BLUEPRINT TO INFORM HEPATITIS C ELIMINATION EFFORTS IN CANADA

Citation

Material appearing in this publication may be reproduced or copied without permission. The following citation is recommended:

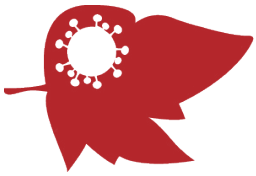
The Canadian Network on Hepatitis C *Blueprint* Writing Committee and Working Groups. *Blueprint* to inform hepatitis C elimination efforts in Canada. Montreal, QC: Available at: canhepc.ca/sites/default/files/media/documents/blueprint_hcv_2019_05.pdf (accessed [date]).

May 2019

This publication is available in English and French on the Canadian Network on Hepatitis C (CanHepC)'s website at:

www.canhepc.ca/en/blueprint/publication.

Visit the website for the most up-to-date version of this publication and for more information on the CanHepC network.



CanHepC

Canadian Network on Hepatitis C
Réseau Canadien sur l'Hépatite C

BLUEPRINT TO INFORM HEPATITIS C ELIMINATION EFFORTS IN CANADA

May 2019

TABLE OF CONTENTS

ABBREVIATIONS

BBI blood-borne infections

BC British Columbia

BCCDC British Colombia Centre for Disease Control

BC-HTC British Colombia Hepatitis Testers Cohort

cAg core antigen

CanHepC Canadian Network on Hepatitis C

CASL Canadian Association for the Study of the Liver

DAA direct-acting antiviral (s)

DBS dried blood spot

ECHO Extension for Community Healthcare Outcomes

gbMSM gay and bisexual men who have sex with men

GHSS Global Health Sector Strategy

HCV hepatitis C virus

HIV human immunodeficiency virus

ICER incremental cost-effectiveness ratio

NSP needle syringe programs

OAT opioid agonist therapy

OPS overdose prevention sites

pCPA pan-Canadian Pharmaceutical Alliance

PHAC Public Health Agency of Canada

PoC point-of-care

PrEP HIV pre-exposure prophylaxis

PWID people who inject drugs

PWUD people who use drugs

QALY quality adjusted life year

SCS supervised consumption services /sites

STBBI sexually transmitted and blood-borne infections

SVR sustained virologic response

TasP treatment as prevention

WHO World Health Organization

FOREWORD

Progress in the hepatitis C virus (HCV) field represents one of the major medical breakthroughs of our time. Discovered in 1989, HCV quickly emerged as the leading cause of liver disease and liver transplantation. For nearly 25 years, we had little to offer people living with the infection and struggling with its complications; treatments were toxic and ineffective. The past few years have seen everything change. We can now offer safe, well-tolerated, simple treatments with cure rates above 95%. Seeing people move on with their lives after HCV is incredibly gratifying. This rapid progress has given us the rare opportunity to eliminate an infectious disease as a public health problem in Canada.

But achieving this ambitious goal is no small task and will take a lot more than effective treatments. The World Health Organization (WHO) is aiming for the global elimination of viral hepatitis as a public health threat by 2030, and has called on all countries to develop national action plans. Although Canada has outstanding expertise across the spectrum of HCV care and research, we do not have a specific national action plan on viral hepatitis.

Healthcare is primarily a provincial and territorial responsibility, making it difficult to develop a single plan that is applicable across the country. However, if we do not coordinate our efforts, despite our effective treatments, the consequences of HCV will continue to rise, and we are unlikely to reach elimination. It was with this in mind that we developed this *Blueprint* to inform hepatitis C elimination efforts in Canada.

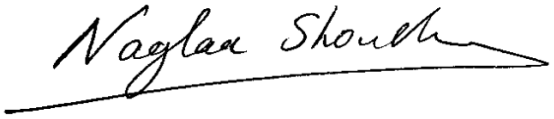
We took on this effort as members of the Canadian Network on Hepatitis C, a national research and training network, which brings together a diverse group of experts and community members from all over the country, and across key disciplines critical to inform HCV policy in Canada. Recognizing that the challenges of HCV vary considerably across the country, we proposed a *Blueprint* rather than a specific national action plan.

The purpose of the *Blueprint* is to define what needs to be done as a public health response to achieve HCV elimination in Canada. High level objectives in the areas of Prevention, Testing and diagnosis, and Care and treatment are broken down into measurable and time-bound targets that we believe are required to meet the WHO elimination goals. Specific considerations are raised for Priority populations, groups that are disproportionately affected by HCV and/or have challenges in accessing HCV services. The *Blueprint* is specific about what must be achieved; the what is clearly defined but the who and the how are not. Ultimately, the *Blueprint* will serve as a menu of options, with specific targets, suggested activities and evidence-based good practices for provinces and territories to develop their own HCV action plans to meet those targets.

We hope the *Blueprint* will help keep us on track for HCV elimination by 2030, ensuring that we monitor our progress collectively, and learn from each other's experiences. We look forward to working with colleagues across the country to turn this *Blueprint* into defined action leading to a Canada free of HCV.

Jordan Feld, MD, MPH

Chairman, *Blueprint* Writing Committee



Naglaa Shoukry, BPharm, PhD

Director, Canadian Network on Hepatitis C

EXECUTIVE SUMMARY

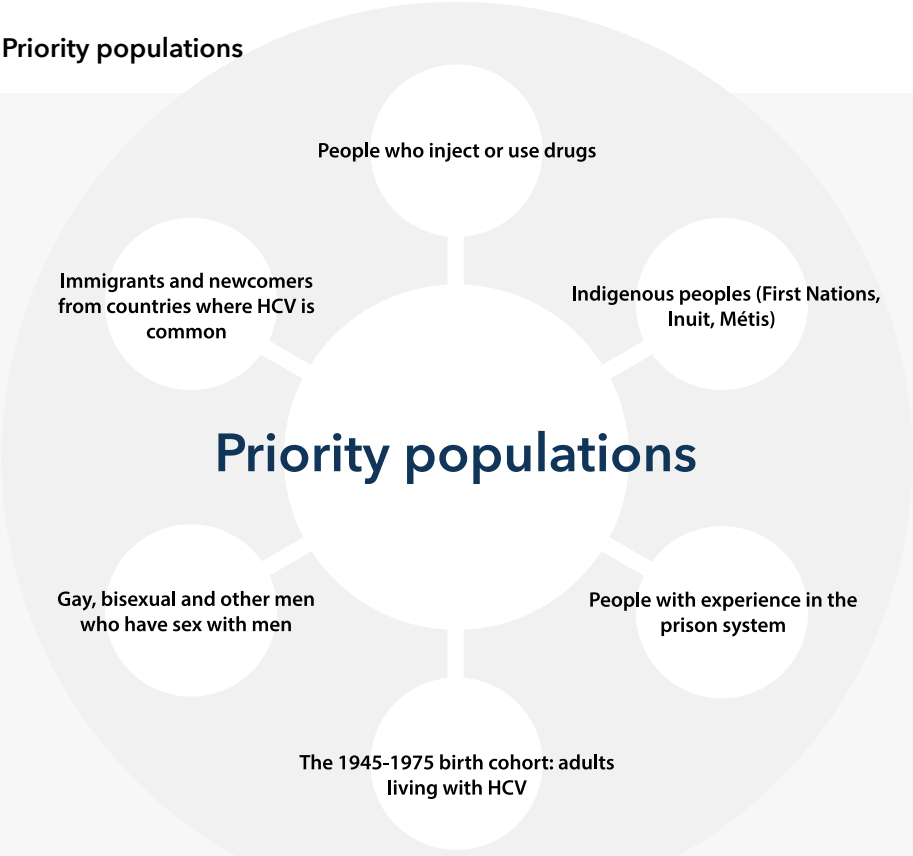
Although preventable and curable, hepatitis C virus (HCV) infection has been described as Canada's "most burdensome infectious illness" since it causes more years of life lost than any other infectious disease in the country.[1] Without urgent actions, HCV will continue to spread, and Canada will face increasing rates of HCV-related illness and death in the coming years, with a corresponding surge in healthcare costs.[2]

There is no vaccine for HCV, and new infections continue to occur at an alarming rate. HCV disproportionally affects a number of populations in Canada, including people who inject drugs (among whom up to 85% of new infections occur), Indigenous peoples, people with experience in Canada's federal and provincial prisons, immigrants and newcomers from countries where there are high rates of HCV, and gay and bisexual men who have sex with men (gbMSM).[3-9]

Addressing HCV in Canada will require specific efforts in these groups that are often left behind by mainstream programs for HCV care. People in these Priority populations (Figure 1) may need tailored interventions to ensure that they have equitable access to high quality HCV services. Many people who are at risk for, or living with HCV face stigma and discrimination, which discourage them from seeking prevention, testing, treatment and care, as well as other essential social services.[10, 11] De-stigmatizing HCV is crucial for successful delivery of services that will reach people who need them most.

Increasing access to HCV testing in Canada is essential, so that people who are living with HCV can be diagnosed and linked to care and treatment. HCV causes few symptoms in most people until liver damage is very advanced, which may explain why over 40% of the estimated 250,000 people living with HCV in Canada are unaware of their infection.[8]

Figure 1. Canada's Priority populations



Canada is facing twin HCV epidemics - one of new infections, primarily among young people who inject drugs (PWID), and one of long-standing HCV infections among people born between 1945 and 1975. People born between 1945 and 1975 account for over 60% of HCV infections in Canada.[3, 9] As they age, rates of liver failure, liver cancer and death among this birth cohort are expected to rise rapidly.[2] In addition to the human toll, the increasing rate of complications from HCV will be very costly to the healthcare system.

Fortunately, unlike other chronic viral infections, HCV is curable. Remarkable progress has led to development of highly effective new treatments, direct-acting antivirals (DAAs), which cure over 95% of people with 8 to 12 weeks of once-daily pills that have few or no side effects. Cure stops HCV progression, reduces the risk for liver-related morbidity and mortality, all-cause mortality, and improves quality of life.[12-16]

HCV treatment has an added public health benefit: prevention. By curing people living with HCV, onward transmission to others is prevented.[17-19] Treatment is not the only preventative approach. Evidence-based harm-reduction strategies such as high-coverage needle syringe programs and opioid agonist therapy can reduce the risk of HCV transmission along with other proven benefits that reduce the devastating toll of opioid overdoses in Canada.[20]

Now that HCV can be easily cured, momentum around global and national strategies to eliminate HCV has been building. In 2016, Canada endorsed the United Nations *Sustainable Development Goals* and the World Health Organization (WHO) *Global Health Sector Strategy* (GHSS) for viral hepatitis and adopted its targets – including eliminating HCV as a public health threat by 2030.[21]

In 2018, the Public Health Agency of Canada (PHAC) launched the *Pan-Canadian Framework for Action to Reduce the Impact of Sexually Transmitted and Blood-borne Infections (STBBI)* - which includes HCV, and is aligned with WHO timelines and targets.[22] This framework is based on a syndemic approach to disease, which considers how different illnesses worsen each other – and how inequities and social, economic, environmental and other circumstances increase their harm.[23, 24] It calls for an approach grounded in cultural relevance, human rights and health equity, and the recognition that services must reflect "…different cultures, genders, orientations, and abilities… and address a range of psychological, emotional, cultural, physical health, and practical needs."[12]

The *Blueprint to inform hepatitis C elimination efforts in Canada* was created to complement the *Pan-Canadian STBBI Framework for Action* with tangible steps built around its pillars, linked to objectives and time-bound, measurable targets (Table 1). It is divided into four sections: ***Priority populations, Prevention, Testing and diagnosis, Care and treatment***, each including key objectives for developing the infrastructure and tools needed to achieve targets. There are many ways to achieve the same goals, and major differences across the country in terms of the HCV burden and healthcare delivery, so each section includes ***Suggested activities*** with recommended ***Good practices*** that highlight evidence-based HCV interventions. A ***Research agenda*** is also included to address key knowledge gaps related to HCV prevention, testing, care and treatment.

The *Blueprint* is designed to offer options that can be tailored to different contexts, cultures, populations and areas, and to ensure equity across its objectives and targets for all Priority populations. Ultimately, the goal of this *Blueprint* is to provide provinces, territories and the federal government with a menu of options for developing action plans relevant to their unique situations, to collectively lead to the **elimination of HCV as a public health threat in Canada**.

Figure 1. The *Blueprint*'s objectives and targets

OBJECTIVES	2025 TARGETS	2030 TARGETS
HCV Prevention		
Reduce new HCV infections	**80%** ↓ incidence*	**80%** ↓ incidence*
Increase the number of sterile needles and syringes provided per person who injects drugs (PWID) per year	**500** sterile needles/syringes	**750** sterile needles/syringes
Increase the number of PWID accessing opioid agonist therapy (OAT)	**40%** of PWID receive OAT	**≥40%** of PWID receive OAT**
HCV Testing and diagnosis		
Increase the number of people living with HCV who have been diagnosed	**70%** of people living with HCV have been diagnosed, all with confirmation of active infection	**90%** of people living with HCV have been diagnosed, all with confirmation of active infection
Increase the number of people with a positive HCV antibody test who receive testing for active HCV infection (e.g. HCV RNA)	**90%** of people with a positive antibody test have received HCV RNA testing	**100%** of people with positive antibody test have received HCV RNA testing
HCV Care and treatment		
Increase the number of people diagnosed with HCV who are linked to care, treatment and ongoing support	**50%** linked to a provider who is familiar with HCV	**90%** linked to a provider who is familiar with HCV
Increase the number of people with HCV who are initiating DAA treatment	**50%** of those living with HCV have initiated DAA treatment	**80%** of those living with HCV have initiated DAA treatment
Ensure high treatment completion rates and documentation of sustained virologic response (SVR)	**95%** treatment completion with 85% documentation of SVR	**95%** treatment completion with 85% documentation of SVR
Reduce HCV prevalence	**50%** ↓ *	**90%** ↓ *
Reduce HCV-related liver transplantation	**30%** ↓ *	**65%** ↓ *
Reduce HCV-related mortality	**30%** ↓ *	**65%** ↓ *

**Compared to 2015;*

***Target to be revised according to mathematical modeling studies.*

GLOBAL SCOPE OF THE HEPATITIS C EPIDEMIC

Globally, an estimated 71 million people are living with chronic HCV infection.[25] In 2015, over 400,000 people died from HCV-related complications, and millions more are expected to develop liver failure and liver cancer in the coming years.[25] Although HCV is preventable, it continues to spread: an estimated 1.75 million people were newly infected with HCV in 2015.[25]

71 MILLION

GLOBAL HEPATITIS C ELIMINATION

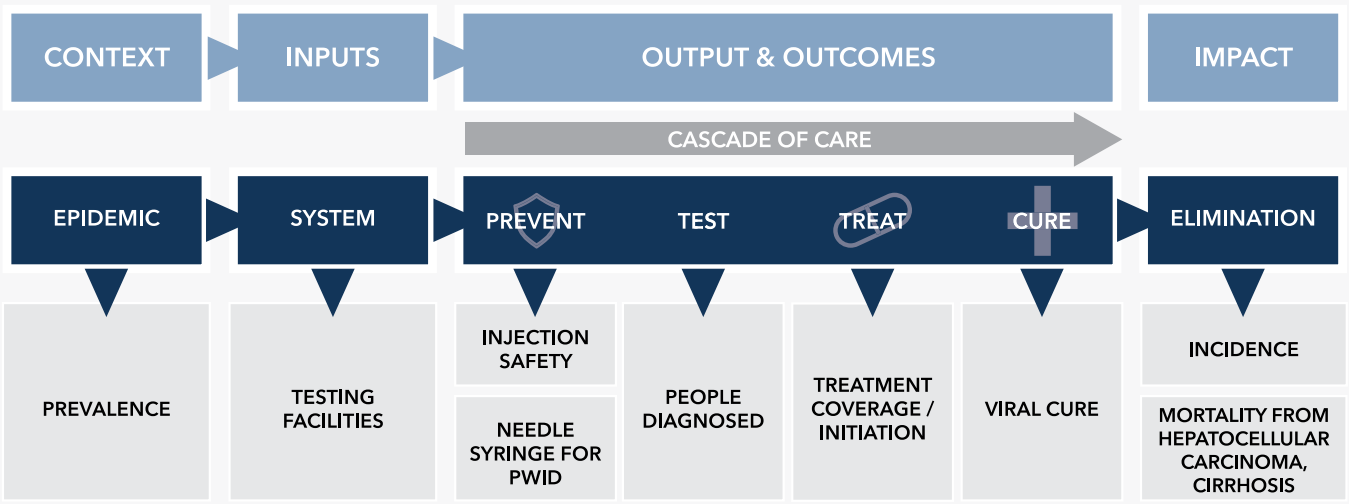
It is currently not possible to eradicate HCV globally, which would mean the permanent reduction to zero infections worldwide. Instead, the WHO has called for elimination of HCV as a public health threat.

The world has the tools to eliminate HCV: evidence-based prevention, simple diagnostic tests, highly effective safe treatment, and a set of global targets to monitor progress from the WHO *Global Health Sector Strategy on Viral Hepatitis (GHSS)* 2016-2021. The GHSS outlines specific targets for synergistic prevention and treatment services with the aim of reducing the number of new HCV infections by 80% and mortality from HCV by 65% by 2030 compared to 2015 levels, effectively eliminating viral hepatitis as a threat to global public health.[21] The GHSS was endorsed by the World Health Assembly's 194 member states, including Canada, in May 2016.

Table 2. GHSS targets for hepatitis C virus (HCV) elimination [21]

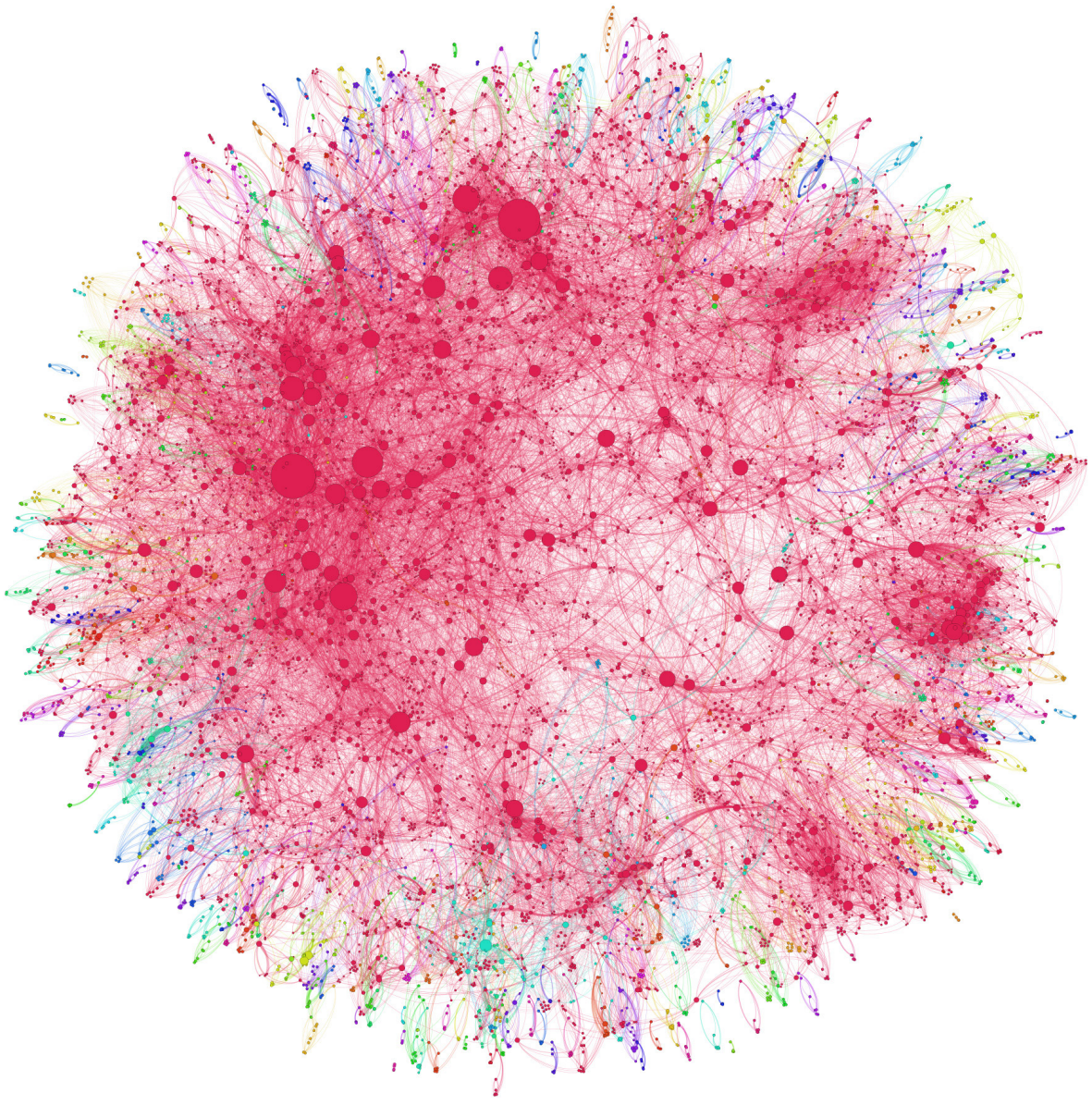
Impact Target	2015 Baseline	2020 Targets	2030 Targets
Incidence of new HCV infections	1.75 million	30% reduction (1.23 million)	80% reduction (350,000)
Mortality from HCV	402,000	10% reduction (361,800)	65% reduction (140,700)
Service Coverage	**2015 Baseline**	**2020 Targets**	**2030 Targets**
HCV diagnosis	>5% ~335,000	30% (21.3 million)	90% (63.9 million)
HCV treatment	<1% ~500,000 with DAAs	~4% (3 million)	80% (56.8 million)

Figure 2. Monitoring and evaluating progress towards hepatitis C virus elimination [26]



There is no effective HCV vaccine. Even with a protective vaccine, it may not be possible to completely eradicate HCV at the global level, but the public health burden can be eliminated with curative treatment, and prevention. Canada has been a leader in vaccine research, and hopefully a vaccine will be developed over the coming years. In the meantime, reaching people who need access to prevention services and/or effective treatment will significantly decrease HCV-related morbidity and mortality and could greatly reduce new HCV infections, by preventing onward transmission. With effective, coordinated strategies, these efforts could reduce the health burden of HCV at the national level to a point where HCV has been eliminated as a public health threat to Canadians.

