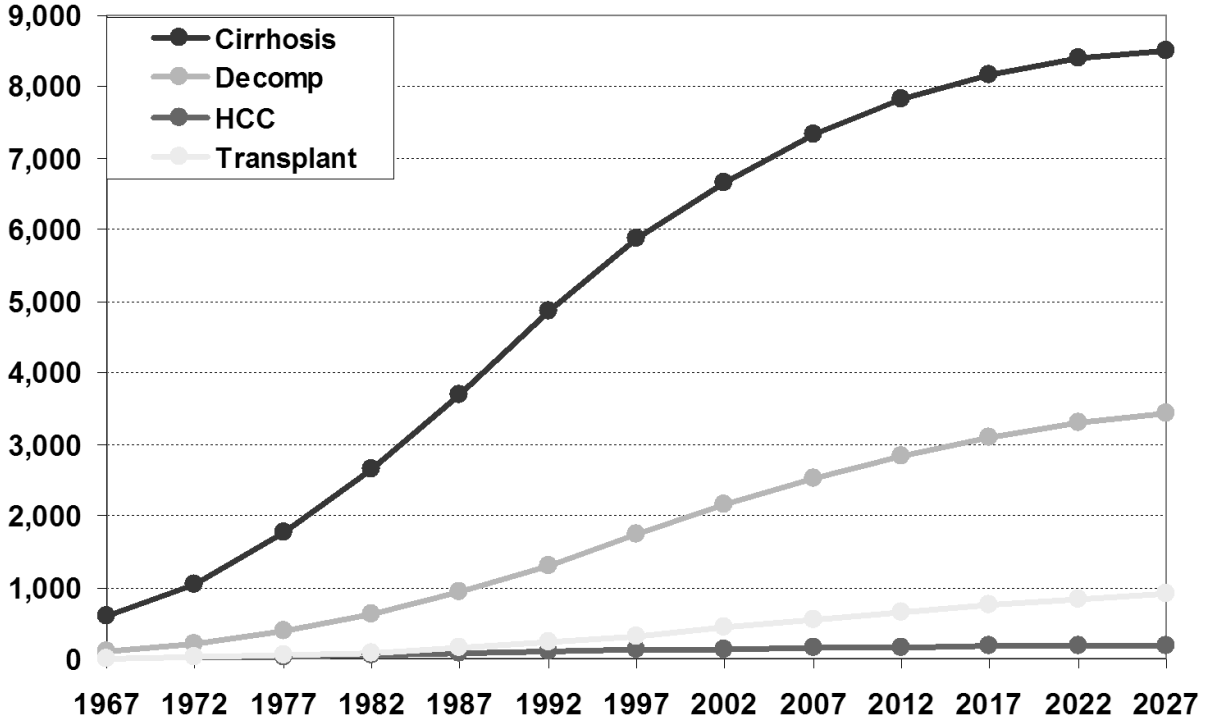
Figure 5 (below) illustrates the projected incidence of serious consequences of untreated hepatitis C in the Ontario population based on current and projected levels of infection to 2027. Figure 6 illustrates the projected prevalence of these consequences, which will result in increased burden on the health care system and associated costs. Sequelae modelled here (Figures 5 and 6) include cirrhosis of the liver; hepatic decompensation ("liver failure"), hepatocellular carcinoma (i.e. primary liver cancer); and liver transplantation, as well as hepatitis C-related deaths.

Figure 5: Modelled incidence of hepatitis C sequelae in Ontario, 1967-2027



Decomp, hepatic decompensation; HCC, hepatocellular carcinoma; HCV, hepatitis C virus.
Source: Dr. Robert Remis, Ontario HIV Epidemiology Monitoring Unit (OHEMU).

Figure 6: Modelled prevalence of hepatitis C sequelae in Ontario, 1967–2027



Decomp, hepatic decompensation; HCC, hepatocellular carcinoma.
Source: Dr. Robert Remis, Ontario HIV Epidemiology Monitoring Unit (OHEMU).

3. Modes of Transmission and Infection Risks

KEY POINTS

- The vast majority of hepatitis C virus (HCV) transmissions involve blood-to-blood contact.
- Most new HCV infections in Ontario are related to unsafe injection drug use practices.
- There is biological and epidemiological evidence for transmission of HCV by non-injection drug use.
- The strongest evidence for sexual transmission of HCV is among human immunodeficiency virus (HIV)-positive people, especially HIV-positive men who have sex with men.
- Most studies of sexual transmission in other populations are of only weak or moderate quality, and in general suggest that the risk of sexual transmission is low in the absence of blood-to-blood exposures.
- No studies are currently available that document hepatitis C incidence in Canadian provincial or federal correctional facilities; however, prevalence is known to be elevated compared to the general population, and there is evidence for higher-risk sharing of drug injection equipment in these settings. Unsterile tattooing and traumatic blood exposures are less well researched but are also likely to result in HCV exposures during incarceration.
- Transmission of HCV to health care workers may occur as a result of needle-stick exposures to the blood of an infected patient; there is no evidence of transmission via exposure of intact mucous membranes, but available evidence is not considered sufficient to definitively rule out this possibility; bodies responsible for regulating health professions are developing guidelines for hepatitis C–infected health care workers.
- Outbreaks of hepatitis C among hemodialysis patients and in personal services settings have been linked to inadequate infection control practices, and guidelines to prevent these have been published.
- Before the availability of screening tests, blood transfusion and organ transplantation were the most common sources of HCV transmission. Some individuals may still be unaware that they are infected, but over time this number is diminishing. Current transmission risk from transfusion is reported to be between 1 per 2.3 million and 1 per 13 million units transfused.
- Perinatal transmission risk is estimated to be 4 to 7 per cent, but is substantially higher with HIV co-infection. Treatment during pregnancy is limited to specific recommendations due to drug toxicity. Breastfeeding is considered safe, but mothers are usually advised to avoid breastfeeding if their nipples are cracked and bleeding.
- HCV testing is not currently part of routine immigration medical testing in Canada. Immigrants and refugees from countries with a high prevalence of hepatitis C due to unsterile medical injections or other practices should be offered education and screening for hepatitis C; this is especially important for those who are positive for HIV or the hepatitis B antigen.

Background

Transmission of hepatitis C occurs via blood-to-blood contact, including use of contaminated syringes and other injecting equipment; sharing of drug inhalation equipment such as straws and pipes; hemodialysis; blood transfusion and blood products; organ transplants; unsterile acupuncture; unsterile medical procedures; unsafe tattoos; and accidental needle-stick exposures among health care workers.

Modes of transmission for which the level of risk is less well documented include sexual transmission and transmission by sharing personal items. The weight of evidence supports the occurrence of both types of transmission, but studies suggest that they are uncommon. In determining the risk of sexual transmission, it is necessary to distinguish other concomitant risks. For example, sexual partners may also share equipment for the injection or inhalation of drugs, or they may share personal items such as razors or toothbrushes. In developing countries, they may have common exposures to unsterile medical injections or other procedures.

Evidence related to these modes of transmission is summarized below and reviewed in more detail in later sections that address prevention and management.

Evidence

Injection Drug Use

A recent systematic review of the global epidemiology of hepatitis C in people who use drugs estimates that 10 million people who use drugs worldwide (95 per cent confidence interval [CI] 6.0–15.2 million) are infected with HCV.[12] Prevalence data for anti-HCV were identified for 77 countries, of which 25 had prevalence between 60 and 80 per cent, and 12 had prevalence over 80 per cent. Studies of people actively injecting drugs in Canada have identified the prevalence of HCV antibodies to be from 47 per cent to 88 per cent.[13,14]

As indicated above, the most common mode of new HCV transmissions in Ontario in recent years is unsafe IDU practices.[10] There is evidence supporting the effectiveness of distributing sterile injecting equipment (needles/syringes and other materials) in preventing transmission of HIV, making harm-reduction programs a high priority for public health action to prevent HIV.[15] Although the evidence for hepatitis C prevention is weaker, there is evidence that harm-reduction programs reduce risky injection behaviour, and this, together with the importance of preventing HIV in the same population, make harm-reduction programs an important part of HCV prevention efforts (see Chapter 6).

Non-injection Drug Use

Studies have found an association between sharing inhalation equipment for non-injection drug use and hepatitis C infection among drug users who have no history of injecting.[16,17] A systematic review by Scheinmann et al in 2007 also concluded that hepatitis C infection is much more common among non-injection drug users than the general population, but that gaps remain in definitively proving that hepatitis C is transmitted via non-injection drug use.[18] Since the Scheinmann review, further evidence has accumulated pointing to elevated prevalence of hepatitis C among drug users who have never injected and identifying sharing of devices for smoking or inhaling drugs as a risk factor for hepatitis C.[19,20] Since randomized trials to define the level of risk will never be feasible or ethical, and because large cohort studies of non-injection drug users are also unlikely because of logistical and cost issues, public health action must be based on this accumulating moderate-quality evidence, together with additional studies demonstrating biological plausibility.

There is evidence that HCV is present in saliva and gingival crevicular fluid. Experiments have shown that injection of saliva from an HCV-infected chimpanzee into another chimpanzee caused infection,[21] and there is a case report of a human bite from a hepatitis C–infected person resulting in productive hepatitis C infection.[22] Furthermore, crack smokers report burns and cuts on their lips when using makeshift inhalation equipment.[23]

There is the potential for contamination of inhalation equipment with blood or serum with these injuries if contaminated drug inhalation equipment is shared; the virus could access the bloodstream of those exposed to contaminated inhalation equipment if they also have burns and/or cuts on their lips. The presence of hepatitis C on used inhalation equipment has been confirmed by a recent Canadian study.[24]

A literature review table summarizing the studies available on hepatitis C and non-injection drug use is included in Appendix C.

Sexual Transmission

Studies have suggested that sexual transmission is significantly higher among men who have sex with men (MSM) than among the general heterosexual population, and that this is linked to co-infections with HIV and/or genital ulcer diseases (particularly syphilis), as well as to specific potentially traumatic practices such as unprotected anal intercourse, fisting and rimming.[25-28] Studies that have attempted to examine specific sexual practices in heterosexuals have also suggested links between hepatitis C transmission and co-infection with other sexually transmitted infections (STIs), exposure to the menstrual blood of an HCV-positive partner, and vaginal trauma resulting in damage to the mucosa.[29] Some studies have identified a correlation between the number of sexual partners a person has and hepatitis C infection. Studies that show higher frequency of specific exposures or behaviours in those with hepatitis C do not in themselves prove causation, however.[30] Some virological studies have attempted to strengthen the evidence by comparing the viral strains of partners and identifying the degree of likelihood that they are the same. However, if a common viral strain is identified in partners, it is still possible that they did not infect each other but were instead both infected by a common source; reliable behavioural information is still needed to address this possibility.[31]

In general, studies of the sexual transmission of hepatitis C should ask detailed questions about sexual behaviour (types of sexual activities, presence of blood, presence of other STIs etc.) and about other potential exposures (sharing of drug use equipment; sharing of personal items with the potential for blood contamination, such as toothbrushes and razors; other potential exposures, such as tattooing, piercing or unsterile medical procedures; receipt of blood or blood products prior to routine hepatitis C testing or in countries that may lack this testing etc.). Many studies have not collected sufficiently detailed information to demonstrate certainty that infection is attributable to sexual transmission. Even in studies where sexual transmission is likely, the questions may not be sufficiently detailed to elicit the specific types of sexual exposures and the degree of risk involved.

A recent major review by Tohme and Holmberg (2010) examined 80 qualifying reports about the evidence for or against sexual transmission of HCV.[30] They confirmed increased risk among people with multiple sexual partners (adjusted odds ratio [aOR] 2.2 to 2.9 in selected studies), but identified potential confounding due to the increased likelihood of IDU with a higher number of sexual partners. Based on the review, the authors found that women infected with HIV or other STIs had an aOR range for HCV infection of 1.9 to 2.7, while HIV-infected MSM had an aOR of 4.1 to 5.7. Risk of transmission in the latter was increased by mucosal trauma (e.g. related to fisting or use of sex toys) and by the presence of genital ulcer disease.

Table 8 reviews the strengths and weaknesses of study designs used to investigate sexual transmission of hepatitis C. A detailed review of studies investigating the sexual transmission of hepatitis C is included in Appendix D.

Table 8: Strengths and weaknesses of study methods used to examine sexual transmission of HCV

Methods	Strengths	Weaknesses
Case investigations of HCV-positive cases	• Can focus on cases without an obvious risk factor (for example no known blood-borne exposures) • May be less selection bias if all cases are investigated • Potential for public health to investigate more cases than in a single clinical setting	• Misattribution is quite likely in at least some cases • Cases may deny unsafe IDU practices due to stigma • Cases may fail to recall potential blood exposures • Cases may be unaware of some exposures, such as contaminated medical equipment
Cohort studies of sexual partners of HCV-positive cases	• Focus is on those with relevant sexual exposure	• Sexual partners may also share drug use equipment or personal items, such as razors and toothbrushes • Studies may not ask sufficiently detailed questions to be sure that sexual exposure has occurred, and to capture the nature and extent of the sexual behaviours
Prevalence studies of hepatitis C in groups thought to be at increased risk for sexual exposure (e.g. sex workers, STI clinic patients, HIV-positive patients)	• Could help to identify specific risks for sexual transmission (e.g. infection with STIs or HIV)	• Groups being studied may have other risk factors (e.g. sharing of drug use equipment) • Unclear if findings are generalizable to other sexual partners without STIs, HIV etc.
Virological studies confirming HCV in semen/spermatozoa of some chronically infected men	• Supports biological plausibility of sexual transmission	• Do not prove infectivity of HCV identified; require large epidemiological studies to prove link between HCV in semen/spermatozoa and sexual transmission • Do not address the question of whether exposure to bloodstream of partner is required to transmit infection
Virological studies confirming similarity of viruses in HCV-positive sexual partners	• Confirms likelihood of one partner having infected the other, or both infected from common source	• Do not prove route of transmission was sexual; do not rule out infection from a common source (e.g. through sharing drug use equipment, receiving medical injections or other services from a common source etc.)

HCV, hepatitis C virus; HIV, human immunodeficiency virus; IDU, injection drug use; STI, sexually transmitted infection.

Incarceration

People who use illegal drugs are at elevated risk for incarceration due to drug-related activities such as trafficking, convictions related to sex work, or property crimes to acquire money for drug purchase. In Ontario provincial correctional facilities, inmates serve sentences of less than two years, and frequently their period of incarceration is quite brief, so that they are less likely to inject drugs while in custody than federal inmates, who are generally serving much longer sentences.

Two studies examined HIV and hepatitis C among inmates in provincial detention in Ontario and in Quebec. In the Ontario study, 30 per cent of adult inmates self-reported a history of IDU.[32] Overall, the prevalence of hepatitis C was 16 per cent among men and 30 per cent among women, but it was much higher among those who reported IDU (54.7 per cent). In the Quebec study, 28 per cent of men and 43 per cent of women reported a history of IDU.[33] Similar to the Ontario study, the prevalence of hepatitis C was much higher among those who reported a history of IDU compared to those who did not. For men, the prevalence of hepatitis C was 16.6 per cent among non-injection drug users and 53.3 per cent among injection drug users. For women, the prevalence of hepatitis C was 29.2 per cent among non-injection drug users and 63.6 per cent among injection drug users. Even those who reported no IDU had markedly higher hepatitis C prevalence than would be expected in a general population sample.

Inmates in federal institutions likely have an even higher rate of problematic substance use, estimated at 70 to 80 per cent,[34] but this estimate includes alcohol problems, and therefore does not provide an explicit estimate of risk related to the injection or inhalation of illicit drugs. IDU may be more common in federal than provincial facilities because inmates have longer sentences, making the desire to use drugs and opportunities to make the necessary contacts more likely. The same source provides somewhat outdated data from a 1995–1997 intake survey, indicating that 18 per cent of federal inmates self-report IDU prior to incarceration, and a 1995 federal inmate survey reporting that 11 per cent of a sample of male inmates reported injecting during their incarceration. Given that the surveys were conducted by correctional authorities, there is a possibility for under-reporting, as a result of selection bias (i.e. who is willing to respond) or concern about providing information that might lead to negative responses from authorities. Despite the limited data from the correctional system, the relatively high prevalence of hepatitis C among injection drug users in the community, together with the data from the Ontario and Quebec studies noted above, makes it reasonable to assume that hepatitis C prevalence in correctional facilities is much higher than in the general population.

No data are currently available on the incidence of hepatitis C in Canadian correctional facilities, but there is evidence of risk behaviours likely to transmit hepatitis C in the context of a relatively high prevalent population. Studies have shown that people who were injecting drugs prior to incarceration inject less frequently in correctional facilities, but when they do inject, there is a high probability of injecting with used equipment, including makeshift equipment with a higher risk of blood contamination.[34] Although bleach has been made available in Canadian federal correctional facilities since the mid-1990s, there are currently no needle-exchange programs, despite their proven efficacy in the community and in correctional facilities in Europe and Central Asia.[35] Current standards of practice recommend that bleach not be used except where provision of sterile needles is not feasible, since it may not reliably eliminate blood-borne infections, especially HCV.[36] Furthermore, World Health Organization (WHO) standards for correctional facility health clearly state that inmates must be provided with the same standards of health care that are available in the community,[37] which in Canada includes access to sterile injecting equipment as provided by needle-exchange services.

Although not extensively researched, tattooing is widespread in correctional facilities and thought to carry risks for hepatitis C transmission in the absence of safe tattooing equipment and techniques. A pilot program to provide safe tattooing materials in federal correctional facilities was undertaken in 2005; however, the program was discontinued prior to dissemination of the evaluation, even though it was subsequently reported that the evaluation supported the effectiveness and even the cost-effectiveness of the program.

Blood-to-blood contact may also occur in correctional facility settings in the context of fights and other forms of violence, but there is very little research on the degree of risk for hepatitis C, that may be associated with this aspect of correctional facility life.

Occupational Exposure

Studies suggest that health care workers are at risk for hepatitis C when they sustain needle-stick injuries involving blood from hepatitis C carriers.[38,39] There is no evidence for transmission via exposure of intact mucous membranes to blood or blood products, but current evidence does not allow a definitive statement that such transmission is not possible. Guidelines for the management of parenteral exposures to HIV, hepatitis B, and hepatitis C have been produced by Health Canada and the U.S. Centers for Disease Control and Prevention (CDC).[39,40] These guidelines state that immunoglobulin and antiviral agents (e.g. interferon with or without ribavirin) are not recommended for post-exposure prophylaxis of hepatitis C. Instead, they recommend that the hepatitis C status of the source and the exposed person be determined, and for health care workers exposed to a hepatitis C–positive source, that follow-up hepatitis C testing be performed to determine if infection develops. The average interval between occupational exposure and seroconversion is six to seven weeks, but it may vary from two to 26 weeks.[41] Should seroconversion occur, there is a high success rate in treatment of newly acquired hepatitis C[4,6,7]; treatment should be considered in this situation.

Dialysis

A recent review of health care–associated hepatitis B and hepatitis C transmission from 1998 to 2008 reported by the CDC identified six hemodialysis-associated outbreaks of hepatitis C involving 40 incident cases among 490 people potentially at risk.[42] Studies have suggested that increased risk for hepatitis C in hemodialysis patients is mainly related to problems with infection control practices, and methods to avoid such infections have been published.[43,44]

Blood Transfusion and Organ Transplants

Before the introduction of effective screening tests for hepatitis C, blood transfusions and organ transplants carried significant risks of transmitting infection. Some individuals living in Canada may have become infected with hepatitis C via a blood transfusion or organ transplant before 1990 and still remain unaware of their infection, but over time this number has been significantly reduced. Current screening tests have greatly lowered the risk of hepatitis C transmission via blood transfusion or organ transplant in Canada. A recent publication reported that the risk of contracting hepatitis C from a blood transfusion in Canada is between 1 per 2.3 million and 1 per 13 million units transfused.[45]

Perinatal Transmission

Hepatitis C can be transmitted from infected pregnant women to their newborns. Rates of transmission are likely to vary depending on maternal viral load, the presence of co-infections such as HIV, and the mode of delivery. Generally, rates of mother-to-child transmission are reported to be 4 to 7 per cent, and it is recommended that all infants born to hepatitis C ribonucleic acid (RNA)–positive mothers be tested for hepatitis C RNA on two occasions: at two and six months and again at 18 to 24 months; HCV antibody testing should be included with the 18- to 24-month test.[46] Rates of hepatitis C transmission from mothers co-infected with hepatitis C and HIV may be two to five times higher than from those with hepatitis C alone.[46] Elective cesarean delivery is not recommended for women with chronic hepatitis C infection alone, and treatment to prevent transmission is limited due to the fetal toxicity of some currently available medications for hepatitis C.[46-47] Infants found to be infected with HCV should be referred to a pediatrician.

There is no evidence that hepatitis C is present in breast milk or transmitted through breastfeeding. Hepatitis C-positive mothers who are known to be HIV-negative can be advised to breastfeed their infants, although it might be wise for mothers to abstain from breastfeeding if their nipples are cracked and bleeding.[47-49]

Immigration from Countries with High Hepatitis C Prevalence

Worldwide, an estimated 170 million people are infected with hepatitis C; it is among the leading causes of cirrhosis and hepatocellular carcinoma. Unsafe injections and other medical procedures received in official health care settings, or via rituals and alternative practitioners are believed to be the most important risk factors for hepatitis C in many countries, particularly where IDU is believed to be uncommon.[50] People living in Canada who may have been exposed to hepatitis C may be at increased risk for chronic hepatitis C infection and are candidates for screening or case finding. Screening for hepatitis C is not currently required as part of immigration or refugee medical assessments. Other mechanisms are required to inform newcomers about potential risks and provide them with access to hepatitis C counselling, testing and education. Newcomers with HIV or chronic hepatitis B infections must be offered hepatitis C testing and care, since co-infection with hepatitis C and HIV or hepatitis B has a much worse prognosis and is more difficult to treat than hepatitis C, HIV or hepatitis B alone. Public health can play an important role in facilitating screening for hepatitis C among newcomers to Canada. Ensuring local health practitioners have appropriate education and are aware of the importance of hepatitis C screening among immigrants is an important component of programming. Outreach programming focused on individuals from highly endemic countries is also an important component of comprehensive care.

Cofactors/Risk Factors for Disease Progression

Most morbidity and mortality arising from hepatitis C occurs as a result of chronic infection that leads to cirrhosis of the liver, liver failure and hepatocellular carcinoma. A number of cofactors increase the likelihood of such progression; some, including male sex and older age,[51] are non-modifiable, but public health can play a role in reducing risk factors that are modifiable. Co-infection with hepatitis A or hepatitis B can accelerate hepatitis C-related liver disease;[51] all hepatitis C cases qualify for publicly funded hepatitis A and hepatitis B vaccination and should be offered appropriate vaccination. In addition, excessive alcohol consumption has been strongly linked to liver disease in people with hepatitis C. [52] Public education and individual counselling about hepatitis C infection should include information about the need to reduce alcohol consumption; referral for alcohol treatment should be available for those who have problems reducing heavy drinking. The degree of impact of low to moderate alcohol consumption and appropriate interventions are less clear. Research in the U.S. published in 2007 found that physician messages are frequently ambiguous for patients who consume alcohol but who are not dependent or problem drinkers.[53] Current practice in Ontario would suggest that clients be advised to ensure alcohol intake is less than one standard drink per day, but complete abstention may be the safest course for those who are able.

Some evidence suggests that daily cannabis use is associated with moderate to severe liver fibrosis, and it has been recommended that people with chronic hepatitis C infection reduce or abstain from marijuana use.[54] At the same time, there is also research showing benefit from the use of oral cannabinoids to reduce hepatitis C treatment-related symptoms that contribute to weight loss.[55]

Cigarette smoking is considered to increase the risk for progression of chronic hepatitis C infection,[56] and the International Agency for Research on Cancer has declared smoking to be a risk factor for hepatocellular carcinoma.[57] A recent review of the risks of alcohol, marijuana and tobacco for the progression of hepatitis C states that patients should be informed of the deleterious effects of all three and offered appropriate supports towards abstinence.[56]

There is some relatively weak evidence that coffee may be beneficial in lowering the risk of death from hepatocellular carcinoma in hepatitis C-positive patients, but not all studies have demonstrated this effect, likely due to confounding factors.[58]

Another potentially modifiable risk factor for progression of hepatitis C is obesity and non-alcoholic fatty liver. Several reviews have suggested that insulin resistance and the metabolic syndrome accelerate fibrosis in

chronic hepatitis C patients and may reduce rates of successful treatment.[59] As a result, weight reduction in an effort to improve insulin response may reduce the rate of development of fibrosis and improve treatment response, although further evidence of efficacy is needed.[59-64]

People with hepatitis C who are infected with HIV are also at risk for more rapid development of severe liver disease. Evidence suggests that MSM with HIV are more likely to become infected with hepatitis C via sexual transmission than those who are HIV-negative.[26-28,65,66] Users of injection drugs are at increased risk of being infected with hepatitis C and HIV, because sharing of injection equipment is a major risk factor for both.[67] People with either of these infections should be tested for the other, as well as for chronic hepatitis B infection (see recommendation 4.9).

4. Surveillance and Testing

RECOMMENDATIONS

Ministry of Health and Long-Term Care, Public Health Ontario and Local Public Health Units

4.1 Public health units, Public Health Ontario and the Ministry of Health and Long-Term Care should use surveillance data to examine the epidemiology of newly acquired hepatitis C infections and human immunodeficiency virus (HIV)/hepatitis C virus (HCV) co-infections; they should use this information to identify possible clusters that require immediate investigation, as well as to identify the need for further prevention measures tailored to the risk factors being reported.

Ministry of Health and Long-Term Care and Public Health Ontario

4.2 Public Health Ontario and the Ministry of Health and Long-Term Care should work towards making both positive and negative hepatitis C ribonucleic acid (RNA) laboratory results reportable to public health (when these are available after a positive antibody result) for surveillance and, where appropriate, case and contact management.

4.3 Public Health Ontario and the Ministry of Health and Long-Term Care should divide the surveillance case definition for hepatitis C into more specific ones for newly acquired and chronic cases.

Ministry of Health and Long-Term Care

4.4 The Ministry of Health and Long-Term Care should use surveillance data to plan and evaluate hepatitis C control in Ontario.

Public Health Ontario

4.5 Laboratories undertaking HCV antibody testing should include with each positive test result a recommendation to clinicians to conduct follow-up RNA testing. They should facilitate this by providing a testing form and information.

Local Public Health Units

4.6 All hepatitis C cases may benefit from (and should have access to) treatment. Where resources are sufficient, follow-up of all newly reported cases of hepatitis C (with collection of risk-factor information) should be undertaken, whether cases are newly acquired or chronic. Where resources are limited, priority should be given to active follow-up of newly acquired cases (those infected within the preceding two years).

4.7 Positive RNA tests after sustained virological response to treatment should be investigated as possible re-infection.

4.8 Public health units and the Public Health Laboratory should work together to improve the identification of newly acquired hepatitis C infections by matching HCV-antibody-positive tests with previous negative tests.

4.9 People infected with HIV or hepatitis B should be strongly encouraged to undergo testing for hepatitis C, and vice versa. If not already immunized for hepatitis A and hepatitis B, people with hepatitis C

should be encouraged to be appropriately immunized for these, unless contraindicated or unnecessary (i.e. already known to be immune to or infected with hepatitis B).

4.10 People who are severely immunocompromised but are potentially chronically infected based on exposures that put them at risk for hepatitis C should have RNA testing, even if antibody testing is negative.

KEY POINTS

- Technical difficulties and data-sharing barriers must be resolved so that surveillance of co-infections (e.g. with HIV, hepatitis B virus and/or STIs) can allow effective case management of co-infected individuals and evaluation and resource allocation for hepatitis C prevention programs.
- The identification of cases with HCV ribonucleic acid (RNA) is needed to determine chronic infection and risk of transmission to others.
- The ability to distinguish between chronic and newly acquired cases among HCV test reports is important for prevention and control efforts.
- People with the HCV antibody but confirmed negative for RNA (two negative RNA results within six months), whether through treatment or spontaneous clearing, can be considered resolved cases and are no longer infectious to others, but remain at risk for re-infection if exposed again.

Surveillance data should be analyzed effectively at both the local PHU and provincial levels to evaluate hepatitis C programs and direct resources most effectively. Surveillance should include identifying and quantifying the extent of co-infections with HIV and HCV. Co-infections with HIV and HCV are very serious health problems, since each infection complicates the other and makes successful treatment more difficult and serious illness more likely. Co-infections are also likely to be an important marker for higher-risk behaviours in affected populations, primarily people who use drugs and some MSM.

Case Definition

Current hepatitis C surveillance case definition in Ontario (as of this document's publication date)
Detection of hepatitis C virus (HCV) antibodies, (if greater than 18 months of age)
OR
Detection of hepatitis C virus (HCV) ribonucleic acid (RNA)

Recommended hepatitis C surveillance case definitions
(Short version—see complete details in Appendix E)

Hepatitis C, newly acquired
Detection of anti-HCV antibody or HCV RNA from a person who has had a negative anti-hepatitis C antibody test recorded within the past 24[1] months (see Appendix E for children less than two years of age),
OR
Detection of anti-hepatitis C antibody or HCV RNA AND appropriate clinical evidence AND exclusion of hepatitis A and B

Hepatitis C, chronic or unspecified
Greater than 18 months of age AND detection of anti-hepatitis C antibody or HCV RNA AND does not meet the definition of newly acquired hepatitis C

As of the publication of this document, the current Ontario case definition for hepatitis C is included in the *Infectious Diseases Protocol, Appendix B: Case Definitions,* which can be accessed at: http://www.health.gov.on.ca/en/pro/programs/publichealth/oph_standards/docs/hep_c_cd.pdf. Users of this document should check this source regularly for updates.

To make hepatitis C surveillance data more specific, meaningful and adaptable for different prevention and control purposes, the Hepatitis C Working Group proposed that the case definition for hepatitis C in Ontario distinguish between newly acquired and chronic infections. This is consistent with hepatitis C case definitions in the United States, the United Kingdom and Australia.[68,69,70] It is also consistent with a 1999 Canadian recommendation by the Expert Working Group for Strain and Laboratory Surveillance of HCV.[71] The recommended newly acquired and chronic hepatitis C case definitions for Ontario, as well as the Public Health Agency of Canada (PHAC), U.S., U.K. and Australian case definitions, can be found in Appendix E.

Any change in the hepatitis C case definitions for Ontario should consider the PHAC definition to ensure compatibility.[72] The recommended new case definitions, separated into newly acquired and chronic or unspecified (above and in Appendix E), are compatible with the PHAC case definition in that the sum of the newly acquired and chronic or unspecified cases should be the appropriate cases to report to PHAC under the undifferentiated hepatitis C case definition.

Ontario's current use of hepatitis C antibody positivity for surveillance provides a very broad case definition that will include both newly acquired and chronic cases, as well as those who have been infected in the past but have cleared the virus and are not chronically infected. It is vital to encourage those with positive anti-HCV tests to also undergo HCV RNA testing and determine if they are chronically infected. Measurement of the number of people with HCV RNA indicating chronic infection will help define future health care needs and

[1] 24 months was chosen because it is more inclusive, more feasible and will ensure that acute cases in Ontario are relatively robust compared to considering a 12-month time period.

transmission risk in the population. Based on the best available science, those who are positive for the HCV antibody but negative for RNA based on two tests done six months apart (whether through treatment or spontaneous clearing) are considered to no longer have active hepatitis C, although they remain at risk for re-infection.

From a prevention and control perspective, it would be valuable to distinguish between newly acquired and chronic infections and to measure the number of newly acquired infections reported each year, since this would allow for investigation of current clusters of disease and risk of transmission. It would also improve surveillance and evaluation of prevention and case management activities. Furthermore, newly acquired cases have been shown to have a better response to treatment.[73] Recent evidence suggests that newly acquired asymptomatic cases are unlikely to clear spontaneously and should be considered for treatment without delay, while a higher proportion of acute symptomatic cases (many of whom are injection drug users) may clear the virus spontaneously; [74] it may be reasonable to delay treatment for a few weeks in this group to avoid unnecessary treatment.

