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This document is best viewed online. There are hyperlinks that appear as underlined words in print versions.



1.0 INTRODUCTION

In British Columbia (BC), all [cases](#) of hepatitis C that have not yet been entered into the electronic public health information system require [documentation](#), geographical [attribution](#) and consideration for follow-up care. This guideline aims to meet the needs of BC health care professionals who are following-up individuals with newly identified hepatitis C infection.

To meet the needs of the Regional Health Authorities (RHA's) and the communities they serve, this document presents information in a flexible way, to encourage client engagement with the health care system. Follow-up may occur directly by public health personnel with a client or indirectly through a primary care provider who is already engaged with the client.

1.1 Authority

Hepatitis C virus is a reportable condition under the [Public Health Act \(2008\)](#) and [Schedule A of the Health Act Communicable Disease Regulation](#).

1.2 Rationale for HCV Follow Up

Follow up of people with newly identified hepatitis C virus (HCV) infections can contribute to positive outcomes for both the individual and the community. This is a key moment in which counselling can be offered for alcohol and substance use, including harm reduction services, overdose prevention and naloxone training, and opioid substitution therapies, where appropriate. Clients can be engaged into care to provide information around treatment, transmission prevention, housing and education around diet, immunization updates and screening for sexually transmitted infections (STIs).

1.3 Goals

To provide public health personnel and primary care providers with information to:

- Prevent transmission of hepatitis C infection.
- Prevent newly identified HCV [cases](#) from acquiring coinfections, including Human Immunodeficiency Virus (HIV), Hepatitis B (HBV) and Hepatitis A (HAV).
- Provide education and counselling to individuals infected with HCV and their contacts.
- Reduce harms. This includes connecting individuals living with HCV infection with harm reduction prevention and support resources, where appropriate. Resources include distribution sites for harm reduction supplies, supervised injection facilities, detox and treatment facilities, opioid agonist therapies (e.g., Buprenorphine/naloxone therapy, methadone maintenance therapy (MMT)), and mental health and outreach programs.
- Educate new HCV [cases](#) about risks associated with HBV coinfection if engaging in activities more likely to result in exposure to HBV, such as intravenous drug use (IDU) and condomless sex with multiple partners.
- Immunize for hepatitis B to reduce morbidity rates of [cirrhosis](#) and hepatocellular carcinoma (HCC) associated with coinfection (1).
- Increase engagement of clients who have and who are at risk of HCV infection, into the cascade of care (see [Figure 6-1](#)).
- Increase access to treatment for clients with HCV infection.
- Prevent adverse sequelae in infants born to mothers who have HCV infection, by timely identification of [cases](#) of HCV vertical transmission.



2.0 DEFINITIONS

Alanine aminotransferase (ALT) - Enzyme produced by the liver. Increased levels indicate inflammation of the liver, but do not always correlate with the severity of the disease process.

Attribution – Refers to the geographic area (e.g. Regional Health Authority (RHA), outside of BC) for the purpose of surveillance reporting.

Case – Defined here for the purposes of surveillance. Clinical criteria are not required. Laboratory criteria:

- **Acute Case** (adults, adolescents & children > 18 months):
 - Anti-HCV positive **or** HCV RNA positive

AND

 - There is an anti-HCV negative test result on record in the prior 12 months
- **Chronic case:**
 - HCV RNA positive

AND

 - There is an anti-HCV negative test result on record more than 12 months ago **OR** there is no documentation available of a prior anti-HCV result
- **Case** - Children ≤ 18 months of age:
 - HCV RNA positive ≥ 4 to 6 weeks of age

OR

 - Anti-HCV positive at 18 months of age

Cases may be further staged depending on the type of electronic public health information system being used in the RHA. See [Table 5-1](#) for staging information specific to Panorama. Case definitions are also available on the [BCCDC website](#).

Contact - Includes any individual who has had a percutaneous or mucosal exposure to the blood or blood products of an individual living with HCV infection.

Direct Acting Anti-Virals (DAAs) - Oral drug formulations used for hepatitis C treatment, that target HCV at various stages in the HCV lifecycle (2). Current therapies combine different DAA classes to avoid resistance.

Documentation – Recording of results and follow-up care provided to those testing for HCV. Guidelines may vary by RHA and agency.

Genotype - There are now 8 genotypes and numerous subtypes of HCV currently identified, of which genotypes 1, 2 and 3 are the most common in North America and BC. With increasing availability of pangenotypic DAA's, the relevance of genotype to treatment selection is becoming less relevant.

HCV Antibody Test (anti-HCV) - HCV antibodies are produced when an individual is exposed to HCV and usually remain present for life. Anti-HCV becomes detectable 5-10 weeks after infection, and confirms that the individual has been infected at some time.

Iatrogenic – Unintentional and unfavourable response to a medical treatment or procedure caused by a healthcare provider.



Immunocompromised - Where the immune response is attenuated by the administration of immunosuppressive therapy, malnutrition or disease processes. Those who have HIV infection and CD4+ cell count < 50 cells/mm³, chronic kidney infection, or who have been on long-term immune suppressants may not be able to mount a normal antibody response to HCV. Those with agammaglobulinemia are unable to make their own antibodies.

Liver fibrosis - An accumulation of extracellular matrix proteins that are produced in excess, inefficiently broken down, or both. Healthy liver cells are replaced with fibrous tissue, leading to disruption of normal liver function. Main causes include chronic hepatitis B or C infection, excessive alcohol intake (>2-3 drinks/day) and non-alcoholic steatohepatitis (NASH), which is associated with obesity, diabetes or metabolic syndrome. Autoimmune hepatitis can also lead to chronic liver inflammation. Symptoms may not be present unless there is severe damage to liver function (3).

May be classified according to a histologic scoring system, such as METAVIR (6):

- F0 = no fibrosis
 - F1 = portal fibrosis without septa
 - F2 = portal fibrosis with few septa
 - F3 = numerous septa without cirrhosis
 - F4 = cirrhosis
- **Cirrhosis** - Progression of fibrosis to scarring and disruption of normally functioning structures in the liver. The presence of extensive 'bridging fibrosis' between portal-vascular structures on liver histology can confirm this diagnosis. It can be predicted by non-invasive investigations, such as Fibro scan[®]. Advanced cirrhosis is supported by marked coagulopathy, portal hypertension, ascites and liver failure (4).

The gold standard for determining the severity of liver damage is liver biopsy.

Non-invasive alternative tools to measure liver fibrosis:

- **Fibroscan[®] (Transient Elastography)** - Ultrasound method that correlates with liver stiffness, and can be used to detect advanced fibrosis and cirrhosis. Results can be influenced by hepatic inflammation, obesity (less reliable results in BMI ≥ 25-28 kg/m²), ascites, narrow intercostal spaces, and increased central venous pressure. These results can be correlated with the METAVIR scoring system(4).
- **Aspartate Aminotransferase-to-Platelet ratio index (APRI)** - An indirect method used to predict significant and severe fibrosis or cirrhosis. APRI score > 1.5 indicates significant fibrosis or cirrhosis, and APRI < 0.7 indicates no significant fibrosis (3).

$$\text{APRI} = \frac{\frac{\text{AST level}}{\text{AST (Upper Limit of Normal)}}}{\text{Platelet Count (10}^9\text{/L)}} \times 100$$

For an online calculator, see <http://www.hepatitisc.uw.edu/page/clinical-calculators/apri>



- **FIB-4** - An indirect method used to help with liver fibrosis staging. FIB-4 < 1.45 indicates no significant fibrosis, and FIB-4 > 3.25 is predictive of advanced fibrosis or cirrhosis (3).

$$\text{FIB-4} = \frac{\text{Age (years)} \times \text{AST (U/L)}}{\text{Platelet Count (10}^9\text{/L)} \times \sqrt{\text{ALT (U/L)}}}$$

For an online calculator, see <http://www.hepatitisc.uw.edu/page/clinical-calculators/fib-4>

Nucleic Acid Test (NAT, NAAT, PCR, HCV RNA) – Detects HCV RNA, confirming active infection. HCV RNA becomes detectable at 1-3 weeks post exposure. It does not determine the severity of liver damage.

Percutaneous Exposure - Contact through the skin with blood (e.g., sharing of needles used for IDU). Non-intact skin exposure when blood or body fluid comes in contact with a wound < 3 days old, or with skin having compromised integrity (e.g., dermatitis, abrasions or other lesions).

Perinatal Exposure - Infection of an infant at birth from a mother. The likelihood of HCV transmission to the infant depends on the viral load of the mother. Coinfection with HIV in the mother may increase the odds of transmission to the infant by approximately 3-fold (5).

Period of Communicability - All persons who are anti-HCV reactive are considered infectious unless there is documentation of a spontaneously resolved infection or virological cure by treatment.

Permucosal Exposure - Contact of the mucous membrane lining body cavities of eyes, nose, mouth, vagina, rectum or urethra with blood or body fluids.

Reactivation – Increase in HBV replication in an individual with HBsAg-positive chronic HBV infection or resolved HBV infection. HBeAg-negative chronic hepatitis can reactivate following HBeAg seroconversion. Can occur spontaneously or after initiation of immune suppressing therapy (e.g., rituximab, HIV-related immunosuppression), corticosteroid therapy, immune modulation therapy, solid organ transplant or organ transplant recipients (6).

Resolved Infection - HCV infections may resolve spontaneously (usually within 6 months of infection) or following a course of antiviral therapy, resulting in a sustained virological response (SVR) indicating that the patient has cleared the virus. Individuals with resolved infection typically have serum that is anti-HCV reactive, but have no detectable HCV RNA. Resolved infection is confirmed after one negative HCV RNA test. If exposure is suspected to have occurred within the past 6 months, repeat HCV RNA testing 6 months after the estimated time of infection.

Seroconversion - An immune response characterized by a change from the absence of HCV antibodies (anti-HCV non-reactive) to the presence of HCV antibodies (anti-HCV reactive) in the serum of an individual at any time.

Sustained virologic response (SVR) - No detectable HCV RNA in plasma 12 weeks (SVR12) after treatment completion. In the past, SVR was measured at 24 weeks after treatment completion (7).

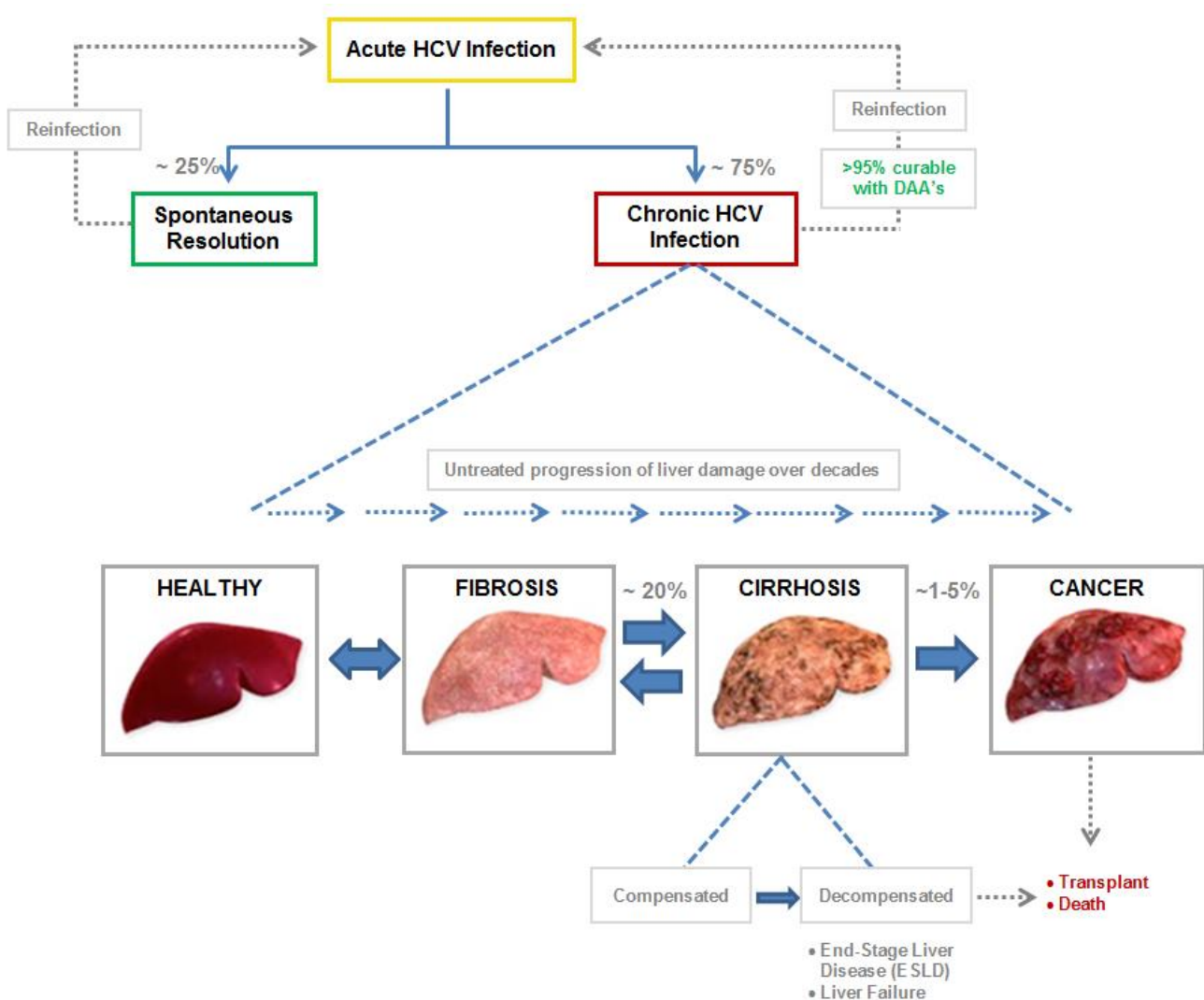
3.0 HEPATITIS C VIRUS

Hepatitis C is a virus that can cause chronic liver disease. HCV is a single-stranded, enveloped, linear RNA virus from the *Flaviviridae* family. HCV is a blood-borne virus that is highly transmissible via [percutaneous exposures](#) to infectious blood. [Per mucosal transmission](#) may occur if blood is present, but is not as efficient.

3.1 Clinical Description

Most people (75%) who have just become infected with HCV have no symptoms. The remaining 25% may experience fatigue, loss of appetite, muscle aches, fever, nausea, or vague abdominal pain beginning approximately 6-7 weeks after infection and resolving after a few weeks. Jaundice, pale stools, and dark-coloured urine occur in less than 10% of cases. Individuals with newly acquired HCV infection may have elevated serum ALT levels. In very rare instances, severe and rapidly progressing hepatocellular death and hepatic failure may develop (fulminant hepatitis).

Figure 3-1: Natural history of HCV infection (6, 8-11)





Approximately 75% of cases become chronically infected, while 25% will naturally clear the virus (spontaneous clearance or [resolved](#) infection) (12). A [BC Hepatitis Testers Cohort \(BC-HTC\)](#) study looking at reinfected individuals reported a spontaneous re-clearance rate of 34%, although reinfection with a heterologous genotype and a history of problematic alcohol use were associated with a reduced rate of spontaneous re-clearance (13). Among those with chronic infection, most remain asymptomatic for years, while some individuals will experience fatigue, depression, lethargy, digestive problems and/or other extrahepatic manifestations.

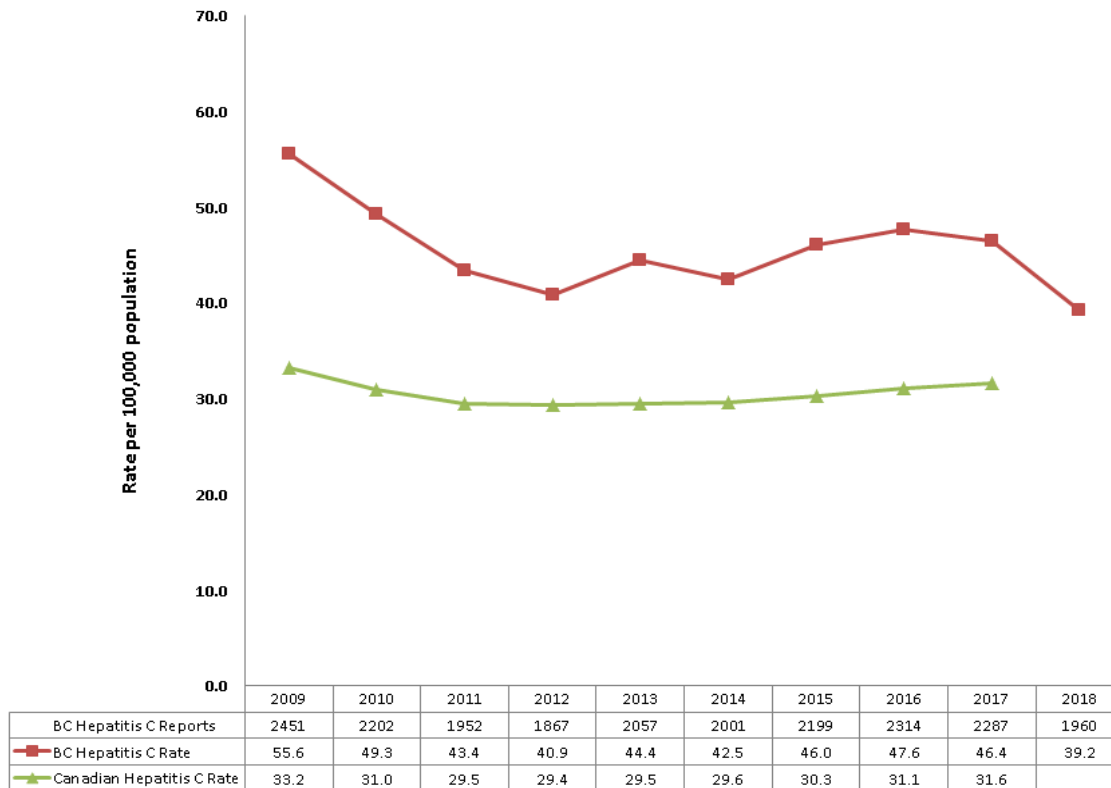
Over decades, 10%-20% will develop [cirrhosis](#). HCV is a leading cause of cirrhosis, end-stage liver disease (ESLD), and hepatocellular carcinoma (HCC). Along with HCC and alcoholic cirrhosis, HCV infection is a major cause of liver transplantation in Canada (14). Cirrhosis is a condition that results from damage or scarring of the liver. This may be reversible in early stages, if the underlying cause is treated. It is the end-stage of many different forms of liver disease and is known to cause a number of other health problems, including variceal bleeding, ascites and hepatic encephalopathy. Approximately 1%-5% of all chronically infected individuals will develop HCC within two decades.