Elimination has benefits beyond liver disease and HCV. Setting up the infrastructure necessary to achieve elimination will greatly strengthen public health systems, from data collection to service delivery. In countries on track for elimination, one of the major benefits of the response to HCV has been the strengthening of the public health system to address many other pressing health issues. These testing and treatment systems can be used for other blood-borne and sexually transmitted infections and the harm-reduction initiatives have major benefits for other health consequences of drug use including the opioid epidemic. Developing improved tools for data collection and linkage allows forw better monitoring across the health system. Recognizing the benefits beyond HCV makes an even stronger case for striving toward elimination.



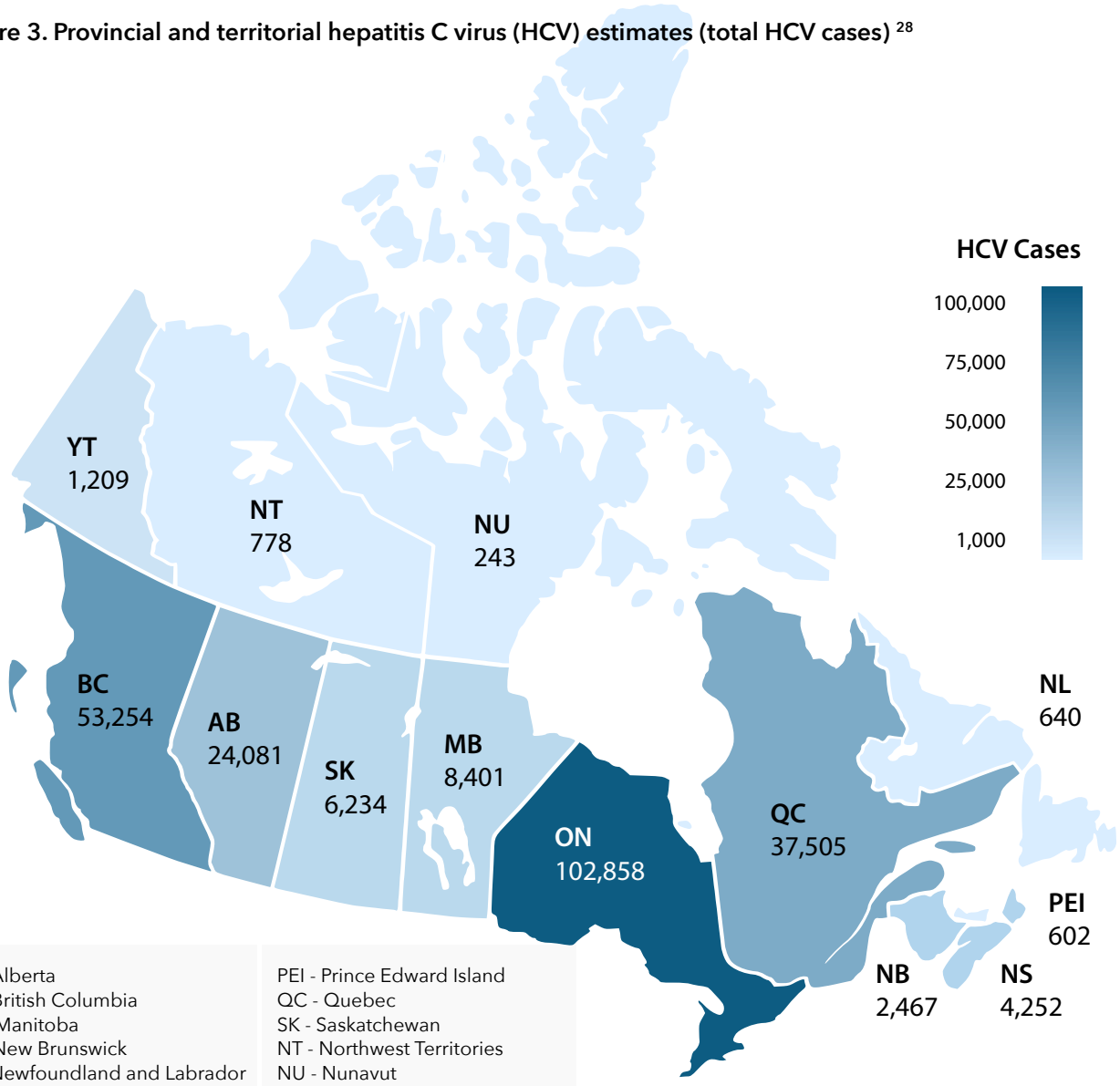
Co-authorship network map of physicians publishing on hepatitis C - Andy Lamb

HEPATITIS C IN CANADA

There are 'twin epidemics" of HCV in Canada: one of new infections primarily among younger people, mainly those who inject drugs who are at ongoing risk for HCV, and one among people born between 1945 and 1975, who acquired HCV years or even decades ago. People with long-standing HCV are at high risk for liver-related illness and death as well as non-liver related complications of HCV if they remain undiagnosed or are not treated. Recent estimates suggest the prevalence may be higher than previously recognized and complications of HCV are on the rise.[27]

High-quality data on the number of people living with HCV in Canada and the number of new infections that occur each year across the country are lacking. Different modeling approaches have been used to develop estimates, with most coming to a similar conclusion: approximately 250,000 Canadians are infected.

Figure 3. Provincial and territorial hepatitis C virus (HCV) estimates (total HCV cases) [28]



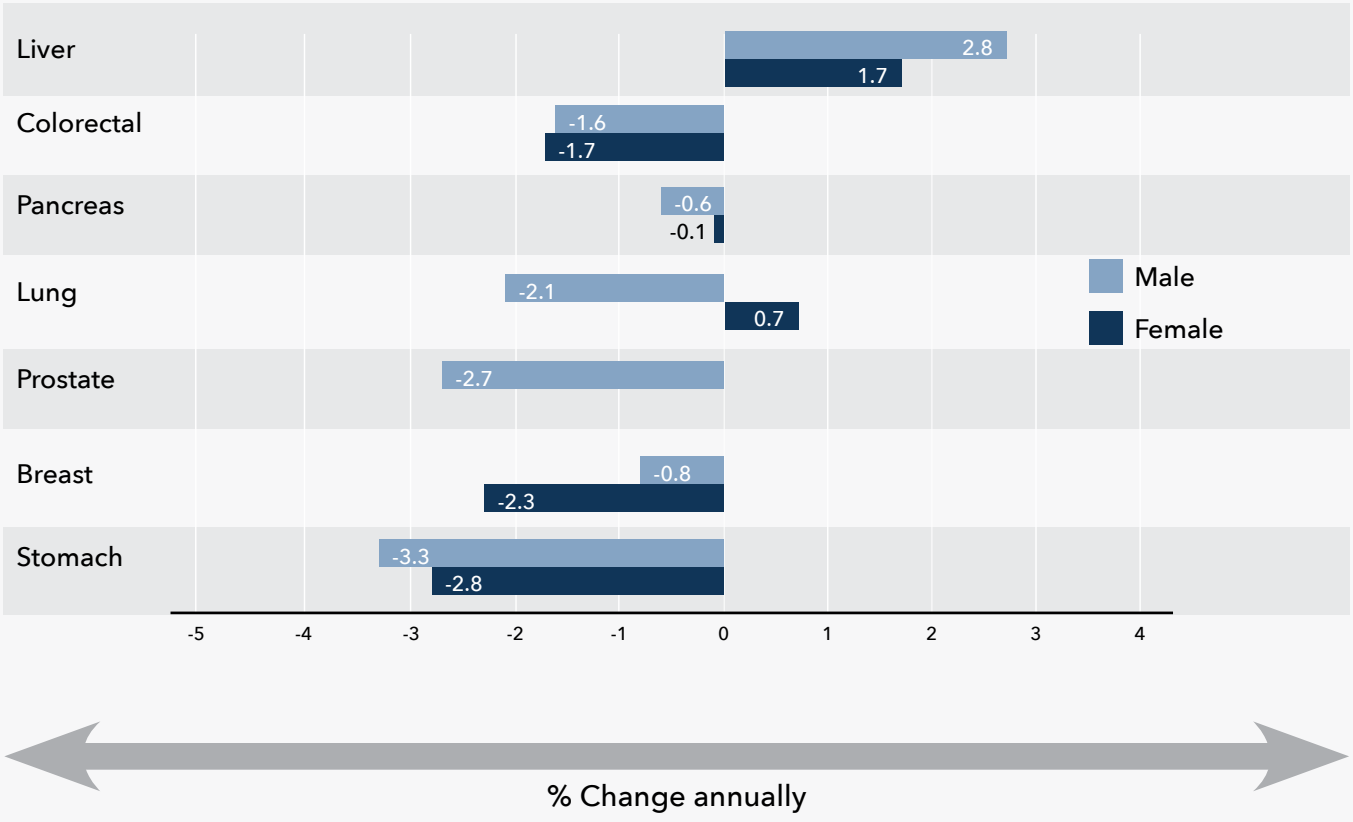
AB - Alberta
BC - British Columbia
MB - Manitoba
NB - New Brunswick
NL - Newfoundland and Labrador
NS - Nova Scotia
ON - Ontario
PEI - Prince Edward Island
QC - Quebec
SK - Saskatchewan
NT - Northwest Territories
NU - Nunavut
YT - Yukon

HCV prevalence is much higher among most Priority populations; it is nearly five times higher among Indigenous peoples, especially women and youth, than among non-Indigenous people in Canada [29, 30] and 5% of Canada's gbMSM have evidence of current or past HCV infection. [31] Up to 85% of new HCV infections occur among the estimated 171,900 PWID living in Canada. [32] HCV can be prevented by scaling-up provision of sterile needles, syringes and all other injecting equipment, and increasing use of opioid agonist therapy. However, access to, and coverage of these evidence-based interventions vary widely across Canada.

HCV causes more years of life lost than any infectious disease in Canada. Most of the HCV-related burden of illness comes from progressive liver damage that leads to liver failure and/or liver cancer. Although the overall number of people living with HCV in Canada may have fallen in recent years, complications from long-standing HCV among people who acquired it many years ago are now increasing. [27] In Canada, the only type of cancer with increasing mortality rates in men and women is liver cancer (Figure 4) - a trend that is primarily related to liver cancer from long-standing HCV infection. Without intervention, by 2035, rates of HCV-related liver failure and liver cancer are expected to increase by 89% and 205%, respectively. [2]

Beyond its obvious effects on the liver, HCV is also a systemic illness that causes problems outside the liver. Non-liver-related complications of HCV range from rare types of lymphoma to common problems like Type 2 diabetes and associated heart disease. [34] People living with HCV also report poor quality of life and reduced emotional well-being, [35, 36] and are up to four times more likely to experience depression than people who do not have HCV. [37] In addition, HCV is associated with high levels of stigma, especially in healthcare settings, [10, 11] which increases the already substantial burden of stigma faced by Priority populations. Stigma and discrimination discourage people living with HCV from seeking prevention, testing, treatment, and ongoing care and support, [10, 11] as well as other essential social services.

Figure 4. Mortality rates by sex and type of cancer [33]



KEY CONCEPTS: INTERSECTIONALITY AND SYNDEMICS

Intersectionality is a framework that explains health inequities among people who are poor, oppressed and/or marginalized. It describes how the overlapping and combined effects of racism, sexism, classism, homophobia and other forms of discrimination intersect, as experienced by marginalized groups and individuals within these groups. It has been conceptualized as a traffic *accident in a busy, four-way intersection, which could be caused by cars* from any number of directions and sometimes from all directions.[38]

Syndemics is a conceptual framework for understanding how multiple illnesses that arise in populations are exacerbated by social, economic, environmental and other circumstances. In a syndemic, two or more conditions worsen each other and inequities increase their harm.[23, 24] Syndemic solutions are illness-based, but focus on approaches that address more than one or all of the syndemic conditions. For HCV, syndemic theory can provide valuable insights into how STBBI prevention, testing, treatment, ongoing care and support can be integrated into comprehensive, wrap-around services for Priority populations that promote health equity.

The syndemic of co-occurring social and economic conditions, problematic substance use, mental illness, and coinfections has a negative health impact among people living with HCV. Addressing HCV without considering the broader health consequences including those related to drug use makes little sense. HCV elimination will require addressing syndemic health issues, particularly other sexually transmitted and blood-borne infections, while recognizing HCV-specific concerns.

In Canada, between 14,000 and 21,000 of the estimated 250,000 people living with HCV are also living with the human immunodeficiency virus (HIV).[39] The highest rates of HCV coinfection are found among PWID, however increasing outbreaks of sexually transmitted HCV, usually in the context of drug use, are occurring among gbMSM, especially those who are living with HIV.[40, 41] Coinfection with HCV increases the risk for liver-related and all-cause death among people living with HIV;[42] and in turn, HIV increases the risk for and progression of liver disease and mortality from HCV.[43]

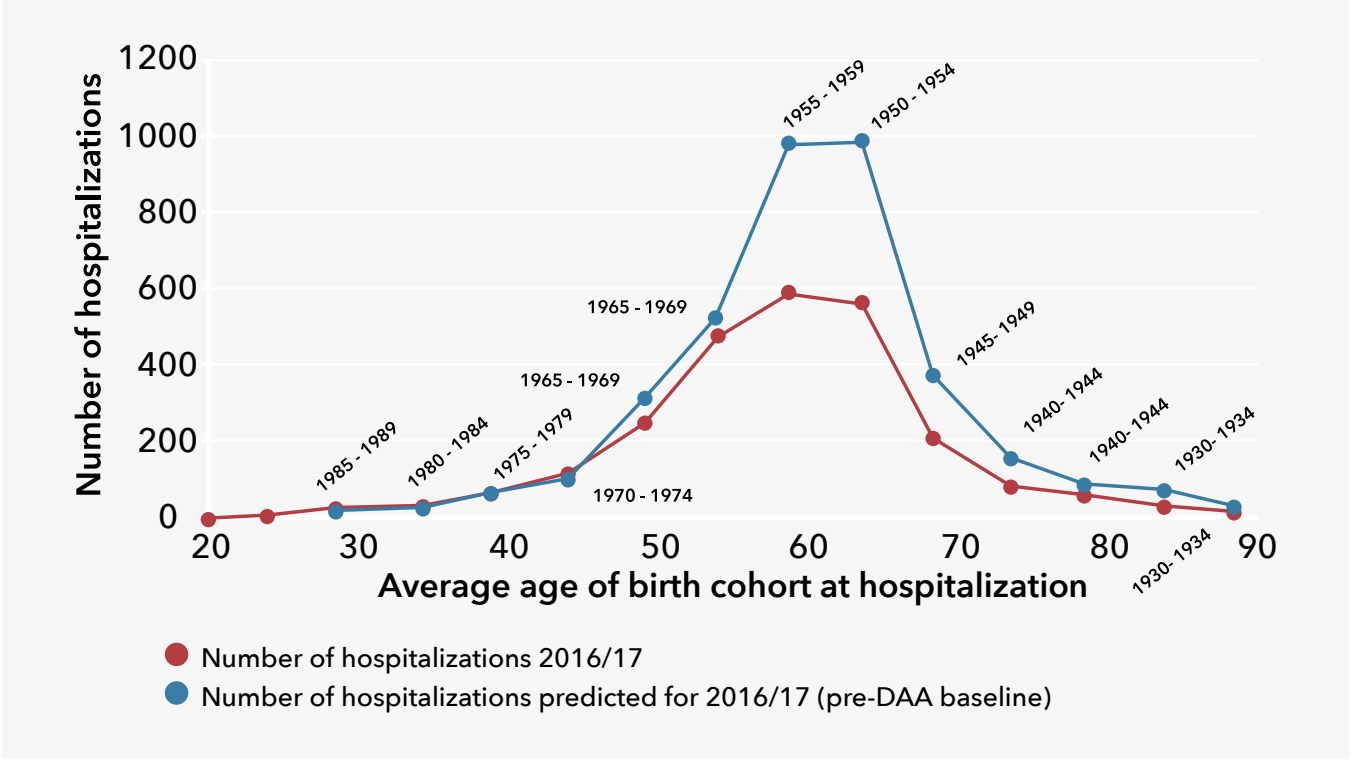
IMPACT OF TREATMENT

Unlike other chronic viral infections, HCV is curable. The development of direct-acting antivirals (DAAs) has transformed HCV care. DAAs cure over 95% of people after 8-12 weeks of once-daily treatment, with few or no side effects.[44-47] Being cured from HCV has many important benefits: it reduces the risk for cirrhosis, end-stage liver disease, liver cancer, transplantation and death and remarkably also nearly halves the risk for stroke and heart attack and can cure or improve other non-liver-related manifestations, and improve quality of life.[48-50] However, it is important to note that people can become reinfected if exposed to HCV again after being cured. This means that for those with ongoing infection risks, linkage to comprehensive prevention will be key.

Before DAAs became available in Canada, rates of HCV-related illness, hospitalization and death and the costs associated with them were projected to increase significantly in the coming years, from $161.4 million in 2013 to $258.4 million in 2032.[2] However, since DAAs were introduced in 2015, modest reductions in rates of HCV-related hospitalization and death in Canada, especially among people born before 1960, have already occurred.[51] These early benefits come from curing people who already have advanced liver disease. Even greater reductions in HCV-related complications will be seen by curing people earlier in the course of infection, since this will prevent the development of advanced liver damage and its complications.

Historically, HCV treatment rates in Canada have been quite low. When DAAs became available, treatment uptake increased to reach 12,000 people per year, in part due to the backlog of people awaiting interferon-free HCV treatment. When people who are already engaged in care have been treated, it will become more and more challenging to maintain the current treatment rate without strategies to find, diagnose and treat everyone who has been left behind.