It should be noted, however, that distinguishing newly infected cases from chronic cases will still not lead to a measure of true incidence, since the majority of newly infected cases are asymptomatic and may not seek clinical care and testing. Mathematical modelling will still be needed to estimate the true incidence of new hepatitis C cases. Encouraging those with ongoing higher-risk behaviour to be tested at least once per year will increase the likelihood of identifying incident cases.

For those who undergo testing and are confirmed to be antibody-positive, the first step at both the provincial and PHU levels should be to look for previous positive tests in the same individual. Individuals with previous positive tests can be considered to not have a newly acquired infection, and if they have been reported in the Integrated Public Health Information System before, they do not require repeat investigation. It may be appropriate to confirm that they have received previous counselling, however (see Chapter 7). For those with no previous positive tests, the Public Health Laboratory (and ideally all laboratories) should try to match the positive test with the most recent negative test if one exists. This gives evidence for when the individual became infected. If this period is less than two years, more intensive efforts should be made to obtain risk-factor information and ensure access to medical care. If an antibody-positive individual has previously donated blood without being notified of a blood-borne infection, this too can help to define a time when he/she was HCV-negative. People who are antibody-positive should be asked about symptoms compatible with hepatitis C in the preceding two years, including jaundice, dark urine and abdominal pain, which may indicate acute infection; testing for acute hepatitis A and B could help rule out these infections as causes of the symptoms. When no previous negative test or recent symptoms compatible with hepatitis C can be identified, the presence of recent risk behaviour (see Chapter 3) does not prove that the case represents newly acquired infection, but it does increase concern about possible transmission to and/or from a positive case and requires more intensive investigation and case management (see Chapter 7).

Appendices F and G provide information about the laboratory testing algorithm and specimen collection for hepatitis C currently used in Ontario (at the time of publication). Readers should check regularly for updates from the laboratory.

Public Health Data Collection from Cases

The highest priority for public health data collection should be cases who are newly infected (within the last 24 months). For surveillance purposes, after determining that the case has not been previously reported, the key data to be collected are demographic characteristics (age, sex and race, including Aboriginal status) and risks for hepatitis C infection. The risks to be assessed have been reviewed and draft definitions developed.

The CDC has recently proposed a hepatitis C case reporting form (http://www.cdc.gov/hepatitis/PDFs/vhsp02.pdf).[75] Based on the Ontario context, where a time frame is specified, we recommend that the maximum duration for risk-factor reporting in acute cases be 24 months and the minimum duration be from the last negative result. The CDC proposes the following risk factors, which can also be considered in the Ontario context:[75]

- Contact of a hepatitis C case since the last known negative result or 24 months (sexual contact, household/non-sexual contact, other)
- Number of sexual partners since last known negative result or 24 months (men and women)
- Ever having a sexually transmitted disease, and year of most recent treatment
- Injection or non-injection drug use since last known negative result or 24 months
- Health care exposures and other parenteral exposures since last known negative result or 24 months: hemodialysis; accidental needle-stick injury or puncture with other blood-contaminated object; transfusion; outpatient intravenous infusion or injection; or any other exposures to someone else's blood
- Employment since last known negative result or 24 months as a health care worker (medical or dental) and contact with human blood
- Employment since last known negative result or 24 months as a public safety worker (e.g. firefighter, law enforcement or correctional officer) and direct contact with human blood
- Receipt of a tattoo since last known negative result or 24 months in a commercial facility, a correctional facility or other
- Body piercing (other than ear) since last known negative result or 24 months in a commercial facility, a correctional facility or other
- Dental work or oral surgery since last known negative result or 24 months
- Surgery (other than oral) since last known negative result or 24 months
- Hospitalization, residence in a long-term care facility or incarceration (correctional facility, jail or juvenile facility) since last known negative result or 24 months
- Ever having been incarcerated for longer than six months

For chronic or resolved cases, the following risk factors are recommended for reporting:

- Blood transfusion or organ transplant prior to 1990
- Receipt of clotting factor concentrates prior to 1987
- Ever on long-term hemodialysis
- Ever injected drugs
- Approximate number of lifetime sexual partners
- Ever incarcerated
- Ever treated for an STI
- Ever a contact of someone with hepatitis (sexual, household, other)
- Ever employed in a medical or dental field involving direct contact with human blood

For some of the risk factors above—such as number of sexual partners or incarceration—the risk factor may be a marker for other unmeasured sources of increased risk (such as blood exposures during risky sexual practices or during fights in correctional facility settings).

Case and contact follow-up based on relevant risk factors is discussed further in Chapter 7.

For surveillance of HIV/HCV co-infections to be effective, PHUs must have access to the necessary data. No barriers currently exist in data sharing for individual case management (i.e. other diagnoses on a named case can be identified), but it is not possible to do effective surveillance examining all cases of co-infections, since

the data can be accessed only on a case-by-case basis at present. For PHUs to estimate the prevalence of co-infections in their area, the public health information system's reporting sub-system has to allow for querying of multiple diagnoses across PHU areas. Co-infections are especially an issue for those with long-standing chronic infections, such as HIV, hepatitis C and hepatitis B. PHUs and Public Health Ontario should work together to remove barriers to data sharing and address technical difficulties in the surveillance of co-infections in current and future public health information systems.

5. Screening

RECOMMENDATIONS

Public Health Ontario

5.1 Research is recommended to determine whether the recent recommendation from the United States Centers for Disease Control and Prevention about birth cohort screening is applicable in Canada.

Local Public Health Units

5.2 Public health units should offer or facilitate access to hepatitis C screening for people at increased risk of infection (see Screening in Public Health Settings).

5.3 Public health units should make specific efforts to offer or facilitate hepatitis C screening to all people at increased risk because of current or former sharing of injection drug use equipment or drug inhalation equipment. Screening may be offered through street outreach and partnership with community agencies or services offering harm-reduction programs.

5.4 Public health units should facilitate access to primary care follow-up for those found to be infected, either on-site at harm-reduction programs or via referral.

5.5 As an essential part of screening, patients must be provided with pre- and post-test counselling about hepatitis C (see Appendix H) so that they understand the reasons for testing and the implications of the results and can provide informed consent. Those who test positive must be given education, the means to prevent transmission to others, information about the availability of treatment, and referral to follow-up care.

5.6 People with ongoing risk of exposure to the hepatitis C virus should be offered counselling and support services to reduce risk behaviour (see Chapters 6 and 7), advised of methods to prevent transmission to others in the event that they do become infected, and should be encouraged to undergo testing at least annually for hepatitis C.

KEY POINTS

- PHUs should offer screening to clients with hepatitis C risk factors, either directly or by referral.
- Although there are currently no specific recommendations about the frequency of screening for people with ongoing risk exposures (e.g. sharing of drug use equipment), it is reasonable to encourage testing at least annually.
- The United States Centers for Disease Control and Prevention has recommended a single screening during routine primary care of all members of the cohort born between 1945 and 1965 as cost-effective, based on elevated prevalence in this age group and the many undiagnosed cases estimated in the United States. Because Canada has a lower estimated prevalence of undiagnosed hepatitis C infections, it is not clear whether the same recommendation should apply in Canada.

Published Guidelines About Screening

Screening refers to the identification of unrecognized disease in those who are asymptomatic and not actively seeking medical care for symptomatic illness. Canadian clinical practice guidelines recommend testing for hepatitis C as part of the investigations of people with evidence of possible chronic liver disease, such as abnormal alanine aminotransferase (ALT) levels,[76] but this would be considered case finding, not screening. The same guidelines recommend the testing of people with risk factors, defined as prior IDU, even if remote and only occasional; transfusion of blood products prior to 1990; and immigration from countries with high prevalence rates of hepatitis C.

The U.S. Preventive Services Task Force (USPSTF) conducted a review of hepatitis C screening in 2004 (see below) and recommended against screening of the general population (Grade D), concluding that the potential harms of screening adults who were not at elevated risk for hepatitis C infection outweighed the potential benefits.[77] This conclusion was drawn using a previous population-based survey estimate that the prevalence of hepatitis C in the general U.S. population was about 2 per cent (1.8 per cent in the general population, 2.3 per cent in adults over 20)[78]—substantially higher than the reported general population prevalence in Canada of 0.8 per cent.[79] The same review concluded that there was insufficient evidence to make a recommendation one way or the other for screening in higher-risk populations (such as injection drug users), because there was insufficient evidence for the long-term benefit of treatment in preventing severe sequelae, and about the potential harms from screening. The World Health Organization released guidelines for the screening, care and treatment of people with hepatitis C infection in low- and middle-income countries and recommended screening (based on moderate-quality evidence) in individuals who are a part of a population with high prevalence of HCV or who have a history of high-risk behaviour.[80]

The USPSTF recommendations differ from those of the CDC and the National Institutes of Health (NIH) Consensus Panel, both cited by the USPSTF.[77] Both the CDC and the NIH recommend screening of groups at increased risk, but with somewhat different definitions of increased risk.[77] Both recommend screening injection drug users, hemodialysis patients and recipients of organ transplants or blood transfusions (CDC before 1992, NIH before 1990). In addition, the NIH panel recommends screening of individuals with multiple sexual partners; spouses or household contacts of HCV-infected people; and those who share instruments for intranasal cocaine use. The CDC recommends screening for children born to mothers infected with hepatitis C; those who received clotting factor concentrates before 1987; those with occupational exposure to HCV-positive blood; and patients with persistently abnormal ALT levels, indicative of possible chronic liver disease. The CDC now recommends that individuals in the 1945 to 1965 birth cohort also be screened for HCV once during routine primary care.[81] Other groups identified by the CDC for whom routine screening is uncertain include recipients of transplanted tissue, those who use intranasal cocaine and other non-injection illegal drugs, those with a history of tattooing or body piercing, those with a history of multiple sex partners or STIs, and long-term steady partners of people with hepatitis C.

A Canadian consensus meeting in 2007 suggested that approximately 35 per cent of HCV-infected people in Canada do not know they are infected, and it recommended that programs be established to identify these people so they can be offered curative therapy and/or lifestyle modification.[82] It is a principle of screening programs that if they are to be established, resources must be available to offer counselling and other care or treatment services to those who are found to be infected. Therefore, public health authorities need to consider what information and resources are available for those who might participate in screening programs, and to balance the financial and human resources required for screening with other potential uses of the resources. For example, offering hepatitis C screening as part of comprehensive harm-reduction and primary care services for injection drug users is likely to be more cost-effective than general population screening.

The Public Health Agency of Canada provides a comprehensive Primary Care Management of Chronic Hepatitis C Professional Desk Reference that gives primary care practitioners with a detailed overview of those at risk of

hepatitis C who should be screened, in addition to further information on laboratory results interpretation and counselling.[83]

Cost-Effectiveness of Screening

Appendix I provides a summary of the literature reviewed with respect to the cost-effectiveness of screening for hepatitis C. The major benefit usually ascribed to screening is the opportunity for treatment and cure of hepatitis C, so that significant future morbidity and mortality from chronic hepatitis—as well as health care costs such as care for decompensated cirrhosis and liver transplantation—can be averted. However, those who do not want to undergo treatment, do not respond to treatment or are ineligible for treatment may still benefit from screening for hepatocellular carcinoma, vaccination for hepatitis A and/or B, and lifestyle modifications such as reduced or eliminated use of alcohol.[84]

No published cost-effectiveness studies on hepatitis C population screening in Canadian settings had been identified as of May 2012. Screening of blood or organ donors was not considered relevant for this review, which focused on public health screening programs. Three recent cost-effectiveness studies from the United States,[81,85,86] using somewhat different methodologies, all concluded that in the U.S. context—with an estimated population prevalence of 1.8 per cent or more, highest in the cohort born between 1945 and 1965—screening of the 1945–1965 birth cohort in primary care settings, and possibly all adults aged 20 to 70, would be cost-effective. This is based on an estimate that approximately 50 to 75 per cent of infected adults have not been tested and do not know their infection status.[81]

One of the key issues in determining the applicability of such cost-effectiveness studies to Canada is the population prevalence of hepatitis C, as well as the proportion of chronically infected adults who are unaware of their infection. A study from Japan found general population screening and higher-risk population screening to be cost-effective, even though the general population prevalence was about 0.36 per cent[86,87]; however, it is not clear whether medical costs in Japan are equivalent to those in Canada, and the cost-effectiveness analysis assumed that all those identified with chronic hepatitis C were treated, which may not be realistic in many settings. One of the U.S. studies indicated that general population screening was cost-effective as long as the general population prevalence was greater than 0.53 per cent,[85] lower than the estimated prevalence for Canada. Further research and consideration specific to the Canadian context is needed to clarify the cost-effectiveness of general population screening, although the consistency of findings from different jurisdictions about the cost-effectiveness of screening for higher-risk people (such as current and former drug users) supports the conclusion that such screening is very likely to be cost-effective in Canada as well.

The recommendations from the three U.S. studies about population screening cost-effectiveness acknowledge that there are few real-world empirical data on this type of screening, and that the benefits of such an approach can only be realized if primary care providers, patients and specialty treatment services all ensure that screening, referral, appropriate management and follow-up are successfully implemented. Potentially relevant to the issue of primary care involvement is a study by Helsper et al in the Netherlands, which demonstrated that hepatitis C information and promotion of testing aimed at higher-risk people on its own was ineffective, but became cost-effective when accompanied by education and support for primary care providers (although not as cost-effective as an active program to promote testing of drug users).[88] In the Netherlands, prevalence in the general adult population is estimated at 0.1 to 0.4 per cent, with only about 25 per cent of chronic cases diagnosed, so screening efforts for the general public in this study were aimed at those with risk factors—including immigrants from higher-prevalence countries, injection drug users, and former injection drug users—rather than at encouraging testing for all adults. As in Canada, hepatitis C prevalence among injection drug users in the Netherlands is very high (estimated at 47 to 79 per cent); in this setting, active education and screening programs introduced into addiction services were cost-effective.[88] The impacts of screening and treatment on people who use drugs are discussed further in Chapter 6.

Screening in Public Health Settings

In Ontario, most hepatitis C cases are detected by primary health care providers. Public health providers are most likely to encounter unscreened people who are at increased risk for hepatitis C while following up reported cases of hepatitis C, providing harm-reduction services or providing clinical services. Epidemiological evidence from the U.K. suggests that STI clinic patients have an increased risk of hepatitis C infection,[89] although it is not clear to what degree this risk is related to higher-risk drug use behaviours rather than higher-risk sexual behaviours. These service situations provide opportunities to screen higher-risk people who may be unlikely to receive regular health care services. However, when such screening is offered, it is essential that resources be available to provide education about hepatitis C, infection and transmission risks and reasons for the test, as well as to ensure that those who test positive are counselled and provided with referrals for follow-up care (see Chapter 7).

Based on the NIH and CDC reviews noted above and evidence provided in Chapter 3, the Hepatitis C Working Group recommends that the groups below be considered at increased risk. PHUs that offer hepatitis C testing should offer screening to these groups. PHUs that do not offer testing should educate health care providers about the need for screening and facilitate referral of these groups to health care providers who offer it:

- Current and former injection drug users
- Those who have shared intranasal or inhalation equipment (especially crack pipes) with others
- Anyone who has had blood-to-blood contact with a person with hepatitis C
- Recipients of blood, blood products or organs (in Canada prior to 1990)—may vary in other countries
- Children born to mothers infected with hepatitis C
- Those who have engaged in high-risk sexual behaviour with a person with hepatitis C or with a current or former injection drug user
- People who have had a tattoo (including permanent makeup) or piercing in a non-professional setting or who have reason to believe that the equipment used was not sterile
- Household contacts of hepatitis C cases who have shared personal grooming items that may have been contaminated with blood, such as razors, nail clippers and toothbrushes
- People infected with HIV or chronic hepatitis B carriers
- Immigrants and refugees from high-prevalence countries

6. Harm Reduction

RECOMMENDATIONS

Local Public Health Units

6.1 Public health units should ensure access to harm-reduction programs for injection drug users, including distribution of sterile needles/syringes and drug and injection preparation equipment as supplied by the Ontario Harm Reduction Distribution Program: sterile water in single-use vials, sterile cookers, new filters, sterile alcohol swabs, ascorbic acid and new tourniquets. Harm-reduction programs should not place arbitrary limits on numbers of needles or other supplies provided; instead, they should provide supplies according to client need. Clients should not be required to return needles to obtain new ones, but they should be encouraged to do so; given sharps disposal containers; and offered counselling on safe disposal of needles, syringes and other injection drug use equipment. Clients should be specifically educated about the risks of sharing needles, syringes and other drug and injection preparation equipment (such as spoons/cookers, filters, water, swabs and tourniquets) at the time these materials are distributed, and they should be educated about the appropriate use of the equipment.

6.2 Public health units should seek to involve people who are currently using or have previously used drugs (frequently referred to as *peers*) to participate in the planning, delivery and evaluation of harm-reduction programs to enhance service relevance and credibility for program users to develop trust in the community that uses drugs.

6.3 Public health units should incorporate harm-reduction measures in their programming (such as distribution of safer inhalation equipment) for smokers of illegal drugs, particularly crack and methamphetamine.

6.4 Clients with a history of illicit drug use and/or imprisonment should be counselled about their risks and offered testing for hepatitis C, hepatitis B and HIV.

KEY POINTS

- Because of the high prevalence of hepatitis C among people in Canada who use drugs and the increased risk of new HIV and HCV infections related to sharing of drug use equipment, harm reduction is an essential component of public health hepatitis C prevention policy and programming.
- Effective harm-reduction programs should include distribution of sterile needles and other injection equipment (cookers, filters, sterile water for injection, ascorbic acid packets, alcohol swabs, tourniquets) and safer smoking supplies (mouthpieces, stems and screens); education and counselling; confidential testing for HIV, HCV and bacterial STIs on-site or by referral; and referrals to other services as required (drug treatment, detoxification, primary care, mental health care, housing etc.).

Injection Drug Use

Studies of people actively injecting drugs in Canada have identified prevalence of HCV antibodies ranging from 47[13] to 88 per cent.[14] The most recent published report of I-Track, the behavioural and risk surveillance study

conducted in several Canadian cities with leadership and funding from PHAC, indicates that 69.1 per cent of recruited injection drug users had antibodies to hepatitis C, ranging from 51.4 per cent in Thunder Bay to 76.7 per cent in Prince George; Kingston was the Ontario city with the highest prevalence (73.3 per cent).[90] Unsafe IDU practices are currently the most important risk factor for new cases of hepatitis C in Canada, accounting for at least 60 per cent of all current hepatitis C transmission.[91]

Risk for transmission of hepatitis C has been linked to sharing of needles and syringes and to sharing of other injection-related equipment, such as cookers, filters and water.[36] The 2014 I-Track report mentioned above also included information on needle-sharing, with 21.9 per cent of participants reporting injection with used needles in the preceding six months (17.9 per cent in Sudbury, 18.5 per cent in Toronto, 19.0 per cent in Thunder Bay and 21.0 per cent in Kingston). [90] Reported borrowing of other used injection equipment apart from needles was much higher (33.9 per cent overall, 35.4 per cent in Sudbury, 35.7% in Kingston, 36.7% in Thunder Bay and 46.4 per cent in Toronto).

There is extensive evidence from many countries confirming the effectiveness of needle-distribution programs as a way to reduce HIV risk among injection drug users.[15] Although less extensively studied, there is also evidence to suggest that such programs can also reduce risk of hepatitis C transmission.[36] To ensure effective coverage levels of syringe provision, needle-exchange programs should not limit the number of needles distributed[92] and should include the goal of ensuring a sterile needle for every injection.[93] Detailed discussion of harm-reduction best practices and supporting evidence are available in Strike et al. *Best Practices for Needle Exchange in Ontario,* 2006. [36]

In addition to the proven importance of sterile needles and syringes to prevent transmission of blood-borne infections (as well as other bacterial contaminants that can cause endocarditis, abscesses etc.), there is evidence that even injectors who are careful to avoid the risks of needle-sharing may share other drug and injection preparation equipment (for example, water, cookers, filters, alcohol swabs, acidifiers and tourniquets).[36] Hagan et al measured hepatitis C seroconversion among a cohort of 317 active Seattle injection drug users who tested negative for HCV antibodies at study entry.[94] Among those who did not share syringes, sharing drug cookers and filtration cotton also elevated the risk of hepatitis C seroconversion six-fold (adjusted relative risk 5.9; 95 per cent CI: 1.1–31.7), and 54 per cent of hepatitis C infections in this group were attributable to cooker/cotton sharing. Hahn (2002) also conducted a prospective cohort study and found that sharing non-sterile drug injection equipment was an independent risk for hepatitis C seroconversion among young injection drug users, in addition to sharing of needles.[95] Thorpe (2002) confirmed that sharing of cookers and filters were independent risk factors for hepatitis C seroconversion in a prospective cohort study of injection drug users under 30 years of age, after controlling for sharing of needles.[96]

There is specific documentation demonstrating that some injection equipment can become contaminated with HIV and HCV, and it can be assumed that the equipment also contributes to transmission. For example, Crofts et al studied used injecting equipment collected in 10 Australian injection settings and found that 25 per cent of spoons/cookers had evidence of HCV RNA, as did 40 per cent of filters.[97]

Use of needle-exchange programs can reduce the sharing of other (non-needle) injection equipment.[98] Comprehensive programs to prevent transmission of hepatitis C and other blood-borne infections through unsafe IDU practices must include provision of safer equipment such as cookers, filters, water for injection etc. With the availability of the Ontario Harm Reduction Distribution Program, all Ontario PHUs have access to provincially funded safer injection materials, which they should be providing as part of comprehensive harm-reduction programs for prevention of blood-borne infections transmission among injection drug users.

It is a reasonable assumption that use of sterile equipment will also reduce infectious complications for users such as abscesses, septicemia and endocarditis. Thus, it is not necessary that harm-reduction programs demonstrate high levels of effectiveness against hepatitis C to be justifiable from a public health perspective,

although an impact on hepatitis C has been demonstrated in some harm-reduction studies. A cohort study from Amsterdam has indicated a major decline in hepatitis C incidence from 1985 to 2005, corresponding to a period in which there were significant declines in drug-using risk behaviours at the population level in Amsterdam, in conjunction with active harm-reduction programs.[99] A secondary analysis of data from four cross-sectional studies of injection drug users aged 18 to 30 in Seattle over 10 years (1994–2004) also found a significant decline in HCV antibody prevalence (from 68 per cent in 1994 to 32 per cent in 2004) after controlling for sociodemographic, drug use and sexual behaviour variables; the same study noted an increase in needle exchange and condom use.[-100] A decline in HCV among young injection drug users is particularly significant because of the evidence for increased risk of HCV acquisition within the first few years of injecting.[101]

An early systematic review exploring the effectiveness of primary prevention interventions for hepatitis C among injection drug users found limited evidence and concluded that interventions such as needle-exchange and methadone maintenance programs remained cost-effective because of their significant impact on the prevalence of HIV but showed less effect in reducing hepatitis C incidence.[102] The authors also concluded that evaluations of new interventions—including the provision of other injecting paraphernalia along with sterile needle distribution— needed to be carried out.

Palmateer et al (2009) evaluated reviews related to hepatitis C prevention by providing sterile injecting equipment (via harm-reduction programs, pharmacies, vending machines or outreach) and found sufficient evidence to support the effectiveness of needle-exchange programs in reducing self-reported injection risk behaviours; tentative evidence to conclude that needle provision had been effective in preventing HIV; insufficient evidence to conclude effectiveness in preventing hepatitis C; and little or no evidence about vending machines, outreach or provision of equipment other than needles.[103]

A more recent systematic review and meta-analysis addressing the primary prevention of hepatitis C in drug users found that interventions combining substance-use treatment and support for safer injections reduced HCV seroconversion by 75 per cent, with a pooled relative risk of 0.25 (95 per cent CI 0.07– 0.83), while single-method interventions had relative risks ranging from 0.6–1.6.[104] Multicomponent programs were evaluated in only two studies, one comparing opiate replacement therapy alone and opiate replacement therapy plus enhanced hepatitis C prevention counselling (showing the latter to be more effective), the other comparing a combination of more than 60 mg per day of methadone maintenance and always using a needle-exchange program with less or no harm reduction. Single-method interventions included peer-education training; drug treatment (unspecified); opiate replacement therapy (mainly methadone maintenance); syringe access programs; and syringe disinfection with bleach. Among these, continuous opiate replacement therapy had a pooled relative risk of 0.52 (95 per cent CI 0.34–0.79), but available studies for other interventions tended to be few in number and/or quite heterogeneous, and did not demonstrate lowered relative risk overall. This review did provide support for the potential benefits of multicomponent prevention, but the limited number of studies and the degree of heterogeneity clearly indicated a need for further research in a variety of settings and populations, with careful attention to what constitutes an adequate dose of intervention and appropriate measures. There is already strong support for multicomponent interventions for HIV infection,[105] and these approaches are likely to also be beneficial for hepatitis C.

Non-injection Drug Use

A combination of virological and epidemiological evidence supports the likely risk of hepatitis C transmission via sharing inhalation equipment used for smoking drugs such as crack and methamphetamine, as well as straws and similar implements for snorting drugs—particularly cocaine.

Some studies have found an association between sharing inhalation equipment for non-injection drug use and hepatitis C infection among drug users who have no history of injecting.[16,17,19,20] A systematic review by

Scheinmann et al (2007) also concluded that hepatitis C infection is much more common among non-injection drug users than in the general population,[18] but that gaps remain in proving that hepatitis C is transmitted via non-injection drug use. The authors pointed to two main possible weaknesses in current studies: misclassification of some current or former injection drug users as non-injectors, and transmission occurring via routes other than non-injection drug use, such as sharing of personal-hygiene items or sexual transmission. However, these alternative explanations are not likely to account for all of the increase attributable to non-injection drug use. First, there is no reason to believe that misclassification of injectors as non-injectors in all studies was substantial—only that it was possible. More recent studies, such as the one by Caiaffa et al,[19] took extensive measures to avoid misclassification of current or former injection drug users as never injection drug users, including examining for needle-track marks, making significant misclassification very unlikely. Second, sexual transmission and sharing of personal-hygiene items are both relatively low-risk activities and are unlikely to explain all of the increased hepatitis C risk among non-injection drug users. Scheinmann et al's review was based entirely on epidemiological studies of risk factors and did not take into account the biological and experimental studies showing the presence of hepatitis C at each stage along the route of transmission associated with non-injection drug use.[18]

For the transmission of hepatitis C by sharing inhalation equipment to be biologically plausible, there must be mechanisms by which the equipment becomes contaminated with hepatitis C, and mechanisms by which the virus is introduced into the bloodstream of someone using the contaminated equipment. There is evidence that HCV is present in saliva and in gingival crevicular fluid. Experiments have shown that injection of saliva from an HCV-infected chimpanzee into another chimpanzee caused infection,[21] and a case report of a human bite from a hepatitis C–infected person resulting in a productive hepatitis C infection.[22] Furthermore, crack smokers report the occurrence of burns and cuts on their lips when using makeshift inhalation equipment,[23] suggesting that contamination with blood or serum is also quite likely. The presence of hepatitis C on used inhalation equipment has been confirmed by a Canadian study.[24] Burns and cuts on the lips, along with damage to the oral cavity associated with persistent cocaine use (such as ischemic mucosal ulceration, rapid gingival recession and dental erosions)[106] provide plausible mechanisms for the virus to access the bloodstream of people exposed to contaminated inhalation equipment.

Although most studies have methodological weaknesses and further research would be valuable, there is sufficient evidence to suggest the biological plausibility of HCV transmission via non-injection drug equipment and to recommend that public health harm-reduction programs provide safer inhalation equipment, including mouthpieces, stems and brass screens—the latter to avoid inhalation of alternative materials such as Brillo, which are otherwise used. Programs frequently include additional materials, such as lip balm to combat the lip damage that can occur with the use of such equipment. An evaluation of a crack kit distribution program in Ottawa found a significant shift from injecting to smoking after implementation of this intervention,[107] suggesting an additional mechanism by which crack kit distribution programs can reduce the risk of blood-borne infections, including hepatitis C.

The provision of kits for safer inhalation allows PHUs to make contact with people who do not inject, to provide education about the risks of hepatitis C and other health problems; encourage testing for hepatitis C and other blood-borne infections and STIs; and provide condoms and counselling about safer sex practices. Establishing trusting relationships with users of crack and methamphetamines can also allow for services and referrals to be provided, addressing other determinants of health and health care needs, including addiction treatment for those who want to undertake it.

There is an urgent need for evaluation research to study the impact of programs providing safer-inhalation kits, with attention to both short-term outcomes (such as accessing and engaging with health and social services) and longer-term health outcomes. A literature review table summarizing the studies available on hepatitis C and non-injection drug use is included in Appendix C.

Counselling and Behavioural Interventions for People at Increased Risk

Public health workers may have opportunities to counsel people at increased risk for hepatitis C about testing when they provide harm-reduction services, street outreach services or sexual health services. Given the high prevalence of hepatitis C among injection drug users in Canada (generally over 50 per cent), the importance of a history of imprisonment as a risk factor, and the elevated rates found in drug users who are not injecting but are sharing various types of inhalation equipment, there is a clear need to offer education and counselling about hepatitis C and access to testing to clients with a history of illicit drug use and/or imprisonment. This is based on the assumption that there is a public health benefit to identifying infected people and offering them care and treatment. There is relatively little evidence about the impact of knowing one's hepatitis C status on subsequent drug-related risk behaviour. The literature on other blood-borne infections supports the value of HIV counselling and testing as a key component of reducing the sexual transmission of HIV.[108] There is less evidence about the effect of knowing one's HIV status on drug use-related risk behaviours, but some research has shown an impact.[109,110]

Despite a lack of direct evidence, the Hepatitis C Working Group recommends that since knowledge of hepatitis C status might reduce behaviours that expose others to infection and is a prerequisite for seeking care and treatment for one's own hepatitis C infection, clients with a history of illicit drug use and/or imprisonment should be counselled about their risks and offered hepatitis C testing.

A recent systematic review and meta-analysis examined behavioural interventions for hepatitis C prevention in people who inject drugs.[111] Six trials evaluating peer-education training and counselling interventions aimed at reducing individual injection-related risk behaviours without explicitly seeking to change population or community norms (such as reducing drug use) were included in the review. There was variation in intervention type (4 counselling, 2 peer-educator training) and duration (30 minutes to 12 hours) across studies. The four counselling interventions all included education about hepatitis C and raised awareness of participants' individual infection risk behaviours; they used motivational interviewing (see chapter 7) to encourage participants to reduce risk behaviours. One of the peer-educator training interventions was among HCV-infected individuals and aimed to reduce onward transmission of HCV; the other was among HIV-negative/HCV-negative individuals and aimed at reducing the risk of infection. Only the two peer-educator training studies (418 and 854 subjects) showed significantly greater reductions in injection risk behaviours in the intervention group compared with the control group. In the studies where HCV incidence was measured, none showed significant differences. Most of the counselling studies had relatively small sample sizes and may have been underpowered to show significant differences. The authors recognized considerable variability among the studies reviewed, but concluded that behavioural interventions alone are unlikely to have a considerable effect on HCV transmission, and that multicomponent interventions are required. In making this recommendation, they referenced a review by Rhodes and Treloar of qualitative research on hepatitis C risk among injection drug users that identified the need for structural interventions to target policing, homelessness and gendered risk.[112] Sacks-Davis et al also referred to a 2010 review by Degenhardt et al identifying the need for individual, structural and combination approaches to prevent HIV among people who inject drugs.[105] In this context, structural approaches can be taken to include access to opioid substitution therapy, needle and syringe exchange programs, and antiretroviral therapy, as well as access to social supports (e.g. housing).

7. Case Management

RECOMMENDATIONS

Local Public Health Units

7.1 Hepatitis C cases should be investigated to determine the reason for the test (whether the case or the physician suggested testing and for what reason); potential sources/risks for infection (see below); and co-infections with HIV, hepatitis B or other sexually transmitted infections. Testing for RNA should be recommended if not already completed.

7.2 Hepatitis C cases should be offered counselling and testing for HIV and hepatitis B virus. They should also be assessed for their risk of bacterial sexually transmitted infections and offered testing as appropriate. All hepatitis C cases qualify for publicly funded hepatitis A and hepatitis B vaccinations and should be offered appropriate vaccination, either by public health units or via their health care provider.