Factors that accelerate liver disease include alcohol consumption (>2-3 drinks per day), older age at the time of infection (> 40 years old), male gender, obesity, and coinfection with HIV or HBV (15, 16). Individuals living with chronic HCV infection have an increased risk of fulminant hepatitis if they are acutely infected with HAV.

3.2 Epidemiology

Refer to the [BCCDC Reportable Diseases Data Dashboard](#) for the most up to date information.

Figure 3-2: Annual rates of newly diagnosed HCV cases in BC and Canada (2009-2018)



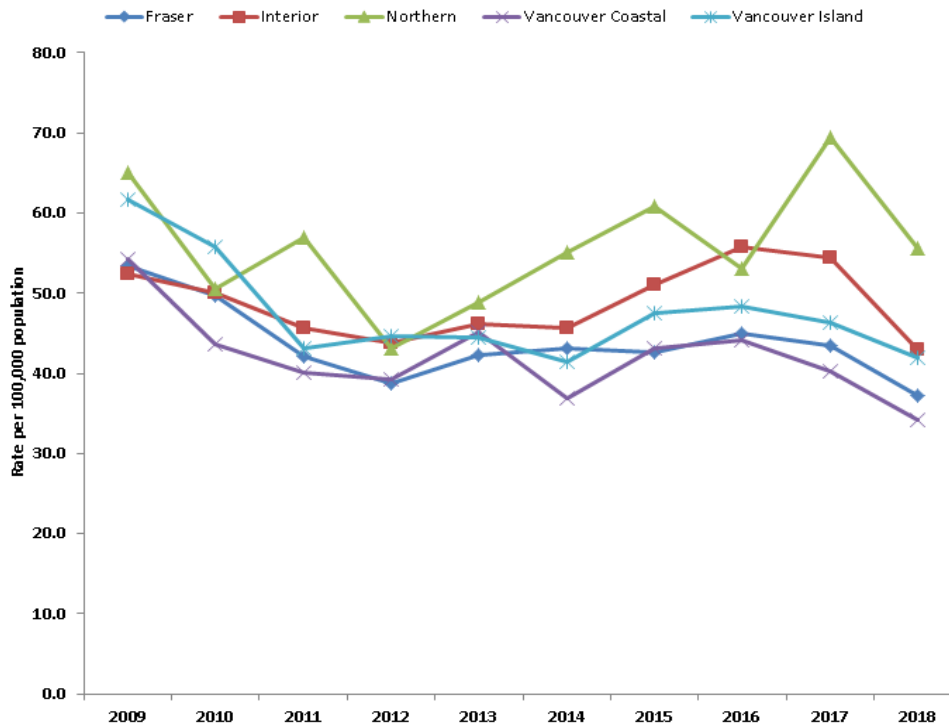


After the discovery of hepatitis A (1973) (17) and hepatitis B (1963) (18), it became clear that many cases of hepatitis that occurred following blood transfusions were due to neither hepatitis A or B. By the mid-1970's, the term "non-A, non-B hepatitis" was used to refer to the virus presumed responsible for these infections. In 1989 the virus was identified and renamed hepatitis C (19, 20). As a result of this discovery and subsequent work to detect infection, Canadian Blood Services has implemented [anti-HCV](#) screening of all blood donors since 1990 and [HCV NAT](#) testing since October 1999 (21).

Between 230,000-450,000 (0.66%-1.3%) Canadians were HCV-infected in 2011 (22-24). A retrospective modeling study estimated the prevalence of chronic hepatitis C in BC to be 1.04%, of which 33.4% remained undiagnosed, compared to 0.91% in Ontario, of which 36.0% remained undiagnosed in 2014 (25).

The annual rate of newly diagnosed HCV cases (acute and chronic) reported in BC has declined over the last decade but remains considerably above the Canadian rate. In 2017, the rate of newly diagnosed HCV cases was 46.5 per 100,000 population in BC, and 31.6 per 100,000 in Canada (see [Figure 3-2](#)) (15). In 2018, the overall rate of HCV infection in BC was 39.3 cases per 100,000 people. Northern Health Authority had the highest rate at 55.6 cases per 100,000 followed by Interior Health Authority at 43.0 cases per 100,000 (see [Figure 3-3](#)) (15). Vancouver Coastal Health Authority had the lowest rate at 34.2 cases per 100,000 (26).

Figure 3-3: Newly Diagnosed cases of Hepatitis C by Health Authority (2009-2018)



In BC, the prevalence of HCV infection is highest in people born between 1945-1964, whereas new infections occur more frequently in younger age cohorts, who are more likely to be affected by socioeconomic marginalization, mental health conditions and HIV and/or HBV infection (27). HCV is endemic among people who inject drugs (PWID), the core group involved in the forward transmission of the present epidemic, accounting for up to 85% of new infections (27-29). Amongst PWID in Canada, it has been estimated that 61.3% have HCV infection (22, 30). Other population groups disproportionately affected by HCV in Canada, include immigrants from HCV endemic countries, individuals who have ever been incarcerated and Indigenous Peoples (31, 32).

There is no vaccine to prevent HCV infection. Treatment based on interferon and ribavirin has been available in BC since 2000. While HCV cure is associated with reduced morbidity and mortality, less than 15% of those with chronic HCV infection had been treated by 2012 (17), in part due to poor tolerability and variable cure rates by genotype. In 2014, better-tolerated, short-course (8-12 weeks), interferon-free direct-acting antivirals (DAA) with cure rates over 95% became available, dramatically improving the opportunity to prevent progressive liver disease.

3.2.1 Coinfection with Hepatitis B Virus (HBV)

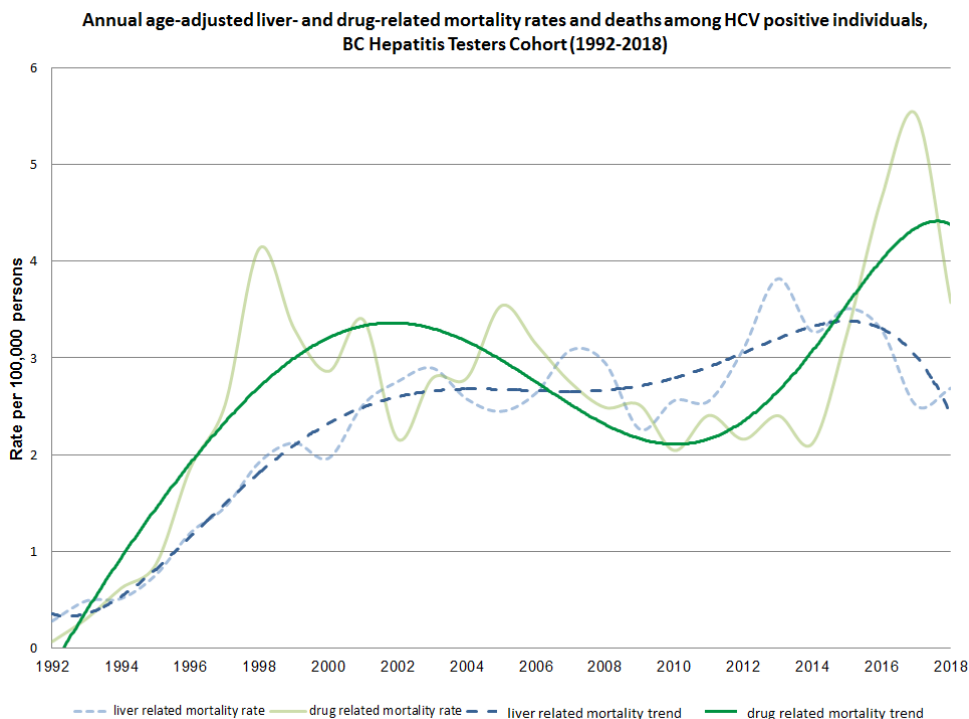
HCV appears to interfere with HBV replication, as HBsAg clearance is 2.5 times higher among people with HBV/HCV infection, compared with HBV mono-infection, and HBV DNA levels are often low or undetectable in people with HBV/HCV coinfection (33, 34). While 25% of individuals with HCV infection will spontaneously clear the HCV virus, 42% of those with HBV/HCV coinfection at baseline will clear the HCV infection (35, 36). Moderate to severe reactivation of HBV infection has been reported when taking DAAs (34, 37-39).

3.2.2 Coinfection with HIV

HIV can have a significant impact on HCV infection. HCV/HIV coinfecting individuals tend to have higher HCV viral loads, impacting HCV treatment response, and lower CD4+ counts. Coinfected individuals with a high degree of immunosuppression have a greater risk of liver fibrosis, and those with cirrhosis progress more quickly to HCC than HCV mono-infected individuals (19).

Estimates of the prevalence of HCV/HIV coinfection vary widely. HCV coinfection can occur in 2-4% of people living with HIV infection in the general population, and 50-90% of HIV-positive PWID (22, 40-42). Compared to HIV mono-infected individuals, HCV/HIV coinfecting groups are characterized by a higher prevalence of injection drug use, poor social conditions, and mental illness. One study in BC, found that of 3,219 HIV positive subjects, 53% were HCV/HIV coinfecting. For those diagnosed with HCV first, the median time to HIV infection was 3.5 years, highlighting the importance of ongoing engagement, support and education (43).

Figure 3-4: Liver and drug-related mortality rates amongst people with HCV infection (30)





3.2.3 Harm Reduction

Harm reduction refers to practices and programs that aim to reduce undue harms of substance use (44). Harm reduction plays a critical role in the prevention of HCV transmission, initiation and completion of HCV treatment, and prevention of adverse health outcomes for people that use substances. In April 2016, the increase in accidental illicit drug overdose deaths prompted the declaration of a public health emergency (45). From January 2016 to November 2020, 6,565 people in BC died due to an illicit drug overdose (46). This is largely attributed to the highly toxic synthetic opioid fentanyl in the illicit drug supply (47).

Of the 1,300,204 individuals in BC who tested for HCV as of December 2018, 27.5% tested positive (30). Among people testing HCV positive, mortality related to acquisition risk factors (e.g., IDU) increased from 1992 to 2000, declined slowly until 2013, and then rapidly increased between 2014 to 2018 (see [figure 3-4](#)). This recent increase coincides with the growing presence of fentanyl in the drug supply and recent surge in opioid overdose deaths (30).

Conversely, liver-related deaths (e.g., HCC, alcoholic and non-alcoholic related liver disease) have declined from 2014 to 2018, likely as a result of the increased availability of [direct acting antivirals](#) for HCV treatment (see [figure 3-4](#)). Liver-related mortality in individuals with HCV infection was more often seen in older people. Similarly, the Canadian Co-infection Cohort Study found that the majority of deaths seen in individuals with HCV/HIV coinfection were related to overdose, followed by factors related to ESLD and smoking (48).

Harm Reduction Programs

Harm reduction supply distribution programs are more effective than one-to-one exchange programs in preventing transmission of bloodborne pathogens (49). BCCDC Harm Reduction Services distributes safer sex and substance use supplies to nearly 400 sites across the province. The number of newly identified HCV and HIV infections among people who inject substances has decreased since 2002, coinciding with a concurrent increase in distribution of harm reduction supplies and scale up of other harm reduction services (50). Although ecological, this is further evidence that policies aimed at reducing harms from substance use have had a positive impact on population HCV and HIV rates.

As of December 2020, there were almost 1,800 sites across BC distributing naloxone kits and more than 75,888 kits had been used to reverse an opioid overdose (51). Observed Consumption Services (OCS) include Supervised Consumption Sites, where people can use substances while being observed by staff trained in overdose response, and Overdose Prevention Services (OPS), where people can connect with peer workers, community services and drug checking services. A Ministerial Order was issued in December 2016 for OPS to be opened where medically needed to prevent overdose deaths (52). At OPS, sterile drug use supplies are provided, reducing the need to share, and thus reducing risk of HCV and HIV transmission.

Many OCS also distribute safer smoking supplies, to prevent transition to IDU and sharing of supplies. It also discourages the use of other materials that could potentially cause burns or injuries that could increase the risk of HCV transmission (53). In a survey with clients of harm reduction sites in 2018, 27% of people who used pipes to smoke substances reported using a second-hand pipe when they couldn't find unused smoking equipment, while 20% injected instead (54).

Opioid agonist treatment (OAT) prescribers, available options and number of clients taking OAT have also significantly increased since 2016. This is partly driven by guidelines, and recommendations for first-line treatment of buprenorphine/naloxone for opioid use disorder (55, 56). OAT has been shown to mitigate transmission of HIV and HCV infection (57-60), reduce illicit opioid use (61-64), and mortality rates (65-69), and increase engagement with health care and social services (70-72).



3.3 Disproportionately affected populations, testing indications and transmission (6, 31, 32, 73-80)

The decision to screen or test for HCV infection depends on the likelihood of prior exposure. The risk for acquiring an HCV infection depends upon the nature of the activity and exposure, with parenteral and [percutaneous](#) routes being considered higher risk. [Per mucosal exposure](#) is lower risk, with greater concern if the integrity of the mucosa in question has been compromised.

Population groups experiencing disproportionately higher rates of HCV infection in BC include:

- People born between 1945 to 1965, likely due to past acquisition risks (e.g., IDU, contaminated blood products or iatrogenic exposures)
- Persons who have ever been incarcerated, where lack of access to harm reduction supplies contributes to needle sharing by PWID and unsterile tattooing practices in correctional settings
- Born or lived in regions where HCV is endemic¹. Select countries of origin of those diagnosed with HCV in BC:

Region	Countries of origin (81) <i>In descending order of prevalence in BC within each region</i>
Central, East or South Asia	China, Hong Kong, Taiwan, Vietnam, Pakistan, India
Eastern Europe	Russia, Romania, Ukraine, Cyprus
Sub-Saharan Africa	Somalia
North Africa or Middle East	Iran, Turkey, Lebanon, Egypt

- Indigenous peoples, where health inequities contribute to national rates that are 4.7 times higher than non-indigenous populations (29)

HCV testing can be considered in certain clinical scenarios:

- First trimester of pregnancy if risk factors (e.g., PWID), repeat in third trimester if ongoing risk
- HIV or HBV infection
- Sexual and household contacts to HCV infection
- Findings suggestive of chronic liver disease:
 - Abnormal liver biochemistry (e.g., persistently elevated transaminases)
 - Hepatomegaly, splenomegaly and jaundice (late findings)
 - Thrombocytopenia
- Findings suggestive of acute liver disease
- Diagnosis of HCC or other liver diseases
- Ever received hemodialysis
- Children born to a parent with HCV infection

Refer to [Table 3-1](#) for a summary of activities and associated level of transmission risk.