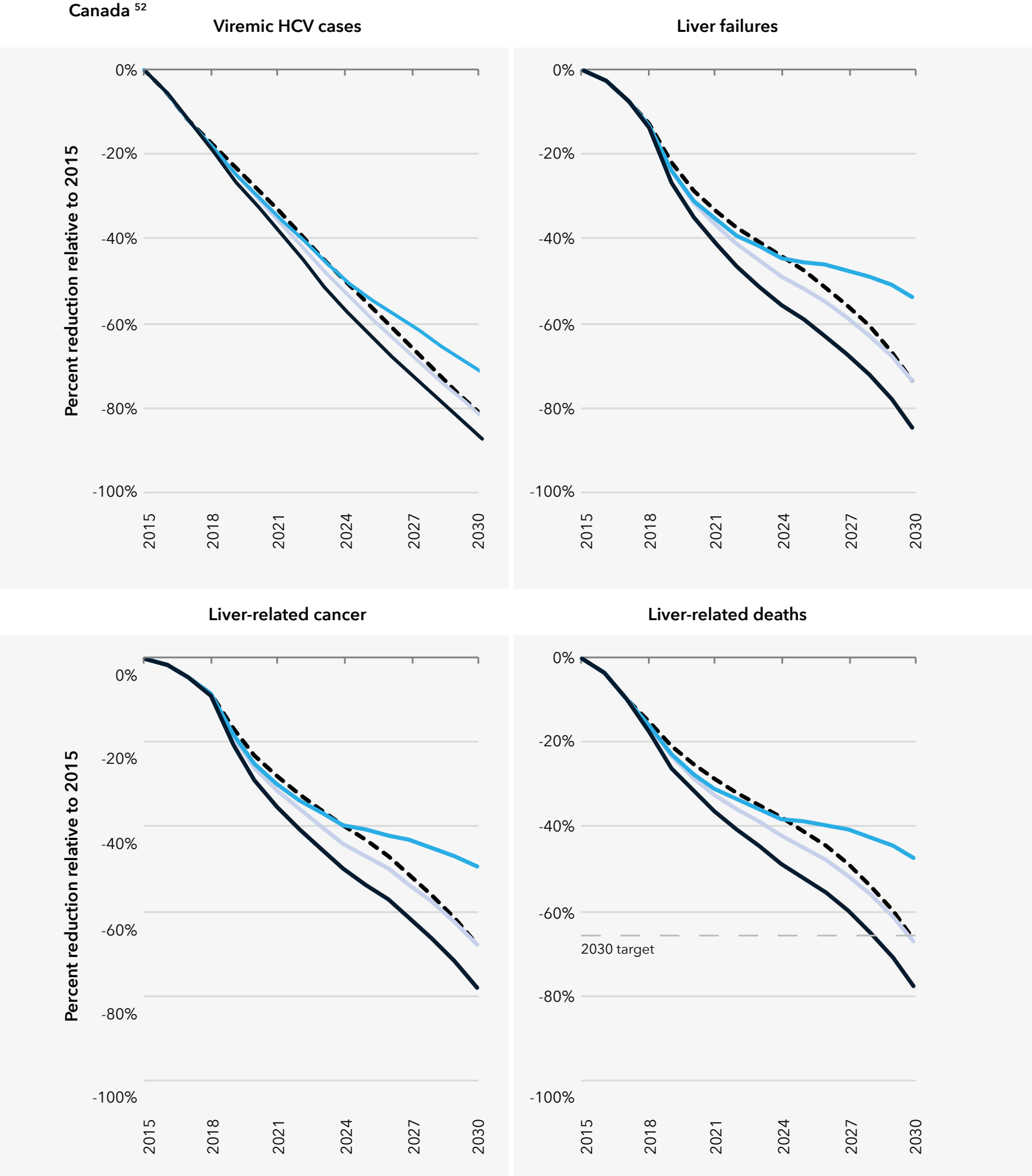
Figure 5. Annual hepatitis C virus (HCV)-associated hospitalizations versus pre-DAA baseline estimates by age, 2016/2017 [51]



Based on modeling of the impact of various DAA treatment scenarios on health outcomes in Canada, to achieve WHO elimination targets, near current treatment rates of 10,200 people per year must be maintained. This will be no small task. Major efforts will be required to ensure that people living with HCV are tested, diagnosed, and linked to care, treatment and ongoing support. As more people are cured, the number of people with HCV will continue to decline, which will make it increasingly challenging to find and treat the same number of people each year.

As the curves clearly show (Figure 6), if treatment rates decline, even marginally, Canada will not reach the HCV elimination targets, particularly if treatment rates drop quickly. The benefits of achieving these targets are clear: reducing liver failure and liver cancer by 70%, accompanied by a 70% reduction in liver-related death by 2030. If strategies are implemented to increase treatment rates, Canada could achieve WHO elimination targets before 2030. If treatment rates are not maintained, HCV-related illness and death will continue to rise, and elimination targets will not be met. [52]

Figure 6. Effect of different hepatitis C virus (HCV) treatment rates on liver-related complications and death in Canada [52]



INNOVATIVE HCV PROGRAMMING IN CANADA

Innovative programming to address HCV is already taking place in Canada. Micro-elimination projects, aimed at eliminating HCV in specific regions or populations, have been successfully piloted across the country. Different provinces have excelled in different aspects of the HCV response, some examples are included below:

- The 'Hepatitis C Teams' in Ontario focus on reaching marginalized populations with a high burden of HCV such as PWID and those with unstable housing; multi-disciplinary teams offer screening, treatment and prevention services, which have been markedly scaled up with the advances in HCV treatment.
- In Saskatchewan, major efforts have been undertaken to address HCV in Indigenous communities with active screening and treatment programs on and off-reserve developed in collaboration with Indigenous leadership.
- British Columbia (BC) has developed sophisticated data tools through the BC Hepatitis Testers Cohort (BC-HTC) by linking HCV testing data with high quality administrative health data, which allows for tracking HCV epidemiology from the spread of new infections to the consequences of HCV on morbidity and mortality at the population level.
- Innovative models of care such as nurse-led treatment and telementoring to link specialists with primary care providers following the Extension for Community Healthcare Outcomes (ECHO) model, have been successfully introduced in Alberta, BC, Ontario and Quebec.
- In both New Brunswick and BC, innovative programs have been developed to address HCV infection among inner-city vulnerable populations using a multidisciplinary, community-based approach, which has produced long-term engagement in care with increases in HCV treatment among PWID; it has also led to reduced overdose-related deaths, showing how HCV programs may play a role in the response to the overdose crisis.
- Expansion of harm-reduction services has occurred to varying degrees across the country, with implementation of supervised consumption services and improved access to needle syringe programs and opioid agonist therapy.
- Indeed, comprehensive action plans to address HCV are under development in many provinces including the Maritimes, Newfoundland, Alberta and BC.
- At the federal level, access to HCV testing and treatment in federal prisons has expanded markedly.

A key to reaching elimination targets will be coordination of efforts and sharing of good practices across the country.

POLICY TOOLS FOR HEPATITIS C ELIMINATION IN CANADA

Canada has been proactive by revising its public health approach and adopting a cohesive plan for addressing all STBBI. To measure impact, specific targets are required, and tools are needed for monitoring progress, to ensure the country remains on track to reach HCV elimination by 2030.

The Public Health Agency of Canada's (PHAC) ***Pan-Canadian Framework for Action to Reduce the Health Impact of Sexually Transmitted and Blood-borne Infections*** **(STBBI)** was released in 2018. The *Pan-Canadian STBBI Framework for Action* uses an integrated approach to reduce the health impact of STBBI, based around four pillars: Prevention, Testing, Care and Treatment, and Ongoing Support – and by tackling the stigma and discrimination that exacerbate HCV and other STBBI by 2030. [22] Canada's *Pan-Canadian STBBI Framework for Action* is aligned with the goals, targets and timelines of the WHO's *GHSS* for viral hepatitis, which allows them to be used for monitoring and measuring its impact.

Although the *Pan-Canadian STBBI Framework for Action*'s is relevant to all STBBI, HCV has some unique aspects; it is curable, yet mortality is high, and diagnosis rates in Canada remain low. As a consequence, HCV-related illness will continue to increase unless actions are taken to improve access to a continuum of prevention, testing, care and treatment services. To date, Canadian HCV prevention and care strategies have been fragmented and collection and quality of data to assess progress is highly variable. Elimination of HCV will require a comprehensive, coordinated plan for prevention, testing, treatment, and ongoing care and support along with well-developed tools to monitor progress.

BLUEPRINT TO INFORM HEPATITIS C ELIMINATION EFFORTS IN CANADA

THE *BLUEPRINT TO INFORM HEPATITIS C ELIMINATION EFFORTS IN CANADA*

The *Blueprint* was developed as a guide for federal and provincial/territorial policymakers, including those in the ministries of health, public health program staff and planners, healthcare providers and the community of people with lived experience of HCV, to complement the *Pan-Canadian STBBI Framework for Action*. The *Blueprint* can help to direct resources and measure progress towards HCV elimination. It offers a menu of options and resources that can be adapted to the specific situation in each constituency - providing the *what*, but not the *how* or the *who*. The distribution of responsibilities varies across the country, meaning that in each jurisdiction, specific components of

the *Blueprint* may fall into different portfolios and even different levels of government. In addition, the current state of the response to HCV differs widely; some provinces already have well developed plans with excellent service provision while others have just begun the process. The *Blueprint* lays out what needs to be done to achieve elimination but how that is operationalized and in what order, will need to be individualized based on the specific situation in each region of the country.

The *Blueprint* is aligned with the WHO HCV elimination targets and timelines, and the *Pan-Canadian STBBI Framework for Action*'s vision, strategic goals, and guiding principles. It supplements them with tangible, actionable and measurable steps. The *Blueprint* includes objectives, targets and activities for each of the *Pan-Canadian STBBI Framework for Action*'s four pillars and provides guidance and practical suggestions for addressing HCV in the Canadian context.

The *Blueprint* includes medium - and long-term targets that are synergistic, evidence-based (wherever possible), and built around proven practices. The targets are based on estimates of current gaps in access and coverage, projections to bring HCV prevention to scale, and by modeling different treatment scenarios to assess their impact on Canada's HCV incidence and disease burden, all with the goal of meeting WHO 2030 elimination targets. The *Blueprint* encourages a forum, ideally federally convened, where good practices, lessons learned, successes and challenges in the Canadian context can be shared.

THE CANADIAN NETWORK ON HEPATITIS C AND THE DEVELOPMENT OF THE *BLUEPRINT*

The *Blueprint* was developed by the **Canadian Network on Hepatitis C (CanHepC)**, a collaborative research and training network funded by the Canadian Institutes of Health Research (CIHR). CanHepC is dedicated to translational research; it links over 100 researchers, trainees, knowledge users (community members, community-based organizations, policy - and decision-makers) working in the HCV field across Canada, as well as international partners. The *Blueprint* confirms CanHepC's interdisciplinary team's commitment to evidence-based HCV elimination efforts.

The *Blueprint* was developed through a **consultative and inclusive process**, drawing from expertise within the CanHepC network and beyond (Figure 7).

In February 2018, CanHepC announced its commitment to develop a *Blueprint* reflecting cross-sector priorities, recommendations and perspectives to inform HCV elimination efforts in Canada. To oversee the work and provide key guidance and leadership on the design and development of the *Blueprint*, a Writing Committee was convened. The Writing Committee included researchers, community-based organizations with wide representation, including people with lived experience and affected populations, clinicians, healthcare workers and others.

In March 2018, four Working Groups (Priority populations, Prevention, Testing and diagnosis, and Care and treatment) reflecting the four pillars of the *Pan-Canadian STBBI Framework for Action* (Prevention, Testing, Initiation of Care and Treatment, and Ongoing Care and Support) were convened. For the purpose of the *Blueprint*, the Ongoing Care and Support pillar was divided and integrated into the Prevention (harm reduction to prevent HCV reinfection) and Care and treatment (post-cure care, support and monitoring) Working Groups. Each Working Group performed an environmental scan of the current situation in Canada with population-specific epidemiology and a survey of existing programs. WHO targets were used as a minimum starting point, from which each

Figure 7. Process for developing the *Blueprint*

Working Group developed the *Blueprint*'s high-level objectives, each with specific measurable targets and a set of indicators to measure progress towards them and identified a range of suggested activities, and systems targets to facilitate achieving them. For each section, *good practices*, rather than *best practices*, are suggested in line with WHO nomenclature, acknowledging that even excellent practices can be improved upon and what is best in one scenario may not be best in another. A consultant writer was hired to collate, synthetize and draft the *Blueprint*, under the Writing Committee's stewardship. See Appendix 2 for a complete list of Writing Committee and Working Group members.

In May 2018, CanHepC held two public webinars to gather feedback on the rationale, development process and overall goal of the *Blueprint*. In June 2018, CanHepC held an open access *Blueprint* National Hepatitis C Stakeholder Workshop in Toronto. Feedback from the workshop and draft objectives and targets were presented at the Global Hepatitis Summit in Toronto for additional feedback, which was incorporated into the *Blueprint*. The outline for the *Blueprint* was also presented to the Communicable and Infectious Disease Steering Committee of the Pan-Canadian Public Health Network to ensure that representatives from all provinces and territories and the federal government were aware of the process.

From July 2018 to February 2019, the consultant writer collated and synthetized the *Blueprint* under the Writing Committee's stewardship.

The consultation process for the draft version of the *Blueprint* took place in February and March of 2019. The draft was sent to stakeholders from provinces and territories including community-based organizations, public health officials and ministries of health. Public webinars in French and English were held in March 2019. The feedback from this consultation process was incorporated into the final *Blueprint*, which was released in Montreal in May 2019 at the 8th Canadian Symposium on Hepatitis C Virus and the Canadian Liver Meeting.

STIGMA

Stigma is a process of exclusion; it occurs when a person - or group of people – are seen as tainted or disgraced. When people perceive themselves as being stigmatized, they may also come to hold the same negative perceptions about themselves, leading to an internalization of stigma and acceptance of a 'spoiled identity'. [53] Stigmatized individuals are also less likely to disclose health conditions (in both healthcare and interpersonal contexts), more likely to avoid healthcare interactions, and less likely to adhere to treatment, which reduces treatment effectiveness. [54-57]

With HCV, stigma arises both from the fear of becoming infected due to misinformation about the consequences and transmissibility of HCV, and negative attitudes about the modes of transmission. [53] HCV-related stigma is relevant across the cascade of HCV services, since it compromises their reach, uptake and effectiveness. People living with HCV experience high levels of stigma in healthcare settings; this discourages them from accessing prevention, testing, care and treatment services. [58] Training about injection drug use-related stigma has, in varying degrees, improved attitudes among healthcare providers, including front-line staff. [59, 60] However, much work remains to be done. Increased training on stigma and its harms, as well as de-stigmatizing approaches must be provided to medical professionals and all those involved in providing HCV services.

Since Canada's Priority populations face greater barriers to accessing healthcare, it is particularly important to provide stigma-free, culturally appropriate HCV prevention, care, treatment and ongoing support services adapted to their needs.

The *Blueprint* calls for actions to decrease HCV-related stigma, by:

- Developing, evaluating and adapting new stigma indicators in Canada:
  - ✧ Evaluate existing stigma indicators, such as promising work from Australia, in a Canadian context*;
- Monitoring HCV-related stigma and discrimination among Priority populations and other groups;
- Developing and implementing curricula and training to increase knowledge among healthcare providers and all those involved in providing HCV services, to reduce stigma and discrimination related to drug use, addictions, HCV and other STBBIs across the continuum of services;
- Developing culturally appropriate and respectful anti-stigma curricula, with full involvement of, and ideally led by people with lived experience and Priority populations;
- Supporting healthcare providers and peer groups in acquiring competencies to reduce stigma in their interactions with people affected by or at-risk of HCV and other related conditions;
- Implementing policy-level strategies to decrease population-level stigma, including decriminalization of drug possession for personal use;
- Implementing and evaluating a substance use curriculum into healthcare education, residency training and continuing education. The curriculum should enable healthcare professionals, particularly front-line workers, to discuss HCV transmission risks with patients, deliver behavioural intervention messages, and/or to provide referrals to appropriate services and information about available community support services;
- Including specific materials in all trainings, curriculum and other educational initiatives that are relevant to the challenges of HCV-related stigma among children and youth under age 18 and their parents and caregivers.

* https://csrh.arts.unsw.edu.au/research/projects/stigma-indicators

PRIORITY POPULATIONS

The importance of an approach that focuses on the needs of Priority populations was identified by the 2015 National Deliberative Dialogue on Integrated Hepatitis C Programming and Services* and through broad community consultation, including members of Priority populations most affected by HCV. The term Priority populations was selected by community members and was meant to refer to populations who experience a disproportionate burden of HCV and/or those with challenges in accessing HCV care and services.

A specific focus on the Priority populations highlighted in the *Blueprint* is essential to the success of HCV elimination. Furthermore, people may identify as being a member of more than one Priority population; syndemic approaches to HCV must address social, economic and other conditions that worsen the health of Priority population members.

People who are members of Priority populations are often excluded from mainstream health services, and face high levels of stigma, discrimination, and other obstacles that make it difficult for them to access and utilize healthcare.

Programs and services need to be informed by, appropriate for, and accessible, available, and acceptable to people who are members of Priority populations to achieve the Pan-Canadian STBBI Framework's vision: "A Canada where STBBI are rare and people living with STBBI receive the care and support they need." [22]

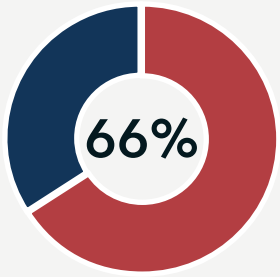
HCV disproportionately affects specific populations in Canada. Overlapping, intersectional, factors such as poverty, homelessness and/or mental health may increase their risk for, and vulnerability to HCV and reduce their access to healthcare services. It is important to understand who these populations are, why they have high rates of new and/or existing HCV infections, and what their needs are.

There are five identified Priority populations and one birth cohort of interest:

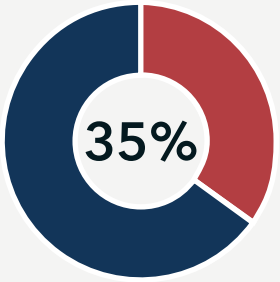
- People who inject or use drugs
- Indigenous peoples (First Nations, Inuit, Métis)
- People with experience in the federal or provincial prison system
- Immigrants and newcomers from countries where HCV is common
- Gay, bisexual and other men who have sex with men
- The 1945-1975 birth cohort: adults living with hepatitis C

* Available at: http://www.catie.ca/sites/default/files/DD-report-2015-en.pdf

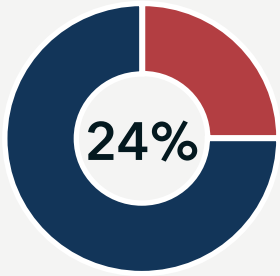
Figure 8. Hepatitis C virus (HCV) prevalence among Priority populations



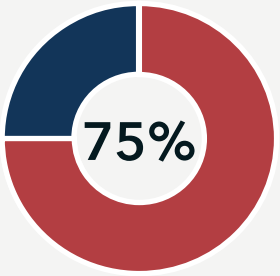
Up to 66% of people who inject drugs have past or current HCV infection.



Up to 35% of all HCV infections in Canada are among immigrants and newcomers, especially those from countries where HCV is common.



Nearly a quarter of prisoners in federal and provincial correctional facilities have a past or current HCV infection.



Up to 75% of all HCV infections in Canada are among people born between 1945-1975.

PEOPLE WHO INJECT DRUGS/PEOPLE WHO USE DRUGS (PWID/PWUD)

The highest incidence and prevalence of HCV are found among PWID in Canada: two-thirds have evidence of current or past HCV infection, and 85% of new HCV infections occur among PWID. [3-8, 61] Criminalization, unstable housing, poverty, stigma and lack of transportation create barriers to services for PWID, and, more broadly, PWUD, and incarceration increases their risk for HCV.

There is need for comprehensive, accessible and available high-coverage harm-reduction programs to support HCV prevention and avert reinfection, including for Indigenous people, women, youth under 18 years of age and people in rural and remote communities.

There is historic and ongoing neglect of the healthcare needs of PWID/PWUD. HCV prevention, care and treatment services for PWID/PWUD need to be considered within the larger context of the health of people who use drugs and the opioid epidemic, with sensitivity to stigma, discrimination and negative interactions with the healthcare system experienced by PWID/PWUD.