7.3 Among women, pregnancy status should be determined; specific treatment recommendations exist for pregnant women. Pregnant women should be advised to notify their health care provider about their infection and discuss treatment options. They should be educated about testing of their infant to determine infection status. Testing for hepatitis C RNA in infants should take place on two occasions: between the ages of two and six months and again at 18 to 24 months; HCV antibody should be included with the 18- to 24-month test. HCV-positive infants should be referred to a pediatrician.

7.4 History of receiving blood, tissue or organs should be determined to define possible eligibility for compensation. History of donating blood, tissue or organs should be assessed to determine possible requirements for follow-up with recipients. Donation history can also be used to establish timing of prior negative hepatitis C screening to help determine approximate time of infection.

7.5 Education/counselling of cases should be ensured. This should include information about the availability and location of harm-reduction services, if appropriate. Individual public health units will determine how much of this counselling they do and how much clinicians will do. Table 9, Appendix H and the Primary Care Management of Chronic Hepatitis C Professional Desk Reference 2009 can be useful for clinicians who may not have experience counselling hepatitis C cases.

7.6 To the extent possible, determine whether reported cases are newly infected (within the preceding two years), and if they are, what their risk factors are and whether they may be associated with other cases (i.e. a cluster or outbreak).

7.7 Current identifiable contacts considered at increased risk for infection (such as known sharing of drug use equipment or higher-risk sexual behaviour involving blood-to-blood contact) should be offered hepatitis C testing. Because of the low risk of sexual transmission in the absence of blood-to-blood contact, routine public health contact tracing of low-risk sexual partners is not recommended, since it is not an effective use of resources.

7.8 Where there is indication of a cluster of cases, public health units should conduct an investigation appropriate to the circumstances and consider outreach to specific contacts to encourage testing and provide counselling and prevention.

KEY POINTS

- Cases infected within the past two years are highest priority for follow-up because of the greater opportunity to identify sources of infection and prevent transmission to others.
- Case investigation should include detailed inquiry about risk factors, including sharing of drug use equipment, higher-risk sexual exposures (see definition below), HIV infection, other STIs within the relevant time frame, or potential blood exposures to people with hepatitis C or to piercing, tattooing or other services that could cause blood exposure.
- Investigation should include inquiry about blood or tissue donation, as well as advice about not donating blood in the future. If careful inquiry suggests that donation may have occurred in the eight weeks immediately following infection, then trace-back efforts are warranted, since screening tests may not be positive during this window period. Canadian Blood Services provides PHUs with a form that can be used to report such cases (see Appendix J).
- Cases should be asked about sexual and household contacts who may have had exposure to their blood during the period of infection so that these contacts can be informed and offered testing.
- Cases should be educated about how to avoid transmission to others: not donating blood; not sharing any drug use equipment or household/hygiene items that may be contaminated with blood; safe disposal of contaminated items; use of bleach to clean blood spills.
- Cases should be assessed regarding drug and alcohol use and offered counselling, referrals and harm-reduction measures as appropriate. Motivational interviewing is a form of brief counselling intervention that can be learned by professionals without specific mental health training and has shown some success in working with substance-use issues.
- Cases should be assessed for other needs (including housing, social support, mental health concerns etc.) and referred to other services, including support groups, as appropriate. Interventions involving peer support have shown some benefit in improving access to services, particularly for people who use drugs.
- Cases should be referred to hepatitis C support groups, as well as other resources, such as the CATIE websites (www.hepcinfo.ca, www.catie.ca), the CATIE information line (1-800-263-1638) and the Canadian Liver Foundation (www.liver.ca). Public health units and individuals can order CATIE's free print hepatitis C resources from www.catie.ca and 1-800-263-1638. See Appendix K for additional resources.
- People who have HCV antibodies but not HCV RNA (shown by two negative RNA tests at least six months apart) should be informed that they will likely remain antibody-positive for life, but do not have current active infection and are therefore not at risk for transmission to others. However, they are at risk of becoming re-infected and should be counselled about reducing any ongoing risk behaviours.

Background

As indicated in Chapter 3, the best-documented risks for hepatitis C involve direct blood–to-blood contact as a result of multi-person use (sharing) of injection or other drug use equipment; receipt of unscreened or inadequately screened blood or blood products; or unsafe medical injections or procedures. Although there is evidence for some degree of sexual transmission (see Chapter 3 and Appendix D for detailed reviews), the extent of the risk is unclear, and is likely to be quite low in the absence of blood exposure during sex, especially in the absence of HIV or other STIs, which appear to increase transmission risk.

In investigating single cases or household clusters of hepatitis C, the first step may be to determine who requested the test and why, and whether the case is under a physician's care or was screened in another setting, such as a harm-reduction program. Inquiry should be made about specific risk factors, including the following: injection or non-injection drug use and sharing of drug injection or inhalation equipment; skin-piercing procedures, such as tattooing, body piercing and acupuncture; receipt of blood/tissue/organs at any time in a developing country, or in a developed country prior to 1990; occupational or non-occupational blood exposures; recent dental procedures or invasive medical procedures, such as hemodialysis; and history of incarceration. For patient counselling and prevention of transmission to others, newly infected cases and recent exposures (within the past two years) are high-priority.

Sexual Exposure Risks

For assessing the risk of a case under investigation and the risk of transmission to others, it is appropriate to determine the case's recent sexual relationships, higher-risk sexual behaviours, and co-infection with STIs or blood-borne infections, especially HIV and hepatitis B virus (HBV). There is some epidemiological evidence suggesting that sexual transmission of hepatitis C may be more likely to occur in the presence of other STIs, including HIV.[27,28] However, it is often difficult to rule out the possibility that HIV and HBV infections may also be related to other risk factors, such as unreported drug use.

Definitions of higher-risk sexual behaviour used in hepatitis C research studies vary, in some cases simply referring to unprotected sex with multiple partners, in others incorporating sexual practices likely to result in blood-to-blood contact. For the purposes of this document, higher-risk sexual contact refers to sexual practices that may cause bleeding or abrasions, resulting in blood-to-blood contact between participants. Examples of higher-risk sexual contact may include anal intercourse, fisting, the use of sex toys, rough sex, sex between participants with open lesions from an STI etc. HIV infection is also known to increase transmission of hepatitis C.

Evidence suggests low rates of sexual transmission of hepatitis C for heterosexual long-term monogamous partners.[113-115] Rates reported among long-term monogamous partners have varied, however, and factors such as high viral load in those with liver disease from serious chronic infection, genotype or other factors may have influenced study results. Many studies have not collected specific information about sexual contact or practices, and may also lack sufficient information to rule out non-sexual household transmission or common source transmission through medical care or services such as acupuncture.

Reported rates of sexual transmission and hepatitis C prevalence among non–drug-using, HIV-negative populations of MSM suggest that even those who engage in risk behaviours such as unprotected anal intercourse have a relatively low incidence of hepatitis C. For example, Alary et al studied hepatitis C seroconversions in the OMEGA cohort of MSM in Montreal being followed for HIV risk.[116] They identified a hepatitis C prevalence at entry of 2.9 per cent, but prevalence among those with no history of IDU was 0.3 per cent. Sixty-two per cent of the cohort reported a history of unprotected anal intercourse over the course of their lifetime, confirming relatively high levels of risk behaviour. Only one seroconversion was identified in 2,653 person-years of follow-up (incidence rate=0.038 per 100 person-years), and this case was in an active

injector who had shared needles. However, although the incidence of hepatitis C seroconversion was very low, this study was limited in its ability to provide strong evidence for or against sexual transmission of hepatitis C because the low population prevalence—especially among the non-injection drug users—would likely make exposure to a hepatitis C–positive sexual partner quite infrequent.

Recent studies of hepatitis C infection among HIV-positive MSM suggest higher levels of risk for sexual transmission in this group. This may be related to higher hepatitis C viral loads, immunodeficiency and lower CD4 counts, and in some cases co-infection with other STIs, such as syphilis. Glosn et al reported on the incidence of hepatitis C among 402 people being followed for a median of 36 months in a French cohort with primary HIV infection (the PRIMO cohort).[28] The two female seroconverters had risk factors related to IDU and body piercing, but the four male seroconverters (incidence 3.5 per 1,000 person-years) reported only unsafe sex with other men as risk behaviours for hepatitis C.

Studies of sexual transmission among injection drug users and non-injection drug users provide very limited evidence for the sexual component of risk in these populations, because of the higher impact of drug-using behaviours and confounding between factors, such as engagement in the sex trade and drug-related risk behaviours.

Based on the available evidence, people diagnosed with hepatitis C should be counselled to avoid unprotected sexual practices that could lead to blood-to-blood contact. Use of condoms in situations that may involve such blood exposure should be recommended, especially since similar behaviours carry risk for HIV, HBV and other STIs. Long-standing sexual partners should discuss the risks and make informed decisions about safer sex practices.

Tables detailing studies of sexual transmission of HCV and their strengths and weaknesses are provided in Chapter 3 and Appendix D.

Pregnancy

Women with newly diagnosed hepatitis C infection should be asked about their pregnancy status and counselled about the implications of hepatitis C infection for pregnancy. There is evidence that 3 to 7 per cent of HCV RNA–positive pregnant women will transmit the infection to their newborn. There are specific hepatitis C treatment recommendations during pregnancy to reduce the risk of harm to the fetus. There is no evidence of hepatitis C transmission through breastfeeding, but women should be advised to refrain from breastfeeding when their nipples are cracked and bleeding. See Chapter 3 for details on infant risk, testing and follow-up.

Blood and Tissue Donation

People with diagnosed hepatitis C infection should be advised that they must not donate blood in the future, but they may be eligible to donate tissues and/or organs. For those who have donated blood in the past, information about the timing and location of the donation(s) should be collected. Current testing is highly effective in screening out infected donations, but if careful investigation suggests that donation may have occurred soon after infection (within eight weeks), then trace-back efforts are needed, since this represents the period when infection may not be detected in donor screening.

Contact Management

Public health investigation should include identification of household and other intimate contacts who are likely to have potential blood-to-blood exposure to the infected person. This includes people with whom they have recently shared needles or other drug-use equipment; people with whom they have recently shared other personal-use items such as razors and toothbrushes; current long-term and short-term sexual partners (with attention to exposures that may involve blood-to-blood contact); and other people with an identified

exposure to their blood. Although sexual and household transmission both appear to be quite uncommon, it is reasonable to offer counselling and testing to recent high-risk sexual partners (i.e. those who may have had blood-to-blood contact with the case), and to family members sharing the same household who might have had relevant blood exposures. Specific contact investigation may be indicated in particular circumstances, including, but not limited to, possible acquisition from a personal services setting, possible health care-related transmission, and possible clusters related to recent or ongoing higher-risk behaviours if public health officials believe that transmission can be reduced through public health intervention.

Education for the infected person should include informing them about risks of such contacts, advising them about how to prevent transmission to their contacts, and encouraging them to discuss their infection with any contacts who may be at significant risk so that the contact can be encouraged to undergo testing. Public health should be available to support the hepatitis C–positive individual in conducting the contact tracing or if requested by the case, public health should provide contact notification.

Where limited public health resources are overwhelmed by the volume of hepatitis C cases, local health units may choose to prioritize case and contact management based on the following priority factors:

- Newly acquired infections
- Cases co-infected with other blood-borne infections, such as HIV and hepatitis B
- Local epidemiology or other local factors (e.g. clusters, outbreaks)

Patient Education

As discussed in Chapter 4, people with the antibody to HCV should be strongly encouraged to have RNA testing. Table 9 provides a summary of the key components of patient education and counselling based on the diagnosis of the patient. For a comprehensive checklist for pre- and post-test counselling, see Appendix H. PHUs will determine how much of this counselling they will deliver and how much is delivered by family doctors or other health care providers. When dealing with clinicians who may not be experienced in counselling patients about hepatitis C, PHUs should provide the information in Chapter 3 and Appendix H to assist in patient counselling and management.

Table 9: Summary of education and counselling tailored to hepatitis C–positive patients' needs (Appendix H)

Type of Counselling	Education and patients' needs
Post-test counselling	• *Antibody-negative:* There is currently no evidence of exposure to the hepatitis C virus; if there was risk exposure in the preceding six to eight weeks, recommend a repeat antibody test in six months and counsel about how to avoid risks of hepatitis C infection • *Antibody-positive (RNA test not yet done):* There is evidence of hepatitis C infection, either current or past; the client requires an RNA test to determine whether he/she is chronically infected (i.e. still has virus present and therefore still infectious to others via blood exposure) • Counsel about modes of transmission and how to avoid transmission to others and/or re-infection if RNA test proves negative; this can be relatively brief if RNA testing and follow-up counselling is assured • Counsel about risk factors for disease progression and provide support and referrals as needed; can be deferred until RNA results available if follow-up is assured

Type of Counselling	Education and patients' needs
Counselling after RNA-positive test	• The client is newly or chronically infected, and is infectious to others • If history suggests new infection, refer for follow-up and consideration of early treatment (if RNA has not cleared spontaneously within six months of infection) • If chronically infected, he/she will remain infectious for life without successful treatment and should be counselled on modes of transmission and how to avoid infecting others, as well as risks for disease progression and how these can be reduced; counsel about the availability of treatment and the importance of regular medical follow-up, and provide referrals as needed
Counselling resolved cases	• Resolved cases are those with antibody to HCV but confirmed RNA-negative based on two tests done six months apart. Note that there is good evidence that a negative RNA test three months after treatment indicates that a sustained virological response will result (i.e. a cure).[67] Once sustained virologic response is achieved with treatment, relapse has never been reported • Inform clients that they are at risk for re-infection; determine the presence of current risks and educate about modes of transmission as needed • If there are ongoing risks, refer for further counselling, harm-reduction services or other needs

RNA, ribonucleic acid.

For those who are HCV-RNA–positive or for whom HCV RNA results are unknown, prevention of transmission to others includes the following:

- Not donating blood, semen, or breast milk, but they may be eligible to donate body organs or tissue
- Not sharing toothbrushes, dental floss, razors, earrings or manicure/pedicure equipment (i.e. articles that might have traces of blood)
- Keeping all open cuts and sores covered until healed
- Putting articles with blood on them (e.g. tampons, pads, tissue, dental floss and bandages) in a separate plastic bag before disposing of them in household garbage
- Disposing of bloody sharp items (razor blades, needles etc.) in a sharps container or a glass jar or hard-sided container with a tight-fitting and puncture-proof lid
- Using bleach to clean up blood spills. Surfaces should be soaked with one part bleach to nine parts water and left for 10 minutes before wiping off (for a more complete discussion of the clean-up of blood spills, see *Best Practices for Environmental Cleaning for Infection Prevention and Control in All Health Care Settings*, available on the PIDAC website[117])
- Informing health care providers (including dental care providers) of disease status where blood exposure is possible

For clients with current high-risk drug use behaviours, assess their readiness to change their behaviour, discuss options, inform them about available addiction treatment and support services, and make appropriate referrals (see Counselling and Behavioural Interventions and Peer Programming for Hepatitis C Prevention and Care sections, below).

For clients who use drugs, discuss the risks from reusing or sharing needles/syringes, water and drug-using equipment (pipes/mouthpieces, filters, spoons/cookers, alcohol swabs, acidifiers [e.g. vitamin C], snorting equipment etc.). Counsel clients to use sterile syringes, injection equipment and drug inhalation equipment (stems, mouthpieces, screens etc.) obtained from a reliable source, never share with anyone else and safely dispose after use. Advise them to ensure that they use a new, sterile syringe and needle for each injection—not just each session. Advise them to use sterile water to prepare drugs or at least use clean water from a reliable source. Advise them to clean bodily injection sites with new alcohol swab before each injection or use soap and water. Advise them to use a new, clean, dry cotton swab after injecting. Provide information and referrals to needle-exchange and other harm-reduction programs that supply needles and other injection equipment.

For all infected people—but especially those with drug- or alcohol-use issues—discuss mental health needs and provide information and referrals to available mental health treatment and support.

Advise clients how to ensure tattoos are being done in locations inspected by PHUs, with sterile equipment, and not with shared or reused tattoo equipment.

Discuss the potential for sexual transmission. In monogamous, long-term relationships without higher-risk sexual practices, the potential for transmission is extremely low; couples should be encouraged to discuss the risks, but use of condoms is a matter of personal choice. In other types of sexual relationships, clients should be strongly encouraged to use latex condoms, partly because of the possibility of sexual transmission of hepatitis C to partners, but also because of the increased risk to their health if they become infected with HIV. Cases should be informed that risk for sexual transmission is higher with multiple partners and with sexual practices that may cause bleeding or abrasions, resulting in blood-to-blood contact. Evidence is sparse regarding the risk of hepatitis C transmission associated with specific sexual practices, including anal intercourse, fisting, the use of sex toys, rough sex, sex between participants with open lesions from an STI etc. Cases should be encouraged to inform all sexual partners about their hepatitis C infection and encourage partners to be tested for hepatitis C.

Educate clients about the potential risks of other types of physical contact that may cause blood contact, such as fighting.

Inform clients that they need not disclose their infection to casual or workplace contacts, but should disclose to any person with whom there is a risk of blood-to-blood contact.

Ensure that clients are aware of factors that can increase their risk for progression to liver disease, including co-infection with hepatitis A virus or HBV (ensure access to counselling, testing for hepatitis B antigen and antibody and appropriate immunization for hepatitis A and B); HIV and other STIs (ensure access to counselling, testing and care); alcohol (provide referrals to treatment as needed); cigarette smoking (offer cessation supports as needed); heavy marijuana use (offer referrals to treatment as needed); and obesity and fatty liver (offer referrals as appropriate). See Chapter 3 for a discussion of evidence regarding the risk factors for the progression of liver disease.

Provide information to pregnant women about mother-to-child transmission of hepatitis C; for those considering hepatitis C treatment, emphasize the restricted treatment options available in pregnancy because some of the treatment drugs are harmful to the fetus. For women who have had or may have children after becoming infected, discuss testing of infants and children.[46] See Chapter 3 for details regarding infant risk, testing and follow-up.

Cases should be referred to community resources, depending on the region and the individual's needs. Examples of community resources may include STI clinics; integrated hepatitis network centres; liver

disease/hepatitis clinics or specialists; peer-support groups; needle exchanges; health care providers prescribing methadone or providing other drug-treatment services. People with Internet access can also find many resources online. Where possible, refer people to hepatitis C support groups, as well as to other resources, such as the CATIE website (http://www.hepcinfo.ca/; http://www.catie.ca), the CATIE information line (1-800-263-1638) and the Canadian Liver Foundation (http://www.liver.ca) (see Appendix K).

Counselling and Behavioural Interventions

There are several areas of public health practice in which counselling and behavioural intervention with those already infected with hepatitis C are relevant. The purpose of such counselling could be:

- To reduce the likelihood of transmitting infection to others (particularly via access to harm-reduction services and changes in drug use-related risk behaviours)
- To increase the likelihood that the client will access medical care and possibly treatment for their hepatitis C
- To increase the likelihood that the client will seek supportive services related to their hepatitis C or other health-related needs (for example, self-help groups, housing workers etc.)
- To increase the likelihood that the client will access addiction care and treatment

A form of brief counselling intervention that has been widely used in encouraging behaviour change—including change among clients with addiction issues—is *motivational interviewing*. This technique was originally developed for use in the addictions field and has since been applied to other health-promoting behaviours. Several systematic reviews and meta-analyses of motivational interviewing have been published[118]; these generally suggest that it can be as effective as other forms of counselling, such as cognitive behavioural therapy, and significantly more effective than no treatment. Motivational interviewing has important advantages for public health practice, since it does not require a trained mental health practitioner; it has been used in interventions delivered by nurses and other health care practitioners after a relatively short training program. It uses active listening skills—important and broadly applicable components of the repertoire of staff who provide outreach and counselling services.

The reviews of motivational interviewing considered for this document are summarized in Appendix L. Motivational Interviewing and other brief intervention approaches to behaviour change are generally based on the Stages of Change model.[119] Determining what stage of the change process people are in enables a counsellor to provide an appropriate type of motivational support. For example, a person at the *pre-contemplation* stage must have his/her consciousness raised before he/she can consider changing behaviour. People who have reached the *contemplation* stage are typically feeling some ambivalence about change and need help to resolve it and choose positive change by weighing the risks and benefits. Once people reach the *preparation* stage, they can be helped to identify and choose appropriate change strategies, while people in the *action* stage may need help and support in carrying out their change strategies. Brief interventions can be used to establish an alliance between client and counsellor and motivate behavioural change at each of these stages. "Regardless of the stage of readiness, brief interventions can help initiate change, continue it, accelerate it, and prevent the client from regressing to previous behaviours."[120]

A key element of brief intervention with any substance user is to motivate and assist change, not to shame or blame; a nonjudgmental approach is essential to success. Because change is often difficult and ambivalence is to be expected, a key principle in interventions such as motivational interviewing is that client resistance is a signal for the counsellor to change strategies and defuse the resistance, rather than to push against resistance and lose trust and alliance. This may be an especially useful feature in work with adolescents, where a systematic review and meta-analysis has shown motivational interviewing to be a useful strategy.[121]

The U.S. Substance Abuse and Mental Health Services Administration has published a document on brief interventions and brief therapies for substance abuse outlining essential knowledge and skills. It states that to provide effective brief interventions, practitioners require knowledge, skills and abilities.[120] Studies have shown that when clinicians apply several skills, they produce good outcomes, including getting clients to enter treatment, work harder in treatment, stay longer in treatment and have better outcomes after treatment (such as higher participation in aftercare and better sobriety rates).[120] These skills include an overall attitude of understanding and acceptance; active listening and helping clients explore and resolve ambivalence; a focus on intermediate (versus long-term) goals; and a working knowledge of the stages-of-change model."[120]

WHO has also published the ASSIST screening tool and guide to brief intervention with substance users: http://whqlibdoc.who.int/publications/2010/9789241599399_eng.pdf?ua=1 [122]

Extensive information about motivational interviewing is available at www.motivationalinterview.org.[123]

Peer Programming for Hepatitis C Prevention and Care

Peer programming is a means of offering more accessible and acceptable services to priority populations by reducing the social distance and mistrust that can make relationships between clients and providers difficult. By employing people who have lived experience with illicit drug use and potentially also with HIV and/or hepatitis C, peer programs can bridge the distance with clients who use drugs, establishing credibility and trust more quickly. Well-developed peer programs can also provide training and employment for people who formerly or currently use drugs, and contribute to community development in communities of people who use drugs. There is a strong human rights argument to be made for involving people who use drugs in the development of policies and services that affect them (e.g. *Nothing About Us Without Us: Greater Meaningful Involvement of People Who Use Illegal Drugs*).[124] At the same time, peer workers may encounter challenges and need additional supports, because their work may expose them to situations that tempt them to use drugs while working or to relapse to drug use if they are not currently using. Such risks should not be seen as reasons to avoid hiring people with lived experience any more than other potential disabilities should block opportunities for employment, but they should alert employers to the need for appropriate supervision and support.

There is limited literature specifically on peer programming related to hepatitis C, but there have been a number of studies of peer programming related to HIV. A recent systematic review addressed the efficacy of peer interventions for HIV in both developed and developing countries, including with people who use drugs.[125] Of the 117 studies reviewed, most were quasi-experimental or cross-sectional, with about one-quarter using randomized controlled designs. Eighteen studies (15 per cent) dealt with substance users as their target population, and 27 studies (23 per cent) reported on substance use as one outcome, including reported behaviours such as needle-sharing, cleaning needles and methamphetamine use. Only 16 studies reported some biological outcome, such as HIV or STI test results, CD4 count or measures of treatment adherence. A descriptive analysis of efficacy was used, with a liberal method of outcome assessment in which studies reporting a positive effect in at least one outcome measure were considered a positive outcome. On this basis, 70 per cent of the studies reporting on substance use supported the efficacy of peer interventions; 100 per cent of studies using outreach; and 56 per cent of studies not using outreach ($p=0.02$). These results are in agreement with a previous meta-analysis of peer interventions in developing countries that reported reductions in equipment sharing among injection drug users.[126] The authors concluded that their findings supported the benefits of peer interventions for HIV prevention, but they also called for more research using the most rigorous study designs and with outcomes less likely to be affected by respondent bias. They acknowledged, however, that there may be situations in which subjective measures are necessary, because studies are underpowered for biological outcomes or focus instead on obtaining valuable qualitative data.

Although no reviews were found on peer interventions specifically for hepatitis C, there were individual studies related to peer interventions for hepatitis C in a treatment context. These reviews reported primarily on the use of peer workers and/or support groups to assist methadone clients or other drug users in accessing hepatitis C treatment and in maintaining adherence to treatment. The studies were mainly descriptive in nature, but emphasized the benefits of such programs in providing treatment opportunities for clients previously denied treatment because of their drug use or other social determinants.[127,128] A summary of research related to peer interventions and hepatitis C is provided in Appendix M.

Given the limited scope of reported research on peer interventions for hepatitis C prevention, it is reasonable to consider the relatively consistent and moderately positive findings of peer interventions for HIV prevention among people who use illegal drugs as supportive of such interventions in harm-reduction programs. It is worth noting the much stronger efficacy of peer interventions that included an outreach component.[125]

8. Public Education and Social Marketing

RECOMMENDATIONS

The Ministry of Health and Long-Term Care and Local Public Health Units

8.1 The Ministry of Health and Long-Term Care and local public health units should partner to identify means of educating the public about harm reduction and drug use, with the goal of increasing acceptance and reducing stigma and discrimination.

8.2 The Ministry of Health and Long-Term Care and local public health units should partner with the Ministry of Education and local school boards to identify and address gaps in education in secondary schools about blood-borne infections, including HIV, hepatitis B and hepatitis C, with attention paid to ensuring understanding of the differences and the similarities between these viruses, as well as the availability and role of prevention and treatment for each.

Local Public Health Units

8.3 Public health units should advocate for measures such as improved access to low-cost housing, healthy food and income support as part of improving the health of people living with hepatitis C and increasing their chances of successfully undergoing treatment.

KEY POINTS

- Mass media educational campaigns aimed at the general public to improve knowledge and awareness and reduce stigma related to hepatitis C have been undertaken in Ontario (2006), as well as in Australia (2008) and France (starting in 1999). Evaluations have suggested that impacts were modest.
- Studies in Australia and France have also suggested low levels of knowledge about hepatitis C and identified a need for better education in secondary schools about hepatitis C, as well as hepatitis A and B, since students may not understand the difference.
- Many subpopulations at increased risk for hepatitis C in Ontario may also be impacted by the broader social determinants of health such as poverty, lack of education, lack of affordable housing etc. Prevention and care in these populations requires policy action, both in the Ministry of Health and Long-Term Care and in other provincial and federal ministries. As front-line agencies charged with prevention of hepatitis C and other blood-borne infections and STIs, PHUs are in a position to help identify the needs of those at risk and newly infected, and promote policies and programs to meet those needs.

Social marketing is described by Health Canada as a planned process for influencing social and behavioural change, using components of marketing and consumer research, advertising and promotion. With respect to hepatitis C, social marketing may play a role in enabling the general public to better understand hepatitis C, who is at risk, and how risk can be reduced. Such marketing could aim to reduce the stigma and discrimination experienced by priority populations, such as people who use drugs. It can also promote tolerance and social support for harm-reduction measures that have been shown to be effective for lowering HIV risk and have the potential to reduce hepatitis C as well (e.g. distribution of safe injection equipment, safer inhalation

equipment, methadone maintenance treatment and supervised consumption sites). Currently, there are no such campaigns in Canada; use of the media to address issues of drug use is limited, and in some cases is inclined to reinforce stigma and discrimination.

The results of an evaluation of a hepatitis C mass media campaign in Australia have been published.[129] The campaign, conducted in April 2008, used television, radio and newsprint advertisements, posters and public display boards, public awareness events and media releases, and included the dissemination of information to health care professionals. Evaluation involved baseline and follow-up interviews in both independent cross-sectional samples and in a cohort providing before-and-after comparisons of the same individuals. The campaign successfully increased public exposure to information about hepatitis C and improved knowledge about means of transmission. In the cohort sample, improved knowledge was associated with reporting exposure to information about hepatitis C following the campaign, postsecondary education and greater knowledge at baseline. Attitudes towards injection drug users and services for them were generally positive (70 per cent or more) at baseline, and although most improved in the cohort at follow-up, they did not change in the independent samples, leading the authors to conclude that the changes may have been associated with pre-test sensitization or social desirability bias. The authors concluded that a sizable proportion of people still did not have some of the basic information after the campaign, and that improvements in knowledge did not directly improve attitudes. They recommended the inclusion of people with hepatitis C in campaigns in an effort to affect attitude changes, as undertaken by campaigns to reduce stigma related to HIV or mental illness.[130,131] However, the campaigns referenced did not directly address the issue of compound stigma (e.g. stigma related to being an injection drug user as well as being HCV-positive).

France also carried out a campaign starting in 1999 to educate physicians, higher-risk populations and the general public about hepatitis C. Repeated cross-sectional surveys in 1997 and 2003 with convenience samples of French adults suggested that knowledge improved significantly on 13 of 26 items and declined on 3. However, the authors concluded that improvements were modest overall, and that even multimodal campaigns can expect only gradual impacts.[132]

A social marketing/public information campaign conducted in Ontario in 2006 was evaluated by a telephone survey company. The outcomes measured included general awareness and familiarity with hepatitis C; knowledge of disease specifics, including awareness of the hepatitis C website being promoted; and response to the recommended action of speaking to a doctor about hepatitis C. The evaluation found improvements in these areas, but concluded that the relevance and personal importance of hepatitis C for the general public were still not high, and that therefore public awareness and action (such as getting tested for HCV) might never be as high as for other diseases such as influenza or West Nile virus.[133]

Social marketing campaigns could also aim to encourage those at higher risk for hepatitis C to undergo counselling and testing, particularly those with hidden risks, such as a history of unsafe IDU practices. Grow and Christopher conducted a focus group study of the responses of members of hepatitis C support groups to television public service announcements produced by the Texas Department of Public Health, concluding that the fear of stigma and discrimination from health care providers and social contacts was an important barrier to seeking hepatitis C testing.[134] Structural barriers, including lack of information or incorrect information, inadequate access to health care and not having a primary health care provider were barriers to seeking testing and treatment. The study also reported that fear-inducing messages increase stigma and may reduce the likelihood that those in the pre-contemplation stage will take action. The study recommended using celebrity appeals, realistic drug-use portrayals, more extensive use of social networking in tandem with non-traditional media, and messages emphasizing self-efficacy but minimizing fear tactics. One concern about the use of social marketing campaigns to encourage testing is the likelihood that they will be least likely to reach those at highest risk, because those populations are less in touch with the mainstream media or less likely to

relate to messages provided there. For a more complete discussion of screening issues relevant to this use of social marketing, see Chapter 5.

Social marketing campaigns could also be considered as a way of preventing non-injection drug users from becoming injectors. Research suggests that current abstinence-oriented drug education campaigns conducted in schools or in the media are ineffective.[135,136] Effective social marketing strategies designed to prevent the initiation of IDU need to be innovative, and need to pay particular attention to reaching more marginalized youth, such as those not in school and especially those who are street-involved (see Chapter 9 on specific populations). The prevention of illicit drug use by young people is a complex and multifaceted issue, and those most at risk are often members of families and communities with substance-use issues related to poverty and other social needs.[137]

An educational campaign aimed at youth has been reported from France.[138] This involved information meetings in 52 classes of 11 general and vocational secondary schools, with students aged 14 to 24 (mean age 15.9). The information sessions were accompanied by a comic strip depicting scenarios involving hepatitis C. Before the information session, 1,509 questionnaires were completed, and 1,419 were completed two months later. Baseline questionnaires indicated poor knowledge of hepatitis C. Knowledge scores improved significantly after the session, with significantly greater improvement among those who said they also read the comic strip. Knowledge was particularly increased concerning transmission by unsafe IDU practices, severity of the disease and lack of a vaccine. The authors recommended integrated education about blood-borne infections, including HIV, hepatitis B and hepatitis C, underlining their differences; this was to address the finding that some adolescents had difficulty distinguishing between hepatitis A, B and C and different aspects of each, including vaccine availability. Although this campaign increased knowledge, no attitudinal measures or behavioural intentions were assessed, so its effectiveness in these areas could not be determined.