¹ For estimates of HCV prevalence, see [Mohd Hanafiah K, Groeger J, Flaxman AD, Wiersma ST. Global epidemiology of hepatitis C virus infection: new estimates of age-specific antibody to HCV seroprevalence. Hepatology \(Baltimore, Md\). 2013;57\(4\):1333-42.](#)

Table 3-1: Likelihood of transmission and activities associated with acquisition of HCV infection

Likelihood	Transmission	Activity	Comments
<p>High</p> <p>Low</p>	Parenteral	Injection drug use (IDU)	<ul style="list-style-type: none"> • Greatest risk in those who have ever shared drug preparation or injecting equipment • In Canada and BC, ~ 85% new infections are related to IDU (27-29)
		Potential iatrogenic exposures	<ul style="list-style-type: none"> • Receipt of healthcare in HCV is endemic areas where basic infection control practices were not followed and/or blood supply was not tested • In Canada, increased risk if receipt of blood transfusion, blood products or organs before 1992
		Tattooing, body piercing or acupuncture	In unregulated premises where unsterile equipment and/or improper technique is used(82)
	Per mucosal	Non-injection drug use	Risk when sharing drug use equipment, where the integrity of the mucosa is compromised or ulcerated (e.g. snorting can damage nasal mucosa, crack pipes can damage oral mucosa)
	Sexual	Condomless sex, multiple partners	<ul style="list-style-type: none"> • Where blood is exchanged, as in sex causing mucosal tearing • More frequently reported in gbMSM engaging in group sex with concurrent substance use (i.e., “party ‘n play” or “chemsex”) • Coinfection with HIV, HBV or other STI’s that can cause sores or lesions can increase the risk
	Vertical	Mother to baby	<ul style="list-style-type: none"> • 6% risk of transmission to infants born to HCV RNA positive mothers (73, 83-86) • Increased risk with higher RNA titres and in the presence of acute hepatitis symptoms • 2-fold increased risk if mother has HIV/HCV coinfection (83)
	Sexual	Condomless sex, with one long-term, partner	Very low risk where blood is exchanged, as in sex causing mucosal tearing
	Horizontal	Sharing personal hygiene items	<ul style="list-style-type: none"> • Household exposure • Examples include sharing of nail clippers, razors and toothbrushes that may have traces of blood on them
	Occupational	Accidental needle stick injury	The average incidence of anti-HCV seroconversion after percutaneous exposure from a source with a history of HCV infection, in an occupational health setting is 2%
		Breastfeeding	

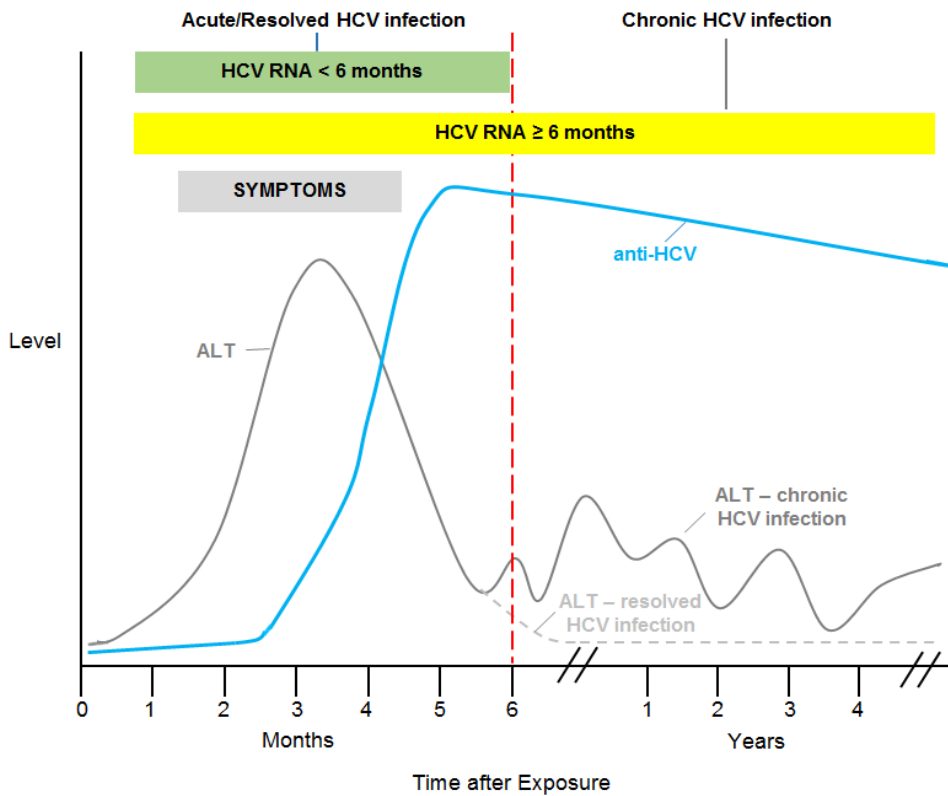
There is no evidence that HCV is spread by coughing, sneezing, hugging, kissing, using the same dishes or cutlery, swimming in a chlorinated pool when a case has cuts or scrapes or when menstruating, being bitten or stung by an insect which then bites or stings someone else, or skin contact by others with the body fluids of a case that are not exposed to blood (such as saliva, urine, feces or vomit).

4.0 LABORATORY INFORMATION

4.1 HCV Testing Window Periods

During the acute phase of HCV infection, ALT levels are markedly elevated, while they can fluctuate widely in chronic cases. [Antibodies to HCV](#) are usually detectable 5 to 10 weeks after infection and generally persist for life. The development of antibodies can be delayed or absent in [immunocompromised](#) individuals (e.g. HIV with CD4+<50 cells/mm³, chronic kidney disease, long-term immunosuppressant use, agammaglobulinemia). [HCV RNA](#) becomes detectable by NAT within 1-3 weeks of infection.

Figure 4-1: Acute HCV Infection with Recovery



4.2 HCV Testing

The BCCDC Public Health Laboratory (PHL) performs the majority (95%) of [HCV antibody](#), and all [HCV RNA](#) and [genotype](#) testing in BC. A sensitive enzyme immunoassay (EIA) screen is used to detect antibodies to HCV. All samples testing reactive by this initial screen are retested using an EIA test from an alternative manufacturer. A quantitative test is used to detect HCV RNA, which has a lower limit of detection of approximately 12 IU/mL.

All persons with an [anti-HCV](#) reactive result are considered infectious unless there is documented evidence of a [resolved](#) infection. While approximately 25% of HCV infected individuals are able to resolve their infection (usually within 6 months of infection) without treatment, most HCV infections become chronic. To distinguish active from resolved infection, HCV RNA testing should be done after an initial anti-HCV reactive result.

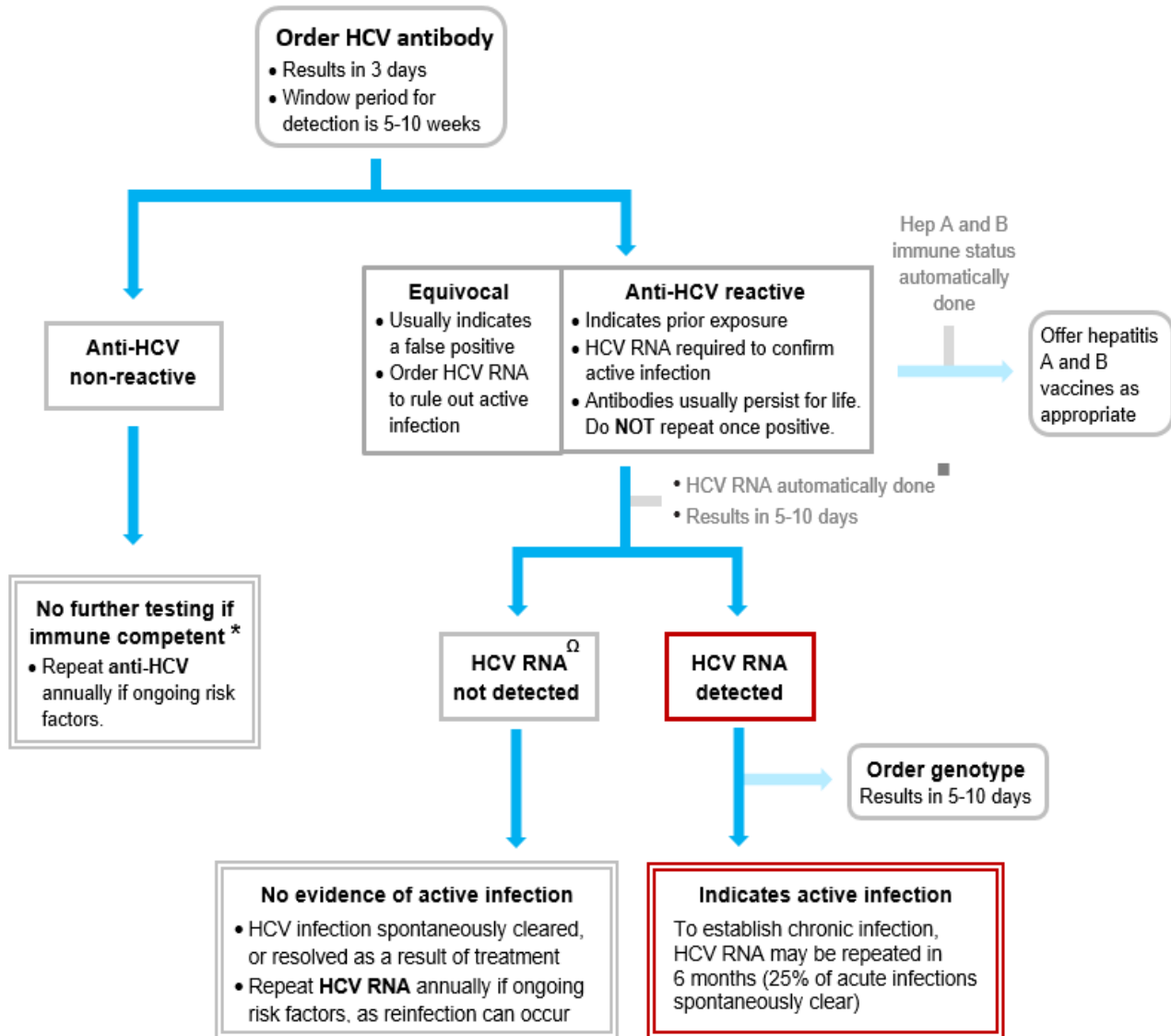
For requisitions and information about testing performed at the BCCDC PHL, refer to the [BCCDC website](#). For information on sample collection and processing instructions, refer to the [PHSA eLab Handbook](#).



Table 4-1: HCV tests.

HCV test	Description and Notes
HCV antibody test (Anti-HCV)	<ul style="list-style-type: none">• Window period: 5-10 weeks• Recommended first screening test for HCV infection• Does not need to be repeated once positive, as antibodies usually persist for life• Response may be blunted in immunocompromised person (e.g., HIV where CD4+ < 50). Even in a seronegative person, HCV infection could be present.• Does not distinguish between past, current and resolved infection• Antibodies are not protective. If an initial HCV infection is cleared spontaneously or due to treatment. A person can get infected with HCV again.
HCV ribonucleic acid test (HCV RNA)	<ul style="list-style-type: none">• Window period: 1-3 weeks• Used to confirm active infection• Does not distinguish between acute and chronic infection• Recommended HCV screening test:<ul style="list-style-type: none">○ If prior anti-HCV positive and cleared HCV infection spontaneously or due to treatment○ In an immunocompromised person○ If the person is still within the window period for testing○ Anti-HCV results are equivocal○ When there is high suspicion for HCV infection, but initial anti-HCV results are negative (e.g., compatible clinical presentation with no other clinical diagnosis identified and high pre-test probability)• In BC, although the majority of HCV RNA positive results likely reflect chronic HCV infection, HCV RNA can be repeated 6 months after the initial test (or date of exposure if known) to rule out spontaneous clearance of infection• There is no correlation between HCV RNA levels and severity of liver disease, or chance of successful completion of treatment (and achievement of SVR-12)
HCV Genotype	<ul style="list-style-type: none">• If the HCV RNA test is reactive, the blood specimen can be screened for genotypes 1-6• The necessity of genotyping is becoming less important with the increased availability of pangenotypic DAA treatments. It can still be useful to help direct treatment decisions in certain scenarios.

Figure 4-2: HCV Testing Flowchart



■ Automatic HCV RNA testing done as of January 13/20 on all **first time** anti-HCV reactive results, and previously anti-HCV reactive results where HCV RNA testing has **never** been done. Instructions will be provided on the BCCDC PHL lab result in situations where an additional EDTA tube is required for HCV RNA testing to be completed.

* False negatives may occur in the presence of major immunosuppression (e.g., HIV infection where CD4+ < 50 cells/mm³ and agammaglobulinemia). Order HCV RNA where appropriate.

Ω Instructions will be provided on the BCCDC PHL lab result to collect an EDTA tube for HCV RNA testing to confirm an initial HCV RNA 'not detected' result.



4.3 Reflex Testing

The following section describes reflexive testing performed at the BCCDC PHL. It is important to check for past test results in the client's file and local electronic laboratory systems (e.g., CareConnect, Excelleris) in order to ensure that the correct tests are ordered and tubes of blood are collected, and to avoid unnecessary accessioning and testing of specimens.

If you are unsure of the individual's prior HCV testing history, contact the [BCCDC PHL Lab Client Services](#) (1-877-747-2522).

On the first reactive [anti-HCV](#) result, the following reflexive testing is done at the BCCDC PHL:

1. HCV RNA testing (87)

As of January 13, 2020, serologic HCV RNA testing is reflexively done on all:

- **First time** anti-HCV reactive results
- Previously reactive anti-HCV results, where HCV RNA testing has **never** been done

The HCV RNA will **not** be reflexed if a sample tests positive for HCV antibodies and there is already a prior HCV RNA result in the system. Be sure to check for past HCV test results so that the correct test is ordered.

Sometimes an EDTA tube of blood is still required to confirm an initial reflexed HCV RNA result. Where indicated, these follow-up recommendations are noted on the patient's lab report. This can occur when the reflexive HCV RNA test result is equivocal or not detected, or if the strength of the initial anti-HCV signal is too low.

2. Hepatitis A and B immune status testing

Reflexive testing for total antibody to hepatitis A (anti-HAV total) and hepatitis B surface antibody (anti-HBs) is performed on all first time reactive anti-HCV results. Where anti-HBs is non-reactive, further testing for hepatitis B surface antigen (HBsAg) and total hepatitis B core antibody (anti-HBc Total) is automatically done. Recommendations can then be made regarding recommended immunizations and case management (e.g., referral to a specialist if HBV infection), based upon these results.

If HAV and HBV results are not available on an anti-HCV reactive laboratory report, check local electronic lab results systems. If you cannot locate them, call the [BCCDC PHL Lab Client Services](#) (1-877-747-2522). If they are not available, HAV and HBV immune status testing can be added on if requested within 7 days of the laboratory receiving the HCV sample.

3. HCV genotype testing

HCV genotype testing can only be performed on specimens collected in EDTA tubes that test HCV RNA positive. Call [BCCDC Lab Client Services](#) (1-877-747-2522) if needing to add this test on to a specimen that has tested HCV RNA positive on an EDTA tube. It can be done reflexively, if requested at the same time as HCV RNA testing ordered on an EDTA tube.

HCV genotype testing has not yet been validated on specimens collected in SST tubes.



4.4 Interpretation of Test Results

See [Appendix A](#) for examples of results as reported out by the BCCDC PHL. Contact the [BCCDC PHL](#) if unsure of how to interpret HCV test results.

4.4.1 [HCV Antibody](#) Test Results

Two sensitive enzyme immunoassay (EIA) platforms are used to detect antibodies to HCV. The incidence of false positive EIA results is extremely low (0.2 - 0.4%).

Practitioner Alert!

Anti-HCV antibodies usually persist for life and do **not** need to be repeated once result is reactive. A reactive result does **not** differentiate between a resolved case and an active infection.

Table 4-2. Interpretation of HCV antibody test results

HCV Antibody test result	Screening HCV antibody assay	Supplemental HCV antibody assay	Interpretation
Anti-HCV reactive	EIA test is reactive	EIA test is reactive	<ul style="list-style-type: none"> Person has antibodies to HCV and therefore has been infected with the hepatitis C virus at some point in their life Reactive result does not indicate active infection or immunity
Anti-HCV non-reactive	EIA test is non-reactive	N/A	<ul style="list-style-type: none"> HCV infection is ruled out in most immunocompetent persons. No further testing is required. If the test was performed before this marker became detectable and the person has high risk behaviours, consider repeating anti-HCV 1-2 months. If immunocompromised, anti-HCV response may be blunted and confirmatory HCV RNA testing may still be required
Anti-HCV equivocal	EIA test is reactive	EIA test is non-reactive	<ul style="list-style-type: none"> If clinically indicated, a HCV RNA test is required to determine if active infection exists Equivocal results usually indicate a false positive

4.4.2 [HCV RNA](#) Test Results

Table 4-3. Interpretation of HCV RNA test results

HCV RNA Test Result	Interpretation
HCV RNA detected	<ul style="list-style-type: none"> Indicates active infection with HCV (i.e. the virus is actively replicating) Does not distinguish between acute or chronic infection
No HCV RNA detected	<ul style="list-style-type: none"> No evidence of active infection The infection has resolved either spontaneously or as a result of therapy Re-infection can occur if the client has on-going risk factors

The HCV RNA test is quantitatively accurate between 12 and 100,000,000 IU/mL. Note that the viral load may be reported outside of this range at < 12 IU/mL, but an active infection can still be detected and reported as "HCV RNA detected".



5.0 PUBLIC HEALTH MANAGEMENT

The following [case](#) definitions described in this section are specific to Public Health [documentation](#) and [attribution](#) of HCV cases in BC. Definitions used in daily clinical practice may employ the same terminology, but can differ significantly in their use and meaning.

Practitioner Alert!

[Case](#) definitions used for the purposes of surveillance in BC differ from their use in a clinical setting.