Policy and service delivery recommendations:

- Create a specific focus on PWID/PWUD populations in national and provincial/territorial HCV strategies;
- Develop partnerships with federal/provincial correctional agencies to ensure HCV treatment access to treatment in these settings, and ensure treatment is low-threshold, non-discriminatory, confidential and accessible regardless of current drug use and liver fibrosis stage, and conforms to professionally accepted standards in the community;
- Decriminalize drug possession for personal use as part of an evidence-based, public health approach to drug policy - this strategy was first adopted in Portugal with funds saved from policing drug use directed to support health and social services leading to reduced rates of HIV, HCV and other health consequences of drug use;

- Scale-up access to harm-reduction services, including needle and syringe programs (NSP), supervised consumption services (SCS) and overdose prevention sites (OPS);
- Ensure that PWID/PWUD are meaningfully involved in the design, delivery and evaluation of HCV prevention and care models, programs and policies;
- Provide youth-focused, accessible harm reduction and addiction services;
- Make stigma-free HCV care, treatment and re-treatment available and accessible for all, regardless of current drug use and liver fibrosis stage;
- Move care and treatment from specialty centers to low-threshold environments, including places where PWID/PWUD are already accessing services (such as harm-reduction programs, Indigenous health services, community-based primary care, nurse-led clinics and pharmacies).
- Incorporate harm reduction and overdose prevention measures across the continuum of HCV services;
- Support community-based harm-reduction treatment models in offering comprehensive, wrap-around care that is client-centered, trauma-informed, responsive to social determinants of health and includes community development:
    - ✧ Provide safe outpatient and inpatient healthcare spaces that provide active addictions medicine support, pro harm-reduction policies, and staff education and awareness;
    - ✧ Develop novel models of care such as use of peers, directly observed therapy, case management and 'bring a friend' approaches;
- Offer voluntary, stigma-free HCV testing, including for reinfection:
    - ✧ Expand rapid testing and diagnosis to minimize loss to follow-up;
    - ✧ Use finger-stick testing technology when possible, particularly for people with poor venous access.

INDIGENOUS PEOPLES (FIRST NATIONS, INUIT, MÉTIS)

There is large diversity in culture, language, and socio-economic differences within Indigenous communities, including differences within and between First Nations, Metis and Inuit peoples. While half of the Indigenous population is located in urban centers, there is much migration between urban and non-urban and on and off-reserve locations, on and off-settlements and to and from the North. Variations in jurisdiction, governance and policies in Indigenous communities affect access to and support for HCV and harm-reduction services.

Although data on the burden of HCV disease in Indigenous people are limited, there is evidence that HCV rates are five times higher among Indigenous peoples than Canada's general population. [4, 29, 30, 62] Complex, intersecting factors have an impact on this population: racism, colonialism, intergenerational trauma and systematic abuse increase vulnerability to HCV among Indigenous peoples, and the same conditions make Indigenous people less likely to trust or access HCV services. [63]

Indigenous-led, culturally safe/responsive care is more effective, but there are limited numbers of Indigenous healthcare providers and respectful, well informed allies.

In addition to HCV-related stigma, many Indigenous people face widespread racism when seeking healthcare. Racism has resulted in long-lasting distrust. This context has had significant detrimental, intergenerational impacts on health, family relationships and Indigenous language and culture. [64] The intersecting experiences of stigma, racism, and distrust must be taken into consideration when responding to the health of Indigenous peoples.

The Truth and Reconciliation Commission investigated the Residential School system through gathering survivors' testimonies, reviewing documents and the policies that sustained the system. The final report included 94 Calls to Action to change the future relationship of Canada and Indigenous people. There are seven specifically health-related Calls to Action (numbers 18 to 24). Number 24, for example, speaks directly to

addressing medical training, holistic care and racism and offers clear direction related to providing HCV services to Indigenous peoples.[65] In addition, Indigenous people have established standards on use and sharing of data that describes them, which are based on concepts for self-determination, data sovereignty and ethical conduct. All Canadian citizens are represented as treaty signatories by the Crown and share in the legacy of these agreements and the Truth and Reconciliation process.

Policy and service delivery recommendations:

- Create a specific focus and/or documents for Indigenous populations in national and provincial/territorial HCV strategies, developed by or with representatives from First Nations, Metis and Inuit leadership;
- Use health equity and structural competency approaches for all HCV services, and establish equitable health targets for Indigenous and non-Indigenous Canadians;
- Ensure that approaches for addressing HCV are Indigenous-led, multidisciplinary (including shared care models that bring together Indigenous and Western approaches to health), and rooted in addressing Indigenous determinants of health (e.g. racism, social exclusion):
  - ✧ Build from Indigenous wellness approaches;
  - ✧ Create culturally safe approaches and resources that address historic, collective and inter-generational trauma;
  - ✧ Work from culturally safe/responsive approaches, building on trust and partnerships;
  - ✧ Enable healthcare practitioners to have enough time with Indigenous clients to address complex needs;
- Provide access to holistic Indigenous healthcare services on and off-reserve through clinics/links to shared care model teams:
  - ✧ Care models that expand capacity to deliver HCV services, including primary, mobile, community-based, eHealth and other means of specialist support will be most effective;
  - ✧ Make approaches flexible and adaptable to diverse geographic settings;
- Build community awareness and readiness for HCV programming, including harm-reduction and care cascades with Indigenous leadership and their communities;
- Be prepared to address broader community needs beyond HCV;
- Create programs to address stigma related to drug use from a comprehensive and Indigenous context;
- Provide funding for dedicated sexual health and HCV training, and staff who work on-reserve, on Métis settlements and off-reserve, including urban, rural, semi-remote and remote settings including Inuit hamlets;
- Address the jurisdictional issues related to Indigenous peoples living off-reserve, including non-status and Métis, in all provinces, so that everyone can access HCV prevention, testing, care and treatment.

CHILDREN AND YOUTH UNDER THE AGE OF 18 ARE VULNERABLE AND OFTEN UNDERSERVED.

HCV incidence and prevalence among children in Canada is unclear. Children whose mothers are living with HCV are at increased risk, since the virus can be transmitted from mother-to-infant (and possibly through other routes as household contacts). HCV is also more common among children who are immigrants or newcomers (including international adoptees) from countries where HCV is common, Indigenous and other teens who are injecting drugs, children of parents who use drugs, and street-involved youth.

PEOPLE WITH EXPERIENCE IN THE PRISON SYSTEM (PROVINCIAL AND FEDERAL)

HCV is far more common among people within Canadian prisons than people outside of them. In federal facilities, 30% of prisoners have evidence of a past or current HCV infection. In provincial facilities, 15% of men and 30% of women have evidence of a past or current HCV infection.[66] HCV-related policies and practices vary between provincial, territorial and federal jurisdictions; this affects access to HCV education, testing and treatment.

PWID/PWUD, Indigenous peoples, and other populations are more likely to have experience in prison systems. People who enter the prison system already have a higher risk of HCV, and their time in prison further increases this risk, since injecting drugs and tattooing with shared equipment in prison are common, and poor access to safe tattooing, piercing and injection equipment forces many individuals to re-use unsterilized equipment. At the same time, inadequate or no access to opioid agonist therapy, lack of support for management of drug withdrawal and sharing razors and nail clippers facilitate the spread of HCV in prison.

Even in jurisdictions with policies that stipulate the availability of HCV treatment for prisoners, regardless of liver fibrosis stage or drug use history, in practice, access to HCV treatment may be difficult in a prison setting. There are many reasons for this, including lack of confidentiality in prison settings; HCV-related stigma among prisoners and prison staff (including healthcare staff); interruption of provincial drug benefit programs while in prison; poor follow-up with inter-facility transfer or upon release and difficulty being referred to HCV specialists or HCV-knowledgeable providers. Short periods of incarceration in provincial prisons pose an additional set of challenges for diagnosis of HCV and engagement into care and treatment.

Policy and service delivery recommendations:

- Create a specific focus for people with experience in the prison system in national and all provincial and territorial HCV strategies;
- Increase funding for ministries responsible for provincial and territorial correctional services to ensure that all prisoners living with HCV receive education and are offered testing, treatment and support, irrespective of liver fibrosis stage and/or drug use history, as is currently done in the federal prison system;
- Implement harm-reduction programs and policies, in consultation with prisoners, correctional health staff and others that include:
  - ✧ Needle syringe programs (NSP) and opioid agonist therapy (OAT) – provide NSP, OAT and the full suite of harm-reduction services, and ensure that these services are accessible, confidentially available, and consistent with good practice in public health;
  - ✧ Provide programs for safe tattooing as well as measures to address transmission from tattooing equipment, razors and nail clippers;
- Develop, institute and evaluate policies and procedures to improve access to HCV prevention, testing and treatment:
  - ✧ Routinely offer voluntary, confidential HCV testing, education and counseling to prisoners at prison entry and during prison stay, facilitated, where possible, by community-based organizations;
  - ✧ Provide HCV education for prisoners and prison workers to reduce stigma;
  - ✧ Provide population-specific HCV prevention resources for women, Indigenous people, youth and other ethno-cultural groups;

- Provide HCV treatment for all prisoners and/or linkage to care upon release for those with short sentences, irrespective of eligibility for provincial drug benefit programs:
  - ✧ Provide access to DAA treatment and harm reduction from an experienced provider;
  - ✧ Create mechanisms for linkage with community care upon release from prison, so that transfer of medical records and access to, and coverage of DAAs are seamless;
  - ✧ Ensure transfer of medical records and continuity of HCV treatment for prisoners who transfer facilities or are released to freedom before completion of DAA therapy;
- Include prison environments in HCV implementation research;
- Provide rapid linkage to harm reduction, social and HCV care services upon release.

IMMIGRANTS AND NEWCOMERS FROM COUNTRIES WHERE HCV IS COMMON

Immigrants and newcomers from countries where HCV is common comprise approximately 35% of all current or past HCV infections in Canada.[8] In their home countries, HCV is primarily transmitted through unsafe medical and dental practices such as via transfusion and/or re-use of unsterilized equipment, although immigrants and newcomers may also be part of other Priority populations with other risks for, or routes of HCV transmission.

Although voluntary HCV screening after arrival in Canada is included in existing national recommendations, immigrants and newcomers are less likely to access the healthcare system than Canadian-born residents, and healthcare providers may be unaware of countries where HCV is common. Immigration status and fear of deportation may prevent access to health services, and cultural and language barriers create obstacles to accessing health information and services. Furthermore, non-status or undocumented immigrants are an important sub-group who face additional barriers to health services.

Newcomers to Canada often experience racism in the healthcare system and at the population level, with additional perceived and/or real fear of deportation; as a result, they may not seek healthcare or disclose their HCV risk and/or status.

Policy and service delivery recommendations:

- Create a specific focus on immigrant and newcomer populations in national and provincial/territorial HCV strategies:
  - ✧ Provide education about how HCV is transmitted in their countries of origin;
- Make voluntary HCV screening and linkage to care accessible to newcomers as soon as they arrive in Canada:
  - ✧ HCV information, referral and voluntary testing should be part of the standard newcomer primary health screening provided to people when they first arrive in Canada;
  - ✧ Integrate screening and treatment into multidisciplinary, community-based models of primary care (i.e. community health centers);
- Educate healthcare practitioners about the increased risk for HCV among immigrants and newcomers from countries where it is common, as well as the benefits of HCV testing;
- Train healthcare providers who treat large numbers of people from countries where HCV is common, such as Pakistani or Egyptian physicians working in Canada, to diagnose and manage HCV;
- Offer linguistically and culturally sensitive services.

GAY, BISEXUAL AND OTHER MEN WHO HAVE SEX WITH MEN (GBMSM)

GbMSM are an emerging priority population because HCV, which is not usually acquired through sexual transmission, has been reported in increasing numbers among gbMSM. An estimated 5% of gbMSM have evidence of past or current HCV infection, and gbMSM may be part of other Priority populations.[31] Sexual transmission and/or drug use are the most likely HCV risk factors among gbMSM, especially rough sex and group sex in the context of drug use. Although HCV rates are higher among HIV-positive gbMSM, new cases have been reported among HIV-negative gbMSM who are using HIV pre-exposure prophylaxis (PrEP),[67,68] and increasing rates of reinfection have been documented among gbMSM at ongoing risk who have been previously treated and cured.[69]

Prevention messaging for gbMSM around condoms and sterile injection equipment has historically been focused around HIV, so there is less awareness of the need for HCV prevention and testing among gbMSM than for HIV and other STBBI. The emergence of HIV prevention strategies that do not involve condoms or sterile needles (i.e. PrEP, undetectable = untransmittable [U=U])[70] and lack of knowledge about HCV risk may facilitate transmission among gbMSM.

Policy and service delivery recommendations:

- Acknowledge gbMSM as an emerging priority population and create a specific focus on gbMSM within national and provincial/territorial HCV strategies:
    - ✧ Involve gbMSM in the design, implementation and oversight of materials and programs;
- Improve awareness and knowledge around HCV prevention, testing, care and treatment among gbMSM;
- Integrate HCV into existing sexual health and HIV strategies and programming for gbMSM:
    - ✧ Offer HCV testing and prevention services in sexual health clinics;
    - ✧ Offer HCV testing to all individuals receiving PrEP;
    - ✧ As gbMSM do not always use traditional NSP, similar services should be integrated into other services and programs for gbMSM;
- Provide regular monitoring for reinfection, along with STBBI testing, for gbMSM who have cleared HCV infection spontaneously or with treatment.

1945-1975 BIRTH COHORT: ADULTS LIVING WITH HEPATITIS C

People born between 1945-1975 have the highest HCV prevalence of any age cohort: they comprise an estimated 66-75% of people living with HCV in Canada.[3,6,9] People living with HCV in this age cohort are five times more likely to develop complications (i.e. cirrhosis, cancer, premature death) than the general population,[71] yet many of them have not been tested for HCV.[72] Furthermore, HCV is the main cause of liver transplants in Canada, and 98% of HCV-related transplants occur in people aged 40 or older.[73]

Most infections among people in this cohort resulted from medical/hospital procedures or past injection drug use. People in this birth cohort may also be a part of other Priority populations with increased HCV risk, such as newcomers to Canada or gbMSM. Stigma of past drug use (or other high-risk activities) may make older adults less likely to disclose risk exposures, and reluctant to access testing or treatment. Healthcare professionals may also be less aware of risk factors among this age cohort, particularly for those with remote risk exposures.

Given the high levels of stigma around HIV and HCV, older Indigenous people, especially those who are considered Elders in their communities, may be even less likely to disclose or seek treatment for fear of losing respect of their family and community, as well as their Elder standing.

Policy and service delivery recommendations:

- One-time, birth-cohort-based testing should be implemented in addition to risk-based and clinically-based testing, to identify people living with HCV who are undiagnosed:
  - ✧ Increase community awareness of the benefits of HCV testing and treatment for older adults;
  - ✧ Provide screening for, and treatment of concomitant conditions that may impact liver disease progression (e.g. fatty liver disease, diabetes, alcohol use);
- Provide education about the rationale for birth-cohort-based HCV testing, as well as about relevant co-morbidities and recognition of advanced liver disease for healthcare providers;
- Conduct real-world studies to evaluate treatment outcomes and health benefits/consequences in people over 65 years who were not included or were under-represented in clinical trials.

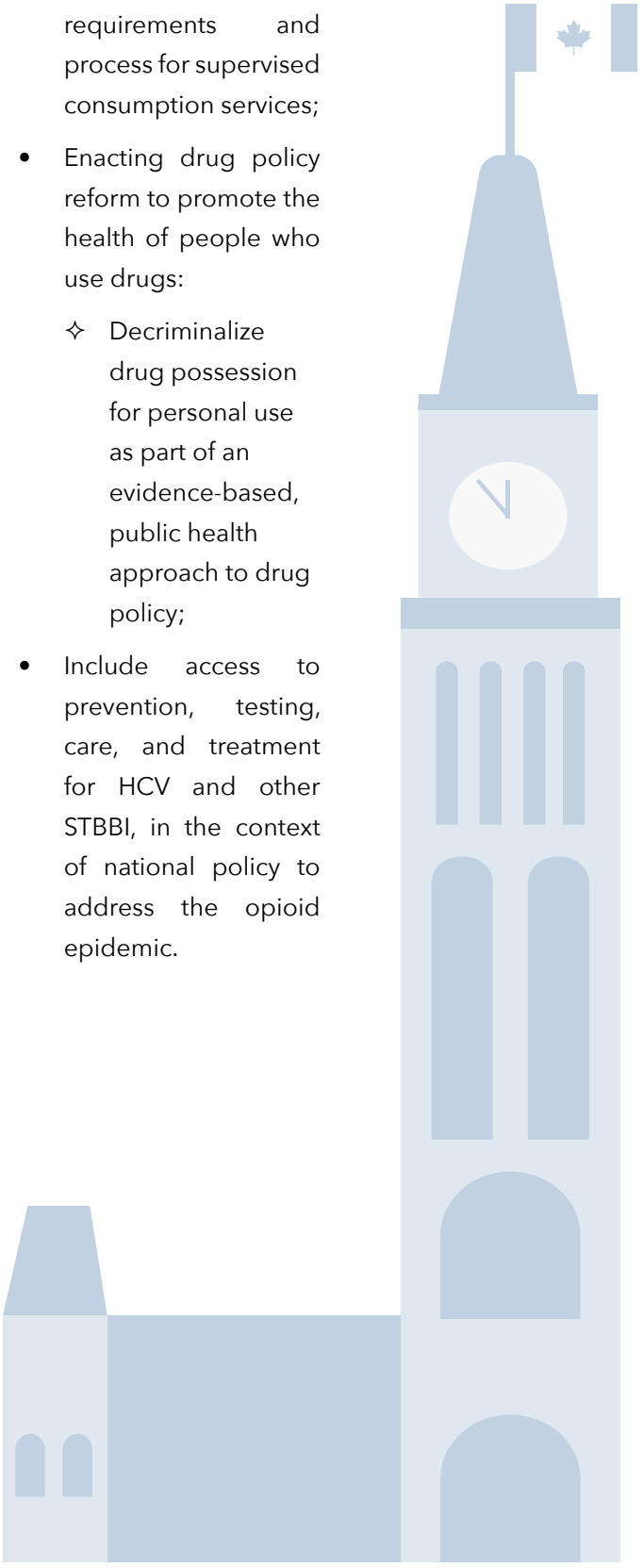
FEDERAL RECOMMENDATIONS

In Canada, healthcare falls under provincial or territorial jurisdiction for most Canadians and, as such, most recommendations in this *Blueprint* must be operationalized at the provincial/territorial level.

However, the federal government also has an important role in health coverage and policy. Indigenous peoples, those in federal prisons and those in the military receive health coverage from the federal government. In addition, some newcomers to Canada receive health services at the provincial or territorial level that are reimbursed by the federal government. The specific recommendations pertaining to these groups, which are outlined in the Priority populations section, need to be implemented by or with the federal government.

The following additional recommendations for policy interventions at the federal level will have a significant impact on Canada's HCV epidemic:

- Expediting, funding and expanding implementation of evidence-based harm-reduction interventions, including supervised consumption services, opioid agonist therapy and needle syringe programs, and enacting legal protection for such services in all Canadian jurisdictions. In particular, to facilitate the expansion of supervised consumption services, the federal government should grant a class exemption under the *Controlled Drugs and Substances Act* protecting clients and staff, including volunteers, from prosecution for drug possession or for activities (such as drug sharing or assisted injection that may amount to "trafficking") when accessing or providing supervised consumption services that meet minimum required conditions. If the federal government insists on maintaining a case-by-base exemption process, it should take measures to further streamline the current application requirements and process for supervised consumption services;
- Enacting drug policy reform to promote the health of people who use drugs:
  - ✧ Decriminalize drug possession for personal use as part of an evidence-based, public health approach to drug policy;
- Include access to prevention, testing, care, and treatment for HCV and other STBBI, in the context of national policy to address the opioid epidemic.



SYSTEMS FOR MONITORING PROGRESS

There are significant gaps in knowledge about Canada's HCV epidemic. High quality data from across the country are required to develop sound policies.

Information is needed about *where we are starting from* (the number of people who become newly infected each year; the number of people who are living with HCV; the number of people who are developing complications from HCV), and *where we are going* (expected rates of new infections; consequences of existing infections). This information is essential for informing effective policies and monitoring progress towards HCV elimination.

WHO has highlighted **three key parameters** to assess the impact of HCV, and progress towards its elimination. Ongoing surveillance in each region (province or territory) is required to monitor:

1. The incidence of new HCV infections;
2. The prevalence of existing HCV infections;
3. The incidence of complications from HCV infection, particularly cirrhosis, liver cancer and HCV-related mortality. [74]

These parameters must be assessed serially, and with adequate sampling of populations at increased risk of HCV infection.

The **Indicators Tables** (see Appendix 1) outline key, WHO-recommended indicators necessary for assessing progress toward HCV elimination. Each target has its own specific indicators and sub-indicators to help monitor and report progress in achieving them. Sub-indicators are included, to provide additional information that is useful for improving overall assessment of national progress.

Integrated data systems are required to assess key indicators. Some data collection and integration systems already exist. These produce relatively accurate assessments of the consequences of HCV, although there is wide variability across the country.