Although no studies were identified regarding Ontario adolescents' knowledge of hepatitis C, a study from Australia also found low levels of knowledge about hepatitis C in a survey of a nationally representative sample of secondary school students conducted in 1997, and recommended more education and health promotion related to hepatitis C among students, with care to avoid conflation of hepatitis C with HIV.[139]

9. Specific Populations

RECOMMENDATIONS

Ministry of Health and Long-Term Care

9.1 The Ministry of Health and Long-Term Care should attempt to collect data on hepatitis C prevalence, incidence, risk factors and sequelae specific to Aboriginal people (including the rates and causes of morbidity and mortality from chronic liver disease) to assist in the development of appropriate public health programming.

9.2 The Ministry of Health and Long-Term Care should work that create policies to address the social determinants of health to better meet the needs of subpopulations at increased risk for hepatitis C.

Local Public Health Units

9.3 Corrections authorities have primary responsibility for the health of inmates. Public health units with correctional facilities, jails or detention centres in their jurisdiction should determine the availability of hepatitis C education, counselling, testing, support and other resources, and help corrections authorities deliver appropriate services where feasible. They should also work with local corrections authorities to help them ensure that inmates being paroled or released into the community are provided with information about and referrals to needle-exchange programs, other harm-reduction programs and other available support services.

9.4 Public health units should seek to ensure effective access to harm-reduction and treatment programs, including appropriate coordination and continuity with federal on-reserve care for Aboriginal people with hepatitis C who are living off-reserve in their jurisdiction.

9.5 Public health units should assess the need for and availability of services for street-involved youth in their jurisdiction; ensure access to hepatitis C counselling, testing and harm-reduction services; and try to facilitate access to care and treatment for those infected with hepatitis C.

9.6 Public health units should work with drug-treatment services in their jurisdiction to ensure access to hepatitis C counselling, testing, care, treatment and support for clients in drug treatment, including methadone maintenance or detoxification facilities. This should include providing information about the availability and location of harm-reduction services and ensuring provision of hepatitis A and B vaccines as indicated.

9.7 Public health units that offer clinical services and hepatitis C counselling and testing may offer hepatitis C counselling and testing to newcomers to Canada who are from highly endemic countries if they have not already been tested, and deliver culturally appropriate counselling and follow-up. Public health units should encourage primary care providers to offer hepatitis C counselling and testing to newcomers to Canada.

9.8 Public health units should offer or facilitate hepatitis C counselling and testing to men who have sex with men who are HIV-positive. Counselling should include discussing the high rates of co-infection with hepatitis C and HIV, the higher risk of sexual transmission of hepatitis C to contacts of those who are co-infected, safer sex practices and harm-reduction approaches, as indicated.

KEY POINTS

- Correctional facilities are high-risk environments for transmission of HCV because of ongoing risk behaviour (e.g. sharing of injection equipment and unsterile tattooing equipment) and no access to harm-reduction measures comparable to those in the community.
- More information is needed about the prevalence and causes of chronic liver disease among Aboriginal people in Canada. Limited studies suggest that Aboriginal injection drug users may have a higher prevalence of HCV than non-Aboriginal people; there are also some limited data suggesting that Aboriginal people may clear HCV at higher rates than non-Aboriginal people.
- Available studies show a higher prevalence of HCV in street-involved youth compared to other Canadians of the same age; this is linked to a history of injecting drugs and to a variety of vulnerabilities that need to be addressed in prevention efforts.
- Hepatitis C testing, treatment and care should be integrated into methadone maintenance and other drug-treatment programs.
- PHUs should consider passive screening of immigrants and refugees from developing countries that have elevated prevalence of hepatitis C by offering education and testing when such individuals present for other services.
- There is preliminary evidence to indicate that people who currently use drugs can be successfully treated for hepatitis C in the context of multidisciplinary care with adequate supports; decisions about treatment should be made on a case-by-case basis involving careful assessment of individual strengths and needs.
- Men who have sex with men who are HIV-positive are at increased risk of acquiring hepatitis C and transmitting hepatitis C to their sexual contacts. Annual testing for hepatitis C and counselling around risk-reduction strategies are important aspects of care for HIV-positive men who have sex with men.

Inmates

As indicated in Chapter 3, epidemiologic and research evidence indicates that inmates have a much higher prevalence of hepatitis C infection than the general population. Studies, mainly in federal correctional facilities with offenders on longer sentences, suggest the presence of risk behaviours such as injection with shared equipment and unsafe tattooing in correctional facilities. The correctional system environment may also involve risks of violence associated with the presence of blood (e.g. fist fights and attacks involving use of weapons).

While there is a great deal of evidence regarding the prevalence of hepatitis C in correctional facilities, there is little evidence to indicate what role PHUs should play with respect to hepatitis C in the correctional system. PHUs can seek to establish relationships with local correctional facilities and offer education about hepatitis C (and other infections) to inmates and correctional officers. PHUs should support and encourage corrections to undertake HCV testing. PHUs may also consider offering counselling and testing for hepatitis C based on local needs. Needle exchange for incarcerated individuals has been shown to be a successful intervention in the context of HIV prevention in several countries[140] but it is not currently available in Canada, owing at least in part to concerns that needles could be used as weapons. There is a need for better education of corrections authorities and staff about the potential benefits of correctional needle-exchange programs, including lowered

risk of accidental needle-stick injury during cell searches and the public health benefits for inmates achieved in some European countries.

PHUs may also be able to play a role in helping corrections officials prepare inmates about to be paroled or released into the community. At the time of parole or release from a correctional facility, former inmates may not remain in the local area, so in most cases local PHUs would not take primary responsibility for linking inmates with harm-reduction, counselling or other services upon their transition from the correctional system to community. However, PHUs in areas that include provincial or federal correctional facilities may be able to work with corrections officials to develop information and referral packages to help ensure that those transitioning to the community can find appropriate public health services in a timely manner.

Aboriginal People

A recent structured review reported that North American Aboriginal people are disproportionately affected by chronic liver disease; indeed, it has become one of the most common causes of death in the Aboriginal population.[141] However, mortality figures are based on studies in the United States, since data are not available on mortality from chronic liver disease among Canadian Aboriginal people. Although the most common cause of chronic liver disease is alcoholic liver disease, hepatitis C is reported to be important and increasing as a cause. [141] The structural review also identified a need for research to monitor the incidence and etiology of chronic liver disease among Aboriginal people, and to study hepatitis C treatment in this population.[141] A review by Minuk et al reported anti-HCV positivity prevalence in studies of Canadian Inuit and First Nations ranging from 1 to 18 per cent, but found that Aboriginal people who were anti-HCV–positive had a lower prevalence of HCV RNA than generally found in non-Aboriginal people. This suggests a higher rate of clearance of the virus and a more benign course for Aboriginal people who do not have additional complications (such as HIV co-infection or heavy alcohol use).[142]

A recent meta-analysis of international studies exploring the distribution of hepatitis C in diverse racial/ethnic drug injector groups found that Canadian and Australian Aboriginal injectors consistently had a higher prevalence of hepatitis C antibody compared to injectors of other ethnicities.[143] Researchers found Canadian and Australian Aboriginal people who inject drugs had a higher relative risk for seroconversion than Caucasians, but this finding was not statistically significant (RR 1.31, 95 per cent CI 0.87–1.99).[143] A meta-analysis of three studies found an odds ratio (compared to Caucasians) of 2.04 (95 per cent CI 1.48–2.82). [143] In Vancouver, Aboriginal injection drug users had an incidence of hepatitis C of 58.4 per 100 person-years, compared to 42.9 per 100 person-years for Caucasians.[144] This suggests that even within the higher-risk population of injection drug users, Aboriginal people may be at especially increased risk and should receive special attention and culturally relevant interventions.

Surveillance and treatment and care for Aboriginal people living on Ontario reserves is the responsibility of the federal government through Health Canada's First Nations and Inuit Health Branch. PHUs in areas where many Aboriginal people live off-reserve need to establish good lines of communication and coordination with on-reserve health services to ensure appropriate follow-up and case management of people living with hepatitis C. It is especially important to ensure access to harm-reduction services when needed, as well as continuity of care for those undergoing hepatitis C treatment.

Street-Involved Youth

A multi-site surveillance study of street-involved youth in Canada reported an overall prevalence of hepatitis C for 1999–2005 of 4.4 per cent, while the rate among the general youth population was reported to be 0.01 per cent.[145] IDU and crack cocaine use have both been associated with hepatitis C infection among street youth.[146] In the PHAC report cited above, 21 per cent of street youth interviewed reported a history of IDU; of these, 18 per cent were hepatitis C–positive, compared with 0.7 per cent of those who reported no IDU (OR 32.8, 95 per cent CI 21.1–51.1). [145] Although this was the strongest association with hepatitis C infection in the study, the findings also highlighted a number of indirect factors associated with hepatitis C among the street youth studied, including ever being in foster care; ever being in a group home; ever being in jail or a detention facility or having a probation officer; having left home because of sexual abuse; engaging in alcohol abuse; and having an illegal primary source of income in the preceding three months. All of these highlight the vulnerability of this population and the need to provide effective services, including services to reduce the risk for acquiring hepatitis C, other blood-borne infections and STIs; address the social determinants of health; provide needed social and personal support; and provide harm reduction for those who are engaged in drug use.

Youth in particular could also be targeted for efforts to reduce transition to more harmful illicit drug use, and for those already using drugs such as opiates and cocaine, to reduce transitions from non-injection to injection routes of administration. Hunt et al reviewed potential interventions to reduce transition from non-injection drug use to IDU,[147] as well as methods to encourage injectors to switch to less harmful routes of administration, but there is very little evidence available addressing the effectiveness of the potential interventions discussed. The same authors evaluated a brief intervention delivered by a drug worker with established injectors who were recruited from drug-treatment services and pharmacy needle exchange; the intervention aimed to reduce inadvertently encouraging non-injectors to start injecting by avoiding injection and talking about injection in front of them, as well as raising injectors' level of disapproval of initiating non-injectors.[148] The evaluation showed declines in IDU initiation, and in desired attitude and behaviour change in the intervention group compared to a control group. This type of intervention has potential, but it would be important to adapt it to the context involved, and use peers or trusted service providers in delivering the intervention to ensure a high level of trust.

Drug Treatment and Withdrawal Management Facilities

Because unsafe practices and behaviours associated with IDU are a leading cause of hepatitis C infection, and because practices and behaviours associated with non-injection drug use are also likely to carry some risk, it is recommended that all people seeking drug treatment (including methadone maintenance) or withdrawal management (detoxification) services be offered screening for hepatitis C if they are not already known to be infected. This can provide an opportunity to link people being tested for hepatitis C or already known to have a chronic infection with needed care and support services. The Substance Abuse and Mental Health Services Administration in the United States has undertaken initiatives to support the integration of hepatitis C services into substance-abuse treatment settings, including training for methadone treatment providers and a program to support combined vaccination for hepatitis A and B in substance-abuse treatment services.[149] Research in Amsterdam supported the feasibility and benefits of hepatitis C management in methadone maintenance patients.[150]

Immigrants and Refugees

Hepatitis C screening is not currently required for immigration to Canada. The epidemiology of hepatitis C worldwide is not precisely known, owing to the difficulty of conducting representative population-based seroprevalence studies, especially in developing countries. A 2005 review suggests that rates of 3 per cent or higher occur in the general populations of many African and Asian countries, including an estimate of 3.2 per cent in China.[50] Egypt has the highest reported seroprevalence in the world, at 22 per cent, related to

contaminated glass syringes used between 1960 and 1987 during a nationwide schistosomiasis treatment campaign.[50] In contrast to developed countries, the main risks for hepatitis C acquisition in developing countries are considered to be transfusion of unscreened blood and reuse of needles and other medical equipment by both professionals and non-professionals, as well as some cultural practices involving blood exposures. The WHO estimates that 43 per cent of donated blood in the developing world is not adequately screened for hepatitis C.[50]

Although population-based data are lacking for most developing countries, seroprevalence studies from the developing world suggest that prevalence among and within developing countries varies greatly depending on local medical and cultural practices. Some subpopulations have very high prevalence, and some appear to have rates similar to developed countries. The WHO has prevalence estimates for various countries and for the six WHO regions, but these estimates were published in 1999. [151] A more recent review of hepatitis C epidemiology in Europe highlights that immigration to European countries from endemic areas of Asia and Sub-Saharan Africa is one factor affecting prevalence in Europe.[152] Because of uncertainty about the prevalence of hepatitis C in populations from whom newcomers to Canada are drawn, there is not enough evidence to determine whether organized screening should be offered to immigrants simply on the basis of their country of origin. Further research and pilot projects in Canada would be useful.

In spite of substantial uncertainties, there are significant concerns about the state of sterile technique in medical practice and the lack of adequate blood screening in developing countries. It also appears likely that many developing countries have hepatitis C prevalence rates that are considerably higher than Canada's. Furthermore, these rates are not necessarily related to well-known behavioural risk factors, such as unsafe IDU practices, that can be ascertained directly from the client. Indeed, clients from developing countries may not even be aware that they have been exposed to a medical procedure such as an injection if it took place when they were young. Therefore, from a practical perspective, PHUs that offer hepatitis C counselling and testing for clients with hepatitis C risk factors may wish to consider those who have lived in a developing country to be at increased risk for hepatitis C and offer counselling and testing when they come into contact with the PHU's clinical services (i.e. passive screening). PHUs should educate and encourage primary care providers to offer counselling and testing for these clients as well.

People Who Use Drugs

As indicated in Chapter 3, a majority of newly infected hepatitis C cases in Ontario will occur because of the practices and behaviours associated with IDU. A smaller but probably not insignificant number of infections may occur as a result of non-injection exposures, such as sharing of inhalation equipment. Harm-reduction as a means of preventing blood-borne infections in this population is supported by research, as discussed in Chapter 6.

Drug users are much more likely to be incarcerated than the general public, and the most marginalized groups of drug users also experience a range of other health and social problems, including poverty, unstable housing, malnutrition and a high frequency of mental and physical health problems. There is some limited evidence to suggest that injection drug users can be successfully treated for hepatitis C if provided with adequate case management and/or other necessary supports.[127,128,153,154] Public health providers can advocate for the provision of holistic health care services for drug users to provide them with opportunities for hepatitis C care and treatment.

HIV-Positive Men Who Have Sex with Men

Evidence suggests that MSM with HIV are more likely to become infected with hepatitis C and have higher rates of transmission of hepatitis C to contacts through sexual transmission than those who are HIV-negative.[26-28,65,66] Acquiring hepatitis C in HIV-positive men who have sex with men is linked to co-infections

with HIV and/or genital ulcer diseases (particularly syphilis), as well as to specific potentially traumatic practices such as unprotected anal intercourse, fisting and rimming.[25-28]

HIV-positive men who have sex with men are also more likely to transmit hepatitis C to sexual contacts. This may be relate to higher hepatitis C viral loads, immunodeficiency and lower CD4 counts, and in some cases co-infection with other STIs, such as syphilis. Glosn et al reported on the incidence of hepatitis C among 402 people being followed for a median of 36 months in a French cohort with primary HIV infection (the PRIMO cohort).[-28] The two female seroconverters had risk factors related to IDU and body piercing, but the four male seroconverters (incidence 3.5 per 1,000 person-years) reported only unsafe sex with other men as risk behaviours for hepatitis C. PHUs should support and/or facilitate hepatitis C testing for HIV-positive men who have sex with men and support the provision of counselling to ensure they are aware of their increased risk of hepatitis C infection and can access appropriate harm-reduction measures to reduce their risk.

Summary: Social Exclusion and Hepatitis C

The epidemiology of newly acquired hepatitis C infections in Canada clearly indicates that the majority of cases are associated with vulnerable groups, such as inmates, Aboriginal people and people who use drugs. Newcomers to Canada and HIV-infected individuals are also more likely to be infected with hepatitis C than the general population. For a variety of reasons, each of these groups is likely to be affected by the social determinants of health. Research involving marginalized users of illicit drugs in Canada confirms that they are likely to have relatively low levels of education and income, live in unstable housing and lack social support. A study published in 2007 found that more than one in five recent (since 1990) immigrants was living in poverty, compared to about one in 10 other Canadians.[155] Addressing the needs of subpopulations at increased risk for hepatitis C for services to address to the social determinants of health requires policy action both within the Ministry of Health and Long-Term Care and in other provincial and federal ministries. As front-line agencies charged with prevention of hepatitis C and other blood-borne infections and STIs, PHUs are in a position to help identify the needs of those at risk for or newly infected with hepatitis C, and to promote policies and programs to meet those needs. Although PHUs can and should promote policies that attempt to address the social determinants of health, this topic is complex and beyond the scope of this document.

Appendices

Appendix A: Hepatitis C Public Health Needs Assessment Survey

The purpose of this survey is to determine the needs of public health staff in responding to hepatitis C case management. In 2007, a practice survey was circulated to public health units across Ontario to determined current hepatitis C case management practices. This survey will help the PIDAC Hepatitis C Working Group formulate evidence-informed guidelines that will best support the public health response to hepatitis C.

If you have any questions concerning this survey, please contact Jennifer Pritchard, Nurse Consultant, Public Health Ontario, at jennifer.pritchard@oahpp.ca.

What is your job title?

Please identify your health unit: (drop down will appear)

Please rate your knowledge of HCV (1 being none; 10 being expert)

1 2 3 4 5 6 7 8 9 10

Based on the list of topics below, please select the top five subject areas about which you feel more information would enhance your practice.

☐ Incidence and prevalence rates
☐ Diagnostic test interpretation
☐ Modes of transmission and infection risks
☐ Cofactors/risk factors for disease progression
☐ Case definition
☐ Public health data collection from cases
☐ Public education and social marketing
☐ Social exclusion and hepatitis C
☐ Investigation of newly reported cases
☐ Patient education
☐ Contact management
☐ Drug users
☐ Prisoners
☐ Aboriginal people
☐ Street-involved youth
☐ Drug treatment and withdrawal management facilities
☐ Immigrants and refugees

Are there additional topics that you would find beneficial? Please specify:

1) 2)

Thank you for taking the time to complete this survey. If you would like more information about Public Health Ontario, please visit our website at www.publichealthontario.ca. If you have any additional questions, please email jennifer.pritchard@oahpp.ca.

Appendix B: Literature Search Strategies

Literature searches for the topics identified for this document, were updated to June or December 2011. The search terms employed are briefly presented in the table below.

Titles of all articles identified were scanned, and abstracts of articles considered relevant to the search topic were reviewed. Relevance was based on the relationship to the question being addressed, as well as relevance to the context of Ontario. In general, studies conducted in Europe, North America or Australia were considered most relevant, although for certain topics (e.g. the question of HCV transmission via non-injection drug use, for which evidence was somewhat sparse) evidence from any country was considered. Articles considered potentially relevant based on abstract review were retrieved and reviewed. Information considered relevant was extracted and then considered by the Hepatitis C Working Group as part of the review of each chapter and the development of recommendations. The quality of studies reviewed was included in this consideration, although this was not a systematic review.

Search for Unindexed (Grey) Literature

Grey literature searches and jurisdictional scans were conducted in Google using synonyms for topic categories: counselling, testing, best practice guidelines, harm reduction, screening, management and education.

Scientific/Academic/Medical Literature Database Searches

Concept and Database(s)	MeSH	EMTREE	PsycINFO	EBSCO	Keywords
Hepatitis C and non-injection drug use (MEDLINE, Embase)	Hepatitis C/ Substance-Related Disorders/ Cocaine/	Hepatitis C/ Hepatitis C Virus/ Drug Abuse/ Substance Abuse/ Cocaine/ "Drug Use"/			hcv "substance-related disorder$" "non injecting drug$" "non-injecting" nonprescription drug$ transmission cannabis cocaine crack
Hepatitis C and harm reduction (MEDLINE, Embase, PsycINFO)	Hepatitis C/ Hepatitis C, Chronic/ Harm Reduction/ Risk Reduction Behavior/ Knowledge/ Health Knowledge, Attitudes, Practice/ Health Status/	Hepatitis C/ Hepatitis C Virus/ Harm Reduction/ Risk Reduction/ Knowledge/ Attitude to Health/ Health Status/ Substance Abuse/Pc, [Prevention]	Harm Reduction/ Drug Abuse/ Needle Exchange Programs/ Behavior Therapy/ Social Marketing/ Health Promotion/ Public Health/ Health Education/		hcv hepatitis c harm reduction ((harm or risk) adj3 reduction) ((IDU or inject$) adj3 drug$) test$ knowledge needle exchange

Concept and Database(s)	MeSH	EMTREE	PsycINFO	EBSCO	Keywords
	Substance Abuse, Intravenous/Pc, Px [Prevention & Control, Psychology] Needle-Exchange Programs/ Behavior Therapy/ Social Marketing/ Community Health Services/ Health Promotion/ Public Health/ Health Education/	Preventive Health Service/ Behavior Therapy/ Social Marketing/ Community Care/ Health Promotion/ Public Health/ Health Education/			safe inject$ injection site injection room consumption site consumption facilit$ consumption room behavior modification social marketing
Hepatitis C and sexual transmission (MEDLINE, Embase)	Hepatitis C/ Hepatitis C/Tm [Transmission] Sexually Transmitted Diseases, Viral/ Sexual Behavior/ Coitus/ Sexual Partners/ Risk Reduction Behavior/	Hepatitis C/ Hepatitis C Virus/ Sexually Transmitted Disease/ Sexual Behavior/ Coitus/ Sexual Intercourse/ Sexuality/ Sexual Health/ Sexual Transmission/ Risk Reduction/			hcv hepatitis c virus intercourse intimate partner spous$ transmit$ infect transmission
Hepatitis C and screening (MEDLINE, Embase)	Hepatitis C/ Hepatitis C/Di, Pc [Diagnosis, Prevention and Control] Mass Screening/ Behavioral Risk Factor Surveillance System/ Diagnosis/	Hepatitis C/ Hepatitis C/Di, Pc [Diagnosis, Prevention] Hepatitis C Virus/ Mass Screening/ Screening/ Screening Test/ Antibody Screening/ Behavioral Risk Factor Surveillance System/ Diagnosis/ Diagnostic			hcv hepatitis c diagnosis screening screen test assessment testing surveillance

Concept and Database(s)	MeSH	EMTREE	PsycINFO	EBSCO	Keywords
		Procedure/ Diagnostic Test/ Early Diagnosis/			
Cost-effectiveness of Hepatitis C screening (MEDLINE)	Hepatitis C Antibodies/ Hepatitis C, Chronic/ Hepatitis, Viral, Human/ Mass Screening/ Economics/ "Costs and Cost Analysis"/ "Cost Allocation"/ Cost-Benefit Analysis/ "Cost Control"/ "Cost Of Illness"/ "Cost Sharing"/ Health Care Costs/ Health Expenditures/ Economics.Fs.				hepatitis screen$ detect$ diagnos$ cost economic expenditure burden invest afford$ (value adj3 money) (value adj3 dollar$)
Hepatitis C and social marketing (MEDLINE, Embase)	Hepatitis C/ Hepatitis C/Ep [Epidemiology] Social Marketing/ "Marketing of Health Services"/ Health Education/ Health Promotion/	Hepatitis C/ Hepatitis C Virus/ Hepatitis C/Ep [Epidemiology] Social Marketing/ Financial Management/ Health Education/ Behavior Change/ Health Promotion/			hcv social marketing behaviour change behavior change "social marketing" "communication campaign" "communication strategy" "communication plan" awareness
Hepatitis C and testing (MEDLINE, Embase, Academic Search Premier)	Hepatitis C/Di [Diagnosis] Community Health Services/ Community Health Centers/	Hepatitis C/ Hepatitis C Virus/ Community Care/ Health Center/ Polymerase Chain		(DE "Hepatitis C Virus") (DE "Hepatitis C") (DE "Routine Diagnostic Tests") (DE "Diagnostic	hcv point-of-care poc "public health clinic$"

Concept and Database(s)	MeSH	EMTREE	PsycINFO	EBSCO	Keywords
	Polymerase Chain Reaction/ "Diagnostic Techniques and Procedures"/ Diagnostic Tests, Routine/ Diagnostic Services/	Reaction/ Diagnostic Procedure/ Diagnostic Test/ Preventive Health Service/		Services")	PCR "diagnostic method$" "diagnostic technique$" "diagnostic procedure$" (anonymous adj3 test$) test$
Hepatitis C and social determinants (MEDLINE, Embase)	Hepatitis C/ Social Environment/ Socioeconomic Factors/ Social Class/ Poverty/ Education/ Educational Status/ Marital Status/ Public Housing/ Housing/ Urban Health/ "Emigration and Immigration"/ Vulnerable Populations/	Hepatitis C/ Hepatitis C Virus/ Social Environment/ Socioeconomics/ Social Status/ Poverty/ Education/ Educational Status/ Lowest Income Group/ Housing/ Health Disparity/ Health Status/ "Social Aspects and Related Phenomena"/ Social Aspect/ Social Background/ Social Class/ Social Discrimination/ Social Problem/ Social Stress/ Cultural Deprivation/ Divorce/ Economic Aspect/ Unemployment/ Income/			hcv social determinant$ (social adj1 determinant$) poverty "low socioeconomic" poor education "low income" inner city disadvantaged health inequity health equity marginalized employ$ unemploy$

Concept and Database(s)	MeSH	EMTREE	PsycINFO	EBSCO	Keywords
		Urban Area/ Urban Population/ Urban Rural Difference/ Urbanization/ Immigrant/ Immigration/ Migration/ Homelessness/ Marriage/ Vulnerable Population/ Health Care Access/			
Hepatitis C and surveillance (MEDLINE, Embase)	Hepatitis C/ Hepatitis C/Ep [Epidemiology] Sentinel Surveillance/ Population Surveillance/	Hepatitis C/ Hepatitis C/Ep [Epidemiology] Hepatitis C Virus/ Sentinel Surveillance/ Health Survey/ Disease Surveillance/			hcv
Hepatitis C and risk factors (MEDLINE, Embase)	Hepatitis C/ Risk Factors/ Substance Abuse, Intravenous/	Hepatitis C/ Hepatitis C Virus/ Risk Factor/ Substance Abuse/			hcv risk factor risk drug use$ inject$ homeless$ street sex unprotected behavior$ culture social network MSM homosexuali$
Hepatitis C and	Hepatitis C/	Hepatitis C/			hcv

Concept and Database(s)	MeSH	EMTREE	PsycINFO	EBSCO	Keywords
body piercing/tattoos (MEDLINE, Embase)	Hepatitis C/ Di, Ep, Pc [Diagnosis, Epidemiology, Prevention and Control] Tattooing/ Body Piercing/ Prostitution/ Unsafe Sex/ Homosexuality/ Substance-Related Disorders/ Inhalant Abuse/	Hepatitis C Virus/ Hepatitis C/Di, Ep, Pc [Diagnosis, Epidemiology, Prevention] Tattoo/ Body Piercing/ Prostitution/ Unsafe Sex/ Homosexuality/ Drug Abuse/ Inhalant Abuse/ Intravenous Drug Abuse/ Drug Dependence/ "Ethnic or Racial Aspects"/ High Risk Behavior/ High Risk Population/			
Hepatitis C and pregnancy (MEDLINE, Embase)	Hepatitis C/ Prenatal Care/ Prenatal Diagnosis/ Pregnancy Complications, Infectious/ Pregnancy	Hepatitis C/ Hepatitis C Virus/ Prenatal Care/ Prenatal Diagnosis/ Pregnancy Complication/ Pregnancy/			hcv antenatal
Hepatitis C management (MEDLINE, Embase, CINAHL)	Hepatitis C/	Hepatitis C/ Hepatitis C Virus/		(MH "Hepatitis C") (MH "Case Management")	hcv contact management case management notification
Hepatitis C and counselling (MEDLINE, Embase, PsycINFO, CINAHL, SocINDEX)	Hepatitis C/ Hepatitis C/Pc, Px [Prevention and Control, Psychology] Hepatitis C/Di [Diagnosis] Directive Counseling/ Counseling/	Hepatitis C/ Hepatitis C Virus/ Hepatitis C/Pc [Prevention] Hepatitis C/Di [Diagnosis] Directive Counseling/ Counseling/	Counseling/ Health Promotion/	(MH "Hepatitis C+/DI") (MH "Hepatitis C+/PF") (MH "Counseling") (MH "Hepatitis C – Psychological Aspects")	hcv hepatitis c psychology risk-taking behavior therapy peer support support group$ client interaction

Concept and Database(s)	MeSH	EMTREE	PsycINFO	EBSCO	Keywords
	Preventive Health Services/ Health Promotion/	Preventive Health Service/ Health Promotion/ Control/			brief intervention referral adherence test$ counsel$ prevention control "directive counseling" behavior therapy
Hepatitis C and motivational interviewing (MEDLINE, Embase, CINAHL)	Hepatitis C/ Motivational Interviewing/ HIV Infections/ HIV/ Behavior Therapy/ Cognitive Therapy/ Community Health Nursing/ Community Health Services/ Public Health Nursing/ Patient Education As Topic/	Hepatitis C/ Hepatitis C Virus/ Motivational Interviewing/ Human Immunodeficiency Virus/ Behavior Therapy/ Behavior Modification/ Cognitive Therapy/ Community Health Nursing/ Community Care/ Preventive Medicine/ Patient Education/ HIV Education/		(MH "Hepatitis C") (MH "Preventive Health Care") (MH "Patient Education") (MH "HIV Education") (MH "Motivational Interviewing") (MH "Human Immunodeficiency Virus") (MH "BEHAVIOR Modification") (MH "Behavior Therapy") (MH "Cognitive Therapy") (MH "Community Health Nursing") (MH "Community Health Services")	"hepatitis c" brief intervention$ motivation$ interview$ nurs$ health public community
Hepatitis C peer interventions (MEDLINE, Embase, PsycINFO)	Hepatitis C/ Patient Education as Topic/ Self-Help Groups/ "Referral and Consultation"/ Counseling/ Behavior Therapy/ Peer Group/	Hepatitis C/ Hepatitis C Virus, Patient Education/ Peer Group/ Support Group/ Patient Referral/ Counseling/ Behavior Therapy/ Peer Counseling/	Client Education/ Support Groups/ Counseling/ Behavior Therapy/ Peer Counseling/		hcv "hepatitis c" test$ blood$ sex$ alcohol$ drug$ inject$

Concept and Database(s)	MeSH	EMTREE	PsycINFO	EBSCO	Keywords
					intraven$ addict$ street homeless shelter mental infectious hepatitis HIV
Hepatitis C and patient education (MEDLINE, Embase)	Hepatitis C/	Hepatitis C/ Hepatitis C Virus/			hcv patient education
Hepatitis C and obesity/fatty liver (MEDLINE, Embase)	Hepatitis C/ Obesity/ Obesity, Morbid/ Fatty Liver/ Disease Progression/ Body Mass Index/	Hepatitis C/ Hepatitis C Virus/ Obesity/ Morbid Obesity/ Fatty Liver/ Steatosis/ Disease Course/ Body Mass/			steatosis disease progression fatty liver “body mass index” obesity
Hepatitis C and smoking (MEDLINE, Embase)	Hepatitis C/ Smoking/ Tobacco/ Nicotine/ Cannabis/	Hepatitis C/ Hepatitis C Virus/ Smoking/ Tobacco/ Nicotine/ “Smoking and Smoking Related Phenomena”/			“hepatitis c” smoking cigarette$ cigar$
Hepatitis C and specific populations (excluding drug users) (MEDLINE, Embase)	Hepatitis C/ Homosexuality/ Bisexuality/ Homosexuality, Female Transsexualism/ Vulnerable Populations/ Homeless Persons/	Hepatitis C/ Hepatitis C Virus/ Homosexuality/ Bisexuality/ Homosexual Female/ Transsexualism/ Vulnerable Population/			hcv “street-involved youth” “men who have sex with men” “sex trade workers” LGBTQ emigrant$ immigrant$

Concept and Database(s)	MeSH	EMTREE	PsycINFO	EBSCO	Keywords
		Homelessness/			refugee$ aboriginal$ native “priority population$”