Laboratory results available to public health may not be adequate to meet clinical requirements for staging the infection, but will generally be sufficient for surveillance purposes of documenting and attributing cases appropriately. The information presented in this section may be used to guide the [documentation](#) and geographical [attribution](#) of confirmed (not suspect, or Person Under investigation, or PUI) HCV cases using an electronic public health information system.

One key distinction in how HCV case definitions are used by public health reporting is the focus on [seroconversion](#). In BC, individuals who have a documented seroconversion ('anti-HCV not detected' to 'anti-HCV detected' within a 12-month time period) are considered an 'acute' case, regardless of whether HCV RNA results are available or not, and regardless of clinical presentation. HCV cases attributed to BC that have not been reported elsewhere in Canada are reported to the Public Health Agency of Canada (PHAC).

The acute stage of HCV infection is important to capture, as these cases represent an important population whose risks reflect current transmission and acquisition risk factors. This provides key opportunities to engage individuals with HCV infection into comprehensive care. The [documentation](#) and [attribution](#) of 'acute' HCV cases can support case management by gathering acquisition risk factors. From this information, the linkage to care can be facilitated by the provision of timely education and service referrals (see [Section 6.0](#)). The documentation of other stages like 'resolved' is useful to have, but is not crucial (see [Table 5-1](#) for Panorama staging).

For individuals with newly identified HCV infections in BC who list their permanent residence as out of province, follow RHA guidelines, and refer to recommendations in the [Surveillance of Reportable Conditions, Chapter 6 of the BCCDC CDC Manual](#).

5.1 Case Definitions

As there is no single serological test available for identification of newly-acquired infections, [seroconversion](#) and time parameters are used as a proxy. Local surveillance systems may be limited by the current reporting of laboratory testing results. For confirmed case definitions, see 'Case' in [Section 2.0 Definitions](#). For Panorama specific staging guidance, see [table 5-1](#). Refer to RHA guidelines for further specific classification requirements related to a particular public health information system.

The flow of individual lab reports can vary, but in general [anti-HCV](#) test results are received first, followed by [HCV RNA](#), and then genotyping. A confirmed HCV case may consist of a single 'anti-HCV detected' test result, with or without other results. An antibody positive client who then receives HCV RNA results ('HCV RNA detected' or 'No HCV RNA detected') remains a confirmed case.

If the only information available is a stand-alone 'HCV RNA detected' test result or [genotype](#) result (without an anti-HCV result), these are also considered confirmed cases.



Table 5-1: Confirmed case definitions of Hepatitis C for the purposes of Public Health reporting in Panorama

Staging	Age	Baseline anti-HCV test result	Present HCV test result
Acute	Adults, adolescents & children > 18 months	Anti-HCV negative result on record within the prior 12 months	Anti-HCV positive OR HCV RNA positive
Chronic [^]	Adults, adolescents & children > 18 months	Anti-HCV negative result on record > 12 months ago OR No documentation available of previous anti-HCV result	HCV RNA positive
Resolved ^{^,Ω}	Adults, adolescents & children > 18 months	Anti-HCV positive	HCV RNA negative
Unstaged*	Adults, adolescents & children > 18 months	Anti-HCV negative result on record > 12 months ago OR No documentation of previous anti-HCV result	Anti-HCV positive AND No HCV RNA result available
Unstaged**	Children ≤ 18 months	N/A	HCV RNA positive ≥ 4 to 6 weeks of age OR Anti-HCV positive at 18 months of age

[^] If an anti-HCV reactive and a HCV RNA positive result are received at the same time, report as an 'acute' case first, and then change to 'chronic' or 'resolved' using the same date.

^Ω For the purposes of surveillance, for all cases > 18 months only a **single** negative HCV RNA is required to confirm resolution (no time parameter)

* Update case within the same investigation when HCV RNA result arrives

** In the case of children ≤ 18 months, leave unstaged until further testing has been completed. This can be revised to chronic or resolved if further HCV RNA results are available after 18 months.

5.2 New case follow-up

This section describes suggested follow-up of new HCV cases, carried out by public health personnel with the assistance of a primary health care provider where possible. Refer to local guidelines for further guidance.

Case Identification

- Lab notification received confirming HCV infection (usually [anti-HCV](#) results, may also see reflexed HCV RNA results)
- Document test results in your health authority's public health information system
- Review prior testing history to determine if new HCV case
- Classify according to age and prior baseline anti-HCV test result (see [Table 5-1](#) for staging information specific to Panorama)



Reporting

- Use your health authority's public health information system to report confirmed cases of HCV
- If reporting a new acute HCV, complete the [Hepatitis C Acute Case Report Form](#)

Case Management

- Engage into care. If appropriate offer referrals and resources for:
 - Primary care provider (MD/NP) for further clinical evaluation
 - If no reflexed result available, recommend HCV RNA testing to confirm current infection. Ensure that the primary care provider has been copied on the result.
 - Immunization update. Check for HAV/HBV testing results and prior immunizations.
 - Alcohol and drug harm reduction care (e.g., OAT referral)
 - Mental health and addictions counselling
 - STI screening
 - General health and education resources (e.g., diet, housing resources)
 - Community support groups and services
- Review transmission information and prevention, providing supports where needed (e.g., local harm reduction sites for safer sex and drug use supplies, supervised consumptions services and overdose prevention sites)
- Discuss potential for stigma and that disclosure is voluntary
- Where possible, offer to assist client with notifying [contacts](#) and provide local testing resources

6.0 ACUTE CASE MANAGEMENT

The following section outlines suggested follow-up for cases of acute HCV. Many of the recommendations below are not exclusive to acute cases and may also apply to cases of chronic HCV.

Individuals may avoid seeking follow-up care due to stigma and discrimination, which can be even more pronounced in rural and remote areas. The creation of a supportive environment that respects the privacy and culture of each individual will help to foster the trust needed to develop a partnership of care. The challenges that face individuals in the context of the broader determinants of health (e.g. housing, coping skills, gender) must be acknowledged when reviewing a new HCV lab test result or diagnosis.

6.1 Management of Adults

[The British Columbia Hepatitis Testers Cohort \(BC-HTC\)](#) is a cohort containing de-identified health information for 1.7 million individuals (as of 2018) who were tested for HCV or HIV, or diagnosed with hepatitis B, hepatitis C, HIV or active tuberculosis from 1990 to 2015. These data are linked with multiple datasets on medical visits, hospitalizations, cancers, prescription drugs, and death records (88, 89).

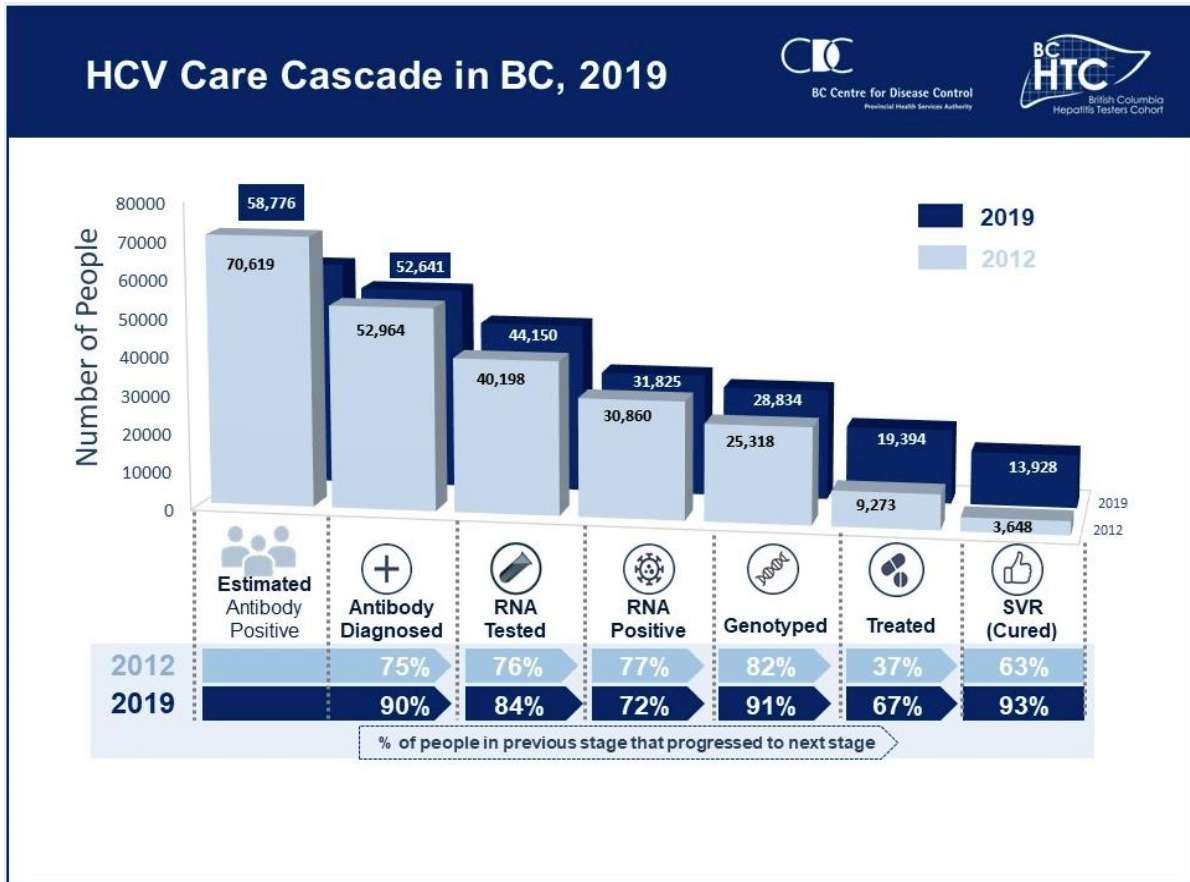
The BC-HTC database reveals how many people living with HCV infection are getting the care that they need. From the care cascade (see [Figure 6-1](#)), it is clear that there are a significant number of people with HCV infection who are being lost to follow-up after initial testing. Where possible, efforts should be made to engage people living with HCV infection into comprehensive care upon initial contact.

6.1.1 First Contact

Check for HCV RNA results to confirm active infection. If direct contact with a client is part of a RHA's routine practice, attempt to confirm that the client is aware of their diagnosis with the primary care provider before initiating contact. In situations where confirmation with the primary care provider cannot be established, direct contact with a client may be appropriate.

If HCV RNA results have not been reflexively performed by the BCCDC PHL, recommend confirmation of infection by [HCV RNA](#) testing (collected in an EDTA tube).. Ensure that the primary care provider (PCP) is copied on the results, and advise client to follow-up with their PCP for results. Having this result at the follow-up visit with their PCP can help with continuity of care. It is within the scope of practice of a STI certified RN to order a HCV RNA test (see [STI assessment DST](#)).

Figure 6-1: HCV Cascade of Care. Data from the BC-Hepatitis Testers Cohort (BC-HTC).



6.1.2 Contact Tracing and Disclosure

It is recommended that the interview for contact information be done by the first health care professional (e.g. public health personnel, primary care provider) who interviews the client, as there may not be another opportunity to do so. Give a rationale as to why the case report information is being collected to provide reassurance regarding privacy and confidentiality.

Where possible, provide assistance to clients with notifying [contacts](#) who may need testing and counselling. Provide resources and education regarding options for local HCV testing and prevention of transmission.



6.1.3 Health Teaching to Prevent HCV Transmission

It is essential to assess for acquisition risk factors. Even after clearing an initial infection spontaneously, or after successful hepatitis C treatment, individuals remain at risk for premature death related to acquisition risk factors (30)

Advise how to prevent transmission:

- Do not share equipment used for injection, snorting or smoking of drugs (e.g., needles, syringes, straws, cookers, water source, mixes/washes and pipes)
- Do not share equipment used for tattooing, body piercing or other acupuncture (e.g., needles, ink)
- Do not share personal care items (e.g., toothbrushes, razors, earrings or manicure equipment)
- Do not donate blood, semen, breast milk, body organs or tissues
- Keep all open cuts and sores covered until healed
- Put articles with blood on them (e.g. tampons, bandages) in a separate plastic bag before disposal in household garbage
- Dispose of bloody sharp items (e.g. razor blades, needles) into a hard-sided container, taped shut
- Wearing clean, disposable gloves, clean blood spills by using absorbent materials first (e.g., paper towels). Then clean the area more thoroughly with soap and water, and then disinfect. To disinfect, use a fresh solution of 1 part bleach to 9 parts water. Allow to sit for 10 minutes before wiping off.
- If considering pregnancy discuss the risk of transmission to the infant. Breastfeeding is generally considered safe (see [Section 6.1.6](#)).
- For additional information on reducing the risk of transmission from blood and body fluids, refer to
 - [HealthLink BC File #97. Contact with Blood or Body Fluids: Protecting Against Infection](#)

6.1.4 General Health and referrals

Assist in obtaining a referral to a primary care provider (PCP) if needed. The PCP can conduct further assessments and tests prior to consulting with and/or referring to healthcare provider experienced with HCV management and treatment (e.g., gastroenterologist, hepatologist, infectious disease specialist or MD/NP with HCV experience) for more specialized care and treatment consideration if needed. See [Figure 4-1](#) for the HCV testing flow chart.

If appropriate, assess for other STI's and offer harm reduction education and counseling. Provide referrals to STI clinics and harm reduction services aimed at reducing the risk of acquiring HIV infection and reducing harms associated with illicit drug use (e.g., drug use supply, distribution and recovery sites, supervised injection facilities, opioid substitution therapies).

[Liver fibrosis](#) can progress in the presence of coinfection with HBV or HIV, alcohol consumption (> 2-3 drinks/day), non-alcoholic fatty liver disease, obesity and insulin resistance. Discuss limiting or avoiding alcohol, avoiding hepatotoxic drugs (e.g. acetaminophen) and eating a well-balanced diet, as part of a healthy lifestyle and to minimize liver damage. Clients should consult with their primary care provider before using over-the-counter medications and herbal remedies².

² Herbal remedies include herbs, herbal materials, herbal preparations, and finished herbal products that contain parts of plants or other plant materials as active ingredients (55). Clients may refer to them as, but are not limited to, the following examples: "natural", "alternative", "traditional" or "Chinese" medicine.



6.1.5 Immunizations

All persons with an anti-HCV reactive result are considered to be at higher risk for certain infections. Regardless of HCV RNA results, the following immunizations are provincially covered for anyone testing anti-HCV reactive:

- hepatitis A vaccine series, if susceptible
- hepatitis B vaccine series, if susceptible
- pneumococcal vaccine
- annual influenza vaccine

Review reflexive testing results for hepatitis A and hepatitis B, that are automatically done by the BCCDC PHL on all new anti-HCV reactive test results (see [Section 4.2](#)), and prior immunization history.

Timely HBV immunization is important for those living with chronic HCV infection, as a better immune response to HBV vaccine is observed if immunization occurs before the onset of [cirrhosis](#) (54). Engaging individuals into care also provides an opportunity to assess for other outstanding routine immunizations.

Practitioner Alert!

Individuals who spontaneously clear a HCV infection (i.e. [resolved infection](#)) should be offered these immunizations for free, as they are still considered to be at higher risk for certain infections.

For more information on routine immunizations for the general adult population and those recommended for persons with chronic liver disease, refer to the [BC Immunization Manual](#).

6.1.6 Pregnancy and Breastfeeding

Recommend pregnant women who are [anti-HCV](#) positive to have confirmatory [HCV RNA](#) testing done. If active infection is confirmed, recommend liver function testing to identify those with compromised liver functioning who may require specialist referral.

Recommend breastfeeding to mothers who are infected with HCV. If the nipples become cracked or bleed, mothers can abstain from breastfeeding until they are healed. To prevent cessation of milk supply, mothers may consider expressing and discarding breast milk until their nipples are healed. Breastfeeding is not recommended for mothers co-infected with HIV.

6.1.7 Private Insurance Testing

Clients identified through insurance applications may go through a different process when reporting to Public Health. The elements of follow up are the same as for other all other newly identified cases. These clients may be contacted directly by public health personnel to begin follow-up and/or a primary care provider, who may complete the follow-up process. Information regarding the appropriate vaccinations, testing and counselling for a case can be provided to the primary care provider.

6.1.8 Transfusion Transmission

If risk factors indicate the possibility of a transfusion transmissible infection, where the client has been a donor or recipient, follow the reporting process in the [BCCDC CD Manual, Chapter 1: Transfusion Transmissible Infections](#).



6.2 Management of Neonate to Determine Vertical Transmission

Maternal antibodies can cross the placenta, yielding a false positive result up until the infant is 18 months of age (90, 91). In 95% of cases, maternal antibody will no longer be detectable in the infant by 12 months of age. In the remaining 5%, maternal antibody will no longer be detectable by 15 to 18 months of age (91). The BCCDC PHL will not normally process requests for antibody testing on infants less than 18 months.

Public Health recommendations for infants born to mothers with HCV infection*

- Anti-HCV testing at 18 months
- Infants testing [anti-HCV](#) reactive at 18 months should:
 - Be referred to a paediatric infectious disease specialist or hepatologist for further testing and care.
 - Receive vaccines as per routine infant and chronic liver disease schedules (see [BC Immunization Manual, Part 1: Immunization Schedules and Part 2: Immunization of Special Populations](#)).