Currently the best available regional data on HCV come from epidemiological cohort studies, serial cross-sectional studies and a collaboration between the British Columbia Centre for Disease Control (BCCDC), the BC Ministry of Health and the BC Cancer Agency that links data from the BC-HTC with laboratory data and administrative healthcare information. The BC-HTC integrated data has made it possible to identify healthcare disparities among people living with HCV, and monitor access to, uptake, completion and outcomes of HCV treatment – data that are essential for informing strategies for, and tracking progress towards HCV elimination targets. While extremely useful, even the BC data could be improved upon and most other jurisdictions do not have such comprehensive data, limiting their ability to plan, monitor and achieve elimination targets.

Many of the targets set out by WHO and the *Blueprint* require improved systems for monitoring and data collection. To ensure that 2025 and 2030 targets are met, systems for collecting and integrating data across the cascade of care, by region and by population, should be up and running by 2020. Testing data must be linked with administrative health data, to enable provincial, territorial, and national-level monitoring, and to assess HCV healthcare outcomes and related

costs. In many regions, the quality of administrative data needs to be improved to provide more comprehensive information, such as identification of individuals living with HCV and the services they have accessed. Disaggregating HCV-relevant data into key sub-populations (Indigenous peoples, newcomers to Canada etc.) is also important for guiding HCV policy and monitoring progress towards elimination.

TO THIS END, THE *BLUEPRINT* CALLS FOR:

Establishing surveillance systems across all regions of Canada by 2020, and to:

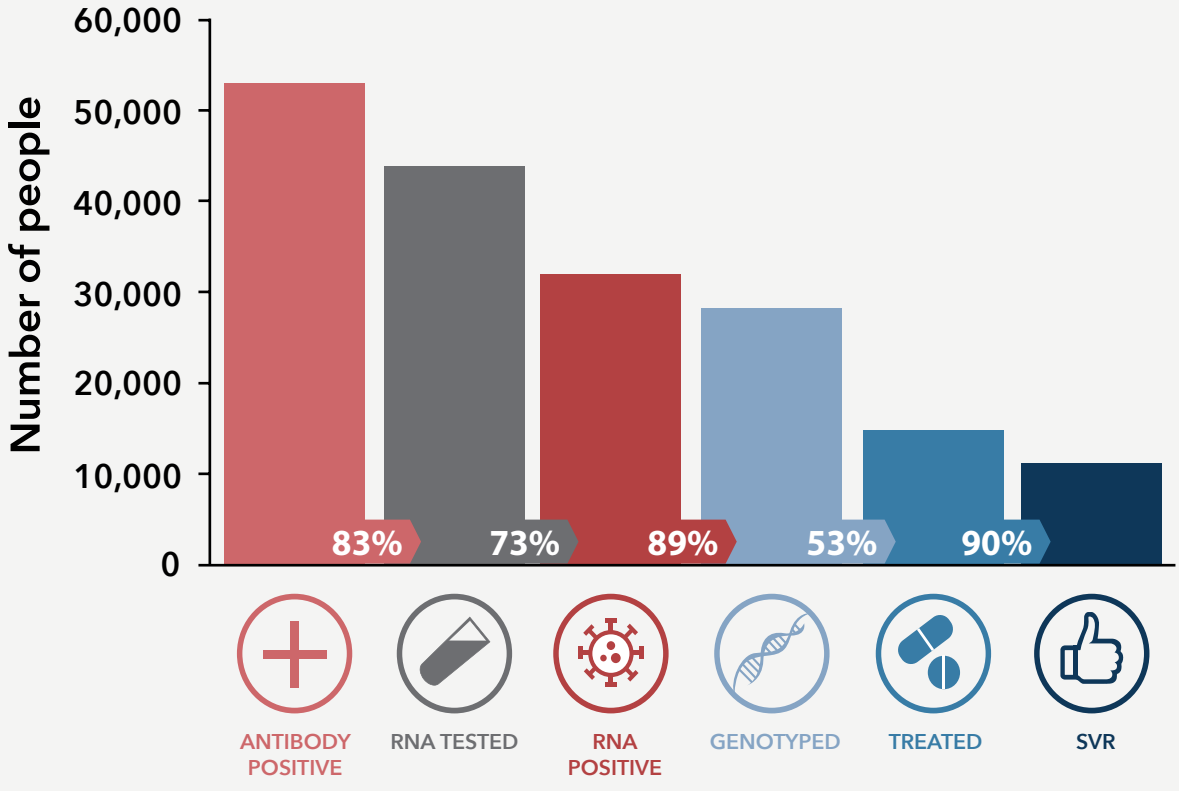
- Carry out systematic, biannual serosurveys, with adequate representation of Priority populations and all age groups, including children and youth, to generate high quality provincial, territorial, and national estimates of HCV prevalence;
- Use enhanced reporting on acute hepatitis, well-designed epidemiological cohort studies, serial cross-sectional studies of populations at ongoing risk, and serial prevalence estimates among youth to estimate HCV incidence (see challenges of measuring incidence, below);
- Leverage ongoing surveillance studies for other diseases by including HCV testing.

Regularly-updated HCV surveillance must include adequate representation of Priority populations, carefully designed efforts to assess HCV incidence (new infections and reinfections) and surveillance of risk behaviors, so that prevention services are responsive to new transmission patterns, and to ensure adequate coverage of harm-reduction services.

Linking surveillance data with provincial and territorial administrative health data:

- Integrating data on HCV incidence and prevalence with administrative health data will enable monitoring of HCV outcomes across the cascade of care and the costs of care, by region and by population;

Figure 9. The British Columbia hepatitis C virus cascade of care [75]



- Administrative datasets should include data on healthcare utilization (outpatient, specialty care, emergency room services, hospitalizations), treatment uptake (including provider-type), cancer incidence (cancer registry), liver transplantation and mortality, which can be linked to specific HCV diagnostic laboratory results.

MEASURING NEW HEPATITIS C INFECTIONS – THE CHALLENGES OF MEASURING INCIDENCE

Currently, neither Canada nor its provinces and territories systematically collect reliable HCV incidence data. Accurate data on HCV incidence are hard to collect; large numbers of people from different risk groups need to be followed over time, with serial testing to identify if and when they acquire HCV. Observational longitudinal cohorts of PWID have reported high incidence rates in many Canadian settings. [76, 77] However, these estimations cannot be generalized, as there is great regional and contextual heterogeneity across the country.

HCV is reportable in all provinces and territories, and information may be collected about the source of infection. Estimates of HCV incidence have been generated from provincial reporting systems, which makes it difficult to distinguish incident (new) infections from prevalent (long-standing) infections. Unfortunately, *new diagnoses* are often reported as *new infections*, making it likely that current estimates of HCV incidence in Canada are unreliable. Furthermore, most new HCV infections are not recognized or reported because they are often asymptomatic.

Although data on both new and long-standing HCV infections are important, new diagnoses of long-standing HCV infections do not provide information about current HCV transmission or incidence, and thus must not be included in incidence estimates. Determining the percentage of newly reported cases that are actually new infections (rather than new diagnoses of long-standing infection) allows estimates of incidence as a fraction of the prevalent cases in the population – which is a much easier number to measure and to model. This can be achieved by careful follow-up of new diagnoses with clear case definitions for new (incident) infections. Other approaches to estimate incident HCV infections may be considered (see Table 3).

As true incidence data are unavailable, the simplest approximation may be to assume that most new infections in Canada occur among young people. There are obvious caveats to such a simplified approach, although this strategy would provide useful data to guide policy and progress toward elimination.

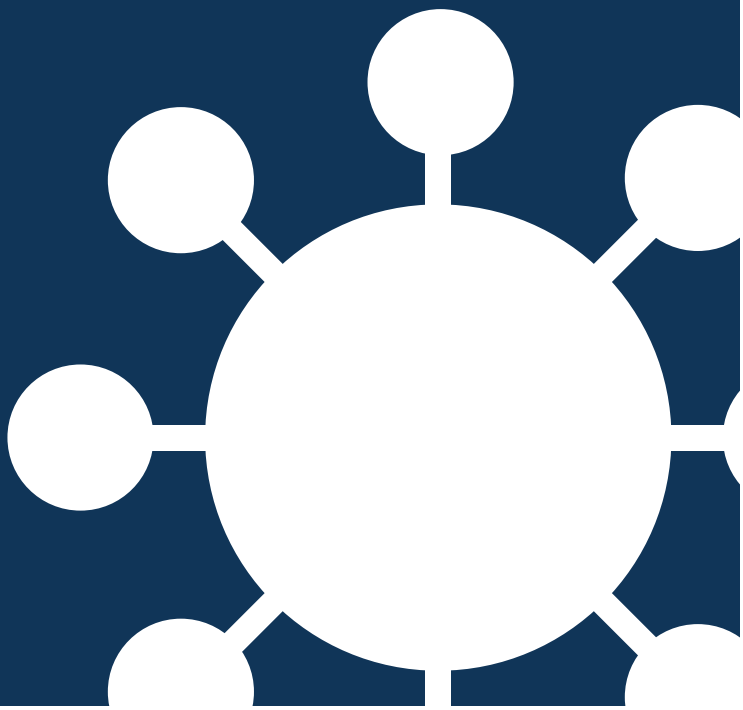
Ideally, each region will use a combination of approaches to estimate incidence by different methods, which will help provide estimates to guide policy.

Table 3. Approaches to measuring hepatitis C virus (HCV) incidence

Methods	Description	Pros	Cons
Longitudinal cohort	Defined population/risk group followed serially, with repeat testing to identify individuals who test positive after initially testing negative	• Precise estimate for specific population	• Costly • Slow (requires years of follow-up) • May not be generalizable to other populations or regions • Must know the size of the studied population (e.g. PWID, gbMSM) in the region/country
Use of HCV antibody avidity index	HCV antibodies produced during recent infection have different properties than those in chronic infection. By measuring HCV antibody avidity in the population, the proportion of recent or incident infections can be determined.	• Simple measurement of HCV antibody avidity in the whole population of HCV antibody-positive individuals	• Assays for antibody avidity are not standardized or widely available • Population sample requires inclusion of those with recent infection, many of whom may not be tested or diagnosed
Repeated sentinel survey	Periodic serosurvey of defined population or general population, with information on risk activities, with incidence based on: i) repeat testers who test positive after initially testing negative, or ii) based on changes in prevalence over time to estimate incidence.	• Relatively reliable incidence estimate in different populations • Potential to collect data on other health outcomes	• Costly • Relatively slow • Requires sampling of at-risk populations • Requires knowledge of treatment uptake and mortality to infer incidence from prevalence data
Enhanced surveillance of acute hepatitis	Detailed case-tracking of all new HCV diagnoses using clinical data to identify acute/new HCV infections. Overall incidence is then determined based on percentage of new HCV infections that result in acute hepatitis.	• Reporting and follow-up of new diagnoses already established • Relatively inexpensive	• Requires reliable data on percentage of new HCV infections that cause acute hepatitis • Likely to provide accurate relative trends in incidence rather than accurate absolute numbers of incident cases
HCV in young individuals (under age 25)	Most HCV transmission in Canada occurs among PWID, the majority of whom are young. Changes in prevalence among youth likely identify the majority of incident infections.	• Relatively simple to collect • Likely fairly reliable	• Requires accurate prevalence data among youth, which requires sentinel serosurveys including at-risk populations due to low routine testing rate • Imprecise: misses transmission in older people and assumes transmission in young people with prevalent infection

HEPATITIS C PREVENTION

- Why is it important to enhance hepatitis C prevention?
- Current situation
- Key objectives and targets
- Good practices and suggested activities
- Research gaps



HEPATITIS C PREVENTION

WHY IS IT IMPORTANT TO ENHANCE HCV PREVENTION?

The highest rates of new and existing HCV infections are found in the estimated 171,900 PWID in Canada [32] who comprise up to 85% of all new HCV infections and 70-80% of existing infections. [3-8] Yet HCV transmission is preventable with evidence-based, WHO-recommended and cost-effective interventions such as needle syringe programs (NSP) [78, 79] and opioid agonist therapy (OAT). Together, these reduce the risk for HCV infection by up to 74%, [80] and their impact can be augmented by HCV treatment as prevention (TasP). Modelling demonstrates greater prevention benefits occur when high-coverage NSP and OAT are combined with rapid HCV treatment scale-up among PWID. [17-19] HCV treatment is most cost-effective among people who are currently injecting drugs and in people with advanced liver disease.[81] Furthermore, the models indicate that rapid scale-up to high treatment coverage is cheaper than slow introduction of treatment in PWID populations, and that HCV treatment is particularly effective when offered in the context of well-structured OAT and other harm-reduction programs. [82]

As HCV treatment is expanded to populations with ongoing risk, an initial increase in reinfection rates is likely to occur, since curing HCV does not protect against reinfection. It is important to recognize that an initial increase in reinfection rates is an indication that the highest-risk populations are being identified, engaged in care, and treated. Reinfection rates can be lowered by rapidly scaling-up HCV treatment among PWID; a reduction in the overall prevalence among PWID means that people who have been cured are less likely to be exposed to HCV during injection drug use, because there is less HCV in the population. When treatment coverage among PWID is very high, reinfection rates will start to fall as the benefits of TasP become apparent. Scaling-up coverage of harm-reduction strategies is also necessary for reducing reinfection rates.

Developing specific targets for reducing reinfection rates over time is difficult. Ultimately, as with new HCV infections, the goal for 2030 is to reduce HCV reinfections by at least 80%, which will require expansion of existing prevention programs. However, intermediate goals are less clear due to the expected initial increase in reinfections as higher-risk populations are treated. Currently, both coverage and reach of Canada's HCV prevention programs are insufficient. Current coverage in Canada is estimated at 291 needle-syringes per PWID per year, with substantial variation across the country, [32] and harm-reduction programs are not evenly distributed throughout regions and territories.

Prevention tools and initiatives for other populations are less well defined. High rates of HCV infection and reinfection have been reported among gbMSM, with little data on the effectiveness of behavioural and/or other interventions on decreasing transmission.

CURRENT SITUATION IN CANADA

People who inject drugs, many of whom use illicit or prescription opioids, have a high incidence of HCV. [90] These people are also experiencing high morbidity and mortality from the overdose epidemic. Given the overlapping nature of these two epidemics in this population, it is imperative that HCV prevention is coordinated with efforts to reduce the risk of opioid overdose and focused on addressing the broader social and healthcare needs of people who are at risk.

Emerging risk factors for HCV among gbMSM and PWID highlight the importance of closely monitoring transmission rates, so that prevention programs are responsive to new risk patterns. As examples, HIV PrEP and condomless sex may have an impact on

AN HCV VACCINE

In addition to harm-reduction and TasP strategies, the ultimate preventative tool would be a protective vaccine. An HCV vaccine has been an elusive target, due to the high mutation rate of the virus. However, Canadian researchers are among world leaders in HCV vaccine development efforts.[83-88]

Vaccines have shown promising results in early trials, and modelling studies suggest that even a vaccine with modest efficacy could reduce HCV transmission among PWID.[89] Support to advance the vaccine agenda in Canada could have major national and global impact.

The *Blueprint* supports:

- Continued funding for research leading to the development of an HCV vaccine;
- Measuring acceptability and feasibility of a vaccination program, if available, in Canada;
- Modelling the potential impact of an HCV vaccine, combined with other strategies, on HCV transmission; evaluating its cost-effectiveness, given varying scenarios of prevention and treatment coverage levels;
- Promoting development of an effective HCV vaccine by providing technical expertise and promoting industrial/academic partnerships for large-scale production of vaccine candidates for clinical trials.

HCV transmission among gbMSM[67,68] and/or PWID,[91] while trends in injection drug use, such as injecting methamphetamine and prescription opioids or injecting binges, could increase HCV risk.[92] However, reliable national-level data on the true rate of new infections are not available.

Some Priority populations have additional HCV risk factors. Sexual transmission of HCV may also occur; the risk depends on the type of exposure,[93,94] with heterosexual couples having the lowest risk.[95] GbMSM who are living with HIV and/or who are using specific recreational drugs (sometimes by injection) in a sexual context, and often in a party environment, have the highest risk for HCV.[96,97] Scant data exist on the most effective strategies to prevent or reduce HCV transmission in this context.

Data on HCV among children and adolescents under age 18 are not currently available. An estimated 6% of infants born to women with HCV are perinatally infected; the rate is twice as high among women with high HCV viral loads, and two to four times higher among women who are HIV/HCV co-infected - especially if they are not on antiretroviral therapy.[98-102]

KEY OBJECTIVES AND TARGETS

The prevention targets were developed using available information about HCV incidence and prevalence and coverage of evidence-based interventions to prevent HCV.

Table 4. Key objectives, targets and indicators for hepatitis C virus (HCV) prevention

Objectives	2025 Targets	2030 Targets	Key indicator label **
Reduce new HCV infections	**80%** ↓ incidence*	**80%** ↓ incidence*	P1, P2
Increase the number of sterile needles and syringes provided per person who injects drugs (PWID) per year	**500** sterile needles/ syringes	**750** sterile needles/ syringes	P3
Increase the number of PWID who are accessing opioid agonist therapy (OAT)	**40** of PWID receive OAT	**≥ 40** of PWID receive OAT***	P4

**Compared to 2015;*

***Refer to the appendix for a list of the Indicators and metrics to monitor and report progress for HCV Prevention;*

****Target to be revised according to mathematical modeling studies.*

GOOD PRACTICES

Evidence and/or expert opinion supports the effectiveness of these good practices; they may need to be adapted to meet the needs of Priority populations, and for certain settings:

- Partnering with community groups is key to strengthening the reach and impact of prevention efforts;
- Scale-up NSP: the gold standard is a new needle/syringe for each injection, which lowers HCV risk by over 50%; [80]
- Scale-up OAT: reduces risk for HCV (and HIV). When used with 'gold standard' NSP, HCV risk is reduced by 74%; [80]
- Implement evidence-based programming to discourage people from initiating injection drug use; [103]
- Implement effective peer-based interventions to deliver education, counseling and linkage, and support engagement in care and services. [104]

SUGGESTED ACTIVITIES

Needle syringe programmes

Needle syringe programs can prevent HCV. Although WHO recommends a minimum of 300 needle/syringe sets per PWID/year, [105] the gold standard for HCV prevention is a new needle/syringe for each injection. This high level of coverage reduces HCV risk by up to 56%. [80] Current median coverage in Canada is estimated at 291 needles/syringes per PWID in 2016, with substantial variation across the country. [32] Harm-reduction programs are not evenly distributed throughout communities, regions, provinces and territories (range: 136-883 needles/syringes per PWID). Based on national I-Track and other Canadian surveillance data, a median of 408 injections occur per PWID/year. With wide regional, temporal and individual variation in injection frequency, more sterile needles/syringes are required per year than the median injection frequency to provide optimal coverage. As such, this *Blueprint* proposes a target of 500 needle/syringes per PWID/year by 2025 and 750 needle/syringes per PWID/year by 2030 to achieve the maximum benefit from NSP.

These targets account for the uncertainty in PWID population size estimates (including delays in producing estimates) and providing needles/syringes to cover >100% of injections. To reach these targets, implementation plans should include consideration of geographic accessibility (short travel distances to obtain needles/syringes) and reflect local drug use patterns, including differing frequency of injecting depending on the substance(s) used in the community.

Suggested Activities

- Offer a sufficient amount and variety of low-dead space syringes (which lower HIV risk and may also reduce HCV risk), [106, 107] and all additional injection equipment (swabs, filters, cookers, water).
- NSP should be easily accessible in terms of proximity, opening hours and access points (e.g., specialized fixed sites and mobile outreach units; traditional service points such as pharmacies and clinics);
- Ensure NSP is available in provincial and federal prisons;
- Expand the reach of NSP by using innovative approaches, such as syringe vending machines. [108]

Opioid agonist therapy

The WHO definition for high-coverage OAT is 40 per 100 PWID, per year.[109] In Canada, OAT includes the use of methadone, buprenorphine in combination with naloxone, slow-release oral morphine and injectable opioids. OAT is prescribed to dependent opioid users, to diminish use and effects of illicitly acquired opioids and reduce the frequency of injection and exposure to unsafe injecting practices.[110] OAT provides a range of benefits, including reductions in risk of HIV and HCV as well as other blood-borne infections, decreases in criminal activity, drug-related incarceration and reductions in mortality from overdose or other causes.[111] By itself, OAT reduces HCV risk by 50%; combining it with high-coverage NSP further reduces HCV risk, by up to 74%.[80]

Current OAT coverage in Canada is estimated at 66 per 100 PWID.[32] However, there is considerable heterogeneity in access to, and the range of pharmacotherapies available by province/territory (range: 29-163 per 100 PWID), and no estimates are available of the real need for OAT. In Canada, according to the most recent I-Track data (2012-2014), an estimated 35% of PWID inject cocaine or crack most frequently, with considerable variation across provinces and territories.[112]

Many of these PWID may not use opioids at all, and consequently may not benefit from OAT. Furthermore, some opioid-using PWID may not be eligible for and interested in OAT (e.g., use may be sporadic).