Appendix C: Literature Review Tables for Non-injection Drug Use

Hepatitis C and Non-injection Drug Use

First Author	Journal Reference	Country/Study Population	Methods	Outcomes	Additional Comments	Strength of Evidence
Rodriguez O, et al[156]	*European Journal of Epidemiology* 1998;14(6):555-61	385 consecutive enrolees in a drug detox program in Spain; 122 injection drug users and 263 non-injection drug users	Tested for HBV markers and for HIV and HCV antibody, as well as anti-hepatitis D	Overall 52% anti-HCV+ (88% in injection drug users and 35% in non-injection drug users, p<0.0001); authors suggested high hepatitis C related to sharing of straws for inhalation	HCV most strongly associated with injection drug users and with HBV infection	+; use of treatment subjects may have reduced denial of IDU, and this was confirmed by looking for puncture marks; study was cross-sectional and lacked behavioural info
Tortu S, et al[157]	*Substance Use and Misuse* 2001;36(4):523-34	Participants in 2 studies in New York City	Recruitment in 2 areas by street outreach; 1 study limited to women; interviewed and tested for HCV and other blood-borne infections	Study A: 524 participants, 29% female; male never-injectors 18% HCV+, females 14%; Study B: 234 females, HCV+ 17% for never-injectors	Authors recommended further research to understand HCV transmission in the group	+; recruitment and study methods were likely to minimize misclassification of IDU as non-injection drug use; lower specificity of test may mean true prevalence was higher; transmission routes not fully addressed
Koblin BA, et al[158]	*Journal of Medical Virology*, 2003;70(3):387-90	Non-injection drug users in New York City; aged 15-40 using no more than 10 years	Street outreach recruitment in drug use areas; screened to rule out ever IDU; risk behaviour interview and HCV test	276 enrolled; 94% had sniffed or snorted cocaine; 80% had smoked crack; 4.7% HCV antibody + (95% CI 2.2–7.2); only sniffing/snorting heroin with cocaine significant risk	Sniffing or snorting cocaine alone, smoking crack and sexual risks all not significant; HCV+ sample and numbers not exposed to cocaine alone and crack alone may have been too small to detect effect	+; street outreach and approach to risk screening were likely effective in ruling out past IDU, but power may be inadequate
Neaigus A,	*Journal of Infectious Diseases*	Non-injection heroin	Cohort study of uninfected non-	493 enrolled at baseline; 277 (56%) followed up; 219	Being an MSM who receives money/	+; prospective design a strength but relatively low

First Author	Journal Reference	Country/Study Population	Methods	Outcomes	Additional Comments	Strength of Evidence
et al[159]	2007;195:1052-61	users in New York City	injection drug users recruited via outreach, interviewed for risks, tested for HCV antibody and followed prospectively every 6 months from Sept 1996 to Feb 2003; had either not injected ever or not in previous 6 months	seronegative for HCV at baseline, and had 592.4 person-years of follow-up; at baseline 9% of never-injectors HCV+; 16 seroconverted to HCV (2.7/100 person-years [95% CI, 1.5–4.2]; cumulative; sharing crack equipment independent predictor of seroconversion	drugs for sex also independently predicted HCV seroconversion	rate of follow-up; relied on self-report to determine non-injection drug use at baseline and at follow-up
Macias J, et al[17]	*Liver International* 2008;28(6):781-6	182 non-injection drug users in treatment in Spain	Cross-sectional survey and HCV testing; previous injection drug users were excluded	HCV, 12.6%; adjusted OR for sharing inhalation tube for crack cocaine 3.6 [1.3–9.8]; tattoos 3.5 [1.3–9.1]; age ≥ 34 3.9 [1.3–11.6]	Sharing of crack-smoking equipment was high	+; cross-sectional survey could not prove causation, but ability to rule out IDU risk was a strength
Martinez A, et al[160]	*Liver International* 2008;28(6):757-60	Studies of HCV in non-injection drug users	Editorial review of evidence about HCV transmission in non-injection drug users	Reviews evidence for HCV in saliva and gingival fluid and for mucosal disruption related to non-injection drug use, especially with cocaine	—	+; supported plausibility of HCV transmission with non-injection drug use
Roy E, et al[146]	*Canadian Medical Association Journal* 2001;165(5):557-60	Street youth in Montreal	437 street youth aged 14 to 25 were interviewed and tested for HCV antibody; multivariate logistic regression used to examine risk factors	Overall prevalence was 12.6% (95% CI 9.7–15.9); OR for injection drug use 28.4 (95% CI 6.6–121.4), OR for crack smoking 2.3 (95% CI 1.0–5.3)	—	+; cross-sectional study could not confirm causation; adjusting for IDU appeared to show independent effect of crack smoking
Scheinmann R, et al[18]	*Drug and Alcohol Dependence* 2007;89(1):1-12	Review of studies Jan 1989–Jan 2006	Systematic review of evidence on prevalence of HCV among non-injection drug users; 28 studies included	Despite methodologic issues related to data quality in studies for which non-injection drug use was a secondary population to be studied with main focus	For studies judged least likely to misclassify IDU as non-injection drug use, prevalence narrowed to 2.3–	++; concluded that studies have not definitively shown whether non-injection drug use behaviours are linked to HCV transmission and stronger studies specific to

First Author	Journal Reference	Country/Study Population	Methods	Outcomes	Additional Comments	Strength of Evidence
				on injection drug users, evidence showed non-injection drug users had higher HCV rates than the general population (2.3–35.3%, median 14%); but causal pathway remained unclear	17%	non-injection drug use risk behaviours are needed
Caiaffa WT, et al[19]	*Addiction* 2010;106:143-51	871 non-injection cocaine users in Buenos Aires and Montevideo	Recruitment mainly through non-governmental service organizations with snowball methods; about 18% recruited from public and private drug-treatment facilities; extensive efforts to determine never-injectors and avoid misclassifying; collected data on drug use, sexual history and criminal records; tested for HCV, HIV, HBV and VDRL; HCV monoinfected and HIV monoinfected compared to group who were negative for both	HCV seroprevalence 8.8% (6.9–10.8), for HIV 7.9 (6.1–9.7), anti-HBV 10.1 (8.2–12.3); VDRL 4.1 (2.8–5.4); HCV monoinfected more likely to have been imprisoned (OR 2.41), arrested due to drugs (OR 3.53) and to report having shared straws (OR 2.21); also more likely to ever have had an HIV+ sexual partner (OR 3.15), and more likely to have positive HBV serology, while HIV+ were more likely to have had injection drug–using sexual partners (OR 2.31), HIV+ sexual partners (OR 2.98), HBV serological markers (OR 3.47) and VDRL+ (OR 5.10)	Almost all non-injection drug use was via straws; only about 1% smoked crack, so this could not be assessed as a risk	+; large sample with careful attention to ensuring never-injectors only in the sample; strongly supported correlation between sharing straws and HCV, but cross-sectional design could not prove causality
Removille N, et al[20]	*BMC Public Health* 2011;11:351	Injection drug users and non-injection drug users in Luxembourg included in a national drug surveillance system (RELIS); included participants from prisons,	Case definition was a current and regular user of opiates, cocaine and/or amphetamines and current contact with a health or law enforcement institution	368 participants (31% of those approached) 14.5% of RELIS participants; 84% injection drug users and 16% non-injection drug users; HCV antibody prevalence 81% for	Low participation rates and small sample size for non-injection drug users preventing analysis of correlates with HCV for that group;	+; provided evidence of high HCV prevalence in non-injection drug use, but no information about related routes of administration; also supported elevated risk of

First Author	Journal Reference	Country/Study Population	Methods	Outcomes	Additional Comments	Strength of Evidence
		in- and outpatient drug treatment and drop-in and assistance centres	due to the listed drugs; recruited a 15% sample from the national database, aiming for similar rates of recruitment from all participating sites; injection drug users were those who had injected at least once in their lifetime	injection drug users and 19% (95% CI 8–30%) for non-injection drug users; 55% of non-injection drug users still susceptible to HBV; correlates of HCV in injection drug users were prison, older age, longer duration of injecting; for multivariate analysis, only age and setting of recruitment (inpatient and prison being higher) were associated with HCV; no covariates were presented for non-injection drug use	non-injection drug users were users of heroin, cocaine and/or amphetamine, but routes of administration were not reported	HCV for injection drug users in prison

HCV/HIV Transmission Routes and Non-injection Drug Use

First Author	Journal Reference	Country/Study Population	Methods	Outcomes	Additional Comments	Strength of Evidence
Abe K, et al[21]	*Lancet*, 1991;337:248	Lab study in primates	HCV RNA detection in saliva of carrier chimps and inoculation into HCV– chimp	HCV in saliva of 2/4 carriers and HCV RNA in serum of chimp after inoculated with saliva	Small study, but interpreted as strongly suggesting saliva infectious	Suggestive lab finding in non-human primates
Ackerman Z, et al[161]	*Hepatology Research* 1998;11(1):26-40	Studies of HCV in various human body fluids in several countries	Systematic review of studies looking for HCV in various human body fluids	Many studies lacked control groups; pooled prevalence in saliva (7 studies), 47%	Pooled prevalence in semen 18.5% (2 studies); breast milk 9.5% (2 studies); vaginal fluids 63.6% (1 study); urine 28.3% (2 studies); ascites 100% (1 study)	+; numbers of studies (and within studies) small; studies did not demonstrate infectiousness per se

First Author	Journal Reference	Country/Study Population	Methods	Outcomes	Additional Comments	Strength of Evidence
Dusheiko G, et al[22]	*Lancet* 1990;336:503	Australia	Case report of HCV transmission by human bite	Single case of confirmed acute HCV infection after human bite with no other known exposures	No information available about source case	+; detailed inquiry seemed to rule out other sources, but would be stronger if source case info available
Faruque S, et al[162]	*Journal of Acquired Immune Deficiency Syndromes* 1996;13:87-92	2,323 people aged 18–29 recruited through street outreach in New York, Miami and San Francisco	Data collected about HIV risk behaviours and oral sores; testing for HIV, syphilis and herpes simplex	Crack smokers 2.4 times more likely to have oral sores than non-smokers; OR 1.9 for oral sores among HIV+ versus HIV–	—	+; did not address the role of HIV in oral sores; rather, suggested oral sex and oral sores may be increasing HIV risk; need longitudinal studies to examine causation
Fischer B, et al[24]	*European Journal of Gastroenterology and Hepatology* 2008;20(1):29-32	Street crack users in Canada	51 pipes collected within 60 minutes of use and HCV RNA testing done on eluate; users tested for HCV and had digital photo of oral cavity to look for sores	43% (n=22) of users HCV+; for 7 users, raters agreed on presence of sores, including the 1 user whose pipe was positive for HCV (2% of pipes)	Full rater agreement for 32/51 photos; 7 with sores, 25 without	+; virus present in some cases, but not proven infectious; small sample needs to be repeated with larger numbers. Many users had received safer pipes, so risks of injury likely lower than usual (may underestimate risk of virus contamination)
Gyarmathy A, et al[163]	*Journal of Acquired Immune Deficiency Syndromes* 2002;30:448-56	483 non-injection heroin users (non-injection drug users) in New York City	Between 1996 and 2001, participants did structured interviews and were tested for HIV, HBV and HCV antibodies; multivariate logistic regression analyses stratified by injection history (ever versus never)	**Never-injectors (70%):** significant correlates were unprotected sex with MSM (HIV, HBV); unprotected sex with non-injection drug user (HIV); self-reported syphilis (HBV); longer heroin use (HBV, HCV); shorter cocaine use (HIV); transfusion before 1986 (HIV); being tattooed (HCV) **Former injection drug users (30%):** receptive syringe sharing (HIV, HBV);	Routes of use for heroin among non-injection drug users were mainly sniffing and inhaling vapours after heating on tinfoil; may have underrepresented risks of using pipes (as for crack) or straws; raised possibility that risk of tattooing could	+; did distinguish between ever and never IDU, but routes of administration made drug use-related risks unclear; emphasized sexual risks as important, including risk for sexual transmission of HIV and HBV from injection drug-using partners

First Author	Journal Reference	Country/Study Population	Methods	Outcomes	Additional Comments	Strength of Evidence
				frequent lifetime injection (HCV); longer sexual history (HBV); being tattooed (HCV)	be related to prison tattoos, but did not provide data to support this	
Howe C, et al[164]	*Drug and Alcohol Dependence* 2005;79(3):389-95	755 street outreach recruited non-injection heroin/crack/cocaine users in New York City; age 15–40; drug use not more than 10 years	No history of injection confirmed at baseline interview and confirmed at a follow-up visit; interview, counselling and testing for HIV, HBV, HCV antibody; logistic regression analysis	3.9% HCV-antibody+ at baseline; median age 30; HCV+s were likely to be older than 30 (aOR 5.7); tattooed by a friend or acquaintance (aOR 3.6); know someone with HCV (aOR 4.3)	Sharing of non-injection drug use equipment was not significant after controlling for age; suggested further study with standardized questions about equipment sharing	+; large sample, likely able to rule out previous IDU with recruitment methods; history of sharing equipment might have covaried with increasing age
Liou T, et al[165]	*Journal of Medical Virology* 1992;37(3):197-202	34 Taiwanese patients with chronic liver disease and positive HCV antibody and RNA in serum	PCR testing for HCV RNA on ascites, saliva, seminal fluid and urine of patients and 5 anti-HCV+ but serum RNA– controls	HCV RNA in 7/7 ascites, 15/31 saliva, 4/17 seminal fluid and 2/29 urine; none of fluids from serum RNA– controls were RNA+	Suggested that fluids of serum RNA– patients have negligible risk based on control group findings	+; supported fluids other than blood as possible sources in cases without blood exposure, including saliva for non-injection drug users
McMahon J, et al[166]	*Journal of Psychoactive Drugs* 2003;35:455-60	Review of virological and epidemiological studies of possible oral or nasal transmission of HCV in non-injection drug users	Not provided	Some epidemiological evidence for non-injection drug use oral and intranasal transmission, but there were methodological limits that point to a need for more research	—	+; included only older studies
McCoy C, et al[167]	*Annals of Epidemiology* 2004;14(8):535-42	Florida; injection drug users, non-injection drug users, control group	Cross-sectional surveys of 3,555 drug users and neighbourhood controls in Miami and 2 rural areas of South Florida	**HIV prevalence:** injection drug users 45.1%; dual users (injection drug users and non-injection drug users) 30.5%; crack smokers 20.1%; controls	All drug use groups reported significantly higher rates of sexual risk behaviour and of STI history; did not	+; supported high HCV prevalence in crack smokers versus controls, but high rates of sexual risk behaviours and STIs, as well as cross-sectional nature of

First Author	Journal Reference	Country/Study Population	Methods	Outcomes	Additional Comments	Strength of Evidence
				7.3% **Multivariate logistic regression, OR versus controls:** injection drug users 9.81; dual 5.27; crack smokers 2.24	allow determination of roles of sexual versus drug use transmission	study made clear attribution to crack use problematic
Porter J, et al[23]	*American Journal of Public Health* 1993;83:1490	Crack smokers in North Philadelphia, Pennsylvania	Qualitative information provided by service users attending HIV prevention presentations and during outreach to shooting galleries	Crack smokers described unsafe smoking materials used and types of lip injuries that occurred (burns, blisters, cuts)	—	+; provided clear qualitative evidence of lip injuries, but could not confirm that these resulted in viral transmission
Tortu S, et al[16]	*Substance Use and Misuse* 2004;39(2):211-24	123 female drug users with no history of injection who had voluntary HIV and hepatitis testing in a study in New York City	Targeted sampling and participant referrals used to recruit women who used drugs by non-injection but had no history of injection; interviews for risk factors and testing; case-control analysis comparing HCV+ to HCV–	19.5% HCV+; ever shared non-injected heroin implements with an injector and ever shared both intranasal and oral drug use implements significantly associated with being HCV+	79% had a history of incarceration; HIV+ women 4.5 times more likely to be HCV+ than HIV–; suggestion that HIV might have facilitated HCV transmission through non-injection routes should be followed up in other studies	+; recruitment methods should encourage valid reporting on previous IDU; sample size too small for adequate power for some variables; may have been selection bias with voluntary testers being higher-risk for HCV

Safe Drug Smoking Initiatives

First Author	Journal Reference	Country/Study Population	Methods	Outcomes	Additional Comments	Strength of Evidence
Collins C, et al[168]	*Canadian Journal of Public Health* 2005;96(5):344-7	Canada	Expert commentary on safer smoking sites	Identified possible benefits of safer smoking sites that could form the basis for evaluation	—	–; did not provide direct evidence, but provided rationale for safer smoking sites
Hendrich D, et al[169]	*European Report on Drug Consumption Rooms.* European Monitoring Centre for Drugs and Drug Addiction (EMCDDA) 2004	European Union countries	Report on drug consumption facilities in EU; included safer-injection and safer-inhalation facilities	62 drug consumption rooms by end of 2003; all those in Netherlands and many in Germany and Switzerland included rooms for safer smoking; evaluations showed reduction in risk behaviours and benefits from access to medical/social services and referrals	Program description and process evaluation could provide guidance for others interested in opening such facilities	Evaluation data were primarily related to injectors and did not provide direct evidence about impact on non-injection drug users; evidence about impact on injectors: +; did not as yet include controlled studies of impact on HCV or other infectious diseases
Leonard L, et al[107]	*International Journal of Drug Policy* 2008;19(3):255-64	Active street-recruited injection drug users who also smoke crack in Ottawa	112–167 interviews and HIV/HCV tests at 4 points 6 months prior to implementing crack kit program and 1, 6 and 12 months post-implementation	Post-implementation injecting declined significantly, with evidence that drug users were shifting to smoking from injecting; sharing of pipes also declined significantly	—	+; study examined pre- and post-intervention behaviour, but used cross-sectional surveys, so did not measure change in same individuals; risk data relied on self-report
O'Bryne P, et al[170]	*Addiction, Research and Theory* 2007;16(2):181-92	Crack pipe program implementation in Ottawa and Toronto	Case study of crack pipe program implementation in Ottawa and Toronto	Identified key factors that influenced program development in each city, such as expert roles, police support/ opposition, community partners	—	Did not provide evidence for effectiveness of crack pipe programs per se, but useful information for public health authorities considering introducing them
Shannon K,	*Harm Reduction*	437 crack smokers in Vancouver; 246 (56%)	Survey of crack smokers regarding willingness to	Willingness to use SSF independent association	Paper included background review	+; focus was on feasibility of SSF based on user

First Author	Journal Reference	Country/Study Population	Methods	Outcomes	Additional Comments	Strength of Evidence
et al[171]	*Journal* 2006;3:1	former or current injection drug users, 191 (44%) no history of IDU	use a safer smoking facility (SSF) and correlation of this with reported risks	with: recent IDU (OR 1.72, 95% CI 1.09–2.70); having equipment confiscated or broken by police (OR 1.96, 95% CI 1.24–2.85); crack bingeing (OR 2.16, 95% CI 1.39–3.12); smoking crack in public places (OR 2.48, 95% CI 1.65–3.27); borrowing crack pipes (OR 2.50, 95% CI 1.86–3.40); and burns/inhaled Brillo due to rushing smoke in public places (OR 4.37, 95% CI 2.71–8.64)	of SSFs in Europe and of their potential value in providing contact with higher-risk non-injection drug users to offer health and social services (including addiction treatment), as well as the possibility of intervening to prevent transition to IDU from non-injection drug use	willingness; association of willingness with risks as seen as evidence for potential benefits of providing SSF; focus on SSF rather than safer smoking equipment per se
Wolf J, et al[172]	*Journal of Drug Issues* 2003;33(3):649-61	Safer consumption facilities, Netherlands	Mixed methods study of 18/21 drug consumption sites in Netherlands in 2001	Provided details of program design and issues in Dutch safer consumption sites, all of which included safer smoking rooms	Provided useful background on issues to be considered in opening safer consumption facilities	+; conclusion from mainly qualitative data that drug consumption sites were reducing public nuisance and health harms; did not distinguish injection from smoking

Appendix D: Literature Review Tables for Sexual Transmission of Hepatitis C

Sexual Transmission of HCV

First Author	Journal Reference	Country/Study Population	Methods	Outcomes	Additional Comments	Strength of Evidence
Rooney G, et al[173]	*Sexually Transmitted Infections* 1998;74:399-404	Review of studies providing evidence about sexual transmission of HCV	Medline search with defined terms and review of references; emphasis on methods used in studies	Prospective study gave rate of 12/1,000 person-years; cross-sectional studies gave prevalence of 1 to 3% of partners with HCV; concluded small but definite risk of sexual transmission	Co-infection with HIV, duration of relationship and chronic liver disease identified as cofactors that may increase risk of transmission	+; basic conclusion appeared well supported but did not address extent of impact of cofactors
Terrault NA[29]	*Hepatology* 2002;36:S99-105	Review of differing study types examining sexual transmission of HCV worldwide	No specific search strategy provided; examined evidence according to study methods	Rate of HCV transmission in long-term monogamous relationships 0–0.6% per year; rate with multiple partners or STI risk 0.4 to 1.8% per year; difference may involve non-sexual transmission risks; reports differing ranges of seroprevalence in partners in different geographic regions (2.8 to 11% in southeast Asia, 0 to 6.3% in northern Europe, and 2.7% in the United States)	HIV likely increases risk; couples in long-term monogamous relationships need not change their practices, but could use barrier methods to reduce the already low risk; for multiple or short-term partners, with STIs, during menses, or with practices that may traumatize mucosa, barrier methods are recommended	++; assessment of strengths and weaknesses of differing study types, and specification of recommended prevention in different situations added to strength of conclusions; emphasized importance of further larger prospective studies, confirmation of concordance in virus of partners, and further study of role of recent infection and viral load in transmission, as well as specific sexual practices

First Author	Journal Reference	Country/Study Population	Methods	Outcomes	Additional Comments	Strength of Evidence
Clarke A, et al[174]	*International Journal of STD and AIDS,* 2006;17:74-80	Review of studies with evidence for modes of transmission of HCV	PubMed search with described strategy and references from identified articles; particular focus on U.K.	Concluded that there was no doubt that HCV is sexually transmissible but at a much lower rate than HIV, HBV etc., and that risk is increased by co-infection with HIV or STIs	—	+
Cavalheiro NP[175]	*Revista do Instituto de Medicina Tropical de São Paulo,* 2007;49(5):271-7	Focus on risk for monogamous heterosexual couples in the general population with 1 partner who has HCV	No search strategy specified; included 92 studies up to 2006	Concluded that sexual transmission does occur; that although studies report rates of infection in heterosexual partners between 0 and 27%, the most plausible estimates were between 0 and 3%, and that co-infection with HIV or other STIs and also certain sexual practices increased risk	Some studies also supported increased risk for male-to-female versus female-to-male transmission; many studies lacked complete evidence to rule out non-sexual routes of transmission, and may not have compared virus genomic sequences to confirm identical virus	+; did not fully critique evidence or summarize weaknesses of studies showing higher rates of transmission
Tohme RA, et al[30]	*Hepatology* 2010;52:1497-1505	Review of both heterosexual and homosexual transmission to provide best possible advice by CDC	Review of literature published since 1995 (total of 80 articles) to summarize best available data; studies rated based on strength of design, representation of population and adjustment of control for potentially confounding HCV risk factors	Heterosexual transmission in regular partnerships—most studies showed no increased risk after controlling for other risk factors; multiple partners aOR 2.2–2.9, pre-existing STIs also likely to increase risk; women with HIV almost twice as likely to acquire HCV after controlling for	Limitations: studies of serodiscordant couples may have selected for those less likely to transmit; people with multiple partners may also have been more likely to have unreported past or current IDU; despite these limitations,	++; comprehensive search of English-language literature and quality assessment of studies; relevance to U.S. was likely to be similar to Canada

First Author	Journal Reference	Country/Study Population	Methods	Outcomes	Additional Comments	Strength of Evidence
				IDU (aOR 1.2–2.9), STD clinic attendees with HIV aOR 4.4 for HCV compared to those who were HIV–; HCV acquisition low in HIV– MSM (0–1.5/1000 person-years), but aOR 4.1–5.7 in several longitudinal cohorts of HIV+ MSM; studies suggest links to higher-risk practices such as fisting and use of sex toys	greatest risk for sexual transmission appeared to be related to HIV infection	

HCV-Positive Cases Without Known Parenteral Risk Factors

First Author	Journal Reference	Country/Study Population	Methods	Outcomes	Additional Comments	Strength of Evidence
Mele A, et al[176]	*Journal of Medical Virology* 1999;57:111–13.	Acute HCV+ cases identified through a surveillance system in Italy covering about 46% of the population	Cases defined as having acute illness compatible with hepatitis, negative for HAV and HBV and positive for HCV; 2-page standard risk-factor questionnaire; HCV cases compared to HAV as control	After adjusting for parenteral risk factors and demographic factors, having 2 or more sex partners gave OR of 2.2 (95% CI 1.7–2.7)	After excluding those who indicated IDU or transfusion, OR for 2 partners was 2.0, while for 3 or more it was 2.8	+; standardized questionnaire may have seriously underestimated some risks, especially drug use; no information on sexual behaviours

Heterosexual Partners of HCV-Positive People

First Author	Journal Reference	Country/Study Population	Methods	Outcomes	Additional Comments	Strength of Evidence
Akahane Y, et al[177]	*Annals of Internal Medicine* 1994;120(9):748-52	Japan; spouses of hepatitis C patients with chronic liver disease	Clinical, serological biological survey of spouses (52 men and 102 women) of patients with chronic liver disease	42 (27%) spouses anti-HCV+, 25 also RNA+; positivity increased with duration of marriage (1–60 years); 3 spouses had genotypes different from their partner	No spouses married less than 10 years, and only 9% of those married less than 30 years were infected	+; authors did not appear to have obtained sexual behaviour information apart from spouses, stating they had no extramarital partners; authors did not address very long time to become infected, or provide information on possible non-sexual risks
Aykn N, et al[178]	*Scandinavian Journal of Infectious Diseases* 2008;40:533-7	Turkey; spouses and family members of chronic hepatitis C patients	HCV prevalence measured in 174 stable sexual partners and 230 offspring of chronic hepatitis C patients	HCV prevalence was 2.7% (6 partners and 5 offspring); however, 6 of these had a history of transfusion; 5/6 spouses had also shared equipment; prevalence no higher than reported in general Turkish population	Severity of liver disease in index cases was associated with infection in partners but not offspring	+; relatively small numbers of infected spouses and family, even fewer without alternative risk factors
Boonyarad V, et al[113]	*Journal of Gastroenterology* 2003;38:1053–59	Spouses of 160 chronic hepatitis C patients (54 male and 106 female) in Thailand	Spouses were tested for HCV antibodies, and positives confirmed with PCR tests for RNA; for positive spouses, phylogenetic studies were done seeking to confirm spousal transmission	HCV RNA was detected in 3 of 160 spouses (1.88%); homology and phylogenetic tree analysis could not confirm spouses as source of these infections	Study could not indicate how long HCV+ spouses identified had been infected; phylogenetic shifts might have occurred in long-standing infections, even if spouse was original source	+; confirmed low rate of transmission, but significance of phylogenetic findings not entirely clear
Caporaso N, et al[114]	*Journal of Viral Hepatitis* 1998;5:67-72	1379 spouses and other household contacts of 585 antibody- and Ag	All contacts tested for antibodies; all positives confirmed with PCR	Prevalence among spouses was 15.6% and among other relatives 3.2% (OR	Authors unable to examine homology of virus in spouses	+; unable to conduct sequencing studies to study homology; relied on self-

First Author	Journal Reference	Country/Study Population	Methods	Outcomes	Additional Comments	Strength of Evidence
		HCV+ cases with chronic liver disease in Italy	testing for RNA	6.5, 95% CI 3.5–8.6); after adjustment for confounders, only age >45 years and any parenteral exposure were significantly associated with HCV+; authors concluded there was no evidence of sexual transmission to spouses	because length of infection unknown and genome evolves rapidly, so might change after transmission to appear different	report of parenteral risk factors
Chayama K, et al[31]	*Journal of Hepatology* 1995;22:431-9	205 spouses of HCV+ people in Japan	HCV antibody testing; genotyping completed in both spouses in 17 of 25 HCV+ couples	8.8% of spouses (25/205) HCV+; 14/17 (82.4%) of spouses had same genotype; 5/8 couples with same genotype had very high homology, suggesting the same virus; none of the 5 reported other transmission risks	Authors suggested household exposures to blood could explain transmission, as well as sexual transmission	+; gave idea of HCV prevalence in spouses but could not clearly delineate sexual transmission versus other household contact as source of infection of spouses
Halfon R, et al[179]	*Journal of Clinical Microbiology* 2001;39(3):1204-6	Female heterosexual partner of chronically HCV-infected man	Case study of female with acute HCV, including sequence analysis of HCV from case and her male sexual partner	Only identified risk factor in preceding 6 months was oral, anal and vaginal sex with chronically HCV-infected male partner; viral sequence analysis confirmed the same virus in the partners	—	+; relied on self-report that sexual contact was the only possible transmission route between the couple
Kao JH, et al[115]	*Journal of Gastroenterology and Hepatology* 2000;15:391-5	Spouses of patients with chronic hepatitis C in Taiwan	Prospective cohort study of 112 index hepatitis C patients and their HCV seronegative spouses	Mean follow-up 45.9 months; 1 spouse seroconverted with acute hepatitis 2 years after enrolment; phylogenetic analysis with spouse's virus suggested they were nearly identical; annual risk 0.23% per year	No parenteral or other exposures identified; no details of sexual activities provided; authors suggested risk may be cumulative and recommended education of	++ for estimate of transmission risk in prospective design with substantial follow-up and in confirmation of index spouse as likely source; –/+ for sexual transmission evidence, since other forms of exposure could not be

First Author	Journal Reference	Country/Study Population	Methods	Outcomes	Additional Comments	Strength of Evidence
					spouses about avoiding possible risks	ruled out
Koda T, et al[180]	*Journal of Gastroenterology and Hepatology* 1996;11:1001-5	121 chronic liver disease patients and their spouses in Japan	Cross-sectional study testing spouses of chronic hepatitis C patients; genotypes compared between spouses; those with matching genotypes were compared for genetic heterogeneity	17 spouses (17.4%) were also HCV+; 12 couples had matching genotype; 2 couples had a single viral clone, the remainder had single or complex quasi-species	Authors attempted to rule out tattoos, transfusions etc. as sources through self-report; HCV infection in spouses correlated with length of marriage; they attributed this to many opportunities for household exposures and not necessarily to sexual transmission	+; relatively large number of cases examined; cross-sectional design made timing of infection very difficult to assess; spouses with differing genotypes suggested considerable unrecognized risks outside household, such as medical or other parenteral exposures
Kumar RM, et al[181]	*Obstetrics and Gynecology* 1998;91:426-31	Spouses and household contacts of HCV+ Egyptian women detected during antenatal care and of HCV– control women	699 women screened; 94 anti-HCV+; 65 studied as index patients; 65 matched antenatal HCV– women as controls; included all family members of both groups; HCV sequencing compared in spouses and in randomly selected non-related control pairs	28% of family members of HCV+ group were HCV+, versus 4% of control group family members ($p<0.004$); among HCV+, 48% of husbands versus 8% of children were HCV+ ($p<0.001$); those with seropositive spouses were significantly older and longer married; in 35 HCV+ couples 33 had same genotype and high homology versus 6 of 25 unrelated control pairs with same genotype, all with low homology	HCV is hyperendemic in Egypt, with rates from 10–25% among volunteer blood donors and up to 51% in segments of the general population; infected spouses denied other exposures, including sharing of razors, toothbrushes etc.	+; no clear reason given why families of 29 of initial women not included, but 25 of these women were used in the non-related pair HCV sequencing comparison; inclusion of control group a strength; control group appeared to have lower than general population levels of HCV—this was not discussed
Marincovich	*Sexually*	Open cohort of 171	Other risks for HCV	529 person-years of follow-	1 HIV	++; prospective design,

First Author	Journal Reference	Country/Study Population	Methods	Outcomes	Additional Comments	Strength of Evidence
B, et al[182]	*Transmitted Infections* 2003;79:160-2	uninfected steady heterosexual partners of people infected with HIV and HCV (152 women and 19 men) attending an HIV care clinic in Spain	acquisition excluded at enrolment; clinical, epidemiological and risk info collected and testing done every 6 months, including detailed sexual contact info	up with 74 (43%) of partners having unprotected intercourse with an index case and another 15.8% having condom failure; total 5,800 unprotected anal or vaginal acts; no HCV seroconversions: 95% CI 0–6.3 per 10,000 unprotected contacts	seroconversion occurred 1.7 per 10,000 unprotected contacts, 95% CI 0–9.5; participants younger on average and with shorter relationships than many other studies of spousal HCV transmission	detailed collection of sexual contact info and attempt to exclude other risks were strengths; more person-years of follow-up would have helped to define rate more precisely; may not be generalizable to non-HIV+ couples, since rate of condom use reflected concerns about HIV risk
Meisel H, et al[183]	*Lancet* 1995;345:1209-11	Spouses of women infected through contaminated anti-D immunoglobulin in Germany	Women were followed over 10–15 years; husbands tested 6 months to 2 years after wives infected and again 10–15 years after	None of 94 husbands had HCV antibody or virus; 3/132 children born to chronically infected mothers were HCV+	—	+; sample size small; all testing prior to 1995; could not rule out possibility that more sensitive tests might have detected infection, but still confirmed that rate would likely be low
Piazza M, et al[184]	*AIDS Patient Care and STDs* 1998;12(8):611-8	Long-term partners of hepatitis C patients (most but not all with chronic liver disease) in Italian trial of immunoglobulin prophylaxis for hepatitis C	899 HCV-antibody– partners given IG every 2 months and risk-factor questionnaire and HCV test every 4 months for 18 months; infected partner genotypes compared	Rate of new infections 12/1,000 person-years; all infections in long-term partners, most >50 years of age and exposed >25 years; 4/7 had identical genotypes	Self-report indicated no other exposures, but this may or may not be reliable; 3 couples whose viruses were not identical attributed by authors to rapid viral mutation, but given short time, another source seems more likely	+; unable to exclude other sources of infection, especially for 3 spouses whose virus differed from partners; uncertain why long-term couples transmitted at this point—authors suggested higher partner viral load in long-term infections and perhaps increased risk of mucosal damage in older people during sexual contact; no specific sexual practices reported
Tahan V, et al[185]	*American Journal of Gastroenterology*	Spouses of HCV-infected patients in Turkey	600 spouses initially tested; 216 seronegative spouses	12 (2%) of 600 spouses HCV+; no seroconversions in HCV– spouses over 3	Prevalence of spouses at baseline in limits of general	+; larger numbers or longer follow-up may have shown seroconversion; may be

First Author	Journal Reference	Country/Study Population	Methods	Outcomes	Additional Comments	Strength of Evidence
	2005;100:821-4		followed over 3 years (partners of treated patients excluded)	years	prevalence; data included frequency of intercourse, which correlated with HCV in spouses infected at baseline	some selection bias, but collection of detailed data on sexual intercourse frequency a strength

Prevalence in Populations at Increased Risk for STIs (STI Clinics, Sex Workers etc.)