* For mothers who have cleared an initial HCV infection spontaneously or after HCV treatment, the chance of transmitting HCV infection to their infant is virtually zero. It is unclear if there is a maternal HCV RNA threshold above which transmission is more likely (92).

Follow-up for HCV testing at 18 months can be very poor. A flag or reminder on the mother and infant's file can help to ensure that anti-HCV testing and routine vaccinations are completed when the infant is 18 months of age. Coordinated efforts amongst primary care providers, specialists and public health, can help to ensure that appropriate testing and follow-up of infants is completed (93-96).

To allay parental anxiety, earlier testing for HCV RNA can be considered when infants are 2 months (73, 92, 97). Consult with or refer to a specialist as needed. Note that if the infant tests:

- HCV RNA negative, absence of infection should be confirmed with repeat HCV RNA 6 months later and anti-HCV testing at 18 months (97)
- HCV RNA positive, presence of infection must be confirmed with repeat HCV RNA after 12 months of age and anti-HCV testing at 18 months of age (98)
 - An earlier diagnosis before 18 months does not change follow-up recommendations, as there are no treatments or interventions currently approved until children turn 3 years of age (92)
 - Infants who develop chronic HCV infection generally experience mild clinical sequelae
 - 25-40% of neonatal HCV infection spontaneously clear by 2 years (up to 7 years of age) (98)

For a sample letter that public health can send to a MD/NP advising of recommended testing for an infant born to a mother with HCV infection, refer to [Appendix B](#).

Recommendations for people of child-bearing potential with HCV infection:

- Ribavirin-containing treatment regimens are teratogenic. There have not been enough studies to confirm the safety of DAAs during pregnancy or while chest-/breast-feeding.
- HCV treatment should be completed before pregnancy or after completion of breast feeding. Individuals who are cured before becoming pregnant cannot pass HCV infection to their infant.

See [Section 6.3 Treatment](#) and [Appendix D](#) for further information on treatment.



6.3 Treatment

Depending on the [genotype](#), prior treatment with ribavirin and injectable pegylated interferon typically lasted 24 to 48 weeks. Cure rates ranged from 40 to 80%, and people often experienced severe side effects (99). The introduction of [direct-acting antiviral agents](#) (DAA's) has dramatically changed the HCV treatment landscape. Newer regimens (6):

- Consistently have cure rates greater than 95%
- Are pangenotypic
- Are all oral and interferon free
- Typically last 8-12 weeks
- Have few side effects

By treating HCV infection early, liver-related morbidity (i.e., liver damage, liver failure and hepatocellular carcinoma) and mortality can be reduced and forward transmission of infection halted. In BC, fibrosis restrictions for the coverage of treatment were lifted in March 2018 (100). Regardless of fibrosis stage, anyone with BC Pharmacare coverage can have their HCV infection treated.

The type and duration of hepatitis C treatment is determined on an individual basis. Treatment type and duration varies depending on multiple factors such as prior treatment history, co-morbidities, and presence of [cirrhosis](#). Treatment work-up can be done by the primary care provider who has experience in HCV care, referring to a specialist as needed. See [Appendix D: Quick Reference Treatment Guide for Health Care Providers](#) for suggested treatment work-up and follow-up care.

A [sustained virologic response](#) is defined as having no detectable HCV RNA 12 weeks after treatment completion (SVR-12). This is synonymous with a virological cure, but patients can still be re-infected if they have on-going risk exposures.

Resources

For national treatment guidelines, see [The management of chronic hepatitis C: 2018 guideline update from the Canadian Association for the Study of the Liver \(CASL\)](#)

For information on available treatments and required diagnostic information for approval in BC, see the [Government of BC's Special Authority Forms](#) section.

For in-depth clinician training, see the [University of Washington's Hepatitis C Online course](#).

7.0 MANAGEMENT OF ACCIDENTAL EXPOSURES

Needle stick accidents should be reported and documented as per agency guidelines.

Refer to the [BCCDC CD Manual, Chapter 1: Communicable Disease Control, Blood and Body Fluid Exposure Management](#) section for:

- Blood and Body Fluid Exposure Management Guideline
- Exposure to Blood and Body Fluid Requisition – HLTH 2339
- Exposure to Blood and Body Fluid Letter for Follow-up Physician – HLTH 2340



Appendix A: Examples of Laboratory Results

Below are some examples of HCV laboratory results, as reported out by the BCCDC PHL. Contact the [BCCDC Lab Client Services](#) (1-877-747-2522) if unsure of how to interpret HCV testing results.

Notes and symbols have been added below in **blue** for the purposes of this guideline.

First time anti-HCV positive, HCV RNA detected		
Hepatitis C Virus Antibody Anti HCV	** Reactive	dd/mmm/yyyy
Hepatitis C Virus Supplemental Anti HCV Supplemental	** Reactive	dd/mmm/yyyy
Anti HCV Report Anti HCV Report	** Reactive Anti-HCV reactivity does not distinguish between current or resolved HCV infection Please inform your medical health officer if this infection might be due to a recent blood product transfusion	dd/mmm/yyyy
Hepatitis C Quant NAT Specimen Description HCV RNA (reflex HCV RNA testing on initial serology, SST tube)	Serum 6.10 log ₁₀ IU/mL HCV RNA DETECTED This assay is quantitatively accurate between 12 and 100,000 IU/mL HCV RNA viral load and log values are used to predict and monitor treatment response but do not correlate with disease progression.	dd/mmm/yyyy dd/mmm/yyyy
Interpretation	This individual has active HCV infection. Refer for treatment.	
First time anti-HCV positive, no HCV RNA detected		
Hepatitis C Virus Antibody Anti HCV	** Reactive	dd/mmm/yyyy
Hepatitis C Virus Supplemental Anti HCV Supplemental	** Reactive	dd/mmm/yyyy
Anti HCV Report Anti HCV Report	** Reactive Anti-HCV reactivity does not distinguish between current or resolved HCV infection Please inform your medical health officer if this infection might be due to a recent blood product transfusion	dd/mmm/yyyy
Hepatitis C Quant NAT Specimen Description HCV RNA (reflexed HCV RNA testing on initial serology, SST tube)	Serum HCV RNA not detected from serum. Please submit an EDTA plasma for confirmation.	d/mmm/yyyy
Interpretation	This individual has been exposed to HCV at some point in their life, but does not appear to have a current HCV infection. The reflexed "HCV RNA not detected" result must be confirmed with subsequent HCV RNA testing on an EDTA tube of blood.	



(cont'd, Appendix A: Examples of Laboratory Results)

HCV RNA Results (previously anti-HCV positive)	
HCV RNA detected Specimen Description Test Name HCV RNA HCV RNA (log 10IU/mL) Interpretation	Plasma Results 316732 5.50 HCV RNA detected The assay is quantitatively accurate between 12 and 100,000,000 IU/mL. HCV RNA viral load and log values are used to predict and monitor treatment response but do not correlate with disease progression. Active HCV infection. Refer for treatment consideration.
HCV RNA detected Specimen Description Test Name HCV RNA HCV RNA (log 10IU/mL) Interpretation	Plasma Results < 12 Not calculated HCV RNA detected at < 12 IU/mL The assay is quantitatively accurate between 12 and 100,000,000 IU/mL. HCV RNA viral load and log values are used to predict and monitor treatment response but do not correlate with disease progression. Active HCV infection. Refer for treatment consideration.
No HCV RNA detected Specimen Description Test Name HCV RNA HCV RNA (log 10IU/mL) Interpretation	Plasma Results 0.021548657 Not calculated No HCV RNA detected The assay is quantitatively accurate between 12 and 100,000,000 IU/mL. No evidence of active HCV infection



Appendix B: Sample letter to MD/NP, new acute HCV infection

Print on letterhead

Date

Confidential

Physician Address

Dear:

RE: Hepatitis Test Results for

DOB:

PHN:

We have recently received a reactive hepatitis C antibody (anti-HCV) laboratory report for your patient listed above. Please review the laboratory report to ensure that a HCV RNA test result is available to confirm active infection, and/or if recommendations have been made for follow-up HCV RNA testing.

Hepatitis C Virus is a reportable condition under the BC Public Health Act (2008) and Schedule A of the Health Act Communicable Disease Regulation.

All persons testing anti-HCV reactive, including people who spontaneously clear an initial infection, are eligible to receive the following publicly funded vaccinations, in addition to those listed in the routine schedules:

- Hepatitis A vaccine (if susceptible)
- Hepatitis B vaccine (if susceptible)
- Pneumococcal vaccine
- Annual Influenza vaccine

Please call *Public Health Unit phone number* if you have any questions regarding completion of the HCV case report form, or vaccine availability in your area.

Please contact me if you have any questions.

Sincerely,

*Name, Position
Contact Information*



Appendix C: Sample Letter to Maternal Healthcare Provider regarding testing of infants born to mothers with HCV infection

Print on letterhead

Date

Confidential

Physician Address

Dear:

RE: *Patient Name*

DOB:

PHN:

We have been advised that your patient, who has hepatitis C infection, delivered *Infant Name* on *Infant's DOB*.

To determine if the infant has acquired a hepatitis C infection, the infant should be tested for HCV antibody (anti-HCV) at **18 months** of age when routine immunizations are due. Please note that maternal anti-HCV can cross the placenta and yield false positive anti-HCV results if anti-HCV testing is done before the infant turns 18 months.

Please refer to the BCCDC Hepatitis C Guidelines for further information.

Please contact me if you have any questions.

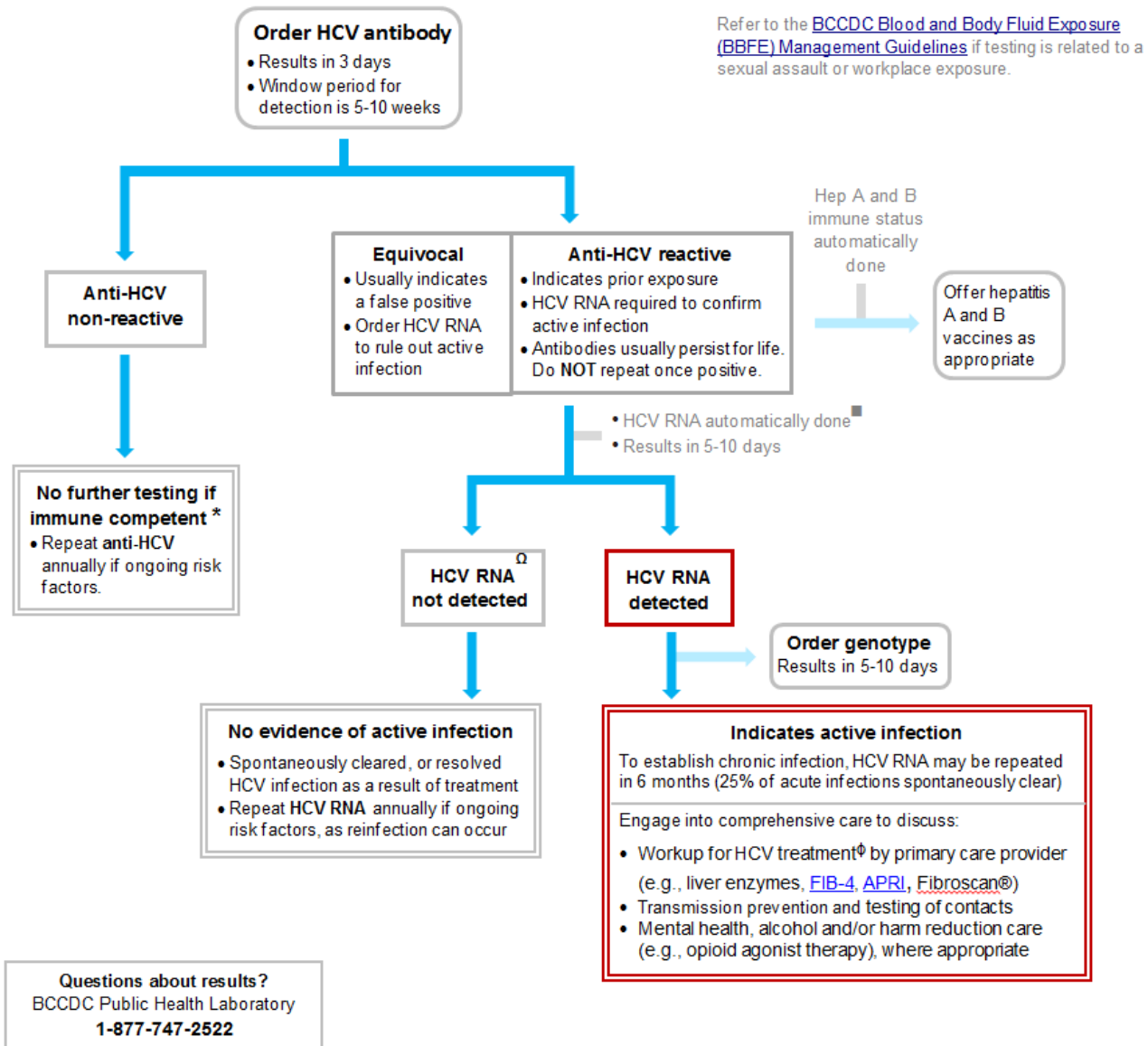
Sincerely,

Name, Position

Contact Information

APPENDIX D: Quick Reference HCV Testing Guide for Health Care Providers

See the [BCCDC CD Manual](#) for pdf and grey scale versions.



■ Automatic HCV RNA testing done as of Jan.13/20 on all **first time** anti-HCV reactive results, and previously anti-HCV reactive results where HCV RNA testing has **never** been done. Instructions will be provided on the BCCDC PHL lab result in situations where an additional EDTA tube is required for HCV RNA testing to be completed.

* False negatives may occur in the presence of major immunosuppression (e.g., HIV+ where CD4+ < 50 cells/mm³ and agammaglobulinemia).
Order HCV RNA where appropriate.

Ω Instructions will be provided on the lab result an EDTA tube is required to confirm an initial HCV RNA 'not detected' result.

φ For treatment information and approval, see the [2018 CASL Hepatitis C Guideline](#) and [BC Special Authority Request Forms](#).



Page 2 - Quick Reference Guide for Health Care Providers

Background

Indigenous peoples continue to be impacted at a significantly higher rate due to historic and present colonial policies and systems that disrupt connection to land, language, and culture, and diminish Indigenous sovereignty. Historical and present intergenerational trauma contributes to the social determinants of health in Indigenous peoples and impacts acquisition risks.

In addition to a lack of support to address social determinants of health, persons who use drugs may lack access to necessary harm reduction supplies and testing that can greatly increase risk for HCV infection.

In BC, injection drug use is the major source of new infections. While prevalent infections are more commonly seen in people born in 1945-65, immigrants from endemic areas (includes regions of Central and East Asia, and North Africa/Middle East, see the [2018 CASL HCV Guidelines](#)) and people who have used illicit drugs in the past.

Direct acting antiviral (DAA) curative treatment is well tolerated and over 95% effective across all genotypes after 8-12 weeks of treatment. Treatment is free for anyone who has current HCV infection and BC medical coverage, regardless of liver fibrosis stage.

Clinical Description
Acute HCV infection (< 6 months)
<ul style="list-style-type: none"> Symptoms are usually absent, but can include a wide spectrum of illness, including jaundice Around 25% will spontaneously clear within 6 months
Chronic HCV infection (≥ 6 months)
<ul style="list-style-type: none"> Symptoms are usually absent Over decades, 20% will develop cirrhosis and 1-5% will develop hepatocellular carcinoma (HCC) Major cause of liver transplantation
Laboratory
HCV Antibody: produced when infected with HCV and usually remains present for life
<ul style="list-style-type: none"> A reactive anti-HCV test does not distinguish between resolved or current HCV infection Does NOT need to be repeated once result is reported as reactive
HCV RNA: confirms active infection
<ul style="list-style-type: none"> Does not correlate with disease progression Performed 12 weeks after treatment completion to assess for a virologic cure, known as a sustained virologic response (SVR-12) Used to screen people who have prior anti-HCV reactive results and have cleared the infection spontaneously or after HCV treatment
HCV Genotype: becoming less important with increasing availability of pangenotypic DAA regimens


Priority populations experiencing a disproportionate burden of HCV infection *

- Born between 1945 to 1965
- Persons who have ever been incarcerated
- Born, lived in or received healthcare in endemic regions
- Indigenous peoples

* See [Blueprint to Inform Hepatitis C Elimination Efforts in Canada](#)

Likelihood of Transmission

Transmission occurs through blood-to-blood contact.