To achieve the maximum benefit from OAT, the *Blueprint* proposes a target of 40 per 100 PWID by 2025. Although this target is below the estimated current median coverage in Canada, many regions in Canada currently are not achieving it. The *Blueprint* proposes to estimate the optimal level of OAT coverage needed to achieve the 2030 HCV incidence target, and to revise the 2030 OAT target, accordingly. This recommendation highlights the need for expanded surveys on drug use among PWID to reflect local patterns of drug use, and the need for treatment.

The optimal targets and how to reach them will be affected by PWID population size estimates, the pharmacotherapies and the available providers; this highlights the need for expanded surveys on drug use among PWID and health surveys to inform these estimates. Implementation of targets should reflect local drug use patterns, including prevalence of opioid dependence in the community, and should recognize that not all opioid-dependent individuals desire OAT.

<u>Suggested Activities</u>

- Offer access to various forms of OAT (including methadone, buprenorphine/naloxone and other opioid agents, such as slow-release oral morphine, and injectable opioids) in adequate dosages, according to user preferences;
- Increase OAT access, by making it available through pharmacists and nurse practitioners, and in various settings, such as primary care, in the community, at NSP sites, hospitals and at emergency service sites;
- Ensure OAT is available in provincial and federal prisons;
- Facilitate linkage to, and initiation of OAT by training healthcare workers to deliver it;
- Provide HCV treatment services where OAT is offered;
- Provide treatment and services for PWID other than opioids.

Discourage Transition to Injecting

Evidence-based interventions such as "Break the Cycle" or "Change the Cycle" can prevent initiation of injecting.[103]

Suggested activity:

- Enhance prevention of HCV and other blood-borne infections (BBI) by educating, promoting and supporting alternatives to injection drug use among PWUD who are at high risk for initiating injection drug use.

Supervised consumption services

Recently, nearly thirty supervised consumption sites have opened throughout the country in response to the opioid epidemic with others pending approval.[113] These sites have the potential to reduce transmission of HCV, other BBI, and overdose, and to promote links to primary care services.[114]

Suggested activity:

- Monitor the impact of supervised consumption sites on transmission of HCV and other harms, by conducting periodic cross-sectional surveys among people who use these services.

Peer-based interventions

Peers (people with lived experience of HCV) can provide education and counseling, build community support networks, offer linkage to harm-reduction, healthcare and social support services, and support engagement in these services.[104]

Suggested activities:

- Expand access to peer-based interventions, including linkage to harm-reduction programs;
- Provide training and resources for peer workers, to support them in better engagement with their communities.

Expand access to ancillary care services

Access to OAT facilitates provision of other services, but not all PWID are eligible for, or desire to be enrolled in OAT at a given time.

Suggested activity:

- Provide access to primary care and mental health services, and to comprehensive addiction services offering treatment other than OAT, including psychosocial interventions such as cognitive behavioural therapy, brief interventions and contingency that have also been shown to reduce the risks associated with injection drug use.

Provide integrated services for, and information that is relevant to Priority populations

Despite the high risk for, and rates of HCV among members of Priority populations, they are often excluded from mainstream health services. To be effective, programs and services for Priority populations need to address the full array of syndemic health needs.

Suggested activities:

- Integrate HCV awareness, testing and prevention strategies for gbMSM with those for other STBBI;
- Monitor the potential effect of HIV PrEP on HCV transmission among gbMSM;
- Research and provide access to services and/or harm-reduction programs specific for reinfection prevention.

Reduce the risk for HCV reinfection

People who have been cured from HCV are susceptible to reinfection from ongoing risk exposures. The risk for reinfection among PWID can be reduced by scaling-up access to harm reduction and TasP, and through offering stigma-free testing, prevention, care, and treatment services, including re-treatment.

Suggested activities:

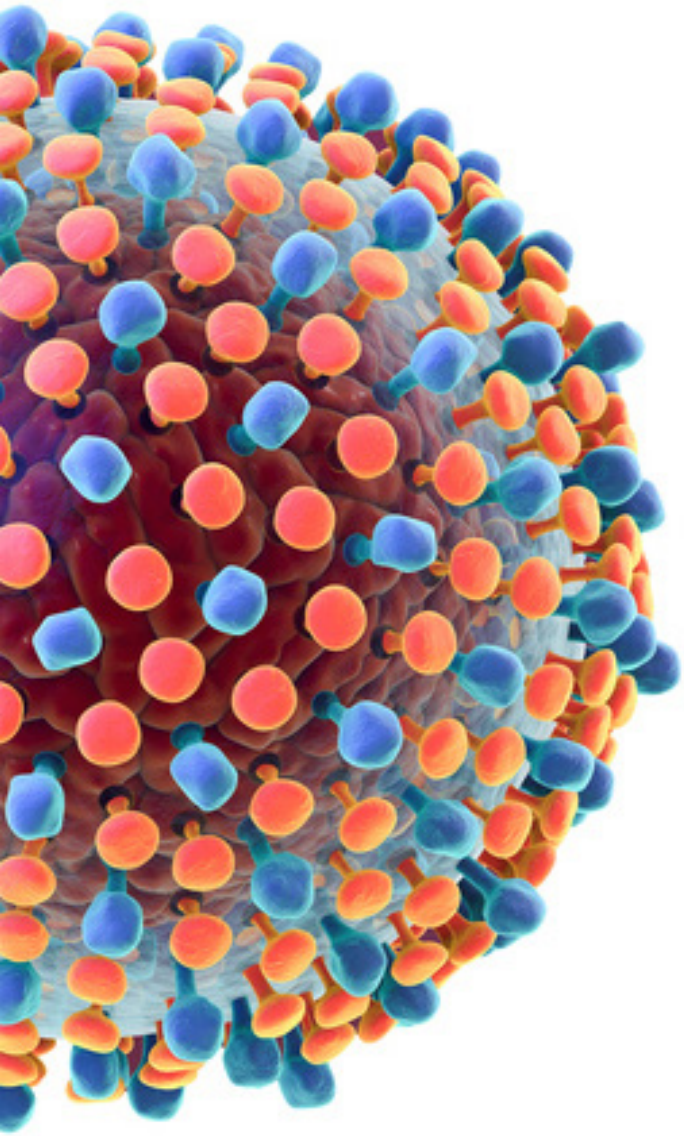
- Develop and provide access to services and/or harm-reduction programs specifically for preventing reinfection;
- Continue testing for HCV with testing for active HCV infection (e.g. HCV RNA) every 6-12 months in people who have cleared HCV and are engaging in risk activities.

Improve care for women of child-bearing potential who are at risk for HCV

Currently, there is no intervention to prevent vertical HCV transmission; the risk is approximately 6% although it is higher if the mother is also living with HIV.[98-102]

Suggested activities:

- Provide counseling and HCV testing as part of pre-natal care for women at high risk;
- Ensure women who test positive for HCV receive testing for active infection and are linked to HCV care and treatment; curing them will also prevent transmission in future pregnancies;
- Provide good HCV-related prevention and care practices to mothers and their babies.



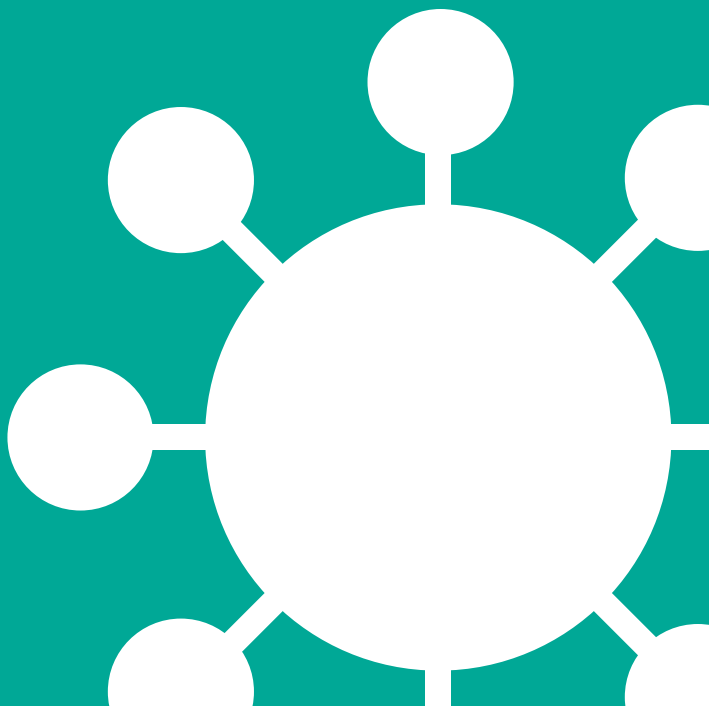
RESEARCH GAPS

HCV prevention can be optimized by research to address key knowledge gaps, such as developing a vaccine, knowing the reach, coverage and effectiveness of prevention interventions, and the scale needed to achieve HCV elimination; therefore, the *Blueprint* supports the following:

- Support development of an HCV vaccine;
- Estimate, through modeling and observational studies, the level of NSP, OAT and HCV treatment scale-up needed to achieve HCV elimination targets;
- Identify optimal models of care to enhance access and retention into OAT;
- Examine the effectiveness of harm-reduction programs in preventing HCV reinfection;
- Examine the effectiveness of behavioural interventions in reducing HCV transmission, overall and in specific populations, particularly in PWID and gbMSM;
- Increase research for the evaluation and scale-up of prevention interventions targeting HCV risk associated with drug use in a sexual context among gbMSM;
- Increase research on interventions to reduce HCV risk among PWID who are not eligible for, or do not desire OAT;
- Increase research to prevent initiation into injection drug use among emergent groups of PWID (e.g. people who engage in drug use in a sexual context, people who use non-injectable drugs);
- Increase research on peer-led interventions that prevent initiation into injection drug use among high-risk populations;
- Evaluate the cost-effectiveness and acceptability of adding HCV to the prenatal screening package for all women, compared to current risk-based targeted screening.

HEPATITIS C TESTING & DIAGNOSIS

- Why is it important to enhance hepatitis C testing and diagnosis?
- Current situation
- Key objectives and targets
- Good practices and suggested activities
- Research gaps



HEPATITIS C TESTING AND DIAGNOSIS

WHY IS IT IMPORTANT TO ENHANCE HCV TESTING AND DIAGNOSIS?

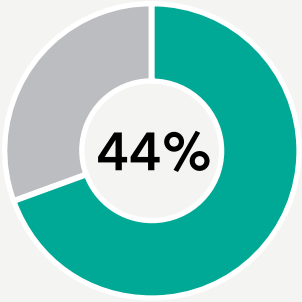
HCV infection often has mild, non-specific symptoms - or none at all - until serious liver damage has developed. Since this process can take decades, HCV often remains undiagnosed.[115]

HCV antibody testing (for evidence of past or current HCV infection) is the gateway to further engagement in confirmatory testing, care, treatment and ongoing support, and it is essential to elimination strategies. In many settings, testing and serial screening have been shown to be cost-effective.[116-121] Different testing strategies are required for different populations. For populations with higher prevalence but few or no ongoing transmission risks, such as the 1945-1975 birth cohort, one-time testing is adequate. For people who are at ongoing risk, serial screening is required. Identifying people who are undiagnosed and linking them with care and treatment before they develop HCV complications will decrease the health consequences of HCV.

CURRENT SITUATION IN CANADA

Nearly half of all people living with HCV in Canada are unaware of their infection.[8]

Figure 10. Hepatitis C virus (HCV) diagnosis in Canada



An estimated
250,000
people in Canada are living with HCV

110,000
of them are **unaware** and **undiagnosed**

Canada has historically advocated for risk-based screening for HCV. However, this approach requires that people and their healthcare providers recognize and acknowledge past risk exposures which may have occurred years or even decades prior. The low diagnosis rate with risk-based screening has led to consideration of other approaches. In the 2018 update of its *Guideline on the Management of Chronic Hepatitis C*, the Canadian Association for the Study of the Liver (CASL) recommended expanding HCV testing beyond those with known risk factors to include the birth cohort of those born between 1945 and 1975, irrespective of their risk exposures.[122] The rationale for one-time HCV testing for this age group is based on the observation that 66-75% of all HCV infections in Canada are among people born between these years, and yet there is a particularly low rate of testing and diagnosis in this group, often because of a perceived low risk of infection.[8] Canadian data suggest that this testing strategy is likely to be both

cost-effective [121] and life-saving, since the highest rates of HCV-related liver failure and liver cancer are found among people born between 1945 and 1964. [3, 4, 8, 9]

Notably, the Canadian Task Force on Preventative Health Care recommended against routine birth cohort testing, citing primarily the high cost of DAA therapy and the lack of access for those with minimal liver damage. Subsequent to their analysis, negotiations by the Pan-Canadian Pharmaceutical Alliance (pCPA) resulted in reduced prices for DAA therapy, which led to removal of fibrosis restrictions across the country, suggesting that the Task Force recommendations should be reconsidered. [123, 124]

Birth cohort screening is controversial because of the significant budget impact of testing a large portion of the population. Well-established models have been developed to evaluate the cost-effectiveness of one-time HCV testing. [121, 125, 126] Although the value of health is hard to monetize, health interventions that cost less than $50,000 per quality adjusted life year (QALY) are generally considered to be good value for money and thus cost-effective. [127, 128] The previously published cost-utility analyses were updated to reflect the current treatments and costs of HCV care in Canada to evaluate whether a strategy of one-time testing and linkage to care would be cost-effective compared to the current model of risk-based testing. The results for different birth cohorts in Canada are shown in Table 5.

The most important determinants of the cost-effectiveness of any widespread testing program are the prevalence of HCV in the population and the proportion with the infection who remain undiagnosed. In the 4th column, estimates from PHAC for the prevalence of HCV and the undiagnosed fraction (44%) were used to calculate the incremental cost-effectiveness ratio (ICER) of an active test-and-treat strategy compared to current practice for each age-band. For all but the oldest group, one-time HCV testing and linkage to treatment would be well below the $50,000 per QALY willingness-to-pay threshold. To determine if more recent data would change the outcome, the analysis was redone with updated estimates for HCV prevalence and the undiagnosed fraction using administrative health data from BC and Ontario (column 5). [27,130] With higher prevalence but a lower undiagnosed fraction than the PHAC estimates, the ICERs are very similar, and still well within the cost-effective range for all but the oldest group. [127,128] Because of the importance of, and uncertainty about the prevalence estimates by age-group, an analysis was performed to determine the threshold prevalence for each age-group above which one-time HCV testing and linkage to treatment would be cost-effective. As shown in column 3, even the lower PHAC prevalence estimates are many times higher than the minimum prevalence thresholds for cost-effectiveness. Overall these data suggest that it would be cost-effective to implement one-time HCV testing in most of the adult population.

However, it is also important to consider the yield of testing and the budget impact. The low prevalence in the youngest age groups means that a lot of testing would need to be done to find the relatively few with HCV. Furthermore, young people are less likely to have advanced liver damage and may still have future risk exposures, reducing the urgency of diagnosis and the efficiency of one-time testing. The overall cost of testing and treating a large sector of the population would be high, thus although 'good value for money' (cost-effective), there would be a significant budget impact. A recent analysis for Ontario suggests that with expected DAA price reductions, a one-time test and treat strategy for those born from 1945 to 1964 would cost an additional estimated $231 million over 5 years, which is in line with many common health expenditures.[126]

Although the situation may vary somewhat across the country, these analyses suggest that in most, if not all jurisdictions in Canada, it would be cost-effective to implement one-time birth cohort testing in the 1945 to 1965 or 1945 to 1975 birth cohort. Risk-based testing should still be performed in those born outside of the birth cohort. Ongoing surveillance data will be required to assess the effectiveness of birth cohort testing and to determine how long testing programs should continue.

Table 5. Cost-effectiveness of birth cohort screening in Canada [125]

Birth cohort	Age range (at 2019)	Threshold for HCV prevalence to be cost-effective at $50,000/QALY	PHAC estimates for prevalence and undiagnosed fraction (44%)		Revised estimates for prevalence and undiagnosed fraction (BC 33%, Ontario 36%) based on BC & Ontario (ON) administrative data	
			Prevalence estimate[72]	Incremental cost-effectiveness ratio (ICER)[27, 129, 130]	Prevalence estimate[27, 129, 130]	Incremental cost-effectiveness ratio (ICER)[27, 129, 130]
>=1995	15 – 24	0.01804%	0.4%	$10,089/QALY	0.53% (BC) 0.52% (ON)	$9,819/QALY (BC) $9,654/QALY (ON)
1985-1994	25 – 34	0.02417%	0.4%	$12,244/QALY	0.53% (BC) 0.52% (ON)	$11,895/QALY (BC) $11,684/QALY (ON)
1975-1984	35 – 44	0.02282%	0.4%	$12,585/QALY	0.53% (BC) 0.52% (ON)	$12,260/QALY (BC) $12,063/QALY (ON)
1965-1974	45 – 54	0.04478%	0.4%	$18,811/QALY	0.53% (BC) 0.52% (ON)	$18,247/QALY (BC) $17,904/QALY (ON)
1955-1964	55 – 64	0.04478%	0.8%	$16,845/QALY	2.31% (BC) 1.93% (ON)	$16,310/QALY (BC) $16,597/QALY (ON)
1945-1954	65 – 74	0.10983%	0.8%	$26,577/QALY	2.31% (BC) 1.93% (ON)	$25,562 /QALY (BC) $26,106/QALY (ON)
<1945	75 +	Not cost-effective to screen at $50,000/QALY	0.8%	$56,593/QALY	0.75% (BC) 0.75% (ON)	$60,700/QALY (BC) $65,525/QALY (ON)

**Key parameters of the model: Lifetime time horizon, Screening uptake rate 90%, HCV Ab cost $21.53, HCV RNA cost $115, Linkage to treatment 80%, SVR rate non-Genotype 3 99%, Genotype 3 cirrhotic 91.7%/non-cirrhotic 97%, Cost of therapy: 70% of current retail price listed in Ontario Drug Benefit Program. Revised estimates for prevalence and undiagnosed proportion based on health administrative data from BC and Ontario showing higher prevalence but lower undiagnosed fraction than previous PHAC estimates.*

The HCV testing process itself can be a barrier to treatment, since it requires two steps (Figure 11). The first step, HCV antibody testing, cannot distinguish a current HCV infection from one that was cleared either spontaneously, shortly after infection (which occurs among 25% of people with HCV), [131] or cured by treatment. People with a positive HCV antibody test result need follow-up testing to document whether they have an active HCV infection (detectable HCV RNA). In most settings, the HCV RNA test requires a second visit and another blood draw - and a third visit to receive those results.