In general, studies of populations at increased risk for STIs may be able to demonstrate increased rates of HCV infection, supporting recommendations for screening in such populations, but are frequently unable to distinguish with certainty between sexual transmission and presence of other risk factors, such as unsafe injection and non-injection drug use practices, and other potential blood exposures.

First Author	Journal Reference	Country/Study Population	Methods	Outcomes	Additional Comments	Strength of Evidence
Balogun M, et al[89]	*Sexually Transmitted Infections* 2003;79:301	Genitourinary medicine attendees in England, Wales, Northern Ireland	Testing of 17,586 unlinked serum specimens from 14 clinics for anti-HCV and HCV antigen genotypes in 1995–1996	HCV among injection drug users, 36.9%; among non-injection drug users, 0.65% (95% CI 0.51–0.78)	Heterosexual injection drug users had higher anti-HCV prevalence than gay/bisexual injection drug users; HCV prevalence increased with age; non-significant difference by birth in U.K. versus abroad, or by HIV status (OR 1.74, p=0.08)	+; potential for under-reporting of IDU; did not include reporting of specific risk behaviours; testing in equivalent of STI clinics should have selected for elevated risk of sexual transmission

HCV Prevalence Among HIV-Positive MSM

First Author	Journal Reference	Country/Study Population	Methods	Outcomes	Additional Comments	Strength of Evidence
Dougan S, et al[65]	*BMC Public Health* 2007;7:7	England and Wales	Matching of routine HCV+ tests, and all tests from HCV sentinel testing sites to HIV diagnoses throughout England and Wales	31 MSM with no other risk factors diagnosed with ion between 1996 and 2003 through routine testing matches; of 242 HIV+ MSM without other risks tested in HCV sentinel system, 11 (4.5%, 95% CI 2.38%) were HCV+	Authors concluded that sexually transmitted HCV in HIV+ MSM has increased over time and that enhanced surveillance is needed for HCV among HIV+ MSM in England and Wales	+; large population a strength; many cases excluded because lacked matching info; much risk-factor information (e.g. IDU) missing; trends might have related to increased testing versus increased ion
Fletcher S[25]	*Journal of the Association of Nurses in AIDS Care* 2003;14(5):87S-94S	London, England; HIV treatment clinic	Investigation of 16 HIV+ MSM diagnosed with acute hepatitis C during 2002	Cases had no history of IDU but reported higher-risk sexual behaviours: unprotected anal intercourse, fisting, rimming and oral sex	6 (37.5%) patients spontaneously cleared HCV, and the rest were treated; 8 (50%) reported a recent STI (e.g. syphilis, GC, HBV)	+; no control group to compare frequency of behaviours; relied on self-report to rule out IDU and other risks
Gambotti L, et al[26]	*Eurosurveillance* 2005;10(5):535-40	HIV+ MSM in Paris, France	Retrospective investigation of recent acute HCV cases among HIV+ MSM	29 cases of acute HCV identified in HIV+ MSM between April 2001 and October 2004; all reported unprotected anal sex; 41% had records of a concomitant STI; 21% fisting; 6/11 completing self-administered questions reported bleeding during sex	Authors concluded unprotected traumatic anal sex caused main risk, with STIs facilitating	+; selection bias possible; only 11/29 completed risk behaviour questions
Glosn J, et al[28]	*Sexually Transmitted Infections*	HIV+ people (MSM and other) in PRIMO primary HIV infection cohort in	Repeat HCV testing in 402 HIV+ people with a median of 36 months	HCV incidence rate of 4.3 per 1,000 person-years—3.5 in males and 7.8 in females; incidence rate was	<1% of cohort were injection drug users	++; prospective study and detailed risk information strengthened evidence of sexual transmission in the

First Author	Journal Reference	Country/Study Population	Methods	Outcomes	Additional Comments	Strength of Evidence
	2006;82: 458-60	France	of follow-up	1.2 per 1,000 person-years before January 2003 and 8.3 per 1,000 person-years after January 2003 (p=0.06); parenteral factors found in women (IDU, body piercing); only identified HCV risk in men was unsafe sex		MSM included
Larsen C, et al[66]	*Eurosurveillance* 2008;13(4-6)	HIV+ patients across France	One-day cross-sectional survey using random and proportional probability sampling of all HIV+ people under care in France	Prevalence of HCV among HIV+ MSM was 3.1%; no evidence of increase from last survey, but methods different	Study confirmed the overall high burden of liver disease (HCV and HBV) in people with HIV	+; study relied on medical records for test results; small refusal rate from patients, higher from clinical sites; may have been biased towards inclusion of those followed more (e.g. those with liver disease)
Rauch A, et al[186]	*Clinical Infectious Diseases* 2005;41:395-402	Switzerland; HIV+ people enrolled in Swiss cohort	Assessed HCV prevalence and incidence in cohort between 1988 and 2004, and association with mode of HIV infection, sex, IDU, and reported condom use	MSM without IDU who reported unsafe sex had an incidence of 0.7/100 person-years; those who did not report unsafe sex had incidence of 0.2 cases per 100 person-years (IRR 3.5)	Younger MSM had higher risk of acquiring HCV; HCV+ MSM had significantly higher rates of seropositivity for syphilis; IDU was by far the predominant risk for HCV incidence (7.4 per 100 person-years)	++; cohort design allowed longitudinal analysis; HCV testing has been routine every 2 years since 1998; limitation lack of info on other HCV risks (tattooing, unsafe non-injection drug use); self-report of risk behaviours

HCV among HIV-Negative MSM or Those of Mixed or Unknown HIV Status

First Author	Journal Reference	Country/Study Population	Methods	Outcomes	Additional Comments	Strength of Evidence
Alary M, et al[116]	*American Journal of Public Health* 2005;95:502-5	Cohort of initially HIV– MSM in Montreal being studied for HIV seroconversion	January–September 2001: 1,085 men tested for HCV; if positive, previously collected baseline serum samples tested to determine timing of infection	HCV prevalence at baseline was 2.9% and strongly associated with IDU (32.9% versus 0.3%); only 1 seroconversion in 2,653 person-years of follow-up (0.038 per 100 person-years); only seroconverter reported IDU with needle-sharing	Men in this study had documented HIV seroconversion and sexual risk behaviours and relatively high levels of HBV antibody and Ag, suggesting that they were experiencing sexual exposures	++; well-designed cohort study, relatively unbiased selection and follow-up with respect to HCV risk; by selecting HIV– men, this cohort may have underestimated HCV in all MSM in Montreal, including MSM/injection drug users
van de Laar TJ, et al[187]	*Journal of Infectious Diseases* 2007;196:230-8	Amsterdam cohorts of MSM; from 1984–1995, MSM of any age or HIV status; since 1996 recruit mainly MSM under 30 who are HCV–; + 34 MSM reported and confirmed as recently acquired cases through reporting system	Study included 6 monthly questionnaires and stored blood specimens; most recent serum specimen tested for HCV; if positive, entry specimen tested; if negative, all other specimens also tested; PCR on first positive sample used to obtain RNA for genotyping and phenotyping	1.3% of cohort HCV+ at study entry; IDU (OR 60.5) and being HIV+ (OR 4.1) only predictors of baseline HCV+; incidence of HCV in cohort 0.18 per 100 person-years for HIV+ and 0 for HIV–; HCV incidence increased after 2000; of the 34 recently acquired cases reported, all but 1 were HIV+	Of the 34 recently acquired cases, a high proportion had STIs and/or reported fisting; genotyping and phenotyping suggested clusters among recently infected HIV+ MSM	++ for cohort study; + for study of recently acquired cases; no control group for the latter, may have been tested more because HIV+ people see doctors more

Biological Plausibility: HCV in Semen

First Author	Journal Reference	Country/Study Population	Methods	Outcomes	Additional Comments	Strength of Evidence
Abou-Setta AM[188]	*Human Reproduction*	Chronically HCV-infected men	Review of studies of sexual transmission of HCV and of HCV in	Variable levels of HCV reported in seminal samples in a number of	Variability may have been due to processing of	+; did not provide a full systematic review, but did provide evidence

First Author	Journal Reference	Country/Study Population	Methods	Outcomes	Additional Comments	Strength of Evidence
	2004;19(12):2711-7		semen samples from chronically infected men	studies	samples; sensitivity of assays used; inhibitors in semen causing false-negative results; rapid changes in viral concentration in seminal fluid	supporting the presence of HCV in seminal samples in at least some studies, and need to consider this in assisted reproduction
Bourlet T, et al[189]	*Journal of Clinical Microbiology* 2002;40(9):3252-5	32 chronically HCV-infected men at an assisted reproduction clinic in France	PCR testing of semen samples for HCV RNA	4/32 (12.5%) of men had HCV RNA detected in semen; detection was correlated with higher HCV RNA in plasma	Infectivity was not proven; would require a prospec-tive study of a larger sample of men with HCV RNA in semen	+; confirmed presence of HCV RNA in some semen samples, but did not prove infectivity
Briat A, et al[190]	*AIDS* 2005;19:1827-35	HCV-infected men drawn from 2 prospective studies conducted in France, which included some HIV –infected men	120 HCV-infected men, 82 (68%) infected with HIV had blood and semen samples collected for HCV PCR	191 semen samples from 120 men: 26.7% of all samples had HCV; 31.6% of men had at least 1 HCV+ sample; with repeat samples, HCV was sometimes intermittent; for HIV+ men, those with HCV in semen had significantly higher viral loads in serum; HCV RNA in 37.8% of HIV-infected men versus 18.4% of HIV– men (p=0.03)	Authors suggested that high rates of HCV in semen of HIV+ men may have been correlated with recent reports of increases in HCV in HIV+ MSM; they emphasized need for protected sex in HIV+ people to prevent HCV	++; large sample allowing comparison of HIV+ and HIV–, which was not possible in smaller samples
Leruez-Ville M, et al[191]	*Lancet* 2000;356:42-3	21 HCV viremic French men, 15 of whom were also HIV+ and on ARVs	Paired blood and semen samples obtained; RNA amplification techniques modified to increase sensitivity of HCV detection in semen	38% of semen samples contained HCV	Infectivity not necessarily proven by HCV in semen; proportion HCV+ and semen HCV viral load did not vary by HIV status	+; confirmed presence of HCV RNA in some semen samples, but did not prove infectivity

Appendix E: Recommended Case Definition for Hepatitis C Surveillance in Ontario and Comparable Case Definitions from Other Jurisdictions

Ontario Provincial Infectious Disease Advisory Committee, Sub-Committee on Communicable Disease, Hepatitis C Working Group, proposes the following surveillance case definition for hepatitis C in Ontario

Hepatitis C, Newly Acquired

1.0 Provincial Reporting
Only confirmed cases of disease

2.0 Type of Surveillance
Case-by-case

3.0 Confirmed Case

3.1 Confirmed Case

A confirmed case of newly acquired hepatitis C is not known to have chronic hepatitis C, and requires either:

1. Laboratory definitive evidence
   OR
2. Laboratory suggestive evidence **AND** clinical evidence **AND** exclusion of other causes of acute viral hepatitis:
   a) IgM antibody to hepatitis A virus (IgM anti-HAV) negative, **AND**
   b) IgM antibody to hepatitis B core antigen (IgM anti-HBc) negative

4.0 Laboratory Evidence

4.1 Laboratory Definitive Evidence

a) Detection of anti-HCV antibody from a person who has had a negative anti-hepatitis C antibody test recorded within the past 24 months,
OR
b) Detection of HCV by RNA testing from a person who has had a negative anti-hepatitis C antibody test result within the past 24 months,
OR
c) Detection of anti-hepatitis C antibody from a child aged 18 to 24 months,
OR
d) Detection of hepatitis C virus by RNA testing in a child aged 1 to 24 months.

4.2 Laboratory Suggestive Evidence
Detection of anti-hepatitis C antibody, or hepatitis C virus by RNA testing.

4.3 Approved/Validated Tests
Anti-HCV line immunoblot assays including recombinant immunoblot assay (RIBA) and line immunoassay (LIA)

4.4 Indications and Limitations

- In immunocompromised cases, HCV RNA testing is recommended, as antibodies may be negative in this population.
- This definition of newly acquired HCV will exclude people with positive anti-HCV and positive anti-HBc IgM, even though it is possible that in rare cases this pattern will be seen in people who have simultaneous acute HBV and HCV. This profile will be much more commonly seen where someone with chronic HCV has newly acquired HBV, and it is considered better to ensure exclusion of this group from reporting as newly acquired HCV.
- HCV antibody testing should not be performed in infants < 18 months of age because of detectable levels of maternal antibody; however, if antibody testing is performed and found to be reactive at 18 months of age, HCV RNA real-time reverse transcription, polymerase chain reaction (RT-PCR) or nucleic acid amplification test (NAT) should be performed to rule out maternal antibody and to confirm viraemia.
- Cord blood should not be used because of maternal blood contamination.
- Testing for RNA earlier than 4–6 weeks of age is not recommended.

5.0 Clinical Evidence

Clinically compatible signs and symptoms are characterized by acute illness with discrete onset of any sign or symptom consistent with acute viral hepatitis (e.g. anorexia, abdominal discomfort, nausea, vomiting), and any of a) jaundice, b) elevated serum alanine aminotransferase (ALT) level or c) bilirubin in urine.

6.0 ICD Code(s)

ICD 10 Code B18.2

7.0 Comments

N/A

8.0 References

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Hepatitis C, Chronic or Unspecified

1.0 Provincial Reporting
Only confirmed cases of disease

2.0 Type of Surveillance
Case-by-case

3.0 Confirmed Case

3.1 Confirmed Case
A case is > 18 months of age, is laboratory confirmed, and does not meet the definition of newly acquired hepatitis C.

4.0 Laboratory Evidence

4.1 Laboratory Confirmation
Either of the following criteria:

Positive for anti-HCV with laboratory confirmation, **OR**
Positive for HCV RNA

4.2 Approved/Validated Tests
Anti-HCV line immunoblot assays including recombinant immunoblot assay (RIBA) and line immunoassay (LIA)

4.3 Indications and Limitations

- In immunocompromised cases HCV RNA testing is recommended, as antibodies may be negative in this population.
- HCV antibody testing should not be performed in infants < 18 months of age because of detectable levels of maternal antibody; however, if antibody testing is performed and found to be reactive at 18 months of age, HCV RNA real-time reverse transcription, polymerase chain reaction (RT-PCR) or nucleic acid amplification test (NAT) should be performed to rule out maternal antibody and to confirm viraemia.
- Cord blood should not be used because of maternal blood contamination.
- Testing for RNA earlier than 4–6 weeks of age is not recommended.

5.0 Clinical Evidence
No clinical evidence of hepatitis C infection is required to diagnose chronic hepatitis C infection.

6.0 ICD Code(s)
ICD 10 Code B18.2

7.0 Comments
N/A

8.0 References
Centers for Disease Control and Prevention. Case definitions for infectious conditions under public health surveillance. MMWR Recomm Rep. 1997;46(RR-10):1-55. Available from: http://www.cdc.gov/mmwr/preview/mmwrhtml/00047449.htm[68]

Heymann DL, editor. Control of communicable diseases manual. 18th ed. Washington, DC: American Public Health Association; 2004. Viral hepatitis C; p. 261-4.[192]
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Communicable Diseases Network Australia (CDNA). Surveillance case definitions for the Australian National Notifiable Diseases Surveillance System [Internet]. Canberra: Australian Government Department of Health; 2004 [cited 2014 June 16]. Available from: http://www.health.gov.au/internet/main/publishing.nsf/Content/cdna-casedefinitions.htm//$File/consolidated-case-definitions-may2014.pdf[69]
Health Protection Agency. Standards for local surveillance and follow-up of hepatitis B and C [Internet]. London: Public Health England; 2011 [cited 2013 Jun 16]. Available from: http://www.hpa.org.uk/web/HPAwebFile/HPAweb_C/1194947376936[70]

Public Health Agency of Canada Hepatitis C Case Definition (Current as of This Document's Publication Date)
The Public Health Agency of Canada has published surveillance case definitions for adults with HCV as follows: [72]

- Anti-HCV–positive (positive tests should be confirmed by dual EIA testing or by immunoblot/PCR based testing)
  OR
- HCV RNA PCR positive, if anti-HCV–negative (PCR testing should only be performed in anti-HCV–negative people when clinically indicated, for example in people with severe immunodeficiency)

For infants less than 1 year of age, the surveillance case definition is:

- HCV RNA PCR positive, regardless of the result of anti-HCV testing

Testing must be done on infant blood rather than cord blood because the latter may be contaminated with maternal blood. Antibody testing should not be used in infants less than one year of age because of the potential presence of maternal antibody. Optimal time after birth for HCV RNA PCR testing is not fully defined. Testing at 4–6 weeks and/or at 6–12 months is recommended.

Comparison Surveillance Newly Acquired Case Definitions from Other Jurisdictions
As indicated in the above references, other countries have case definitions which aim to distinguish newly acquired from chronic HCV among newly tested cases.

United States
The U.S. Centers for Disease Control and Prevention considers an acute case of HCV to be confirmed if it meets the following clinical case definition, as well as being laboratory confirmed as indicated below, and is not known to have chronic hepatitis C.[68]

Clinical case definition
An acute illness with a discrete onset of any sign or symptom consistent with acute viral hepatitis (e.g. anorexia, abdominal discomfort, nausea, vomiting), and either a) jaundice or b) serum alanine aminotransferase (ALT) levels >400 IU/L.

Laboratory criteria for diagnosis
One or more of the following three criteria:

- Antibodies to hepatitis C virus (anti-HCV) screening-test-positive with a signal to cut-off ratio predictive of a true positive as determined for the particular assay as defined by CDC (signal to cut-off ratios: http://www.cdc.gov/ncidod/diseases/hepatitis/c/sc_ratios.htm)[194] **OR**
- Hepatitis C virus recombinant immunoblot assay (HCV RIBA) positive, **OR**
- Nucleic acid test (NAT) for HCV RNA–positive

  AND, meets the following two criteria:

  IgM antibody to hepatitis A virus (IgM anti-HAV) negative **AND**
  IgM antibody to hepatitis B core antigen (IgM anti-HBc) negative

United Kingdom
The U.K. also focuses on defining an acute case of HCV, with a slightly different definition:[70]

Recent seroconversion OR HCV RNA–positive and antibody-negative or equivocal in an immunocompetent individual OR anti-HCV–positive, anti-HAV IgM negative and anti HBc IgM negative and abnormal liver function tests with a pattern consistent with acute viral hepatitis in someone with recent exposure to HCV (e.g. needle-stick injury, dialysis, recent injecting drug use).

Australia
Australia also has a case definition for reporting newly acquired cases of hepatitis C. Newly acquired is defined according to the following laboratory definitive evidence.[69]

Laboratory definitive evidence
- Detection of anti-hepatitis C antibody from a person who has had a negative anti-hepatitis C antibody test recorded within the past 24 months **OR**
- Detection of hepatitis C virus by nucleic acid testing from a person who has had a negative anti-hepatitis C antibody test result within the past 24 months **OR**
- Detection of anti-hepatitis C antibody from a child aged 18 to 24 months **OR**
- Detection of hepatitis C virus by nucleic acid testing in a child aged 1 to 24 months

A newly acquired case can also be confirmed by having both laboratory suggestive evidence and clinical evidence, as follows.

Laboratory suggestive evidence
Detection of anti-hepatitis C antibody, or hepatitis C virus by nucleic acid testing.

Clinical evidence
Clinical hepatitis within the past 24 months (where other causes of acute hepatitis have been excluded) defined as:
1. Jaundice **OR**
2. Bilirubin in urine **OR**
3. Alanine transaminase (ALT) seven times the upper limit of normal.

Manitoba
Some other Canadian provinces have also included efforts to distinguish acute hepatitis C cases in their surveillance. For example Manitoba has the following definition for an acute case of hepatitis C.[195]

Either a documented seroconversion over a period of under six months, of all of the following:

- Confirmed positive serology for hepatitis C
- Clinically compatible illness (e.g. jaundice, nausea, malaise, fatigue, dark urine, loss of appetite)
- Laboratory evidence of hepatitis (hyperbilirubinemia or aminotransferase levels >2.5 times the upper limit of normal)
- Negative test for HBsAg or anti-HBc IgM
- Negative test for anti-HAV IgM

Cases of longer than 6 months duration, or of unknown duration, are considered non-acute.

Appendix F: Labstract—Testing, Interpretation and Follow-up Testing for Hepatitis

NOTE: LABORATORY INFORMATION PROVIDED IN THIS APPENDIX IS CURRENT AS OF THE DATE OF PUBLICATION OF THIS DOCUMENT – READERS SHOULD CHECK FOR UPDATES AT www.publichealthontario.ca

Labstract—February 2008

Hepatitis C Virus (HCV) RNA and Genotype Testing and Interpretation—Update

To Health Care Providers

For Hepatitis C RNA testing, the Public Health Ontario Laboratory (PHOL) has replaced the Cobas Amplicor Qualitative and Quantitative HCV RNA assays with the new Roche Taqman Real Time HCV RNA PCR assay. The linear range of the new Roche Taqman HCV RNA assay is 15 IU/mL to 10 E+8 IU/mL. For comparison, the previously used Roche Cobas Amplicor quantitative HCV RNA assay has a linear range of 600 IU/mL to 10 E+6 IU/mL.

For Hepatitis C Genotype testing, PHOL has replaced the AutoLipa HCV Genotype assay with the Invader® HCV Genotype assay. The Invader® HCV Genotype assay is a research use only assay that provides rapid differentiation of HCV genotypes 1 to 6 based on sequence variation within the HCV 5' non-coding region. The precision of the Invader® HCV Genotype assay is 99.9%.

1. Hepatitis C RNA Testing

Clinical Utility
Quantitation of HCV RNA by PCR is used to measure viremia in anti-HCV–positive individuals who are on treatment or who are being considered for treatment. Detection of HCV RNA can also be used to assess active HCV infection in immunocompromised anti-HCV–negative individuals.

Specimen Requirements
A minimum of 2.5 mL of frozen serum or plasma is required to perform the Roche Taqman HCV RNA assay. Samples received with less than 2.5 mL will be rejected. All requests for HCV RNA testing must include a completed PHOL Test Requisition Form and a Laboratory Information Form (F-C-HE-036), available at: http://www.publichealthontario.ca/en/ServicesAndTools/LaboratoryServices/Pages/Requisitions-and-forms.aspx .

Results Interpretation
The following table is a guide to aid in the interpretation of HCV RNA results.

HCV RNA Result	Interpretation	Comments
Detected	Hepatitis C RNA detected, >15 IU/mL	Viral load will be provided

HCV RNA Result	Interpretation	Comments
Detected	Hepatitis C RNA detected, <15 IU/mL	The result for HCV RNA is below the linear range of the assay, and thus the exact value cannot be calculated
Not detected	No detectable Hepatitis C RNA	Refer to comments on laboratory report if follow-up testing is required

2. Hepatitis C Genotype

Clinical Utility

Genotyping of HCV is useful in evaluating the likelihood of response to currently available antiviral therapy. Patients with HCV genotypes 2 or 3 generally respond better to therapy and typically require approximately 24 weeks of treatment. Patients with HCV genotypes 1 and 4 to 6 may require up to 48 weeks of treatment. HCV genotypes are sufficient for treatment evaluation; HCV subtypes are not required.

Specimen Requirements

No additional sample is required. The first pre-treatment (i.e. baseline) sample submitted for HCV RNA is automatically used to perform HCV genotyping.

For Further Information

- Call the Customer Service Centre at 416 235 6556 or toll free at 1 877 604 4567.
  - Refer to the Specimen Collection Guide at
  - http://www.publichealthontario.ca/en/ServicesAndTools/LaboratoryServices/Pages/Specimen-Collection.aspx
  - To view our Labstracts, visit http://www.publichealthontario.ca/en/ServicesAndTools/LaboratoryServices/Pages/Labstracts.aspx
- To subscribe to future PHO Labstracts, please email labstracts@oahpp.ca.

Document Change History

Revision Number	Date of Implementation	Description and Change
001000	January 28, 2008	New document
	March 18, 2010	Updated visual identity
	October 12, 2012	Updated URL Links

LABSTRACT—APRIL 2008

Hepatitis C Virus—Anti-HCV–Positive Results, Next Steps

To Health Care Providers

If you receive a reactive hepatitis C antibody (Anti-HCV) result on your patient, this result indicates exposure to the hepatitis C virus (HCV). If you receive an inconclusive Anti-HCV result on your patient, this result indicates possible exposure to HCV or a non-specific antibody reactivity.

Next Steps

For reactive or inconclusive Anti-HCV results, additional testing for the active virus is recommended to determine your patient's accurate status and to assist with treatment.

Please submit a 2.5 mL frozen serum or frozen plasma sample to the Public Health Ontario Laboratory for HCV RNA testing accompanied by a completed PHOL Test Requisition Form and a Laboratory Information Form (F-C-HE-036).

These two forms are available at:
http://www.publichealthontario.ca/en/ServicesAndTools/LaboratoryServices/Pages/Requisitions-and-forms.aspx

Attached is an HCV Testing Algorithm for supplementary reference.

For Further Information

Call the Customer Service Centre at 416 235 6556 or toll free at 1 877 604 4567.

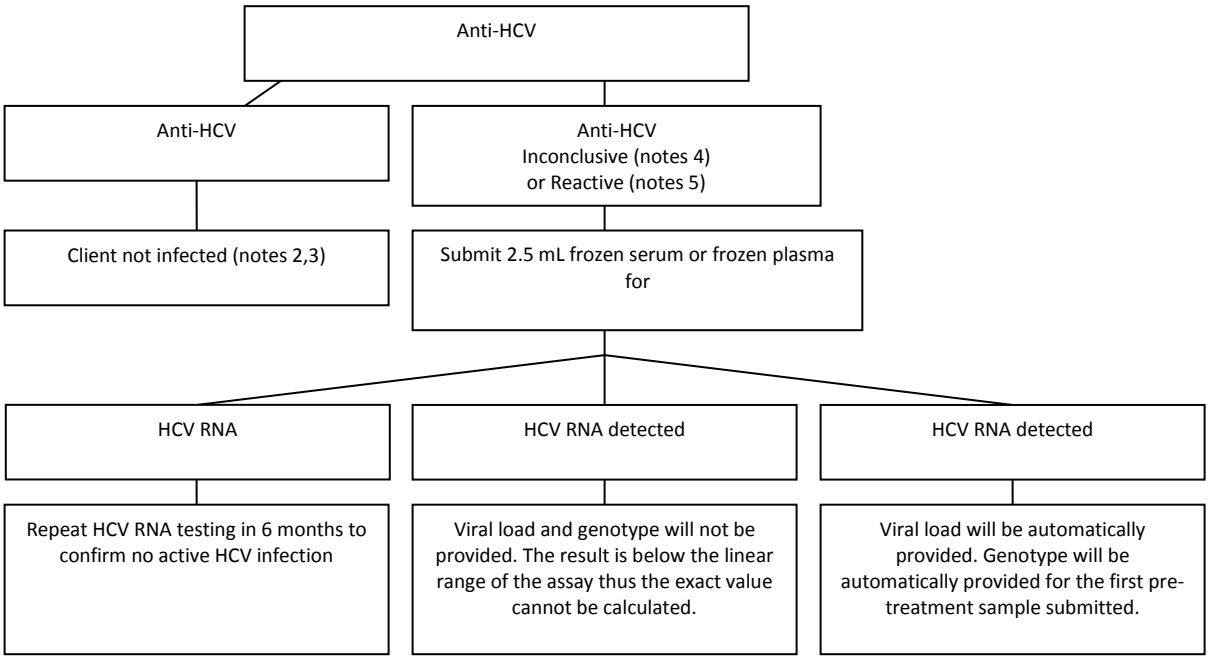
Refer to the Specimen Collection Guide at
http://www.publichealthontario.ca/en/ServicesAndTools/LaboratoryServices/Pages/Specimen-Collection.aspx

Ontario Public Health Laboratories (2008). Hepatitis C Virus (HCV) RNA and Genotype Testing and Interpretation – Update. Labstract, February 2008.

To view our Labstracts, visit
http://www.publichealthontario.ca/en/ServicesAndTools/LaboratoryServices/Pages/Labstracts.aspx

To subscribe to future PHO Labstracts, please email labstracts@oahpp.ca.

HCV Testing Algorithm



Notes

1. The previous qualitative and quantitative tests have been replaced with a single, more sensitive HCV RNA test.
2. If the patient is immunocompromised (e.g. HIV), submit 2.5 mL of frozen serum or frozen plasma for HCV RNA testing to determine if the patient has an active HCV infection. These patients may not exhibit a positive anti-HCV result.
3. If the patient has been exposed to HCV, they may be within the incubation period (6–8 weeks) post-exposure and may not yet have detectable antibody. Submit a serum sample for a repeat anti-HCV test 6–8 weeks post-exposure.
4. If the anti-HCV result is inconclusive and the patient has been exposed, the patient is still susceptible to HCV infection. Patients should continue to be tested after any future exposures. Inform patients that they should not donate blood, blood products and/or organs.
5. If an infant has a mother who is anti-HCV reactive, then submit 2.5 mL frozen serum or frozen plasma from the infant for a HCV RNA test. Retesting the infant for anti–HCV is recommended between 12 months and 18 months of age, as anti-HCV results are presumed to be maternal antibodies.