- 
- Injection drug use (IDU) past or present
 - Receipt of healthcare in HCV endemic area where infection control practices were not followed and/or blood supply not tested
 - In Canada, receipt of blood transfusion, blood products or organ transplant before 1992
 - Tattooing, body piercing or acupuncture where there were poor infection control practices
 - Non-IDU (e.g. snorting, smoking), past or present
 - Condomless sex, multiple partners (more frequently reported in gbMSM engaging in group sex and/or party 'n play)
 - Mother to infant, where mother is HCV RNA positive
 - Condomless sex with one long-term partner
 - Sharing personal care items (e.g. razors, nail clippers)
 - Workplace exposure (e.g. accidental needle sticks)

Education

After testing - engage into care

- Assess alcohol and substance use, providing harm reduction and mental health care as appropriate.
- Review immunizations (e.g., hep A and B vaccines)
- Offer STI screening, counsel about safer sex
- Healthy liver (e.g., diet, acetaminophen use)

Active infection - transmission prevention

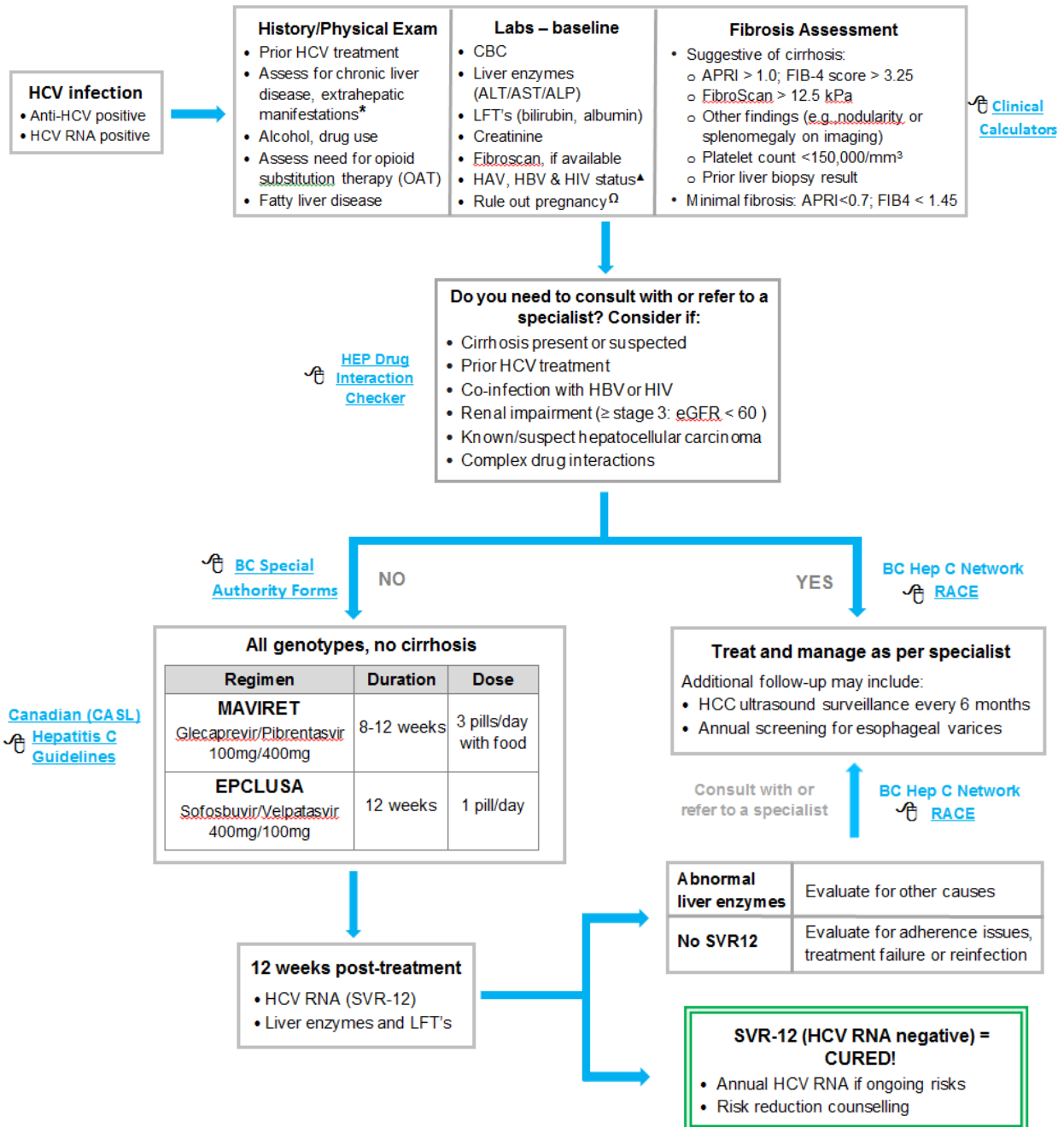
- Do not share personal care items
- Do not donate blood, semen, breast milk or body organs/tissues
- Dispose items and sharps with blood in separate bags or containers
- Keep open cuts and sores covered with bandages
- Blood spills can be cleaned with a solution of 1 part bleach to 9 parts water. Apply and let sit for 10 minutes before rinsing.
- There is no immunization and no post-exposure prophylaxis for HCV

Resources

- [BCCDC PHL](#) – requisition forms
- [eLab Handbook](#) – BCCDC PHL information on lab tests
- [BCCDC Hepatitis C course for public health providers](#)
- [University of Washington - HCV Online Course](#)
- [Hepatitis Education Canada](#)
- [Help4Hep](#) – peer-to-peer helpline

Appendix E: Quick Reference HCV Treatment Guide for Health Care Providers

See the [BCCDC CD Manual](#) for a pdf version.



* Assessment can include: ascites, jaundice, peripheral edema, hepatomegaly, splenomegaly and palmar erythema
 ▲ HBV reactivation can occur if co-infected HBV/HCV individuals are being treated with HCV DAA therapy
 Ω Treatment not recommended if pregnant or breast-/chest-feeding



Appendix F: Case Studies

The scenarios below provide suggested follow-up for the purposes of training and education. These are not meant to be prescriptive, as there may be other considerations unique to each individual situation, in addition to local health authority and site specific processes and guidelines.

Case studies #1 to #5 have a more narrow focus on HCV, while case study #6 is comprised of four parts that include comprehensive care considerations.

Note: Non-reactive = Negative
Reactive = Positive

Case study #1 HCV RNA reflex testing, Low but detectable HCV RNA levels	
Clinical History and Lab Results	
Zane tested for HCV for the first time last week. He has come in to review the following results:	
<i>Anti-HCV screen:</i>	<i>Reactive</i>
<i>Anti-HCV supplemental:</i>	<i>Reactive</i>
<i>Anti-HCV Report:</i>	<i>Reactive</i>
<i>Anti-HCV reactivity does not distinguish between current or resolved HCV infection. Please inform your medical health officer if this infection might be due to a recent blood product transfusion.</i>	
<i>HCV RNA detected</i>	<i>(active infection)</i>
<i>Specimen Description</i>	<i>Plasma</i>
<i>Test Name</i>	<i>Results</i>
<i>HCV RNA</i>	<i>< 12</i>
<i>HCV RNA(log 10IU/mL)</i>	<i>Not calculated HCV RNA detected</i>
How would you interpret these results?	
Explanation	
The BCCDC PHL has performed both anti-HCV and HCV RNA testing on the initial serology specimen. HCV RNA reflexive testing on first-time positive anti-HCV results came into effect on January 13, 2020. The presence of HCV RNA indicates an active infection. Although below the lower limit of detection of 12 IU/mL, HCV RNA was detected somewhere between zero and 12 IU/mL, and reported as an active infection.	
General follow-up considerations	
<ul style="list-style-type: none"> • The anti-HCV reactive result indicates that Zane has had a HCV infection at some point • The HCV RNA detected result indicates that Zane currently has an active infection. • Refer to a MD/NP with HCV experience or to a specialist for further assessment and follow-up testing. • Approximately 25% of initial infections spontaneously clear, which generally occurs within 6 months. Re-testing for HCV RNA 6 months after the date of exposure (or if unsure, date of testing if ongoing risks) will clarify current HCV status. • Review transmission prevention information 	
Public Health reporting considerations	
<ul style="list-style-type: none"> • Following regional guidelines, enter as a confirmed chronic case of hepatitis C. Enter as “unstaged” in the public health electronic documentation system where appropriate, as there is no prior HCV testing history. 	



References and Resources

- BCCDC Hepatitis C Guidelines:
 - [Section 4.4 Interpretation of Test Results](#)
 - [Section 5.0 Public Health Management](#)
 - [Section 6.0 Acute Case Management](#)
 - [Appendix A: Examples of Laboratory Results](#)

Case study #2
Anti-HCV equivocal results

Clinical History and Lab Results

Lloyd was tested for HCV as a part of [HIV PrEP](#) work-up. The HCV test is as follows:

Anti-HCV: EQUIVOCAL

If clinically indicated, please submit an EDTA blood for HCV RNA testing to confirm active infection

How would you interpret this result and what would your next steps be?

Explanation

There was disagreement between the screening and supplemental anti-HCV tests. Usually this reflects a false positive result. If clinically indicated (e.g., immunocompromised, recent or ongoing higher risk exposures), consider testing for HCV RNA.

General follow-up considerations

- Ask Lloyd about any recent possible exposures. In meeting eligibility criteria for HIV PrEP, there may be ongoing risks for HCV exposure. Confirmation of HCV status with EDTA blood collection for HCV RNA testing should be considered.
- Review general safer sex and transmission prevention education
- Provide referrals to harm reduction sites if appropriate

References and Resources

- BCCDC Hepatitis C Guidelines:
 - [Section 4.2 HCV Testing](#)
 - [Section 4.4 Interpretation of Test Results](#)
- [SmartSex Resource: Pre-Exposure Prophylaxis \(PrEP\)](#)
- [BC Centre for Excellence in HIV/AIDS: HIV Pre-Exposure Prophylaxis \(PrEP\)](#)

Case study #3
Anti-HCV reactive, no HCV RNA reflex testing done

Clinical History and Lab Results

Cole had previously tested anti-HCV nonreactive just less than 1 year ago. Now you review the following result from a week ago:

Anti-HCV screen: Reactive

Anti-HCV supplemental: Reactive

Anti-HCV Report: Reactive

Anti-HCV reactivity does not distinguish between current or resolved HCV infection. If clinically indicated please submit an EDTA blood for HCV RNA to confirm an active infection. Please inform your medical health officer if this infection might be due to a recent blood product transfusion.

How would you interpret this lab report and what would you do to prepare for Cole's upcoming visit?



Explanation

Reflex HCV RNA testing on first time anti-HCV positives started January 13, 2020; however, when the signals from the screening or supplemental testing platforms are low, HCV RNA reflex testing cannot be done on serology samples (SST tubes) and an EDTA tube is required. The BCCDC PHL will note on the laboratory report when an EDTA tube is required for HCV RNA testing to be done.

General follow-up considerations

- Cole has been exposed to HCV at some point since last testing less than 1 year ago. Another blood draw for an EDTA tube to test for HCV RNA to see if an active infection is present.
- Review transmission prevention information
- Complete as much of the [case report form](#) as possible, as there may not be another chance to do so
- Review acquisition risk factors and provide referrals and resources as appropriate

Public Health reporting considerations

- Report as an acute case of HCV infection, as there is documentation of an anti-HCV nonreactive result from less than 1 year ago.
- Follow local health authority documentation guidelines and processes

References

- BCCDC Hepatitis C Guidelines:
 - [Section 4.4 Interpretation of Test Results](#)
 - [Section 5.0 Public Health Management](#)
 - [Section 6.0 Acute Case Management](#)
 - [Appendix A: Examples of Laboratory Results](#)
- [BCCDC Public Health Laboratory Update: Hepatitis C reflex testing](#)

Case study #4
Sexual transmission, regular partner

Clinical History and Lab Results

Skylor is wondering if there is any risk for getting HCV infection if condoms are no longer used with a long-term partner, who is living with chronic HCV infection.

What would you tell Skylor?

Explanation

- It is relatively rare to see sexual transmission of HCV between long-term couples
- Compared with parenteral exposure, sexual transmission is not a very efficient means of acquiring an HCV infection, but it has been more recently reported in the context of gbMSM engaging in ChemSex/Party 'n Play and gbMSM who have HIV infection. Sexual activities that may lead to potential blood exposure include those that can cause mucosal tearing, such as condomless receptive anal sex.

General follow-up considerations

- Skylor's partner should be encouraged to complete HCV treatment
- In making a decision, Skylor and her partner should keep in mind that consistent condom use is also recommended for STI prevention and as an option for birth control (if appropriate)
- Although sexual transmission is not commonly seen, recommend HCV screening at least annually
- Recommend routine STI screening

**References**

- BCCDC Hepatitis C Guidelines:
 - [Section 3.3 Disproportionately affected populations, testing indications and transmission](#)

Case study #5

Ongoing risk exposure, HCV testing

Clinical History and Lab Results

Jay and Nya have come to inquire about HCV testing for Nya. Jay has chronic HCV infection, but does not have a regular healthcare provider. They are not sure if they got their syringes mixed up a couple of days ago. Jay often has to help Nya inject, as it is difficult to find a suitable vein. Nya cannot recall getting tested for HCV before.

How would you proceed?

Explanation

- Sharing of drug-use equipment is an efficient means of acquiring an HCV infection

General follow-up considerations

- Recommend anti-HCV testing for Nya today
- Recommend HCV treatment for Jay
 - Offer to start pre-treatment work-up where possible
 - Refer Jay to a primary care physician or NP, preferably someone with HCV experience
- Recommend routine STI testing for Nya and Jay, including HCV for Nya until Jay has cleared the virus
- Review transmission prevention information
- Inquire about any other priorities that they may need help with (e.g., housing, food security)
- Address acquisition risk factors:
 - Review [safer injecting](#) tips
 - Refer to the [Toward the Heart](#) website. The 'Find a Site' feature can help to locate distribution sites in BC where safer sex and drug use supplies, and naloxone kits are available.
 - Offer training on how to respond to an overdose, including [Naloxone training](#)
 - Offer referrals for opioid agonist therapy (OAT) if appropriate

References and Resources

- BCCDC Hepatitis C Guidelines:
 - [Section 3.3 Disproportionately affected populations, testing indications and transmission](#)
 - [Section 4.2 HCV Testing](#)
 - [Section 6.3 Treatment](#)
 - [Appendix E: Quick Reference HCV Treatment Guide for Healthcare Providers](#)
- [Toward the Heart](#)
 - [Overdose prevention training and resources](#)
 - [Find a site](#)
- [BC Centre for Substance Use](#)
 - [Healthcare Provider Resources](#) > OAT Clinics Accepting New Patients
 - [People Who Use Drugs Resources](#)
- [Pathways Medical Care Directory: Search for Care](#)

**Case study #6 – part 1 of 4**
Prior anti-HCV reactive**Clinical History and Lab Results**

Kai presents for routine STI testing. Upon taking a medical history, you check the file and local laboratory system:

September 2019:

Anti-HCV screen: Reactive

Anti-HCV supplemental: Reactive

Anti-HCV Report: Reactive

Anti-HCV reactivity does not distinguish between current or resolved HCV infection. If clinically indicated please submit an EDTA blood for HCV RNA to confirm an active infection. Please inform your medical health officer if this infection might be due to a recent blood product transfusion.

Kai tells you that he hasn't seen a healthcare provider since getting the anti-HCV results because "the visit didn't go very well". The [Case Report Form \(CRF\)](#) and contact follow-up remain outstanding. Complete hepatitis A and B vaccine series are noted on file, including anti-HBs ≥ 10 mIU/mL.

What are your next steps?

Explanation

The BCCDC PHL began [HCV RNA reflexive testing](#) on first-time positive anti-HCV results beginning on January 13, 2020. Before that, people had to be recalled to see their healthcare provider to obtain an additional lab requisition to have another blood draw for HCV RNA testing on an EDTA tube of blood.

General follow-up considerations

- Provide an opportunity to further discuss concerns about the last clinic visit and to help determine how to create a safer space for Kai to receive care
- Recommend testing for HCV RNA to see if an active HCV infection is present
- Review transmission prevention
- Explore acquisition risk factors and offer appropriate supports and referrals
- Review [pre-test counseling information](#), including HCV transmission and reportability
- Try to complete as much of the CRF as you can, taking care not to overwhelm Kai. Ask if it is OK to be in contact with any further questions later if needed.
- Discuss which mode of patient education would work best for Kai (e.g., in person follow-up, mobile texting supports, online resources)

Public Health reporting considerations

Following regional guidelines, enter as a confirmed chronic case of hepatitis C. Enter as "unstaged" in the public health electronic documentation system where appropriate, as there is no prior HCV testing history.

References

- BCCDC Hepatitis C Guidelines:
 - [Section 4.4 Interpretation of Test Results](#)
 - [Section 5.0 Public Health Management](#)
 - [Section 6.0 Acute Case Management](#)
 - [Appendix A: Examples of Laboratory Results](#)
- [Hepatitis Education Canada Resources: Pre- and Post-Test Checklists](#)



Case study #6 – part 2 of 4
Spontaneous Clearance

Clinical History and Lab Results

Kai returns for the HCV RNA results, and they are as follows:

December 2020:

No HCV RNA detected	(no active infection)
Specimen Description	Plasma
Test Name	Results
HCV RNA	0.011566657
HCV RNA (log 10IU/mL)	Not calculated No HCV RNA detected

All other STI results were negative. At the last visit you were able to complete the CRF, and Kai had mentioned that there is sometimes sharing of crack pipes with partners and condomless anal sex. Kai had also injected “down” a few times, but felt it was “nothing serious” and declined any referrals at the time.

You review the results with Kai. What are some things that you would try to talk with Kai about today?