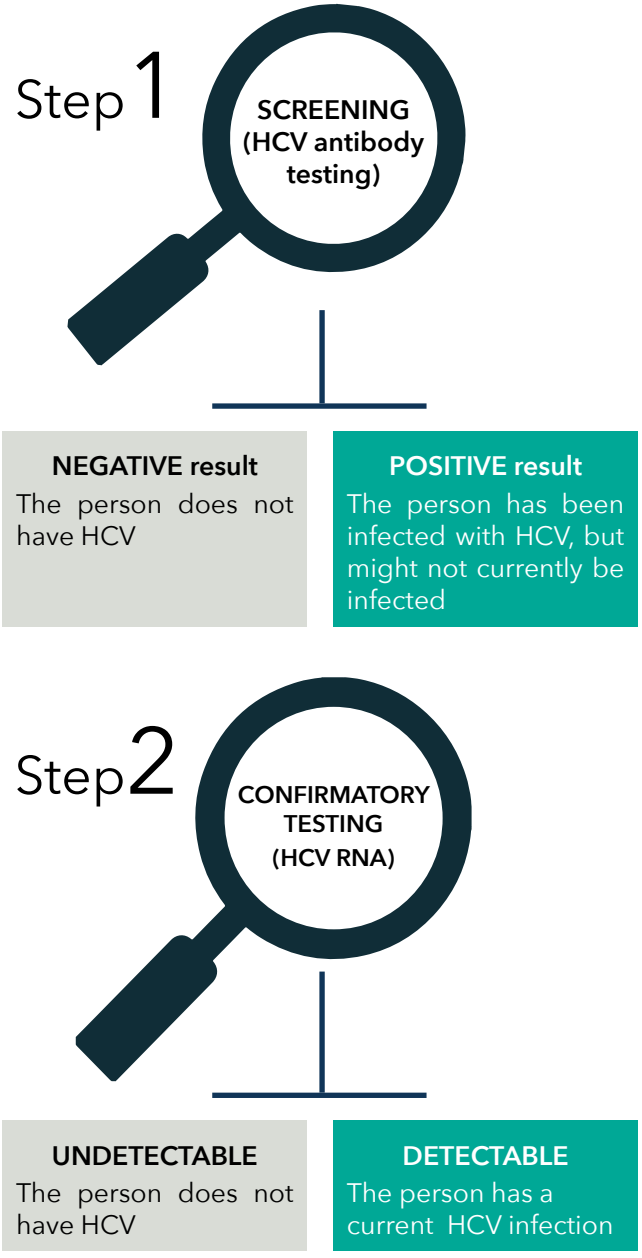
Most studies find that 25-35% of people who test antibody positive never have a follow-up HCV RNA. Loss to follow-up rates are even higher among Priority populations, with studies reporting that 46-73% of people with a positive antibody test result never receive a follow-up test for HCV RNA. [132-134] Notably, data from BC have suggested better follow-up with HCV RNA testing among PWID than has been reported in other countries. [135] However, BC has better coverage of harm-reduction services than most other regions. Whether the BC data are generalizable to the rest of Canada is unclear, but the lack of follow-up HCV RNA testing among both PWID and non-PWID populations is a major impediment to elimination efforts.

The two-test requirement is particularly problematic for 'opportunistic screening' such as at health fairs, in the emergency room, and in other places where people would not have an easy way to receive results, or to arrange for follow-up testing. Commercial labs in other countries have shown that reflex testing for HCV RNA can be performed with the same tube of blood used for HCV antibody testing, but this approach has not been adopted in Canada.

Common patient and provider-level barriers to HCV testing can be addressed to improve the reach and access to HCV testing. For patients, barriers include embarrassment and stigma; concerns about privacy and confidentiality; inconvenient clinic or physician location and/or hours of operation, and fear of, or difficulty in having blood drawn. Provider-level barriers include lack of knowledge about HCV, including optimal testing algorithms; not offering testing due to assumptions about an individual's risk for HCV; lack of time for counseling, and personal discomfort, including HCV-associated stigma.

A range of effective strategies can address the HCV testing gap. Some are systems-based and others provider-based, such as physical and electronic medical chart prompts that remind healthcare providers to follow up on positive antibody test results, [136-140] performing reflex HCV RNA testing for all positive antibody test results so people do not have to undergo a second blood draw, [141, 142] and implementing call-back programs for people with positive antibody test results who have never had follow-up testing. Access to HCV testing can be expanded, by providing pre-test counseling, education and on-site testing outside of medical settings, [143-147] and through peer [148] and prison-based [149] outreach programs that deliver counseling and testing and incentivized peer referral initiatives. [150]

Figure 11. Hepatitis C virus (HCV) screening and testing algorithm



New, simpler diagnostic methods can increase the number and type of sites where HCV testing can be performed, and they facilitate task-sharing by broadening the range of providers who can deliver testing and care. [151-153] Point-of-care (PoC) HCV testing [154] enables testing at pop-up clinics, community fairs, rural sites and needle syringe programs. PoC tests have been developed for HCV antibody and, more recently, for HCV RNA, which allows rapid two-step testing; HCV RNA testing can be performed immediately after a positive PoC antibody test result. [155, 156] These tests only require a drop of blood from a finger-prick. PoC tests using oral/salivary fluid have also been developed for HCV antibody; despite having slightly lower sensitivity, this form of testing is non-invasive and may be particularly useful in certain settings and/or in specific populations, including for PWID, where drawing blood can be a barrier to testing.

Dried blood spot (DBS) testing involves collecting a drop of blood on four or five spots of filter paper. It enables reflex HCV RNA testing for all positive antibody test results by testing the next spot on the card if the first spot tests positive for antibody. DBS testing also allows for testing for other infections (e.g. HIV, hepatitis B) using other spots on the DBS card. [157-164] Staff or peers with limited or no medical background can be trained to carry out DBS testing under supervision or a medical directive from authorized health professionals, reducing costs and potential barriers to engagement with testing.

HCV TESTING TECHNOLOGIES

There are minimally invasive methods for HCV screening and testing that can be administered at the PoC. Rapid antibody testing can be done with saliva or a finger-stick; results are available in 20 to 40 minutes (only the finger-stick assay is approved in Canada).[165] HCV core antigen (cAg) testing is an alternative to HCV RNA, as it also detects active HCV infection. It is cheaper than HCV RNA testing, but it still requires a central laboratory and is less sensitive than HCV RNA, potentially missing up to 3% of those with chronic HCV infection. As such, if the HCV antibody test is positive and HCV cAg test is negative, an HCV RNA test is still required to confirm absence of active infection.

Dried blood spot (DBS) testing is particularly useful for rural and remote regions. Because only a finger-stick is required, the test can be delivered by peer and other outreach workers and the card can be sent by regular mail to a laboratory for processing. However, the results are not immediately available, creating a risk for loss to follow-up. Rapid, PoC HCV RNA testing can be performed with a finger-stick sample with results available in one hour (not currently approved in Canada).[166]

Some of these proven technologies are available in Canada, but they are not reliably funded, making them largely inaccessible.

KEY OBJECTIVES AND TARGETS

The testing and diagnosis targets were developed using available information about HCV incidence and prevalence and the number of people who remain undiagnosed.

Table 6. Key objectives, targets and indicators for hepatitis C virus (HCV) testing and diagnosis

Objectives	2025 Targets	2030 Targets	Key Indicator label *
Increase the number of people living with HCV who have been diagnosed	**70%** of people living with HCV have been diagnosed, all with confirmation of active infection	**90%** of people living with HCV have been diagnosed, all with confirmation of active infection	T1, T2, T3
Increase the number of people with a positive antibody test who receive testing for active HCV infection (e.g. HCV RNA)	**90%** of people with a positive antibody test have received HCV RNA testing	**100%** of people with positive antibody test have received HCV RNA testing	T1, T2, T3

**Refer to the appendix for a list of the Indicators and metrics to monitor and report progress for HCV testing and diagnosis*

GOOD PRACTICES

Evidence and/or expert opinion supports the effectiveness of these good practices; they may need to be adapted to meet the needs of Priority populations, and for certain settings:

- Educate healthcare providers on HCV screening and testing algorithms, and about Priority populations;
- Provide stigma reduction training for healthcare providers;
- Implement one-time HCV testing for the 1945 – 1975 birth cohort;
- Offer routine, voluntary screening and testing to people at ongoing risk, including people who are members of Priority populations;
- Use physical chart prompts and call-back programs to facilitate initial testing (e.g. birth cohort 1945-1975, newcomers to Canada) and follow-up HCV RNA testing for those with an initial positive antibody result;
- Implement reflex testing for HCV RNA or HCV cAg for all HCV antibody positive samples;
- Approve and fund simpler, evidence-based HCV testing technologies, including PoC HCV antibody testing, PoC HCV RNA testing, DBS collection and testing, and HCV cAg testing;
- Expand reach and access to testing by decentralizing and task-sharing;
- Ensure that test results are delivered in the context of engagement and care plans that support linkage to prevention, care and treatment services;
- Integrate HCV testing into STBBI services and vice versa, as appropriate;
- Link HCV test results to administrative data to allow for evaluation of the continuum of care and health outcomes.

SUGGESTED ACTIVITIES

Increase diagnosis among the 1945-1975 birth cohort

HCV can remain asymptomatic for years, while liver disease may be worsening. Simple, one-time testing will identify people who are living with HCV and who would benefit from DAA treatment. For this to happen, HCV testing needs to be followed by reflex HCV RNA testing and connected to strategies for linkage to care, to ensure that all those who test positive are promptly engaged in care. Importantly, one-time testing for people in the 1945 to 1975 birth cohort would prevent nearly 50% of HCV-related deaths in this group and has been shown to be cost-effective in the Canadian context (see Table 5).[121,125,126]

<u>Suggested Activity</u>

- Enhance testing in populations with a higher prevalence of HCV infection:
  - ✧ Implement one-time HCV testing for people in the 1945-1975 birth cohort;
  - ✧ Improve reach of, access to, and availability of HCV screening and testing services across all medical settings.

Increase diagnosis among people who are members of Priority populations, and/or at ongoing risk, by expanding the reach and access to testing

Testing needs to be fully integrated into an individual's healthcare. Innovative approaches can extend access to, and increase reach, availability, acceptability and convenience of HCV testing. Different testing tools and approaches can be effectively used in various settings and populations; these must be available and funded.

HCV testing can become part of care by ensuring that it is offered at locations where people seek care. In turn, HCV PoC testing should be offered as part of a comprehensive care framework, including testing for all related STBBI.

Implementing reflex testing (when samples from a person with a positive HCV antibody test result are immediately tested for HCV RNA or HCVcAg)

eliminates the need for a second blood collection. There are many ways to operationalize reflex testing, including by using the same tube of blood for both tests, collecting a second tube of blood, or using dried blood spots for collection.

Ultimately, new testing technologies such as finger-stick testing, which can be done outside of healthcare settings, by peers and others with limited or no healthcare background, and PoC testing with rapid results could close the HCV diagnostic gap and facilitate immediate linkage to care. These approaches can greatly expand the reach of testing, particularly in rural areas with limited healthcare facilities and among Priority populations who may have experienced stigma from healthcare professionals.

As new testing technologies are approved, quality assurance programs are required to ensure that high standards for testing are maintained in all settings. Test results must be reported centrally, and systems should be developed to facilitate linkage to care through self-referral or automatic referral immediately upon a positive test result.

Access to HCV testing, care and treatment among individuals living in rural and remote communities and mobile populations can be monitored, by creating consolidated health records. Reporting to public health should follow the same guidelines as for phlebotomy-based tests done in commercial and/or public health laboratories.

People who have been treated and cured, or who have spontaneously cleared HCV and are at ongoing risk of infection should be offered frequent serial testing. In this circumstance, screening must be done with HCV RNA because people remain antibody positive for decades or for life, even after being cured or having cleared HCV.[118]

Suggested Activities

- Approve and fund simpler testing technologies to enable expansion of on-site screening and testing at drug treatment clinics, community health centers, needle/syringes programs, services for homeless or unstably housed people, supervised consumption services, prisons, mental health services, sexual health clinics, HIV and PrEP clinics, refugee/newcomer clinics and other decentralized sites;
- Implement reflex testing when antibody test results are positive;

HCV TESTING FOR CHILDREN AND YOUTH UNDER THE AGE OF 18

There is a general lack of awareness about recommendations for testing high-risk pediatric groups. Most HCV infections occur at the time of delivery. HCV antibody testing should not be performed in infants until they are 18 months of age, because infants may retain their mother's antibodies until this time. Infants older than 18 months who have a positive HCV antibody test result need HCV RNA testing to confirm active infection. If early detection of perinatal transmission is desired, the infant can be tested for HCV RNA at 4 to 6 weeks after birth, since testing done in younger infants can yield false negative HCV RNA test results. A negative result from early HCV RNA testing (>6 weeks of age) reliably implies that the infant has not been infected. However, some children will spontaneously clear HCV infection without treatment during their first two years of life, so a positive result from early HCV RNA testing does not predict chronic infection.

Policy and service delivery recommendations:

- Update HCV testing guidelines for children, particularly if they are at increased risk of infection, and improve awareness of these guidelines among healthcare workers;
- Include pedriatric healthcare providers in education programs;
- Increase testing and diagnosis among children born from mothers living with HCV by implementing strategies to ensure confirmatory testing when they are 18 months old.

- Use minimally invasive testing technologies that do not require drawing blood, to increase engagement with people who use harm-reduction, healthcare and social support services;
- Enable task-sharing, by training allied healthcare workers, peers and others to deliver HCV screening and testing with simpler testing technologies;
- Explore innovative testing and reporting approaches, such as online testing (e.g., getcheckedonline.com), online reporting and/or texting of results; and self/home testing;
- Offer routine screening and testing to people at ongoing risk, including people who are members of Priority populations;
- Address syndemic testing needs, by including an offer of HCV testing with other STBBI testing, and vice versa.

Initiate testing reminders

Testing can also be facilitated by reminders and by encouraging people with a positive antibody test to return for confirmatory testing.

Suggested Activities

- Implement electronic medical chart prompts to remind providers when testing is required;
- Implement 'call-back' initiatives for people with a positive antibody test result with no follow-up test for HCV RNA or HCVcAg.

Link HCV test results with administrative data

Developing policies for, and monitoring progress towards HCV elimination requires ongoing evaluation. Centralized reporting of HCV results with subsequent linkage to administrative databases makes it possible to monitor the engagement and retention of people living with HCV across the cascade of care at the provincial/territorial level.

Suggested Activities

- Ensure all positive HCV test results are reported to a central public health body for the province/territory;
- Link administrative data with HCV test results.

RESEARCH GAPS

HCV testing and diagnosis can be optimized by research to evaluate new testing technologies and strategies; characterizing the reach, coverage and effectiveness of testing, and use of testing data to monitor progress towards elimination. Therefore, the *Blueprint* supports the following actions:

- Enhance national and provincial/territorial surveillance of HCV testing and diagnosis;
- Identify remaining barriers to HCV antibody and HCV RNA testing;
- Generate data to get single and multiplex (tests for multiple infections from a single sample) PoC tests approved in Canada;
- Evaluate uptake of novel testing strategies, e.g. finger-stick HCV RNA testing, among Priority population groups;
- Evaluate the cost-effectiveness of alternative testing strategies in different settings;
- Evaluate the cascade of care at the provincial/territorial level, using HCV test results and administrative health data to monitor progress towards elimination targets.

HEPATITIS C CARE & TREATMENT

- Why is it important to enhance hepatitis C care and treatment?
- Current situation
- Key objectives and targets
- Good practices and suggested activities
- Research gaps

HEPATITIS C CARE AND TREATMENT

WHY IS IT IMPORTANT TO ENHANCE HCV CARE AND TREATMENT?

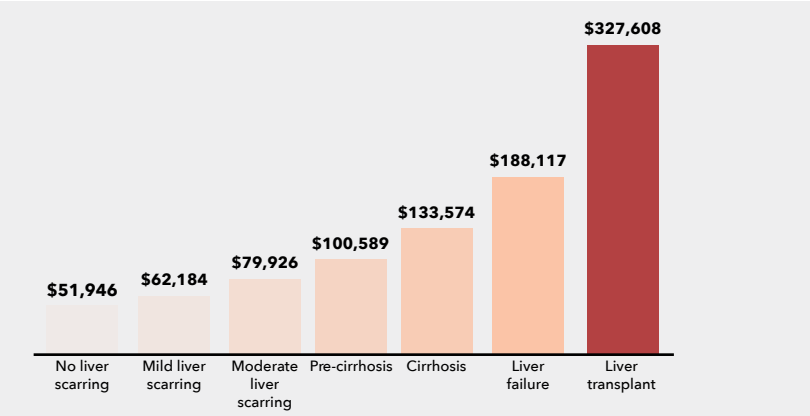
Untreated HCV-related liver disease advances over time, and is associated with a range of systemic health problems, progressive liver damage, decreased quality of life, and increased healthcare costs.[2, 34]

Progressive liver damage, even the development of cirrhosis, is usually asymptomatic. This underscores the need for HCV testing so that the infection can be diagnosed, treated and cured before complications arise. Once cirrhosis is present, people are at risk for end-stage liver disease and liver cancer. Canada's healthcare costs related to HCV-associated liver disease - not including treatment - are projected to increase by 60% from 2013 to 2032, from $161.4 million to $258.4 million.[2] Also, HCV causes a range of other health problems beyond the liver, known as extrahepatic manifestations. These include serious health problems, such as Type 2 diabetes, heart disease, cryoglobulinemia (a condition that can block blood vessels and lead to kidney and nerve damage), and types of lymphoma.[34]

Beyond its impact on physical health, people living with HCV report poor quality of life,[35, 36] and high rates of depression,[37] fatigue, anxiety, and cognitive impairment.[167] In addition, people living with HCV may experience substantial stigma, including in healthcare settings, which discourages them from seeking care and treatment for HCV, and, potentially, other conditions.[10, 11] Diminished physical and emotional well-being lead to higher rates of absenteeism, short and long-term disability and lower productivity as well as HCV-related healthcare costs.[168]

Even after HCV has been cured, ongoing care and support is important for people with advanced HCV-related liver disease and cirrhosis. They require aftercare that includes monitoring for liver cancer, and, where appropriate, follow-up with a liver care specialist.

Figure 12. Lifetime healthcare costs of untreated hepatitis C virus (HCV), by stage of liver disease [2]



Fortunately, HCV treatment has been transformed by DAAs. They cure over 95% of people after 8-12 weeks of treatment, usually with once-daily pills that have few or no side effects.[44-47] DAAs are safe and effective for people with advanced liver disease, HIV coinfection, and other medical problems. Additionally, in many cases, HCV treatment can be safely and successfully completed in people who are using alcohol and/or other substances.[169, 170]

Being cured of HCV has a transformative effect. A cure reduces the risk for cirrhosis, end-stage liver disease, liver cancer, transplantation and death. It improves insulin resistance (pre-diabetes), nearly halves the risk for stroke and heart attack, and it can cure or improve other extrahepatic manifestations, and improve quality of life.[12-16, 48-50]

The individual and public health benefits of DAAs led WHO to issue a 'treat-all' recommendation in its 2018 *Guidelines for the Care and Treatment of Persons Diagnosed with Chronic Hepatitis C Infection*.[171] There is growing evidence of public

health benefits from HCV treatment from the added contribution of TasP, [17-19] since a cure stops onward transmission. However, people who have been cured are not protected from HCV reinfection. Preventing and promptly treating reinfection without stigma is an essential part of ongoing care and support, and underscores the importance of linkage to prevention and harm-reduction programs for people who have been cured and are at ongoing risk of infection.

CURRENT SITUATION IN CANADA

HCV treatment is essential for addressing Canada's epidemic, and DAAs provide the opportunity to strengthen and modernize multidisciplinary approaches to care, while adapting them to the needs of Priority populations.

In 2015, oral DAA regimens were introduced in Canada, replacing lengthier, less effective, more toxic interferon-based treatments. High DAA prices initially limited access to HCV treatment in Canada, where liver fibrosis-based restrictions were imposed. In 2017, the pCPA negotiated an agreement to lower DAA prices. As of 2018, all provinces (except for Newfoundland), territories, federal prisons and on-reserve health jurisdictions have removed fibrosis-related restrictions, [172] allowing treatment for all people living with HCV.

In 2018, the CASL issued a 'treat-all' recommendation. [122] Yet, based on available estimates, over 178,000 people living with HCV in Canada have not been treated. [4,8]

Accurate national data on the number of people living with HCV who have been linked to care and treatment and their outcomes are unavailable. The quality of data varies around the country, with the most comprehensive data coming from BC, through the BC-HTC. [75] With centralized HCV testing linked to administrative databases that house information on treatment rates and HCV-related health outcomes, BC has adequate infrastructure to assess the burden of HCV and progress towards the elimination targets. [175] Unfortunately, in most other regions, such comprehensive data are lacking, making it difficult to generate robust national estimates. Estimates from BC suggest that by end of 2017, 73% of those diagnosed had an HCV genotype test, which is a

EXPANDING ACCESS AND REDUCING BARRIERS TO HCV TREATMENT

HCV treatment is expensive. In Canada, and worldwide, most people living with HCV cannot afford to pay for DAAs out-of-pocket, and many do not have private insurance for medications. Collective bargaining by the pCPA has reduced the cost of DAAs and facilitated coverage in most jurisdictions in Canada. Continuing the pCPA process, ideally with more transparency about costs, will be important for enabling unrestricted access to DAAs while limiting budget impact.

A national pharmacare program could help ensure that all people living with HCV receive equitable access to treatment. Such a program would also enable tracking of people who have been treated for HCV and their outcomes, which is critical for evaluating progress towards elimination targets. Other approaches to remove administrative barriers would allow for same-day prescription and approval, which would minimize loss-to-follow-up. Further savings can be realized by streamlining access to and delivery of HCV care, and by reducing budget silos, so that savings in one aspect of care are applied to support other costs of care.