For information on treatment of HCV, please refer to the *2007 Canadian Consensus Guidelines for the Management of Chronic Hepatitis C.*

Document Change History

Revision Number	Date of Implementation	Description and Change
000	April 8, 2008	New document
	March 18, 2010	Updated visual identity
001	October 12, 2012	Updated URL links and changed OAHPP hotline to CSC

Appendix G: Hepatitis Specimen Collection Guide from Ontario Public Health Laboratories

NOTE: LABORATORY INFORMATION PROVIDED IN THIS APPENDIX IS CURRENT AS OF THE DATE OF PUBLICATION OF THIS DOCUMENT – READERS SHOULD CHECK FOR UPDATES AT www.publichealthontario.ca

Public Health Ontario Laboratories: September 2012

Introduction

The Testing Guideline provides an overview of the laboratory testing available through the Public Health Ontario Laboratories (PHOL).

The guideline is listed in alphabetical order by disease, syndrome and/or causal agent. Information includes:

- Laboratory tests available
- Laboratory test code
- Appropriate specimens
- Collection kit numbers
- Section/location where test is performed
- Turn-around-times for negative and for positive or confirmatory results
- Additional information as required
- Please note that the turn-around-times are based on Monday to Friday business working days.

For further assistance, please contact the Customer Service Centre at 416-235-6556 or toll free 1-877-604-4567 and your call will be appropriately directed.

Criteria for Acceptance of Patient Specimens by Ontario Public Health Laboratories

1. Who can submit:

Legislated Health Care Professionals authorized to submit a specimen and receive a report defined by *Section 9 (1) Ontario Regulation 682* of the *Laboratory and Specimen Collection Centre Licensing Act* (http://www.e-laws.gov.on.ca/html/regs/english/elaws_regs_900682_e.htm) indicates *Section 9 (1)* refers to five types of requestors who can order tests from a laboratory.

a) a legally qualified medical practitioner or a dentist,
b) a midwife, in respect of a test specified in Appendix B of the *Ontario Regulation 682*,
c) a person who lawfully practices a health profession in a jurisdiction outside Ontario, if in that jurisdiction a laboratory may lawfully examine specimens at the request of that person,
d) of an insurer or an agent within the meaning of the *Insurance Act* (https://www.e-laws.gov.on.ca/html/statutes/english/elaws_statutes_90i08_e.htm), in respect of HIV Antibody testing, or
e) a registered nurse who holds an extended certificate of registration under the *Nursing Act, 1991* (http://www.e-laws.gov.on.ca/html/statutes/english/elaws_statutes_91n32_e.htm), in respect of a test specified in Appendix C of the *Ontario Regulation 682*.

2. Definitions:

   a) Non-critical specimen — routine specimens
   b) Critical specimens difficult or impossible to recollect (i.e. CSF, tissue, autopsy material)

3. Criteria for determining Acceptance of Non-Critical Specimens:

    a) Patient identifiers; preferably patient name in full and / or identification number must be on both specimen container and requisition and must match one another. The exception is outbreak specimens, which are received with a numeric outbreak number and no patient name. For smear specimens, the patient identifier (patient initials are acceptable due to space limitations) must be written on the frosted portion of the slide. Patient initials are also acceptable for specimen containers with space limitations e.g. Bordetella specimen containers
    b) A second identifier is essential to distinguish between individuals with the same name, i.e. date of birth or OHIP number or date of collection (mo / day / yr). This second identifier must be on both requisition and container
    c) Legally authorized (as specified in *Ontario Regulation 682* of the *Laboratory and Specimen Collection Centre Licensing Act* at http://www.e-laws.gov.on.ca/html/regs/english/elaws_regs_900682_e.htm) requester's name. Patient test requisition forms received from a clinic staffed by rotating physicians (e.g. hassle-free clinic) shall include the name of the attending physician. Patient reports may be addressed to the Coordinator of the Clinic
    d) Test(s) must be requested or implied (i.e. specimen in a test specific transport media such as SAF for parasitology)
    e) The specimen packaging meets the minimum Federal Regulation – Transportation of Dangerous Goods packaging requirements
    f) The specimen is not leaking

4. Criteria for determining Acceptance of Critical Specimens:

    a) Any critical specimen that is received without patient identifiers will be processed if tests specified but will not be reported, until a signed waiver has been received from the health care provider.

5. Verbal Requests for Additional Tests:

    a) No additional test will be added to previously submitted specimens except under exceptional circumstances. If additional tests are required, please submit a new specimen with an appropriately completed Public Health

Laboratory (PHL) Test Requisition form as follows:

1. HIV and/or HTLV serology: Use the "HIV Serology Test Requisition"
2. Prenatal serology (including Rubella, Hepatitis B, Syphilis and HIV): Use the "Prenatal Test Requisition"
3. For all other serology requests: Use the "General Test Requisition"

Specimen Handling and Transportation

Specimens must be collected in an appropriate specimen container to maintain the integrity of the specimen. To obtain information on the type of container or collection kit that should be used to collect the sample, consult the Specimen Collection section of the Public Health Laboratories at http://www.publichealthontario.ca/en/ServicesAndTools/LaboratoryServices/Pages/Specimen-Collection.aspx

Collection information is provided in the Kit Instruction sheets for each kit. To view the Collection Kit instructions follow the link to the Specimen Collection site at http://www.publichealthontario.ca/en/ServicesAndTools/LaboratoryServices/Pages/Specimen-Collection.aspx

After collection, specimens should be labelled with two (2) identifiers, placed in a plastic bag and sealed. Ensure all container lids are tightly secured before packing.

Most specimens should be stored between 2–8°C however there are exceptions. Specific handling/storage information is included in the Kit Instruction sheet for each kit.

Packing
All specimens must be packaged carefully to avoid breakage or leakage of the specimen. All diagnostic specimens, cultures or biological products must be packed in compliance with the Transportation of Dangerous Goods Regulations. To view these regulations follow the link provided: https://www.tc.gc.ca/eng/tdg/clear-tofc-211.htm

Complete one (1) Public Health Lab requisition per patient. Requisitions are available at: http://www.publichealthontario.ca/en/ServicesAndTools/LaboratoryServices/Pages/Requisitions-and-forms.aspx

Never place the requisition inside the plastic bag with the specimen. Place in outside pouch of clear plastic bag.

All packages sent to the PHO-Public Health Laboratories must be constructed, filled, closed and secured so that under normal conditions of transport, including handling, there will be no accidental release of the substance that could endanger public or employee safety.

The PHO-Public Health Laboratories provides approved specimen transport bags (TC125 IB, Blue Transport Bags) to our clients for surface/road transport of Category B specimens. To obtain Blue Transport Bags for transporting specimens to a Public Health Laboratory or to arrange the pick-up of a Public Health Laboratory specimen; call the Customer Service Centre at 416-235-6556 or 1-877-604-4567 or your local Public Health Laboratory. For information about Lab locations and Contact Information visit our web site at: http://www.publichealthontario.ca/en/ServicesAndTools/LaboratoryServices/Pages/laboratory-location-and-contact.aspx

Place all bagged samples, racks etc in a large zip lock bag or plastic insert provided with the Blue Bag.
All packages must meet the requirements of the National Standards of Canada CAN/CGSB-43.125-2003.
PART 1 – 4.1 Type 1A (TC-125-1A) is used where a high integrity package is required.
PART 2 - Type 1B (TC-125-1B) is suitable for most routine shipments of diagnostic specimens.

Specimen Transportation
The packaging and transportation of all diagnostic specimens, cultures or biological products must comply with the Transportation of Dangerous Goods Regulations. All packages sent to the Ontario Public Health Laboratories must be constructed, filled, closed and secured so that under normal conditions of transport, including handling, there will be no accidental release of the substance that could endanger public or employee safety.

All packages must meet the requirements of the National Standards of Canada CAN/CGSB-43.125-2003.
PART 1 – 4.1 Type 1A (TC-125-1A) is used where a high integrity package is required.
PART 2 - Type 1B (TC-125-1B) is suitable for most routine shipments of diagnostic specimens.

Further information regarding these regulations and compliance packaging can be obtained from the Transport Canada web site at http://www.tc.gc.ca/eng/tdg/moc-infectious-cgsb43125-281.html

For general enquiries email: Questions@tc.gc.ca
Phone: 613-990-2309 Toll Free: 1-866-995-9737 Fax: 613-954-4731
Mailing Address: Transport Canada 330 Sparks Street Ottawa, ON K1A 0N5

Testing Guidelines

Disease/ Syndrome/ Causal Agent/Test	Test Code	Specimens	Collection Kit	Test Available	Section	TAT Negative Results Reported	TAT Positive or Confirmatory Results Reported	Notes
Hepatitis A (HAV) (Infectious Hepatitis)	V11 V12	Blood, clotted or serum	BL–S	Anti-Hepatitis A Virus Total (IgG and IgM) Anti-Hepatitis A Virus IgG (Central PHOL only) Anti-Hepatitis A Virus IgM	Virology	6 days	Within 6 days	Specify test requested: Immunity (Total IgG and IgM or Specific IgG) OR Acute Infection (Specific IgM)
Hepatitis B	V13	Blood, clotted or serum	BL–S	Hepatitis B Surface Antigen (HBsAg)	Virology	6 days	Within 6 days	Specify whether submission is for diagnosis or immunity Immunity – Anti-HBs Diagnosis – HbsAg Anti-HBc IgM, HbeAg and Anti-Hbe – tested only if HbsAg is reactive
	V14	Blood, clotted or serum	BL–S	Anti-Hepatitis B Surface Antigen (Anti-HBs)	Virology	6 days	Within 6 days	
	V15	Blood, clotted or serum	BL–S	Hepatitis B early Antigen (HBeAg)	Virology	6 days	Within 6 days	
	V16	Blood, clotted or serum	BL–S	Anti-Hepatitis B early Antigen (Anti-HBe)	Virology	6 days	Within 6 days	
	V17	Blood, clotted or serum	BL–S	Hepatitis B Core IgM	Virology	6 days	Within 6 days	
	V18	Blood, clotted or serum	BL–S	Anti-Hepatitis B Core Antigen (Anti-HBc)	Virology	6 days	Within 6 days	
		Autopsy			Refer all samples to TML–Mt Sinai Hospital, Toronto, at 416-586-4432			
Hepatitis B–DNA	V13	Frozen serum (minimum of 2.5 mL required) OR Whole blood (red or tiger top) to be received at your local Public Health Laboratory within 4 hours of collection of the blood	BL-S	Hepatitis B Virus-PCR	Virology	10 days	Within 10 days	Details are provided in the Hepatitis B–DNA Specimen Collection Guidelines Include the Hepatitis Information form with the requisition
Hepatitis C	V19	Whole blood,	BL–S	Hepatitis C Virus-PCR	Virology	10 days	Within 10	To determine genotype, pre-

Disease/ Syndrome/ Causal Agent/Test	Test Code	Specimens	Collection Kit	Test Available	Section	TAT Negative Results Reported	TAT Positive or Confirmatory Results Reported	Notes
Genotyping		(red or tiger top) Frozen serum (Minimum of 2.5 mL required)					days	treatment More information is available in the Specimen Collection Details Section of this guide Include the Hepatitis Information form with the requisition
Hepatitis C RNA Quantitative	V19	Frozen serum (minimum of 2.5 mL required) or Whole blood (red or tiger top) to be received at your local Public Health Laboratory within 4 hours of collection of the blood	BL–S	Hepatitis C Virus-PCR	Virology	10 days	Within 10 days	Use test to: • establish HCV viral load prior to treatment • monitor treatment • determine HCV infection in antibody-negative patients who are immunocomprom-ised or recently exposed (6-10 weeks) to HCV • resolve antibody inderminate results for symptomatic patients 1.2.1.1.1.1.1 Include the Hepatitis Informatio n form with the requisition More information is available in the Specimen Collection Details Section of this guide
Hepatitis C Virus	V19	Blood, clotted or serum Heparinized blood not appropriate	BL–S	Anti-Hepatitis C Virus	Virology	6 days	Within 12 days	The detection of antibodies to HCV cannot be used to differentiate between a previous infection (chronic) and an acute infection Details are provided in the Hepatitis C-rNA Specimen

Disease/ Syndrome/ Causal Agent/Test	Test Code	Specimens	Collection Kit	Test Available	Section	TAT Negative Results Reported	TAT Positive or Confirmatory Results Reported	Notes
								Collection Guidelines
		Autopsy			Refer all samples to TML–Mt Sinai Hospital, Toronto, at 416-586-4432			
Hepatitis D Virus Delta Hepatitis Hepatitis E Virus	V20	Blood, clotted or serum	BL–S	Enzyme-linked Immunosorbent Assay	Virology Referred to NML, Winnipeg, MB	14 days	Within 14 days	This test is processed only when HBsAg is positive (HDV is a deficient virus and multiplies only in the presence of HBV)
	V45	Blood, clotted or serum	BL–S	Enzyme-linked Immunosorbent Assay	Virology Referred to NML, Winnipeg, MB	14 days	Within 14 days	Submit relevant clinical details including travel history

Specimen Collection Details—Hepatitis

Hepatitis B—Clinical Course and Antibody Response

1. Incubation period averages 60–90 days, with the range being 45–180 days.
2. HBV is frequently asymptomatic. In those who do develop clinical symptoms, these may include anorexia, malaise, nausea, vomiting, abdominal pains, muscle or joint aches, mild fever, dark urine. Jaundice develops in 25–35 per cent of patients with symptoms.
3. About 90–95 per cent of HBV-infected adults will recover within six months and develop immunity.
4. Of those infected with HBV, 5–10 per cent of adults, 30–50 per cent of children (ages 1 to 5 years), and 80–90 per cent of infants progress to chronic infection.

Abbreviations

HBsAg — Hepatitis B surface antigen

aHBs — Hepatitis B surface antibody

aHBc — Hepatitis B core antibody

HbcIgM — Hepatitis core IgM

HbeAg — Hepatitis B e antigen

aHBe — Hepatitis B e antibody

Ref., *Manual of Clinical Microbiology,* 8th Edition, ASM Press 2003, Editors: P. Murray, E.J. Baron, M. Pfaller, J. Jorgensen, R. Yolken, p. 14

Specimen Collection Details—Hepatitis

Hepatitis B DNA—Specimen Collection Guidelines

This test is useful for:

- Monitoring or assessing drug therapy for chronic hepatitis B.
- Monitoring at 12-week intervals (e.g. 12, 24, 48 weeks)

Test is not useful for:

- Diagnosis

Collection:

1. Collect a tiger-top or red-top tube.
2. Centrifuge blood within 4 hours of collection.
3. Remove serum from clot (2.5 mL serum is required).
4. Freeze within 4 hours of collection in a screw cap cryovial tube.
5. Individually package specimens in a biohazard bag according to Transportation of Dangerous Goods requirements.
6. Complete the information requested on the PHOL Lab Information Form (F-C-HE-036). Attach the information form to the requisition form. Place both forms in the biohazard bag pouch.
7. Ship on dry ice or on an ice pack.
8. Transport specimen in accordance with the Transportation of Dangerous Goods regulations.

Note: If unable to centrifuge and separate the whole blood specimen, ensure that the sample will be received by your local Public Health Laboratory within 4 hours of collection of the blood. Whole blood received after this time frame will not be processed for PCR testing.

Specimen Collection Details—Hepatitis

Hepatitis C RNA—Specimen Collection Guidelines

This test is useful for:

1. Determining HCV infection in antibody-negative patients who have been exposed to a positive HCV source (collect 6–10 weeks post-exposure).
2. Resolving antibody-indeterminate results for symptomatic patients.
3. Testing for HCV infection in HIV-immunosuppressed, antibody-negative patients.
4. Monitoring or assessing patient's quantitative levels for treatment.

This test is not useful and will not be performed for:

1. Assessing disease "activity". Patients may be intermittently PCR-negative, even with active liver disease (elevated liver enzymes). Liver enzyme testing is the preferred method for assessing disease activity.
2. Assessing "infectivity" of patient — all hepatitis C antibody-positive patients are considered potentially infectious.
3. Monitoring therapy by performing multiple PCR (NAA) assays. (To monitor therapy, submit tests pre-treatment, at 12 weeks and at end of treatment.)

Collection:

1. Collect a tiger-top or red-top tube.
2. Centrifuge blood within 4 hours of collection.
3. Remove serum from clot (2.5 mL serum is required).
4. Freeze serum within 4 hours of collection in a screw cap cryovial tube.
5. Individually package specimens in a biohazard bag according to Transportation of Dangerous Goods requirements.
6. Complete the information requested on the PHOL Lab Information Form (F-C-HE-036). Attach the information form to the requisition form. Place both forms in the biohazard bag pouch.
7. Ship on dry ice or on an ice pack.
8. Transport specimen in accordance with the Transportation of Dangerous Goods regulations.

Note: If unable to centrifuge and separate the whole blood specimen, ensure that the sample will be received by your local Public Health Laboratory within 4 hours of collection of the blood. Whole blood received after this time frame will not be processed for PCR testing.

Appendix H: Pre/Post Hepatitis C Testing Counselling Checklist

Pre-Test Discussion	□ Determine whether test is for screening or diagnosis because of symptoms; identify risk factors □ Distinguish hepatitis C from hepatitis A and hepatitis B □ Discuss what will happen if the test is positive (reporting, follow-up RNA test after antibody test, referral for medical follow-up if RNA-positive) □ Discuss antibody versus RNA tests and what each means □ Discuss the implication of a positive test which includes involvement of public health and notification of contacts	
Post-Test Counselling	**Antibody-negative**	**Antibody-positive (RNA test not yet done)**
	□ There is currently no evidence of exposure to the hepatitis C virus □ If there was risk exposure in the preceding 6–8 weeks, recommend a repeat antibody test in 6 months and counsel about how to avoid risks of hepatitis C infection □ Counselled about reducing exposure risks	□ There is evidence of hepatitis C infection, either current or past □ The client requires an RNA test to determine whether he/she is chronically infected (i.e. still has virus present and therefore still infectious to others via blood exposure) □ Counsel about modes of transmission □ How to avoid transmission to others □ How to avoid re-infection if RNA test proves negative (this can be relatively brief if RNA testing and follow-up counselling is assured) □ Counsel about risk factors for disease progression and provide support and referrals as needed (can be deferred until RNA results available if follow-up is assured)
Post-RNA Testing Counselling	**RNA-negative result**	**RNA-positive result**
	□ Resolved cases are those with antibody to HCV but confirmed RNA-negative based on 2 tests done 6 months apart. Note that there is good evidence that a negative RNA test 3 months after treatment indicates a sustained virological response (i.e. a cure).[81] Once sustained virological response is achieved with treatment relapse has never been reported. □ Inform clients that they have evidence of previous infection now resolved □ Inquire about risk and treatment history □ Determine the presence of current risks	□ The client is newly or chronically infected, and is infectious to others □ If history suggests new infection, refer for follow-up and consideration of early treatment (if RNA has not cleared spontaneously within 6 months of infection) □ If chronically infected, he/she will remain infectious for life without successful treatment □ Counsel about • Appropriate lifestyle measures to reduce the risk of disease progression;

	□ Counsel about reducing exposure risks □ If there are ongoing risks, refer for further counselling, harm-reduction services, or other needs □ Educate about modes of transmission as needed	• The availability of treatment • The importance of regular medical follow-up, and provide referrals as needed □ Should be counselled on modes of transmission □ How to avoid infecting others • Not donating blood, semen, breast milk, body organs or tissues • Not sharing toothbrushes, dental floss, razors, earrings or manicure/pedicure equipment (i.e. articles that might have traces of blood) • Keeping all open cuts and sores covered until healed • Putting articles with blood on them (e.g. tampons, pads, tissue, dental floss and bandages) in a separate plastic bag before disposing of them into household garbage • Disposing of bloody sharp items (razor blades, needles etc.) in a sharps container or a glass jar or hard-sided container with a tight-fitting and puncture-proof lid • Using bleach to clean up blood spills. Surfaces should be soaked with one part bleach to nine parts water and left for 10 minutes before wiping off (for a more complete discussion of the cleanup of blood spills see *Best Practices for Environmental Cleaning for Infection Prevention and Control in All Health Care Settings*, available on the PIDAC website).[117] • Informing health care providers (including dental care providers) of disease status where blood exposure is possible

Appendix I: Literature Review Tables for HCV Screening Cost-Effectiveness

First Author	Journal Reference	Country/Study Population	Methods	Outcomes	Additional Comments	Strength of Evidence
Jusot JF, et al[19]	*European Journal of Public Health* 2001;11(4):373-9	Developed (France); screening strategy needed to detect previously or newly infected HCV cases; 3 groups of blood recipients were evaluated: (1) adults younger than 40, (2) adults who received low-volume blood transfusion or were hospitalized in a surgery department or (3) adults between 40 and 65 who received a high-volume blood transfusion	A decision-analytic model was built and divided into 4 successive trees: (1) screening strategies, (2) the confirmation test, (3) treatment choice and (4) the Markov model. The screening strategies were selected from a qualitative study of screening strategies used in France (9 strategies). Confirmation test determined status by detecting the HCV RNA. If ALT was elevated, a liver biopsy was performed and results expressed in the Knodell's score. A Knodell's score < 5 led to surveillance with ALT. After 3 successive normal ALTs, true positive cases were followed a Markov model. Probabilities derived from analysis of the current literature were used to construct Markov models. Data sources for the model were extracted from previously published studies. The costs of the biological tests were obtained from a previous study carried out in 12 French hospitals. One-way and 2-way sensitivity	Except for high-volume transfusions, the strategy using post-transfusion EIA3 confirmed by HCV RNA detection had the lowest cost-effectiveness ratio. In high-volume transfusion, the EIA3 screening strategy prescribed before and after transfusion and confirmed by HCV RNA detection had the lowest undiscounted cost	Focused on clinical screening strategy, not population screening program (birth cohort or higher-risk group)	–; not evaluated for strength, since not related to population screening

First Author	Journal Reference	Country/Study Population	Methods	Outcomes	Additional Comments	Strength of Evidence
			analyses were performed on the prevalence of HCV, the recovery rate after treatment, the sensitivity of ALT, EIA3 on HCV RNA detection and the cost of testing with ALT EIA3 and HCV RNA detection			
Stein K, et al[197]	*Journal of Hepatology* 2003;39(5):814-25	Developed (England); this study investigated the cost of screening for HCV in genitourinary medicine clinics; considered (1) all patients at increased risk of HCV carriage, (2) screening of current or former injection drug users and (3) screening in a larger minority of patients	Developed a screening program and integrated Markov model of combination therapy. The model calculated the utility cost of screening versus not screening. Three elements of screening program: (1) screening—asymptomatic individuals were offered serological testing, (2) diagnosis—people who were positive were offered liver biopsy and (3) treatment—treatment element followed Markov's chain process. Patients in treatment were assumed to be 32 years of age, proportion of males to females was equal, the model ran for 50 years and simulated the natural history of disease. Death rates were estimated from British life tables. Literature search and survey of screening practices were conducted to estimate the parameters of the model and costs. One-way and multi-way sensitivity	The model was sensitive to the prevalence of HCV in a population likely to present to genitourinary medicine clinics; costs per QALY increased once prevalence decreased below 3%. Acceptance of screening determined utility cost: with 100% acceptance, utility cost remained above £60,000 per QALY. There was little difference in utility cost if acceptance of treatment was over 70%, or was 100%. Universal screening would yield benefits of £85,000 per QALY.	Study suggested that universal screening in these clinics was probably not cost-effective, and the most cost-effective approach to screening HCV in genitourinary medicine clinics (equivalent to our STI clinics) would be risk-based; restrict screening to those with a history of IV drug use	+; model considered a single age cohort—did not consider how the model would change if the average age was younger or older than 32; perception of disease, willingness to acceptance screening and treatment may differ among older cohorts; parameter values identified through literature search, and opinions shared by survey and expert opinion may not be truly representative of population. However, sensitivity analysis performed to validate parameters considered in model, which gives strength to results and sensitivity of result to the different conditions hypothesized

First Author	Journal Reference	Country/Study Population	Methods	Outcomes	Additional Comments	Strength of Evidence
			analyses were performed to validate results			
Josset V, et al[198]	*Gastroenterology Clinical Biology* 2004;28(4):351-7	Developed (France); 127 voluntary physicians used a questionnaire to search for risk factors in 10,041 patients aged 18 to 70 years	Free HCV screening test recommended to patients who had at least 1 risk factor for HCV and whose HCV serology was unknown. A reference screening strategy was defined in compliance with official recommendations; 5 other screening strategies were defined from the data collected during the survey; for all 6 strategies, number of patients and number of positive serology previously unknown were noted; physician's fees and test costs were considered. Three funding modalities were hypothesized to estimate to cost of screening practices. Cost-effectiveness analysis performed	Of the 10,041 patients, 54% presented with at least 1 risk factor; of the 924 higher-risk patients HCV was known for 15.5%, screening test performed for 3,550 patients with at least 1 risk factor detected 49 positive patients (1.4%). The prevalence of HCV infection was 2.6%. Seroprevalence not related to age or sex. Cost lowest for reference screening strategy and detected 19 of the 49 positive serologies. Two of the extended strategies detected additional positive patients (15, 8). The other 3 detected 5 more positive patients than the reference strategy	The cost-effectiveness ratio was higher than the mean cost of the reference strategy. Extending HCV screening beyond people with a history of drug abuse or transfusion was not effective	+; tests were not recommended to patients aged 70 and over. Voluntary physicians were not representative of general practitioner population, since a greater proportion of patients were illicit drug users
Shah B, et al[84]	*Clinics in Liver Disease* 2006;10(4):717-34	Developed (United States and Europe); global burden of HCV included	Reviewed global burden of HCV disease and future projections for several European countries + U.S.; reviewed cost-effectiveness of HCV treatment; reviewed early studies of cost-effectiveness of screening and studies of prevention of HIV which may be relevant to HCV	Global burden substantial: 1 of top 10 causes of death from infectious diseases, costs projected to increase over time in all countries reviewed. Review suggested therapy with pegylated interferon and ribavirin was cost-effective, but treatment coverage was low. Early screening studies in U.S. reviewed; 1 study found screening average-risk 35-year-olds cost-effective only if half of	This was a narrative rather than a systematic review, but provided a strong review of global burden data	+; not a systematic review; may have been missing some relevant studies; publication date meant that many more recent cost-effectiveness studies were not included and there was no information about directly acting antivirals included.

First Author	Journal Reference	Country/Study Population	Methods	Outcomes	Additional Comments	Strength of Evidence
				infected were treated, but data suggested treatment rates were much lower. Review of conditions for prevention programs to be cost-effective; no studies directly related to HCV, although some evidence for cost-effectiveness of HIV behavioural interventions, which could be analogous		Provided a clear discussion of cost-effectiveness study issues and methods with respect to HCV
Tramarin A, et al[199]	*Current Pharmaceutical Design* 2008;14(7):1655–60	Developed (Italy); a mathematical model was applied to estimate the possible reduction of socioeconomic burden of HCV by early treatment of patients with recently acquired hepatitis C. Cost and consequences of the current approach based on treatment of chronic hepatitis C were compared to a hypothetical screening program to identify and treat asymptomatic seroconverted individuals at risk for progressed HCV disease. Population for analysis was the Veneto region of Italy	Developed a Markov model to simulate the disease progression in 2 cohorts, chronic hepatitis C or recently acquired infection to estimate life expectancy, QALY and lifetime costs associated with the 2 treatment strategies. The recently acquired hepatitis group consisted of 2 subcohorts (1) injection drug users living in the Veneto Region in 2007 and (2) people at risk for nosocomial HCV—patients who had minor or major surgery in 2007. The incidence of HCV in the population was considered, as well as rates of drug abuse and the annual probability of surgery in the general population. Clinical costs were derived from the Italian National Tariff system. Although screening schedules for both groups had a different frequency, (every 6 months for the IDU	All injection drug users would contract HCV infection during the time period considered (45 years). Of the 9,460 subjects, 862 would have symptomatic hepatitis and be eligible for treatment, even in the absence of screening. Additional values determined for the predicted number that would spontaneously clear HCV or develop end-stage liver disease. Estimates were made for individuals with surgery. The impact of screening in individuals who had surgery was much lower	Early treatment of IDU led to reduction of people with chronic hepatitis C. The cost of screening individuals who have had surgery was high, with a calculated cost-effectiveness ratio of €500,000 per QALY gained. Screening the non-injection drug use population was not cost-effective practice	+; this study assessed the possible reduction in socioeconomic burden of HCV infection by screening and early treatment of 2 populations exposed to risk by drug-use practices and in a general population of people who had surgery. The study of HCV in a specific group at (unknowingly) increased risk was somewhat relevant to the literature review. Also, the conclusion that the risk of disease in the population who have had surgery but no other risk factors (assumed) was too low to make a screening program cost-effective was equally interesting,

First Author	Journal Reference	Country/Study Population	Methods	Outcomes	Additional Comments	Strength of Evidence
			group and at 0 and 6 months for the subjects with surgery), the model assumed absolute compliance to the screening campaign			but the article did not adequately address issues of birth cohorts to be further considered
Nakamura J, et al[87]	*Tohoku Journal of Experimental Medicine* 2008;215(1):33-42	Developed (Japan); to evaluate the cost-effectiveness of a systematic strategy for the screening for HCV in the higher-risk and general populations. Participants from Niigata Prefecture, Japan, from 2003–2006	Screening costs based on medical fees in Japan. (Costs quoted in dollars; not stated if USD). Markov model based on previous cost-effectiveness analysis and combination therapy for HCV infection. Assumptions were made about treatment of all patients, prevalence of viral genotypes present in the population. Overall cost and life expectancies were calculated using a 30-year follow-up period. Comparisons were made in the general population and higher-risk group. Stratified analysis by age was performed, and death rate was estimated by the Abridged Life Table for Japan in 2004	99,001 people in the general population were screened, and 42,538 in the higher-risk group were screened; 0.36% (358) patients were positive in the general population and 0.81% (345) patients were positive in the higher-risk population. In both groups, the infection rate was lower in the 40–49 and 50–59 age group. Screening in the general population resulted in a greater overall cost in comparison to a no-screening strategy. However, since a screening strategy in both populations was below $50,000/ life expectancy year gained, a national screening strategy was considered cost-effective compared to a no-screening strategy.	The younger age group would benefit more from a national screening program	+; the cost conversion should be clarified to determine if the true cost of test and treatment in Japan can be equated to the true cost of screening and treatment in the U.S. or Canada. Acceptable threshold for incremental cost-effectiveness ratio appeared comparable to the usual threshold in U.S. and Canada. Prevalence based on actual data; assumed all identified through screening and did not address whether any of population previously screened/ diagnosed; assumed all cases identified chronic and all received treatment. Life expectancy in Japan may be higher than Canada and therefore life expectancy gains greater, which would increase cost-effectiveness

First Author	Journal Reference	Country/Study Population	Methods	Outcomes	Additional Comments	Strength of Evidence
Sroczynski EE, et al[200]	*European Journal of Public Health* 2009;19(3):245-53	Developed (United Kingdom, United States, France); systematic review including health technology assessment reports, systematic reviews, long-term clinical trials, health economic and decision-analytic modelling studies	7 studies were included: 3 from the U.K., 2 from France, 2 from the U.S. Long-term effectiveness based on decision-analytic modelling studies that included analysis of long-term effectiveness of screening for HCV and early treatment in terms of undiscounted life years and/or QALYs gained compared to no screening and standard care. Only 3 studies evaluated screening plus treatment with peginterferon plus ribavirin, versus older treatments; some studies compared to no treatment of unscreened, rather than to spontaneous case finding	Incremental cost-effectiveness ratios for screening had a huge range (€18,300–1,151,000/QALY) HCV screening in high-prevalence populations such as current or former injection drug users was considered cost-effective. General HCV screening in average-risk adults was unlikely to be effective and cost-effective	Authors noted that ethical considerations such as fairness and equity must be considered in decisions about screening programs because of the substantial number of prevalent iatrogenic HCV cases. Authors also pointed out difficulty in transferring results from 1 country to another because of differing epidemiology, health care systems, disease management practice patterns and treatment costs, as well as the lack of a standard threshold for cost-effectiveness	+; studies included were older, very heterogeneous, many basing models on older treatments no longer standard. Conclusions about the cost-effectiveness of screening higher-risk/higher-prevalence populations were likely to hold for Canada also, but conclusions about general population screening may or may not apply
Coffin PO, et al[85]	*Clinical Infectious Diseases* 2012;54(9):1259–71	Developed (United States); comparison of 1-time screening of U.S. population aged 20–69 to current guidelines with screening of higher-risk population only	Estimated population-level impact and cost-effectiveness using a decision-analytic model for the screening intervention and a Markov model for annual transitions to estimate natural history of HCV; sub-analyses considered newer therapy	Incremental costs per QALY were $7,900 for general population screening and $4,200 for screening by birth year 1945–1965 compared to current guidelines. Screening by birth years 1945–1965 dominated general population screening if cost, clinician uptake and median age of	Estimate 1% of liver-related deaths averted per 15% of population screened; significantly reducing HCV-related morbidity and mortality would require improved	Internal validity: ++ External validity for Canadian context: + Considered only direct medical costs; these could vary substantially from those in Canada; assumed screening