Explanation

It looks like Kai has spontaneously cleared the HCV infection and cannot pass an HCV infection on to others. This can happen in approximately 25% of initial infections

General follow-up considerations

- Review [post-testing counseling information](#), noting that reinfection can still occur even after an infection has cleared, whether spontaneously or due to successful treatment
- Revisit acquisition risk factors and concerns about potential for exposure through IDU, sharing of crack pipes and drug prep materials, and condomless anal sex:
 - Refer Kai to the [Toward the Heart](#) website. The ‘[Find a Site](#)’ feature can help to locate distribution sites in BC where safer sex and drug use supplies are available.
 - Review eligibility for [HIV PrEP indications](#)
- Inquire about any other priorities that Kai needs help with (e.g., housing, food security)
- Talk to Kai about STBBI risks associated with increased IDU, especially in light of the provincial emergency overdose response. Provide or offer resources for Naloxone training

Public Health reporting considerations

Following regional guidelines, update staging to “resolved” HCV infection in the public health electronic documentation system where appropriate.

References

- BCCDC Hepatitis C Guidelines:
 - [Section 4.4 Interpretation of Test Results](#)
 - [Section 5.0 Public Health Management](#)
 - [Appendix A: Examples of Laboratory Results](#)
- [Toward the Heart](#)
 - [Overdose prevention training and resources](#)
 - [Find a site](#)
- [BC Centre for Substance Use](#)
 - [Healthcare Provider Resources](#) > OAT Clinics Accepting New Patients
 - [People Who Use Drugs Resources](#)
- [SmartSex Resource: Pre-Exposure Prophylaxis \(PrEP\)](#)
- [BC Centre for Excellence in HIV/AIDS: HIV Pre-Exposure Prophylaxis \(PrEP\)](#)

**Case study #6 – part 3 of 4**

Contact to HCV/HIV, subsequent testing after prior anti-HCV reactive

Clinical History and Lab Results

A few months have passed (now March 2021). Kai has returned, after being notified by a Public Health Nurse about being a contact to someone who tested positive for HIV and HCV infection. Kai is clearly anxious, teary and upset; but after some discussion, you determine that it is safe to proceed with testing.

Which HCV test(s) would you order? What are some referrals that you could offer?

Explanation

Once someone has tested anti-HCV reactive, it will generally remain reactive for life. HCV RNA should be ordered for any future HCV testing.

General follow-up considerations

- Recommend STI testing, including HCV RNA
- Inquire about recent exposures, offering HIV PEP and CT/GC coverage if appropriate
- Refer to sexual assault services and recommended care if appropriate
- Follow local health authority guidelines regarding follow-up of contacts to HIV and HCV infection.
- Revisit Kai's desire to proceed with supports and referrals regarding increasing drug use, and other priorities for Kai (e.g., housing, food security)
- Provide counseling support options if appropriate (e.g., follow-up visit, referral, text/phone/online counseling support)

References and Resources

- BCCDC Hepatitis C Guidelines:
 - [Section 4.2 HCV Testing](#)
- [Toward the Heart](#)
 - [Overdose prevention training and resources](#)
 - [Find a site](#)
- [BC Centre for Substance Use](#)
 - [Healthcare Provider Resources](#) > OAT Clinics Accepting New Patients
 - [People Who Use Drugs Resources](#)
- [SmartSex Resource: Pre-Exposure Prophylaxis \(PrEP\)](#)
- [BC Centre for Excellence in HIV/AIDS: HIV Pre-Exposure Prophylaxis \(PrEP\)](#)
- [BCCDC Non Certified Practice Decision Support Tool for Prophylaxis Post Sexual Assault](#)
- [BCCDC Blood and Body Fluid Exposure Management Guideline](#)

Case study #6 – part 4 of 4

HCV RNA detected

Clinical History and Lab Results

Several months have passed since the last visit, but Kai has just shown up to be seen at clinic today. The HCV test result is as follows:

<i>HCV RNA detected</i>	<i>(active infection)</i>
<i>Specimen Description</i>	<i>Plasma</i>
<i>Test Name</i>	<i>Results</i>
<i>HCV RNA</i>	<i>215532</i>
<i>HCV RNA(log 10IU/mL)</i>	<i>5.30 HCV RNA detected</i>



The rest of the STI & HIV tests from March 2021 have returned negative.

Kai appears fatigued and is pacing back and forth as you enter the room. Heroin use has increased to daily injections, in addition to smoking crack six or more times a day with a group of friends. Kai started to try to use safe consumption sites for injecting, but sometimes can't wait to get in there.

Kai is quite scared after waking up in hospital last week, being told that emergency ambulance attendants had to use 3 ampoules of Narcan before Kai started to breathe again. An initial prescription for HIV PrEP was filled, but Kai had difficulties remembering to take it, so just stopped. How would you proceed?

Explanation

The presence of HCV RNA indicates an active infection. Individuals with new active HCV infection should be referred to a GP/NP with HCV experience or a specialist to discuss possible HCV treatment for acute infection. There is still a chance that the infection will spontaneously clear again within 6 months.

Note: In this particular scenario, Kai cleared an initial infection spontaneously. However, if an initial infection is cleared after achieving [SVR12](#), it can be difficult to determine if a subsequent HCV infection is a reinfection or relapse after treatment. Review of prior laboratory testing and clinical history, and consultation with the BCCDC PHL, Medical Microbiologist and Surveillance teams, can help to determine case classification in such situations.

General follow-up considerations

- Review the result with Kai: there is an active infection now that can be passed to others.
- Review transmission information, including concerns about ongoing risk for transmission, emphasizing that this is more likely when engaging in IDU, sharing of crack pipes and condomless anal sex
- Provide a referral for HCV treatment:
 - Discuss the availability of highly effective, short duration HCV treatment
 - Do as much of the pre-treatment work-up where possible, as timely follow-up may not be assured
- Given prior challenges taking HIV PrEP without support, try to anticipate potential need for adherence support before challenges arise.
 - Explore local outreach and pharmacy services to see if additional supports can be put in place if Kai starts HCV treatment and HIV PrEP.
- Inquire about other priorities for Kai (e.g., housing, food security), offering referrals for Opioid Agonist Therapy (OAT), Safe Supply sites and counselling as appropriate.
- Work with Kai to see which method of partner notification works best.

Public Health reporting considerations

Following regional guidelines, update the public health electronic documentation system to 'reinfection' where appropriate. Consult with the BCCDC Surveillance team if unsure of how to proceed.

References and Resources

- BCCDC Hepatitis C Guidelines:
 - [Section 4.2 HCV Testing](#)
 - [Section 5.0 Public Health Management](#)
- [Toward the Heart](#)
 - [Overdose prevention training and resources](#)
 - [Find a site](#)
- [BC Centre for Substance Use](#)
 - [Healthcare Provider and People Who Use Drugs Resources](#) > OAT Clinics Accepting New Patients
- [SmartSex Resource: Pre-Exposure Prophylaxis \(PrEP\)](#)
- [BC Centre for Excellence in HIV/AIDS: HIV Pre-Exposure Prophylaxis \(PrEP\)](#)



Appendix G: Resources for Public Health Personnel and Clients

- 1) BCCDC
 - a) BCCDC Public Health Laboratory (PHL): 1-877-747-2522
 - b) [eLab Handbook](#), for information on tests, specimen collection and handling and transport
 - c) [BCCDC PHL Lab Requisition Forms](#)
 - d) [BCCDC Case Definitions](#)
 - e) [BCCDC Case Report Forms](#)
 - f) [BCCDC Communicable Disease Control Manual](#)
 - g) [BCCDC Hepatitis C page](#), for general information
 - h) [Chee Mamuk](#), an Indigenous program providing training, educational resources, and wise practice models in STI, hepatitis and HIV
 - i) [GetCheckedOnline](#), for information on online STI testing (including HCV) availability in BC
 - j) [Harm Reduction Guidelines](#), for information on manuals, newsletters, decision support tools, and links to other harm reduction resources
 - k) [Hepatitis Education Canada](#), for culturally sensitive, multilingual educational resources for clients and health care providers, including an online Indigenous education course
 - l) [ImmunizeBC](#)
 - m) [SmartSexResource](#), for information on STIs for clients and healthcare providers
 - n) [Toward the Heart](#), for information on the take-home naloxone (THN) program, provincial distribution sites for safer sex and drug use supplies, and overdose training and resources
- 2) General Information about HCV
 - a) [HealthLinkBC Files](#)
 - a) [Canadian Liver Foundation](#)
 - b) [Canadian AIDS Treatment Information Exchange \(CATIE\)](#)
 - c) [Dieticians of Canada](#)
 - d) [Canadian Hemophilia Society](#), for information on HCV and HIV tainted blood and compensation
- 3) Advocacy and Community Support Groups
 - a) [Help4HepBC](#), peer-to-peer HCV support by phone or text: 1-888-411-7578
 - b) [BC Hepatitis Network](#), formerly Pacific Hepatitis C Network and HepCBC
- 4) Addictions Training and Guidelines
 - a) [BC Centre on Substance Use](#), for information on addiction research, training and treatment support program, and opioid agonist treatment guidelines
 - b) [College of Physicians and Surgeons of BC](#), for information on Overdose Prevention and Response Training and Methadone Guidelines



REFERENCES

1. Zarski J-P, Bohn B, Bastie A, Pawlotsky J-M, Baud M, Bost-Bezeaux F, et al. Characteristics of patients with dual infection by hepatitis B and C viruses. *Journal of Hepatology*. 1998;28(1):27-33.
2. Pacific Hepatitis C Network. The Four Classes of Hep C Treatment DAAs. Hepatitis C: Treatment Information Project, [Internet]. 2016; 2016(March 10). Available from: <http://www.pacifichepc.org/hepctip/daas/>.
3. University of Washington. Hepatitis C Online. A comprehensive resource that addresses diagnosis, monitoring, and management of hepatitis C virus infection [Internet]. 2016. Available from: <http://www.hepatitisc.uw.edu/>.
4. Ministry of Health, Medical Beneficiary and Pharmaceutical Services Division. Determining fibrosis stage for the treatment of chronic hepatitis C. Information for Prescribers [Internet]. 2014. Available from: <http://www2.gov.bc.ca/assets/gov/health/practitioner-pro/special-authority/fibrosis-info-sheet.pdf>.
5. Polis CB, Shah SN, Johnson KE, Gupta A. Impact of Maternal HIV Coinfection on the Vertical Transmission of Hepatitis C Virus: A Meta-Analysis. *Clinical Infectious Diseases*. 2007;44(8):1123-31.
6. Shah H, Bilodeau M, Burak KW, Cooper C, Klein M, Ramji A, et al. The management of chronic hepatitis C: 2018 guideline update from the Canadian Association for the Study of the Liver. *CMAJ : Canadian Medical Association journal = journal de l'Association medicale canadienne*. 2018;190(22):E677-E87.
7. Yoshida EM, Sulkowski MS, Gane EJ, Herring RW, Jr., Ratziu V, Ding X, et al. Concordance of sustained virological response 4, 12, and 24 weeks post-treatment with sofosbuvir-containing regimens for hepatitis C virus. *Hepatology (Baltimore, Md)*. 2015;61(1):41-5.
8. Lingala S, Ghany MG. Natural History of Hepatitis C. *Gastroenterology clinics of North America*. 2015;44(4):717-34.
9. Westbrook RH, Dusheiko G. Natural history of hepatitis C. *Journal of Hepatology*. 2014;61:S58-S68.
10. Freeman AJ, Law MG, Kaldor JM, Dore GJ. Predicting progression to cirrhosis in chronic hepatitis C virus infection. *Journal of Viral Hepatitis*. 2003;10(4):285-93.
11. Hajarizadeh B, Grebely J, Dore GJ. Epidemiology and natural history of HCV infection. *Nature reviews Gastroenterology & hepatology*. 2013;10(9):553-62.
12. Islam N, Kraiden M, Gilbert M, Gustafson P, Yu A, Kuo M, et al. Role of primary T-cell immunodeficiency and hepatitis B coinfection on spontaneous clearance of hepatitis C: The BC Hepatitis Testers Cohort. *Journal Of Viral Hepatitis*. 2016.
13. Islam N, Kraiden M, Shoveller J, Gustafson P, Gilbert M, Wong J, et al. Hepatitis C cross-genotype immunity and implications for vaccine development. *Scientific Reports*. 2017;7(1):12326-.
14. Canadian Institute for Health Information. Organ replacement in Canada: CORR annual statistics, 2020. Extra-renal transplant data tables. 2020.
15. Vento S, Garofano T, Renzini C, Cainelli F, Casali F, Ghironzi G, et al. Fulminant Hepatitis Associated with Hepatitis A Virus Superinfection in Patients with Chronic Hepatitis C. *New England Journal of Medicine*. 1998;338(5):286-90.
16. Alberti A, Chemello L, Benvegnù L. Natural history of hepatitis C. *Journal of Hepatology*. 1999;31:17-24.
17. Feinstone SM, Kapikian AZ, Purcell RH. Hepatitis A: Detection by Immune Electron Microscopy of a Viruslike Antigen Associated with Acute Illness. *Science*. 1973;182(4116):1026-8.
18. Blumberg BS, Alter HJ. A "New" Antigen in Leukemia Sera. *JAMA*. 1965;191(7):541-6.
19. Choo QL, Kuo G, Weiner AJ, Overby LR, Bradley DW, Houghton M. Isolation of a cDNA clone derived from a blood-borne non-A, non-B viral hepatitis genome. *Science*. 1989;244(4902):359-62.
20. Kuo G, Choo QL, Alter HJ, Gitnick GL, Redeker AG, Purcell RH, et al. An assay for circulating antibodies to a major etiologic virus of human non-A, non-B hepatitis. *Science*. 1989;244(4902):362-4.



21. Canadian Blood Services. Surveillance Report 2014. Available from: <https://www.blood.ca/sites/default/files/blood/blood-safety/External-Surveillance-Report-2014.pdf>.
22. Remis R. Modelling the incidence and prevalence of hepatitis C virus infection and its sequelae in Canada Ottawa: Public Health Agenc of Canada; 2007 [Available from: <https://www.phac-aspc.gc.ca/sti-its-surv-epi/model/pdf/model07-eng.pdf>].
23. Trubnikov M, Yan P, Archibald C. Estimated prevalence of Hepatitis C Virus infection in Canada, 2011. Canada communicable disease report = Relevé des maladies transmissibles au Canada. 2014;40(19):429-36.
24. Myers RP, Krajden M, Bilodeau M, Kaita K, Marotta P, Peltekian K, et al. Burden of disease and cost of chronic hepatitis C infection in Canada. Canadian journal of gastroenterology & hepatology. 2014;28(5):243-50.
25. Hamadeh A, Haines A, Feng Z, Thein H-H, Janjua NZ, Krahn M, et al. Estimating chronic hepatitis C prevalence in British Columbia and Ontario, Canada, using population-based cohort studies. Journal of viral hepatitis. 2020;27(12):1419-29.
26. BCCDC. Reportable Diseases Dashboard Vancouver2021 [cited 2021 January 28]. Available from: <http://www.bccdc.ca/health-professionals/data-reports/reportable-diseases-data-dashboard>.
27. Janjua NZ, Yu A, Kuo M, Alvarez M, Cook D, Wong J, et al. Twin epidemics of new and prevalent hepatitis C infections in Canada: BC Hepatitis Testers Cohort. BMC infectious diseases. 2016;16:334-.
28. Dudani AK, Wu HX, Li Q, Andonov A, Wong T, Jayaraman G, et al. Enhanced Surveillance of Reported Acute Hepatitis C in Canada, 1998 to 2007. Journal of Hepatology. 2010;52:S409-S.
29. Wu H, Wu J, Wong T, Donaldson T, Dinner K, Andonov A, et al. Enhanced surveillance of newly acquired hepatitis C virus infection in Canada, 1998 to 2004. Scandinavian journal of infectious diseases. 2006;38(6/7):482-9.
30. Krajden M, Cook DA, Wong S, Yu A, Butt ZA, Rossi C, et al. What is killing people with hepatitis C virus infection? Analysis of a population-based cohort in Canada. The International journal on drug policy. 2019;72:114-22.
31. The Canadian Network on Hepatitis C Blueprint Writing Committee and Working Groups. Blueprint to inform hepatitis C elimination efforts in Canada. Montreal, QC2019 [cited 2021 Jan 15]. Available from: <https://www.canhepc.ca/en/blueprint/publication>.
32. Krajden M, Cook D, Janjua NZ. Contextualizing Canada's hepatitis C virus epidemic. Canadian Liver Journal. 2018.
33. Said ZNA. An overview of occult hepatitis B virus infection. World Journal Of Gastroenterology. 2011;17(15):1927-38.
34. EASL. EASL 2017 Clinical Practice Guidelines on the Management of Hepatitis B Virus Infection (in press). Journal of Hepatology. 2017;2017.
35. Islam N, Krajden M, Gilbert M, Gustafson P, Yu A, Kuo M, et al. Role of primary T-cell immunodeficiency and hepatitis B coinfection on spontaneous clearance of hepatitis C: The BC Hepatitis Testers Cohort. Journal Of Viral Hepatitis. 2017;24(5):421-9.
36. Micallef JM, Kaldor JM, Dore GJ. Spontaneous viral clearance following acute hepatitis C infection: a systematic review of longitudinal studies. Journal Of Viral Hepatitis. 2006;13(1):34-41.
37. Lok ASF, McMahon BJ. AASLD Practice Guidelines, Chronic Hepatitis B: Update 2009. Hepatology. 2009;50(3):1-35.
38. Coffin CS, Fung SK, Ma MM, Canadian Association for the Study of the L. Management of chronic hepatitis B: Canadian Association for the Study of the Liver consensus guidelines. Canadian Journal Of Gastroenterology = Journal Canadien De Gastroenterologie. 2012;26(12):917-38.
39. Government of Canada. Direct-acting antivirals, used for hepatitis C, may reactivate hepatitis B Ottawa2016 [Available from: <http://healthycanadians.gc.ca/recall-alert-rappel-avis/hc-sc/2016/61274a-eng.php>].