First Author	Journal Reference	Country/Study Population	Methods	Outcomes	Additional Comments	Strength of Evidence
			with protease inhibitors, and screening the birth cohort 1945–1965 rather than whole population 20–69. Used published literature to obtain estimates; lifetime, societal perspective for cost-effectiveness	diagnoses were considered equivalent; however, general population screening was still cost-effective versus current guidelines. Sensitivity analyses still supported conclusions even when assumptions relatively unfavourable to general population screening were used; general population screening considered cost-effective as long as prevalence >0.53%	rates of referral, treatment and cure along with the changes in screening considered	and treatment in the initial year, rather than over several years as is more likely; did not consider costs of scaling up clinical services to manage chronic HCV cases
Helsper CW, et al[88]	*Epidemiology and Infections* 2012;140(1):58–69	Developed (Netherlands); general population; general population and support program for primary care; drug users	Data from pilot campaigns intended to improve HCV awareness and case finding was used to build a mathematical model to estimate incremental cost-effectiveness ratio of 3 different campaign strategies: (1) campaign aimed at people at increased risk within the general public without support for primary care, (2) campaign aimed at general public with support for primary care and (3) campaign aimed at drug users	Prevalence in the general population in the Netherlands estimated 0.1–0.4%; estimated only 25% of chronic HCV carriers have been diagnosed; estimated prevalence in injection drug users 47–79%. Pilot study of general population campaign without primary care support did not lead to any new HCV diagnoses, so this strategy determined not cost-effective. The same campaign but with primary care supports (courses + 2 facilitators who visited general practitioners by appointment to provide info about HCV, and the campaign was considered cost-effective (QALY €17,000 per case identified). The drug user campaign trained addiction care professionals in HCV counselling that was actively and systematically offered to injection drug users, as well as doing information	Key issues affecting cost-effectiveness of the general public and primary care support campaign were number of cases found and referral rate. Key issue for drug users campaign was age at testing, but influence of 10 different parameters was considered, and this campaign was still cost-effective, even though QALYs were reduced by the assumption of a 15-year shorter life expectancy for drug users. Concluded that focusing on regions with higher prevalence of	Internal validity: ++ External validity for Canada: + Results were particularly strong with respect to the importance of active screening for drug users, and this component was likely to be applicable to Canada; it was more difficult to determine the comparability of primary care in the Netherlands and how results of the general public campaign + primary care support would apply here. The results strongly suggested that campaigns to try to increase testing of higher-risk people within the general

First Author	Journal Reference	Country/Study Population	Methods	Outcomes	Additional Comments	Strength of Evidence
				meetings for injection drug users about HCV. This was more cost-effective than the general population and support campaign, and would be cost-effective with any reasonable assumptions in sensitivity analysis (QALY – €6,700 per case identified)	higher-risk people might improve outcomes. Recommended consideration of integrating screening for HBV and HIV as well, since same groups at higher risk	public in the absence of supports to improve primary care response are likely to be ineffective
McGarry LJ, et al[86]	*Hepatology* 2012;55(5):1344-55	Developed (United States); developed a Markov model of the natural history of HCV to assess the potential costs and benefits of a birth-cohort screening program by considering screening, diagnosis, treatment and outcomes of HCV in the U.S. population. Model population for the primary analysis consisted of individuals born 1946–1970 eligible for screening. Population born before 1946 or after 1970 assumed to be screened based on risk-based screening protocols	Only direct medical care costs was considered for the study. Several estimations were made based on results from published studies. Disease progression and mortality rates from advanced liver disease by sex and age at infection were derived from a published model that synthesized data from primary sources. Mortality rates were estimated from U.S. population averages. Administrative claims analysis was used to estimate the population proportion screened, and the probability of infection among screened individuals under current risk-based screening practice. Treatment eligibility was estimated from studies, and treatment efficacy from clinical trials. Utility values for each health state were derived from published studies and	Outcomes evaluated were cases of advanced liver disease avoided and HCV-related deaths averted. Current risk-based screening for all 40- to 64-year-olds in 2010 was the least costly strategy. Targeted birth cohort screening for all 40- to 64-year-olds yielded the most benefits in terms of QALYs. Targeted screening of the older subgroups 45–64 and 50–59 were more costly and less effective and were removed from consideration. A 5-year program of birth cohort screening led to fewer cases of compensated cirrhosis and advanced liver disease. Mortality associated with HCV was reduced. The cost of cohort screening was $80.4 billion versus $53.7 billion for risk-based screening, although cohort screening provides additional quality-adjusted survival	Study estimated that a screening program targeting birth cohort born from 1947–1970 was likely to be cost-effective at a U.S. and European willingness-to-pay threshold. The birth cohort screening program provided benefits by identifying HCV-infected people who would not otherwise have been screened. Other studies that found cohort screening not cost-effective did not examine specific age groups at elevated but moderate risk of HCV	+; several estimates and assumptions were made based on results of other studies. Since data were combined from a variety of sources, validity could not be verified. Also cost estimates originated from multiple data sources and may not have reflected the true cost of diagnosis and management. Use of expert opinion for utility values may not have adequately reflected opinion of the population. Higher population prevalence of HCV and higher estimated proportion of infections undetected versus Canada, so results could not be directly applied to Canadian setting

First Author	Journal Reference	Country/Study Population	Methods	Outcomes	Additional Comments	Strength of Evidence
			applied to age-specific national norms. All costs were expressed in 2010 U.S. dollars or inflated to 2010 U.S. dollars using the U.S. Bureau of Labor Statistics consumer price index for medical care services. Sensitivity analysis was based on estimates from the literature and expert opinion.			
Rein DB, et al[81]	*Annals of Internal Medicine,* 2012;156(4):263-70	Developed (United States); adults born 1945–1965	Cost-effectiveness simulation for 1-time HCV antibody test screening of all adults having 1 or more visits to a primary care provider annually; took a lifetime, societal health care perspective	In the U.S., HCV is most prevalent in adults born from 1945–1965, and about 50–75% of infected adults are unaware of their infection. In the base case analysis, birth cohort screening identified 808,580 more cases of chronic HCV than the status quo, at a cost of $2,874 per case; assuming treatment with pegylated interferon and ribavirin, screening would increase QALYs by 348,800 at a cost of $5.5 billion, or $15,700 per QALY gained. If screening was followed by direct-acting antiviral plus pegylated interferon and ribavirin treatment, screening would increase QALYs by 532,200 at a cost of $19 billion, or $35,700 per QALY saved. Concluded that birth-cohort screening for HCV in primary care settings was cost-effective	Sensitivity analysis showed incremental cost-effectiveness ratio most sensitive to sustained viral response to antiviral therapy, cost of therapy, discount rate used, and QALY losses assigned to disease states. Study was limited by lack of empirical data on screening and on direct-acting antiviral treatment in ordinary clinical settings	Internal validity: ++ External validity for Canada: + Limitations with respect to empirical data noted would not negate the incremental cost-effectiveness ratio reported with screening and current treatment, which was quite favourable. Main limitation was the lack of information on the feasibility/uptake of such an approach to screening: will providers and patients do this, and will referral and treatment uptake follow? Estimated prevalence of undiagnosed adults in Canada was substantially lower

First Author	Journal Reference	Country/Study Population	Methods	Outcomes	Additional Comments	Strength of Evidence
						than the estimates given here, and treatment costs may also differ, so it would be desirable to have this study replicated using Canadian data

Appendix J: Form for Notification of Canadian Blood Services About Newly Reported Infections

Canadian Blood Services
Société canadienne du sang

EXTERNAL TRANSMISSIBLE DISEASE NOTIFICATION TO CANADIAN BLOOD SERVICES
CONFIDENTIAL

CLIENT INFORMATION		
Surname:	First Name:	Middle Name:
All Previous Names:		
Gender: ☐ Male ☐ Female	Date Of Birth: (yyyy-mm-dd):	Telephone:
Mailing Address:		
City:	Province:	Postal Code:

TRANSMISSIBLE DISEASE MARKER	
☐ HCV ☐ HIV ☐ HBV * ☐ HTLV ☐ WNV ☐ OTHER: * For HBV, Please Indicate Which Marker Was Tested: _____	
Copy Of Positive Test Report: ☐ Yes ☐ No (If available, please attach copy)	Test Date (yyyy-mm-dd):
Is Client Aware Of His/Her Diagnosis? ☐ Yes ☐ No	
Has Client Been Advised That This Information Will Be Reported To Canadian Blood Services? ☐ Yes ☐ No	

HISTORY OF BLOOD DONATIONS: ☐ YES ☐ NO	
City/Province	Donation Date (yyyy-mm-dd)

HISTORY OF BLOOD TRANSFUSIONS: ☐ YES ☐ NO		
Hospital	City/Province	Transfusion Date (yyyy-mm-dd)

Does Public Health Require A Summary Of The CBS Investigation? ☐ Yes ☐ No		
Initiated By:	Date (yyyy-mm-dd):	Telephone:
Public Health Branch:	Mailing Address:	

Fax The Completed Form To The Lookback/Traceback Manager, Canadian Blood Services, **905-494-8120 or email it to LBTB@blood.ca**

F800021

Appendix K: Sources of Hepatitis C Treatment Fact Sheets

Ontario Ministry of Health and Long-Term Care

Hepatitis C for health care providers [cited 2012 Nov 29]:
http://www.health.gov.on.ca/english/providers/program/hepc/hepc_mn.html

Hepatitis C for the public [cited 2012 Nov 29]:
http://www.health.gov.on.ca/en/public/programs/hepatitis/hep_c.aspx

Toronto Western Hospital Liver Centre

Home page [cited 2012 Nov 29]: http://www.torontoliver.ca/main.html
Hepatitis C [cited 2012 Nov 29]: http://www.torontoliver.ca/content/hepatitisc.html

Canadian Liver Foundation

Home page [cited 2012 Nov 29]: http://www.liver.ca
Hepatitis C [cited 2012 Nov 29]: http://www.liver.ca/hepatitis/hepatitis-c.aspx

Canadian Haemophilia Society (for patients and families)

Hepatitis C Information Booklet [cited 2012 Nov 29]:
http://www.haemophilia.ca/en/hcv-hiv/hepatitis-c--an-information-booklet/

CATIE (patient-level information for front-line workers)

Information toolkit for front-line staff [cited 2012 Nov 29]: http://www.hepcinfo.ca/index_sp_e.html

Appendix L: Literature Review Tables for Behaviour Change Interventions in People Who Use Drugs

Behaviour Change Interventions in People Who Use Drugs

First Author	Journal Reference	Country/Study Population	Methods	Outcomes	Additional Comments	Strength of Evidence
Smedlund G, et al[201]	*Cochrane Database of Systematic Reviews* 2011;(5):CD008063	Cochrane review including 59 RCTs with total of 13,352 participants dependent or abusing substances	Comprehensive search up to November 30, 2010; main outcome extent of substance use, not able to assess other outcomes such as treatment retention or change motivation	Compared to no treatment controls motivational interviewing showed a significant reduction in substance use over short- and medium-term follow-up, which waned over the long term; motivational interviewing was not significantly different from other forms of treatment, except for significantly better results at medium-term follow-up compared to assessment and feedback	Much of the evidence assessed as being of low quality, so further stronger studies are needed	++; this was a very strong review showing that motivational interviewing was better than no treatment and may have been as effective as other forms of treatment for reducing substance use
Jensen CD, et al[121]	*Journal of Consulting and Clinical Psychology* 2011;79(4):433-40	Detailed search of electronic databases (PsycINFO, MEDLINE, ERIC) for interventions using motivational interviewing for substance using adolescents	21 independent studies analyzed; 5,471 total participants	Small but significant weighted mean effect size post-treatment (mean d=0.173, 95% CI 0.94–0.252); small but significant effect sizes as follow-up. Motivational interviewing interventions effective across a variety of substance-use behaviours, varying session lengths, different settings and with clinicians with different levels of education	—	++; effect sizes small, but still significant; length of follow-up variable; did not compare to other forms of intervention, but fit with other findings that motivational interviewing can be used in a variety of settings by clinicians with varying levels of education (i.e. did not necessarily need to be mental health professionals)
Sacks-Davis, et al[111]	*International Journal of Drug Policy* 2012;23(3):176-84	Studies of controlled behavioural interventions that attempted to change individual behaviour without explicitly	Used PRISMA methods; eliminated observational studies without control groups; searched MEDLINE, Embase,	Duration varied from 30 minutes to 12 hours; 4 counselling studies with HCV education and using motivational interviewing to	Some studies required HCV+ to be eligible, some HCV–, some both; no indication that	++; review methods strong small number of studies, each with own biases, did not examine effects of context; overall conclusion

First Author	Journal Reference	Country/Study Population	Methods	Outcomes	Additional Comments	Strength of Evidence
		attempting to change population norms (or address risk environments)	Cochrane trials registry, PsycINFO and Cochrane reviews to October 2010; 568 records screened, 151 studies fully evaluated by 2 investigators, 6 studies included	raise awareness of risk and encourage reduction; 2 peer-educator training studies—1 for HCV+ aimed at reducing onward transmission, 1 for HIV/HCV– teaching to mentor other people who inject drugs to reduce their risk behaviours; 3 studies reported HCV incidence rates—none showed statistically significant differences with controls; 1 peer-intervention training study (Latka et al) found significant reductions in injecting in the intervention group after 3 and 6 months; the other studies found non-significant differences; both peer-intervention training studies found significant reductions in participant injecting risk behaviours, while none of the 4 counselling interventions did, although 2 found significant decreases over time in both intervention and controls	outcome varied by HCV status; some studies were relatively small and may have been underpowered to find differences; most indicated positive changes in intervention group but not reaching significance	that individual behaviour intervention alone not likely to be sufficient; multifactorial intervention needed

Multisession Individual Counselling Interventions*

First Author	Journal Reference	Country/Study Population	Methods	Outcomes	Causal Pathway Linkages	Additional Comments
Robles R, et al[202]	*Journal of Substance Abuse Treatment* 2004;27(2):145-52	People who use injection drugs in Puerto Rico	6 weekly sessions, case management for 1.5 months, 2 HIV counselling and testing sessions	—	Reduced injection drug use, reduced needle-sharing	Involved case manager, outreach worker and nurse; delivered in drug-treatment centres and by community outreach as well as at study site
Sterk CE, et al[203]	*AIDS Education and Prevention* 2003;15(1):15-32	Heterosexual African American women drug users	4 sessions, total 2 to 2.5 hours; focused on woman- and culture-specific negotiation skills	—	Reduced exchange of sex for money or drugs, increased condom use	Delivered by counsellor and female health facilitator
Abou-Saleh M, et al[204]	*Harm Reduction Journal* 2008;5:25	U.K. drug-service attendees, HCV seronegative	Randomized trial of 4 session enhanced prevention counselling, incorporating motivational interviewing methods versus 10 minute standard educational session	No HCV measures included Post-intervention	Both groups improved from baseline; power inadequate to measure differences between 2 groups; pre- and post-test counselling may have reduced risk behaviours	Majority in enhanced prevention counselling attended only 1 session; authors concluded may not be better to offer more than brief (1 session) intervention in regular setting (without research personnel)
Zule WA, et al[205]	*American Journal of Public Health* 2009;99 Suppl 1:S180-6	851 out-of-treatment injection drug users in North Carolina	Randomly assigned to either 6 educational sessions or 6 motivational interviewing–type sessions	Main outcome was to reduce alcohol use; participants receiving MI were significantly less likely to drink alcohol post-intervention (OR 0.67; 95% CI 0.46–0.97; followed 1 year) versus educational intervention	No significant differences between interventions in use of new syringe at last injection or use of condom at last sex	All sessions 30 minutes to 1 hour; motivational interviewing sessions delivered by trained lay people from the community

**Some interventions with special populations or requiring very extensive interventions (more than 10 sessions) are not included here since they are considered well beyond the resources of most public health programs.*

Group or Individual and Group Counselling Interventions

First Author	Journal Reference	Country/Study Population	Methods	Outcomes	Causal Pathway Linkages	Additional Comments
Latkin C, et al[206]	*Health Psychology* 2003;22(4):332-9	Drug users in Baltimore, United States; predominantly African American	SHIELD study; 10 sessions, 15 hours	Reduced needle-sharing and IDU, and increased condom use	Emphasis on pro-social roles and social identity	Delivered by male and female peer facilitators and outreach workers

Appendix M: Literature Review Tables for Peer Interventions in People Infected with or at Risk for Chronic Hepatitis C

First Author	Journal Reference	City/Study Population Country	Methods	Outcomes	Additional Comments	Strength of Evidence
Grebely J, et al[127]	*International Journal of Drug Policy*, 2007;18(5):437-43	Vancouver, Canada; Current and former injection drug users who were HCV+ and attendedan inner-city multidisciplin-ary health clinic	Prospective observational efficacy trial; Subjects with detectable HCV RNA and interested in receiving treatment were referred to the group; attendance at the once-weekly group was recorded on the first day they attended and monitored subsequently; the end point was end of treatment response; Mann-Whitney tested used to assess differences in median attendance between groups of patients; Fisher exact test was used to assess differences in proportions	High uptake of HCV treatment among peer support group attendees; of 80 referred, 21 (26%) initiated or completed treatment for HCV, (18 enrolled in the study), and 23 (29%) were lost to follow-up; individuals who initiated/ completed treatment had 22.7 median group meetings, and the group lost to follow-up had 3.4 meetings; 51% of group attendees received or were about to receive therapy; 75% of these had to discontinue treatment early due to side effects	Injection drug users made up a large proportion of newly diagnosed HCV cases; injection drug users were engaged in care through the peer-support group ; Low subject number	+; provided qualitative information
Garfein RS, et al[207]	*AIDS* 2007;21(14):1923-32	Baltimore, Chicago, Los Angeles, New York, Seattle, United States HIV– and HCV– injection drug users (injected illicit drugs in the past 6 months) between 15 and 30 years of age (had to speak English)	Randomized, controlled trial; Target population was recruited and participated in small-group, 6-session, cognitive behaviour, skills-building intervention where they were taught peer-education skills and	A 29% decline in injection risk 6 months post-intervention compared to the control group; from baseline information, there was a 76% decrease in injection risk	Interventions such as peer-education training providing information, enhancing risk-reducing skills and motivating behaviour change can reduce injection risk behaviours	+

First Author	Journal Reference	City/Study Population Country	Methods	Outcomes	Additional Comments	Strength of Evidence
		with no plans to move within 12 months	compared to a control group; psychosocial and behavioural factors were measured at baseline and 3 and 6 months post-intervention, along with HIV/HCV testing; injection risk indicators included injection with a syringe used previously by another injection drug user, using a new sterile syringe to divide drugs with another injection drug users when drugs were split, sharing cookers, sharing cotton filters, sharing rinse water		Participants had to return for test results to learn of their eligibility and then return again for random selection—participants lost in the process; potential for biased results due to socially desirable responding, attrition; sample population potentially not representative	
Craine N, et al[208]	*Journal of Substance Use* 2006;11(3):217-27	Rural northwest Wales (small market town of 5,000 with areas of high deprivation) 13 current injection drug users (heroin use and integrated in the local IDU network) were trained to be peer educators	Structured Q&A used to get educational messages out; materials also distributed; evaluation of peer-education program was completed through measurement of self-reported risk among injection drug users in the geographic area targeted by the project (collected at baseline and after cycles of education); Primary purpose of the project	Risk data collection found a high level of injecting risk (80% of injection drug users questioned by peer educators reported using a dirty needle in 30 days prior to the interview); peer-education group met 25 times for formal sessions; study suggests peer education is a feasible approach to harm reduction; study found the symptoms of withdrawal from opiate use increase sharing of used needs; results indicated the match between	Risk reduction was feasible through peer education; it allowed messages to be passed into communities' injection drug culture Follow-up sample was not large enough to evaluate changes in behaviour; reliance on self-reported behaviours	+

First Author	Journal Reference	City/Study Population Country	Methods	Outcomes	Additional Comments	Strength of Evidence
			was education, but peer educators collected research data as well	frequency of injecting and number of clean needs used; difficult to determine the efficacy of the intervention and the acceptability of the interventions		
Norman J, et al[209]	*Harm Reduction Journal,* 2008;5:8	Melbourne, Australia Clients from the healthy liver clinic where peer workers engage clients were recruited for the study (9 participants)	Qualitative data collection via semistruc-tured interview ; Peer worker was taught to facilitate referrals and recruitment to the service, provide support to people considering and undergoing treatment and enhance patient adherence and support within the service	Client interviews identified the overall supportive aspects of the peer worker, not just medical support but psychological and social support; clients felt having access to the peer worker made the process of screening and treatment easier and felt it was an essential service to the program success; clients identified the benefit of having someone who is aware of what they have endured giving them no reason to hide information; the majority of clients identified the importance of sharing the lived experience as being desirable— not essential, but remained important	Peer-based integrated model of HCV care for injection drug users was acceptable by the population and feasible Small sample; peer worker was an author of the study (not involved in the analysis)	+
Rowe M, et al[210]	*Psychiatric Services* 2007;58(7):955-61	Urban public mental health centre in Connecticut, United States Adults who had criminal charges with the 2 years before enrolment	2x3 prospective longitudinal, randomized, controlled trial with 2 levels of intervention (group and peer support and standard services for controls); Participants completed interview at baseline, 6 months, and	The intervention group showed significantly reduced alcohol use compared to the control group; no significant changes in non-alcoholic drug use and criminal justice charges compared to the control group; alcohol use decreased in the intervention group, and increased in the	Peer- and community-oriented group support and learning may facilitate decreased alcohol use over time in individuals with a history of mental illness and	+

First Author	Journal Reference	City/Study Population Country	Methods	Outcomes	Additional Comments	Strength of Evidence
			12 months and responded to questionnaires; 41 participants were placed in the control group, whereas 73 were in the intervention group, including a peer mentor support	control group	criminal justice involvement Small sampling; researchers were not able to determine the importance of peer mentor, class and valued role components in producing findings; the focus group was not a full qualitative study	
Treloar C, et al[211]	*International Journal of Drug Policy* 2005;16(1):46-53	Urban Sydney, urban Brisbane, rural Northern Rivers area of New South Wales, Australia 16–25 years of age; reported an injecting history of 4 years or less and had injected illicit drugs within the last 6 months; qualitative interview participants were mostly from those who completed the quantitative interview with a small number recruited from snowball sampling out of Sydney	Quantitative survey of 336 injection drug users (less than 25 years of age) from 3 sites in Australia; 24 young injection drug users also participated in qualitative interviews; Quantitative study completed to report patterns of information exchange and qualitative interview further understanding of information access and change	The majority of those surveyed passed on information to their peers; information gathered about HCV was from pamphlets, and close to 50% of information was provided by friends; individuals with hepatitis C were more likely to pass on information to other injection drug users; many varied topics were discussed between peers, and sometimes inaccurate information was exchanged; injection practices were not related to knowledge or information access, but individuals with riskier practices were more likely to pass information onto their peers; information regarding safe injection practices was not passed along generally until after initiation of IDU	Findings suggested the peer group was a natural source of information and therefore the need for accurate information was evident Findings were not generaliz-able because of the convenience sampling used	—

First Author	Journal Reference	City/Study Population Country	Methods	Outcomes	Additional Comments	Strength of Evidence
Dutcher MV, et al[212]	*AIDS Patient Care and STDS* 2011;25(7):403-11	Diverse locations in the United States 23 HIV+ peers	Semistruc-tured interviews followed by qualitative analysis using QSR NVivo; Purposeful selection techniques used to select participants based on race/ethnicity; sex (included both) and geographic location (rural and urban) and reflecting peers who were new to providing peer services and those who were more experiences; qualitative analysis by 2 independent researchers using coding, and thematic content analysis	Peers reported that peer characteristics (HIV status, common experiences and self-care) enabled them to engage clients; peers required flexibility to address clients' needs; activities spanned 4 types of social support: informational, emotional, instrumental and affiliational	— Peers selected were a small purposeful sample of peers participating in the PETS initiative—their experiences may not have been reflective of all peers participating in the initiative; interviews were conducted by different interviewers, and although a common guide was used, there was variance in extensive-ness of follow-up questions	—
Dyer J, et al[213]	*Health Promotion Journal of Australia* 2009;20(1):37-41	All states and territories of Australia; each region represented by 2 to 5 interviewees23 health professionals (18 women, 5 men) who were involved in the management of provision of hepatitis C education/ support to inmates	Semistruc-tured telephone interviews; Participants chosen using snowballing method and facilitated by state and territory hepatitis councils; interviewees employed as nurses, educators psychologists, policy makers or service coordinators; semistructured interviews conducted by telephone ≥20 questions derived from unpublished guidelines	Participant reports varied greatly between prisons and across states; successful services and barriers to improvement included limited time, insufficient funding and frequent personnel changes; prisons had individual needs, and external educators were not always aware of procedures and methods of harm reduction available in particular facilities	Small sample size; not randomized sampling	+; provided qualitative information

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			developed by the Ministerial Advisory Committee on AIDS, Sexual Health and Hepatitis and covered a variety of questions; action research framework used			
Bailey SL, et al[214]	*Drug and Alcohol Dependence* 2007;91 Suppl 1:S18-29	Baltimore, Chicago, Los Angeles, New York, Seattle, United States Injection drug users between the ages of 15 and 30	Surveys, multivariate modelling; Participants recruited using street outreach and respondent-driven referrals; surveys of drug use, sexual behaviours and correlates were administered via audio-computer assisted self-interviews of those enrolled in an HIV/HCV prevention intervention trial at 3 months and 6 months post-baseline; the proportions of injections involving receptive syringe sharing (RSS) at baseline and at follow-up were used at outcomes in multivariate models that adjusted for intervention effects	At baseline, 54% of 3,128 participants reported RSS in the previous 3 months; RSS decreased to 21% at 6 months post-baseline for the combined trial arms	Perceived risk, peer influences, and type of injection partner were predictors of RSS; peer influences and perceived risk can be altered; Not generalizable; potential self-report bias	+; provided qualitative information
Repper J, et al[215]	*Journal of Mental Health* 2011;20(4):392-411	United Kingdom	Literature review; An inclusive search of published and grey literature was undertaken to identify	The literature demonstrated that PSWs can lead to a reduction in admissions among those with whom they work; additionally, associated	Lack of framework to critically analyze the included articles; wide scoping aims of the	+

First Author	Journal Reference	City/Study Population Country	Methods	Outcomes	Additional Comments	Strength of Evidence
			all studies of intentional peer support in mental health services; articles were summarized and findings analyzed using systematic critical analysis based on nature of the article	improvements were reported on numerous issues that could impact the lives of people with mental health problems	review meant that findings had to be more generalized	
Mahat G, et al[216]	*Journal of HIV/AIDS & Social Services* 2009;9(4):371-84	Newark, New Jersey, United States 106 ninth-graders	Quasi-experimental design; Intervention used a modified 10-session (45-minute sessions) program based on "Teens for AIDS Prevention" and implemented by peer educators; used convenience sampling; questionnaire was used to gather demographic information, HIV knowledge and self-efficacy before and after intervention (3 months post-intervention)	Result showed HIV knowledge improved significantly with peer-led program; results demonstrated self-efficacy improved significantly with peer-led program	Teens for AIDS Prevention peer-led education program was effective at increasing adolescent HIV knowledge and self-efficacy Some findings based on self-reported data; used convenience sampling; participants from only 1 school; sample size small; no long-term follow-up	—
Purcell DW, et al[217]	*Drug and Alcohol Dependence* 2007;91 Suppl 1:S73-80	5 U.S. cities 854 18- to 30-year-old injection drug users (must have injected within the past 12 months); weren't currently in treatment and didn't expect to move in 12 months; HIV– and HCV–	Randomized, controlled trial; Researchers developed a peer-education intervention to reduce the injection and sexual behaviour risk among young injection drug users using CBT and peer education; used RCT of	Peer education intervention participants were more likely to identify that the group intervention motivated them to make more positive life changes and think about their own injection behaviour; there was no difference in the intervention group regarding motivation to think	Future research should be conducted to determine effective interventions for sexual risk Self-reported data; no long-term follow-up; no	+

First Author	Journal Reference	City/Study Population Country	Methods	Outcomes	Additional Comments	Strength of Evidence
			6-session behaviour intervention versus control; after baseline assessment, participants were randomized into either 6-session behavioural intervention or 6-session comparison intervention; peer-education intervention was developed collaboratively in multiphase approach; at 3- and 6-month follow-ups, participants were asked to rate the intervention on 10 items that assessed effects	about their own sexual behaviour; peer-education intervention group participants were significantly more likely than controls to be motivated to think about their infection risk; no difference in thinking about sexual risk behaviour	indication of active behaviour change	
Purcell DW, et al[218]	*Journal of Acquired Immune Deficiency Syndromes* 2007;46 Suppl 2:S35-47	Baltimore, Miami, New York, San Francisco, United States 966 HIV+ injection drug users recruited from variety of community venues; 18+ years old, IDU in the past year at least, with at least 1 opposite-sex partner in last 3 months, self-identified as HIV+ (486 peer mentoring intervention; 480 control)	Randomized, controlled trial; Intervention to reduce sexual and injection transmission risk behaviours and increase utilization of medical care and adherence to HIV medications among this population; participants randomly assigned to a 10-session peer mentoring intervention or an 8-session control group (video discussion intervention); participants completed audio assisted self-interviews and viral	Sexual and injection risk behaviours decreased significantly from baseline over time in both groups; the differences in risk behaviour changes were not significant between the 2 groups; use of health care slightly decreased over time for both groups (not significant); adherence increased significantly in both groups over time at 6 and 12 months	Both interventions led to decreases in risk behaviours with no medical changes Sample not representa-tive of HIV+ injection drug users; use of incentives to increase attendance and report back may have affected ability to generalize results	+

First Author	Journal Reference	City/Study Population Country	Methods	Outcomes	Additional Comments	Strength of Evidence
			load and CD4 count at baseline 3-, 6- and 12-month follow-ups			
Boisvert RA, et al[219]	*Occupation-al Therapy International* 2008;15(4):205-20	Florida, United States 18 adults between 19 and 62 years of age participated (7 removed from the program, so 10 available for post-test at 9 months post-program)	Mixed methods, including semistruc-tured interviews, participant observation and pre-test/post-test to evaluate changes in the quality of life at baseline and at 9 months; The peer-supported community program was designed by an occupational therapist; therapist presented and residents had the opportunity to discuss and develop skills to become peer leaders and form their own peer support recovery community	Participants had a significant reduction in risk of relapse; quality of life rating improved for those in the program but was not significant	Suggestion that peer-supported community program focused on self-determination can have a significant positive impact on recovery from substance addictions and homelessness Small sample size; poor external validity of tool; no randomized control group used; potential selection bias	—
Deering KN, et al[220]	*AIDS Patient Care and STDS* 2009;23(8):603-9	Vancouver, British Columbia, Canada 20 HIV+ women enrolled	Self-reported data; assessment of pharmacy data and viral loads; Participants enrolled on a rolling basis referred by health care provider, family, friend or self; peer-driven interventions included weekly peer support meetings, health advocate buddy system, peer outreach service and on-site	Self-reported adherence high (92%); number of viral load tests ≤50 copies/mL increased by 40% during the peer-driven intervention; pharmacy adherence increase was greater among those with increased frequency of IDU and more unstable housing; findings similar for changes in viral load	Evidence suggested that peer-driven interventions may have had a positive impact on adherence outcomes No indication of long-term success; small study sample; experiment-tal design limited by lack of control group; reliance on	+

First Author	Journal Reference	City/Study Population Country	Methods	Outcomes	Additional Comments	Strength of Evidence
			nursing care; adherence determined via assessment of pharmacy data, self-reports, viral loads		self-reported data	

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