40. Platt L, Easterbrook P, Gower E, McDonald B, Sabin K, McGowan C, et al. Prevalence and burden of HCV co-infection in people living with HIV: a global systematic review and meta-analysis. *The Lancet Infectious Diseases*. 2016;16(7):797-808.
41. Centers for Disease Control and Prevention. Atlanta: US Department of Health and Human Services, Centers for Disease Control and Prevention 2017. Available from: <https://www.cdc.gov/hepatitis/populations/hiv.htm#ref08>.
42. Garg S, Brooks JT, Luo Q, Skarbinski J. 1588: Prevalence of and Factors Associated with Hepatitis C Virus Testing and Infection Among HIV-infected Adults Receiving Medical Care in the United States. *Open Forum Infectious Diseases*. 2014;1(Suppl 1):S423-S.
43. Buxton JA, Yu A, Kim PH, Spinelli JJ, Kuo M, Alvarez M, et al. HCV co-infection in HIV positive population in British Columbia, Canada. *BMC public health*. 2010;10:225-35.
44. British Columbia Centre for Disease Control. BC Centre for Disease Control Position Statement: Harm Reduction. Vancouver, BC: British Columbia Centre for Disease Control; 2018 Oct.
45. Government of British Columbia. Provincial health officer declares public health emergency. BC Gov News 2016 Apr 14 [2021 Jan 14]. Available from: <https://news.gov.bc.ca/releases/2016HLTH0026-000568>.
46. British Columbia Coroners Service. Illicit Drug Toxicity Deaths in BC: January 1, 2010 – November 30, 2020 British Columbia Ministry of Public Safety & Solicitor General; December 21, 2020 [cited 2021 Jan 14]. Available from: <https://www2.gov.bc.ca/assets/gov/birth-adoption-death-marriage-and-divorce/deaths/coroners-service/statistical/illicit-drug.pdf>.
47. British Columbia Coroners Service. Fentanyl-Detected Illicit Drug Toxicity Deaths January 1, 2012 to November 30, 2020: British Columbia Ministry of Public Safety & Solicitor General; December 21, 2020 [cited 2021 Jan 14]. Available from: <https://www2.gov.bc.ca/assets/gov/birth-adoption-death-marriage-and-divorce/deaths/coroners-service/statistical/fentanyl-detected-overdose.pdf>.
48. Kronfli N, Bhatnagar SR, Hull MW, Moodie EEM, Cox J, Walmsley S, et al. Trends in cause-specific mortality in HIV-hepatitis C coinfection following hepatitis C treatment scale-up. *AIDS (London, England)*. 2019;33(6):1013-22.
49. Kerr T, Small W, Buchner C, Zhang R, Li K, Montaner J, et al. Syringe sharing and HIV incidence among injection drug users and increased access to sterile syringes. *American journal of public health*. 2010;100(8):1449-53.
50. Papamihali K, Ng J, Buxton J. Harm Reduction Strategies and Services Policy Indicators Report: Review of data to December 2019. Vancouver, BC: BC Centre for Disease Control (BCCDC); July 2020.
51. British Columbia Centre for Disease Control. Take Home Naloxone Program in BC: Towards the Heart; December 2020 [cited 2021 Jan 14]. Available from: <https://towardtheheart.com/thn-in-bc-infograph>.
52. British Columbia Centre for Disease Control. BC Centre for Disease Control and Provincial Health Officer Position Statement: Observed Consumption Services: British Columbia Centre for Disease Control; 2019 [updated June 14, 2019; cited 2021 Jan 14]. Available from: http://www.bccdc.ca/resource-gallery/Documents/Statistics%20and%20Research/Statistics%20and%20Reports/Overdose/Final_OCSStatement_June2019.pdf.
53. Strike C WT, Gohil H, Miskovic M, Robinson S, Arkell C, Challacombe L, Amlani A BJ, Demel G, Gutiérrez N, Heywood D, Hopkins S, Lampkin H, Leonard L, Lockie L, Millson P, Nielsen D PD, Young S, Zurba N. The Best Practice Recommendations for Canadian Harm Reduction. Programs that Provide Service to People Who Use Drugs and are at Risk for HIV, HCV, and Other Harms: Part 2. Toronto, ON; 2015.
54. British Columbia Centre for Disease Control. 2018 BC Harm Reduction Client Survey: BC Overall 2019 [Available from: http://www.bccdc.ca/resource-gallery/Documents/Statistics%20and%20Research/Statistics%20and%20Reports/Overdose/BC_HR_survey_2018_May2.pdf].



55. British Columbia Centre for Disease Control. Overdose Response Indicator Report Vancouver, BC: BCCDC; November 2020 [cited 2021 Jan 14]. Available from: <http://www.bccdc.ca/resource-gallery/Documents/Statistics%20and%20Research/Statistics%20and%20Reports/Overdose/Overdose%20Response%20Indicator%20Report.pdf>.
56. British Columbia Centre on Substance Use British Columbia Ministry of Health. A Guideline for the Clinical Management of Opioid Use Disorder. Vancouver, BC; June 2017.
57. Gowing L, Farrell MF, Bornemann R, Sullivan LE, Ali R. Oral substitution treatment of injecting opioid users for prevention of HIV infection. The Cochrane database of systematic reviews. 2011(8):CD004145.
58. J. Macarthur G, Minozzi S, Martin N, Vickerman P, Deren S, Bruneau J, et al. Opiate substitution treatment and HIV transmission in people who inject drugs: systematic review and meta-analysis. *BMJ: British Medical Journal*. 2012;345(7879):16-.
59. Nolan S, Dias Lima V, Fairbairn N, Kerr T, Montaner J, Grebely J, et al. The impact of methadone maintenance therapy on hepatitis C incidence among illicit drug users. *Addiction*. 2014;109(12):2053-9.
60. Platt L, Minozzi S, Reed J, Vickerman P, Hagan H, French C, et al. Needle and syringe programmes and opioid substitution therapy for preventing HCV transmission among people who inject drugs: Findings from a Cochrane Review and meta-analysis. *Addiction*. 2018;113(3):545-63.
61. Fullerton CA, Kim M, Thomas CP, Lyman DR, Montejano LB, Dougherty RH, et al. Medication-assisted treatment with methadone: Assessing the evidence. *Psychiatric Services*. 2014;65(2):146-57.
62. Mattick RP, Breen C, Kimber J, Davoli M. Methadone maintenance therapy versus no opioid replacement therapy for opioid dependence. The Cochrane database of systematic reviews. 2009(3):CD002209.
63. Nielsen S, Larance B, Degenhardt L, Gowing L, Kehler C, Lintzeris N. Opioid agonist treatment for pharmaceutical opioid dependent people. The Cochrane database of systematic reviews. 2016(5):CD011117.
64. Thomas CP, Fullerton CA, Kim M, Montejano L, Lyman DR, Dougherty RH, et al. Medication-assisted treatment with buprenorphine: Assessing the evidence. *Psychiatric Services*. 2014;65(2):158-70.
65. Bell JR, Butler B, Lawrance A, Batey R, Salmelainen P. Comparing overdose mortality associated with methadone and buprenorphine treatment. *Drug and Alcohol Dependence*. 2009;104(1-2):73-7.
66. Liao D-L, Chen P-C, Chen C-H, Hsieh C-J, Huang Y-F, Shih W-Y, et al. Higher methadone doses are associated with lower mortality in patients of opioid dependence in Taiwan. *Journal of Psychiatric Research*. 2013;47(10):1530-4.
67. Marteau D, McDonald R, Patel K. The relative risk of fatal poisoning by methadone or buprenorphine within the wider population of England and Wales. *BMJ open*. 2015;5(5):e007629.
68. van Ameijden EJC, Langendam MW, Coutinho RA. Dose-effect relationship between overdose mortality and prescribed methadone dosage in low-threshold maintenance programs. *Addictive Behaviors*. 1999;24(4):559-63.
69. Pearce LA, Min JE, Piske M, Zhou H, Homayra F, Slaunwhite A, et al. Opioid agonist treatment and risk of mortality during opioid overdose public health emergency: Population based retrospective cohort study. *BMJ: British Medical Journal*. 2020;368.
70. Joseph LP, Rachlin JA. Use and effectiveness of chest radiography and low-back radiography in screening. *Journal of occupational medicine : official publication of the Industrial Medical Association*. 1986;28(10):998-1003.
71. Palepu A, Tyndall MW, Joy R, Kerr T, Wood E, Press N, et al. Antiretroviral adherence and HIV treatment outcomes among HIV/HCV co-infected injection drug users: the role of methadone maintenance therapy. *Drug and alcohol dependence*. 2006;84(2):188-94.
72. Perlman DC, Jordan AE, Uuskula A, Huong DT, Masson CL, Schackman BR, et al. An international perspective on using opioid substitution treatment to improve hepatitis C prevention and care for people who inject drugs: Structural barriers and public health potential. *International Journal of Drug Policy*. 2015;26(11):1056-63.



73. Boucher M, Gruslin A. No. 96-The Reproductive Care of Women Living With Hepatitis C Infection. *Journal of obstetrics and gynaecology Canada : JOGC = Journal d'obstetrique et gynecologie du Canada : JOGC.* 2017;39(7):e1-e25.
74. Schillie S, Wester C, Osborne M, Wesolowski L, Ryerson AB. CDC Recommendations for Hepatitis C Screening Among Adults - United States, 2020. *MMWR Recommendations and reports : Morbidity and mortality weekly report Recommendations and reports.* 2020;69(2):1-17.
75. The American Association for the Study of Liver Diseases and the Infectious Diseases Society of America (AASLD-IDSA). Hepatitis C Guidance 2018 Update: AASLD-IDSA Recommendations for Testing, Managing, and Treating Hepatitis C Virus Infection. *Clinical Infectious Diseases.* 2018;67(10):1477-92.
76. Centers for Disease Control and Prevention. Hepatitis C Questions and Answers for the Public Atlanta, GA: U.S. Department of Health & Human Services; [updated July 28, 2020; cited 2021 Jan 15]. Available from: <https://www.cdc.gov/hepatitis/hcv/cfaq.htm>.
77. Centers for Disease Control and Prevention. Hepatitis C Questions and Answers for Health Professionals Atlanta, GA: U.S. Department of Health & Human Services; [updated August 7, 2020; cited 2021 Jan 15]. Available from: <https://www.cdc.gov/hepatitis/hcv/hcvfaq.htm>.
78. Tohme RA, Holmberg SD. Is sexual contact a major mode of hepatitis C virus transmission? *Hepatology (Baltimore, Md).* 2010;52(4):1497-505.
79. Terrault NA, Dodge JL, Murphy EL, Tavis JE, Kiss A, Levin TR, et al. Sexual transmission of hepatitis C virus among monogamous heterosexual couples: the HCV partners study. *Hepatology (Baltimore, Md).* 2013;57(3):881-9.
80. Vandelli C, Renzo F, Romanò L, Tisminetzky S, De Palma M, Stroffolini T, et al. Lack of evidence of sexual transmission of hepatitis C among monogamous couples: results of a 10-year prospective follow-up study. *The American journal of gastroenterology.* 2004;99(5):855-9.
81. British Columbia Hepatitis Testers Cohort (BC-HTC). Countries of origin of persons diagnosed with Hepatitis C between 2011-2015 as identified with the validated name-recognition software Onomap. Unpublished data. Note: China, Hong Kong and Taiwan are grouped due to similarities in naming.
82. Jafari S, Buxton JA, Afshar K, Copes R, Baharlou S. Tattooing and risk of hepatitis B: a systematic review and meta-analysis. *Canadian Journal Of Public Health = Revue Canadienne De Santé Publique.* 2012;103(3):207-12.
83. Benova L, Mohamoud YA, Calvert C, Abu-Raddad LJ. Vertical transmission of hepatitis C virus: systematic review and meta-analysis. *Clinical infectious diseases : an official publication of the Infectious Diseases Society of America.* 2014;59(6):765-73.
84. Roberts EA, Yeung L. Maternal-infant transmission of hepatitis C virus infection. *Hepatology (Baltimore, Md).* 2002;36(5 Suppl 1):S106-S13.
85. Garcia-Tejedor A, Maiques-Montesinos V, Diago-Almela VJ, Pereda-Perez A, Alberola-Cuñat V, López-Hontangas JL, et al. Risk factors for vertical transmission of hepatitis C virus: a single center experience with 710 HCV-infected mothers. *European journal of obstetrics, gynecology, and reproductive biology.* 2015;194:173-7.
86. Chappell CA, Hillier SL, Crowe D, Meyn LA, Bogen DL, Krans EE. Hepatitis C Virus Screening Among Children Exposed During Pregnancy. *Pediatrics.* 2018;141(6).
87. BCCDC Public Health Laboratory. BCCDC Public Health Laboratory Update: Hepatitis C reflex testing Vancouver, BC: SmartSexResource; January 16, 2020 [cited 2021 Jan.19]. Available from: <https://smartsexresource.com/health-providers/blog/202001/bccdc-public-health-laboratory-update-hepatitis-c-reflex-testing>.
88. Janjua NZ, Kuo M, Chong M, Yu A, Alvarez M, Cook D, et al. Assessing Hepatitis C Burden and Treatment Effectiveness through the British Columbia Hepatitis Testers Cohort (BC-HTC): Design and Characteristics of Linked and Unlinked Participants. *PloS one.* 2016;11(3):e0150176-e.



89. Bartlett SR, Yu A, Chapinal N, Rossi C, Butt Z, Wong S, et al. The population level care cascade for hepatitis C in British Columbia, Canada as of 2018: Impact of direct acting antivirals. *Liver International: Official Journal Of The International Association For The Study Of The Liver*. 2019;39(12):2261-72.
90. Polywka S, Pembrey L, Tovo P-A, Newell M-L. Accuracy of HCV-RNA PCR tests for diagnosis or exclusion of vertically acquired HCV infection. *Journal of medical virology*. 2006;78(2):305-10.
91. England K, Pembrey L, Tovo P-A, Newell M-L. Excluding hepatitis C virus (HCV) infection by serology in young infants of HCV-infected mothers. *Acta paediatrica (Oslo, Norway : 1992)*. 2005;94(4):444-50.
92. The American Association for the Study of Liver Diseases and the Infectious Diseases Society of America (AASLD-IDSA). HCV Guidance: Recommendations for Testing, Managing, and Treating Hepatitis C. HCV in Children 2021 [cited 2021 Jan 21]. Available from: <https://www.hcvguidelines.org/unique-populations/children>.
93. Jhaveri R. We Need a New National Strategy for Hepatitis C Virus Screening. *Pediatrics*. 2020;145(3).
94. Towers CV, Fortner KB. Infant follow-up postdelivery from a hepatitis C viral load positive mother. *The journal of maternal-fetal & neonatal medicine : the official journal of the European Association of Perinatal Medicine, the Federation of Asia and Oceania Perinatal Societies, the International Society of Perinatal Obstetricians*. 2019;32(19):3303-5.
95. Hojat LS, Greco PJ, Bhardwaj A, Bar-Shain D, Abughali N. Using Preventive Health Alerts in the Electronic Health Record Improves Hepatitis C Virus Testing Among Infants Perinatally Exposed to Hepatitis C. *The Pediatric infectious disease journal*. 2020;39(10):920-4.
96. Gowda C, Smith S, Crim L, Moyer K, Sánchez PJ, Honegger JR. Nucleic Acid Testing for Diagnosis of Perinatally-Acquired Hepatitis C Virus Infection in Early Infancy. *Clinical infectious diseases : an official publication of the Infectious Diseases Society of America*. 2020.
97. Greenaway E, Biondi M, Feld J, Ling S. Hepatitis C virus infection in mothers and children. *Canadian Liver Journal*. 2019;2(4):210-24.
98. Mack CL, Gonzalez-Peralta RP, Gupta N, Leung D, Narkewicz MR, Roberts EA, et al. NASPGHAN practice guidelines: Diagnosis and management of hepatitis C infection in infants, children, and adolescents. *Journal of pediatric gastroenterology and nutrition*. 2012;54(6):838-55.
99. Manns MP, Wedemeyer H, Cornberg M. Treating viral hepatitis C: efficacy, side effects, and complications. *Gut*. 2006;55(9):1350-9.
100. Government of BC. Chronic hepatitis C medication now available for all British Columbians March 13, 2018 [cited 2021 Jan 26].