The ECHO model was developed to increase access to HCV care and treatment, especially for people in rural and remote settings. This model is built around a low-cost, 'many to many' approach, using video and/or teleconferencing between specialists and community-based providers known as 'telementoring'. The ECHO model has proven effective: a trial comparing HCV treatment outcomes from community-based ECHO model sites and an academic medical center found no difference. [173] The ECHO model is being used in Ontario, Alberta, BC and Quebec, [174] to expand access to, and the reach of treatment.

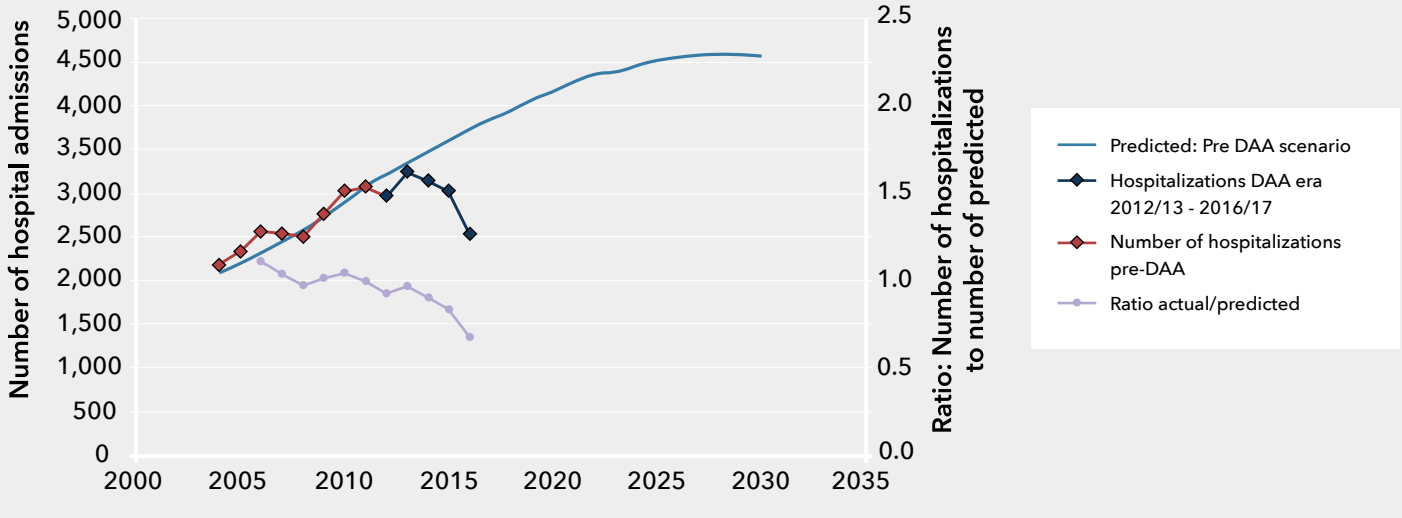
good indicator of linkage to a healthcare provider who is knowledgeable about HCV.[176]

Since 2015, HCV treatment uptake has increased significantly, going from 5,127 people in 2014 up to an estimated 12,000 people in 2017.[52] Already, instead of the projected increase in HCV-related hospitalizations and death, DAAs have brought modest decreases in HCV-related hospitalization and death rates – especially among people in the 1945 to 1975 birth cohort, who are at the highest risk for HCV-related liver failure and liver cancer.[51]

Models of expected HCV-related outcomes in Canada make it possible to estimate the impact of various DAA treatment scenarios, and to determine the treatment rates required to reach the 2030 elimination targets. As an example, if the increased treatment rates seen in recent years can be maintained - an estimated 12,000 people in 2017 – this could bend the curve of Canada's HCV epidemic. Instead of the 89% increase in the number of people who have liver failure and the 205% increase in the number of people developing liver cancer projected to occur by 2035 if no actions are taken,[2] Canada could witness a 70% decrease in the number of people progressing to HCV-related liver failure and liver cancer - and a 70% reduction in HCV-related deaths, in just over a decade.[52] With an aggressive HCV strategy, increasing treatment rates to 14,000 per year, elimination targets could be reached before 2030.[52] However, even maintaining current treatment rates, let alone increasing them, will be very challenging. As the number of people living with HCV decreases, finding those left behind will become more and more challenging. Furthermore, if effective prevention strategies are not developed, new infections and reinfections will reduce the effect of increased treatment rates. If treatment rates decline, particularly if they fall off rapidly (see Figure 6), the health burden of HCV will persist and elimination targets will not be met.

Removing fibrosis restrictions makes it possible to treat more people, but even countries with unrestricted access to DAAs have reported a decline in treatment rates after an initial expansion.[177] The initial surge in treatment occurred from treating the backlog of people in care who were awaiting the new, more effective DAA treatments. To maintain or exceed the current treatment rates, it will be essential to find people with HCV, many of whom have been disenfranchised from the healthcare system, and engage them in care that is adapted to their needs. To achieve increased treatment rates, particularly among marginalized populations, new models of care that rely less on specialists to oversee HCV treatment will be required. With the high efficacy and excellent safety of DAAs, treatment can be effectively delivered by family doctors, addiction specialists, nurse practitioners, nurses and even in non-traditional healthcare settings like pharmacies, prisons and addiction centers.[178-182]

Figure 13. Predicted pre-direct anti-viral (DAA) hospitalization rates and impact of DAAs [51]



KEY OBJECTIVES AND TARGETS

The care and treatment targets were developed using available information about HCV incidence and prevalence; the number of people who are untreated; the effectiveness of DAA treatment, and projections of the burden of untreated liver disease in Canada.

Table 7. Key objectives, targets and indicators for hepatitis C virus (HCV) care and treatment

Objectives	2025 Targets	2030 Targets	Key indicator label**
Increase the number of people diagnosed with HCV who are linked to care, treatment and ongoing support	**50%** linked to a provider who is familiar with HCV	**90%** wlinked to a provider who is familiar with HCV	C1
Increase the number of people with HCV who are initiating DAA treatment	**50%** of those living with HCV have initiated DAA treatment	**80%** of those living with HCV have initiated DAA treatment	C2, C3
Ensure high treatment completion rates and documentation of sustained virologic response (SVR)	**95%** treatment completion with **85%** documentation of SVR	**95%** treatment completion with 85% documentation of SVR	C3
Reduce HCV prevalence	**50%** ↓ *	**90%** ↓ *	C4
Reduce HCV-related liver transplantation	**30%** ↓ *	**65%** ↓ *	C5
Reduce HCV-related mortality	**30%** ↓ *	**65%** ↓ *	C6

**Compared to 2015;*
***Refer to the appendix for a list of the Indicators and metrics to monitor and report progress for HCV care and treatment*

GOOD PRACTICES

Evidence and/or expert opinion supports the effectiveness of these good practices; they may need to be adapted to meet the needs of Priority populations, and for certain settings:

- Increase awareness of HCV via partnerships with community-based organizations, particularly among Priority populations;
- Expedite linkage to care and initiation of DAA treatment, and reduce delay between entry to care and treatment initiation;
- Increase the number and type of providers treating HCV by eliminating provider-based prescribing restrictions;
- Provide stigma reduction training for healthcare providers;
- Eliminate barriers to treatment for people who currently use drugs;
- Expand treatment and care sites to reach Priority populations and others at high and ongoing HCV risk by co-locating HCV treatment with OAT, harm-reduction, addiction, mental health and social services (e.g. housing, food);
- Simplify on-treatment monitoring;
- Provide follow-up care, including serial HCV RNA testing for people at ongoing risk of reinfection, and re-treat HCV reinfection without stigma or discrimination;
- Continue to provide post-cure liver cancer surveillance with ultrasound surveillance every six months for people known to have cirrhosis prior to HCV treatment.

SUGGESTED ACTIVITIES

Expedite linkage to care and treatment initiation

There are major gaps in the cascade of care for HCV. In 2012, only 35% of people in BC who were diagnosed with HCV went further than having a viral load test, and only 12% initiated treatment.[75] In 2017, 83% of antibody positive individuals had an HCV RNA test done and 38% of those diagnosed with HCV initiated treatment in BC.[133] Now that DAAs have dramatically simplified HCV treatment delivery, many barriers to treatment can be removed, and people can be engaged in care in as little as a week. In some circumstances, HCV treatment can even be started on the first visit with an HCV care provider. Care should ideally be initiated within no more than two months of a new diagnosis.

Suggested activities

- Increase access to rapid and/or simplified diagnostic tests to confirm chronic infection, paired with access to counselling for those found to be living with HCV;
- Simplify referral pathways;
- Allow and promote self-referral;
- Provide information regarding available HCV care and treatment centers at the time of public health contact to newly identified HCV cases (which may occur after documentation of new positive HCV result);
- Reduce time between diagnosis and treatment initiation to a maximum delay of eight weeks, by:
    - ✧ Eliminating routine pre-treatment genotype testing now that pan-genotypic treatments are available;
    - ✧ Eliminating requirements for repeat HCV RNA testing for treatment approval in those with clinical or other evidence of chronic HCV infection;
    - ✧ Capitalizing on e-health systems to ensure shared access to laboratory data between providers to avoid duplication and delays due to repeat testing;
    - ✧ Eliminating restrictions based on provider-type (e.g. specialists or hospital centers) to avoid the need for referral of uncomplicated cases;
    - ✧ Increasing access to non-invasive methods for fibrosis assessment, to identify people with advanced liver disease who may require specialist care and post-cure follow-up;
    - ✧ Eliminating the need for unnecessary appointments (e.g. same day/rapid treatment decision);
    - ✧ Expediting the approval process for medication reimbursement (e.g. same day as prescription);
    - ✧ Link rural and remote patients to care and treatment via electronic means, including HCV telemedicine programs such the ECHO model, ensuring adequate support is available to providers to participate in telementoring programs.

Increase the number and type of providers treating HCV and the sites where treatment is delivered

A broad range of healthcare providers can be educated on HCV testing, liver disease staging, treatment, and surveillance for liver cancer and reinfection, particularly providers who deliver primary healthcare services to Priority populations.

Because of their safety, simplicity and tolerability, DAAs can be delivered by non-specialist providers in low-threshold and community-based settings, including nurse-led treatment, by family doctors and other primary care providers, in prisons, co-located with substance use treatment, harm reduction programs and STBBI clinics.[177-180]

HCV-related stigma in healthcare settings discourages people from accessing and engaging in care;[10,11,53] all provider trainings should include stigma reduction.

Suggested Activities

- Eliminate provider-type restrictions for prescribing HCV treatment;
- Create and increase capacity and support for treatment delivery by non-specialists, and in low-threshold settings:

- ✧ Experts in HCV management may help to identify and train interested healthcare providers;
- Use telemedicine to expand reach and access to rural and remote areas, and to train and support local providers;
- Increase the number/type of providers able to treat HCV through task-sharing.

Expand treatment to reach Priority populations and others at high risk for HCV

Suggested Activities

Despite the high risk for, and rates of HCV among members of Priority populations, they are often excluded from mainstream health services.

- Co-locate HCV care and treatment with OAT, harm-reduction, addiction, alcohol misuse, mental health and social services (e.g. consider housing and food support);
- Work with provinces and territories to resource regional HCV treatment centers that will enable multi-disciplinary care;
- Develop pathways to link prisoners to care and treatment in prison and after release;
- Emphasize active roles for peers and those with lived experience in planning and implementation of new approaches to delivering treatment;
- Re-engage people who were previously diagnosed but lost to follow-up through active case-finding;
- Consider new venues, community health workers and peers for dispensing and delivering harm reduction, prevention and treatment.

Simplify on-treatment monitoring

In the past, with interferon-based treatment and in DAA clinical trials, HCV RNA testing was used at different time points during and at the end of treatment, to monitor response (as well as 12 weeks afterwards, to assess treatment outcome). However, on-treatment viral load monitoring does not reliably predict the outcome of treatment and is no longer necessary except in specific circumstances.[183]

Suggested Activity

- Minimize laboratory monitoring during treatment to avoid unnecessary medical appointments and reduce costs;

HCV TREATMENT FOR CHILDREN AND YOUTH UNDER THE AGE OF 18

There is a lack of knowledge about pediatric HCV among healthcare providers. In addition, access to HCV DAAs for children and youth has been delayed, and some medications will not be studied in and approved for children.

Policy and service delivery recommendations:

- Update HCV treatment guidelines for children;
- Improve awareness of these guidelines among healthcare workers;
- Include pediatric healthcare providers in education program;
- Ensure that HCV education and treatment programs and providers embrace services for children/youth;
- Provide family-centered care for children who are living with HCV;
- Develop practitioners skills for delivering family-centered care, age-appropriate patient education and communication with teens;
- Expedite and expand approval of, and funding for DAA therapies for children and youth;
- Encourage testing, licensing and cost-coverage of HCV treatment for children and youth.

- Ensure access to HCV resistance testing is available when clinically indicated, particularly for people who do not achieve sustained virological response (SVR) with an initial course of treatment.

Ensure continued follow-up care, including HCV RNA testing every 6 to 12 months, for people at ongoing risk of reinfection

Once there is unrestricted access to DAAs, it is likely that people who are at ongoing risk will be treated and cured, but some may become reinfected. HCV reinfection rates differ, based on local epidemiology, access to, and coverage of NSP and OAT, PrEP and other harm-reduction services. In the Canadian Co-infection Cohort (HIV/HCV), people who frequently injected methamphetamine and cocaine were six times more likely to become reinfected with HCV than their low-risk counterparts. [184] High rates of HCV reinfection have been reported among HIV-positive men who have sex with men, usually through chemsex (drug use in a sexual context). [67-69, 185] Stigma-free and expedited diagnosis and treatment of HCV reinfection are essential, for individual benefit and the public health benefit of reducing further transmission.

Suggested Activities

- Provide continued follow-up care, including HCV RNA testing, every 6 to 12 months for people at ongoing risk of infection;
- Retreat HCV reinfection without stigma or discrimination;
- Increase awareness of HCV via partnerships with community-based organizations, particularly among Priority populations.

Ensure continued follow-up care for people with cirrhosis diagnosed prior to HCV treatment

Fortunately, DAAs are safe and effective, even for people with cirrhosis - including those with decompensated cirrhosis. Although being cured reduces the risk for liver cancer among people with cirrhosis, it does not eliminate the risk; ongoing ultrasound surveillance for liver cancer is required even after cure of HCV. Non-invasive tools to assess liver fibrosis are only reliable for diagnosing cirrhosis before HCV treatment, highlighting the need for a pre-treatment fibrosis assessment.

Ultrasound performed every 6 to 12 months is the preferred surveillance strategy to detect early liver cancer. Early diagnosis of liver cancer prior to symptoms allows for treatment, and often a cure.

Suggested Activities

- Continue to identify people at increased risk of mortality and provide them with HCV treatment;
- Ensure access to and reimbursement for liver fibrosis assessment with non-invasive tools, to enable diagnosis of cirrhosis prior to initiation of HCV treatment;
- Continue to provide post-cure ultrasound every 6 months for liver cancer surveillance among people diagnosed with cirrhosis prior to HCV treatment;
- Continue to provide post-cure liver-related care including alcohol control programs for people with cirrhosis.

Provide comprehensive, multidisciplinary care that is relevant to the needs of Priority populations

Experts in HCV care should partner with experts in providing other services that are relevant to people living with HCV, such as addiction and mental health services and treatment and management of other STBBIs, to ensure that HCV treatment is part of comprehensive healthcare.

Suggested Activities

- Provide and develop community-focused, population-specific, culturally sensitive awareness and education campaigns on HCV and the benefits of HCV diagnosis, care and treatment, in collaboration/partnership with representatives from Priority populations and the organizations that provide them with services.

RESEARCH GAPS

Research on HCV care and treatment could further optimize HCV treatment and re-treatment outcomes; explore new service delivery models to expand the reach and effectiveness of DAAs, and explore their safety and efficacy in understudied populations. Therefore, the *Blueprint* supports the following actions:

- Explore shorter duration treatment regimens and alternative formulations of treatment (e.g. long-acting injectable therapies);
- Document treatment outcomes using novel models of care including telemedicine, nurse-led, and pharmacy-led care;
- Assess new models for dispensing and delivering medications to unstably housed, mobile or homeless people;
- Determine the role of DAA resistance testing in selection of therapy after DAA failure;
- Develop tools for risk stratification for people with HCV-related cirrhosis prior to treatment, to determine optimal hepatocellular carcinoma surveillance post-therapy;
- Determine optimal duration and regimen for acute HCV infection;
- Evaluate alternative models of care to help increase treatment uptake among the most marginalized population groups (e.g. DAA treatment in opioid agonist therapy centers; correctional settings);
- Evaluate patient outcomes following DAA therapy, e.g. 'real-world' studies;
- Evaluate and identify optimal educational interventions that will assist multidisciplinary teams in implementing HCV treatment in community-based settings;
- Conduct real-world studies that look at treatment in people over age 65, who were not included or under-represented in clinical trials;
- Investigate the safety of DAAs during pregnancy and potential efficacy of treatment for preventing vertical transmission by establishing a registry and considering interventional trials.

APPENDICES

1. *Blueprint* Indicators and metrics
    - Prevention
    - Testing and Diagnosis
    - Care, Treatment and Ongoing Support
2. Writing Committee and Working Groups

APPENDIX 1: *BLUEPRINT* INDICATORS AND METRICS

Table 8. Indicators and metrics for hepatitis C virus (HCV) prevention

Key indicators and metrics to monitor and report progress

LABEL	INDICATOR	DEFINITION	NUMERATOR	DENOMINATOR	BREAKDOWN BY POPULATIONS	MEASUREMENT METHODS	EXAMPLES OF DATA SOURCES
P1	Size of priority populations	Estimate of number of people in each at-risk group	NA	NA	• Geographic region • Priority Population • Setting (e.g., community, prison, rural, urban)	• Census and other population surveys • Enhanced surveillance in priority populations • Use and linkage of routinely collected data, such as electronic medical records, administrative claims, registries and judicial data*	• Adult and Integrated Correctional Services Surveys • Canadian Community Health Survey • SurvUDI Study • The Tracks Enhanced Surveillance Systems, such as I-Track, M-Track, A-Track and Y-Track • Prescription monitoring programs
P2	HCV incidence	i) Rate of new infections with HCV (anti-HCV positive) (WHO indicator) ii) Rate of new infections with HCV in those known to be negative previously (main indicator) iii) Rate of HCV infection cases reported among younger age groups (proxy indicator) iv) Reported rate of acute HCV infection (proxy indicator)	i) Number of new infections, defined as anti-HCV positive ii) Number of people with a previous negative HCV test who test positive for anti-HCV and/or HCV RNA iii) Number of people with a new HCV diagnosis among younger age groups (e.g. ≤25 or ≤30) iv) Number of people with a new HCV diagnosis in which clinical information suggests acute infection	i) Total population, minus people living with HCV ii) People at risk of HCV infection, or total population minus people living with HCV iii) People at risk of HCV infection, or total population within younger age group (e.g. ≤25 or ≤30) iv) People at risk of HCV infection or total population minus people living with HCV	• Age • Sex • Geographic region • Previous HCV infection (anti-HCV positive) • Priority Population • Setting (e.g., community, prison, rural, urban)	• Enhanced surveillance in priority populations • Serial HCV testing in cohorts conducted among Priority populations • Use and linkage of routinely collected data, such as electronic medical records, administrative claims, laboratory data and registries	• BC Hepatitis Testers Cohort • Notifiable Disease Surveillance System (Federal, Provincial and Territorial) • Ongoing cohort studies (e.g. HEPCO, VIDUS/ARYS) • SurvUDI Study • The Tracks Enhanced Surveillance System such as I-Track, M-Track, A-Track and Y-Track

P3	Coverage of needle and syringes programs (NSP)	Number of needles/ syringes distributed per PWID, per year	Number of sterile needles/syringes distributed per year by NSP	Number of PWID	• Geographic region • Setting (e.g., community, prison, rural, urban)	• Enhanced surveillance in Priority populations • Use of routinely collected data such as harm-reduction program data	I-Track Enhanced Surveillance System
P4	Coverage of opioid agonist therapy (OAT)	Proportion of PWID accessing OAT at a given point in time	Number of PWID receiving OAT at a given point in time	• Number of PWID • Number of PWID eligible for OAT	• Type of medication (e.g., methadone, buprenorphine/ naloxone; slow-release morphine; injectables) • Setting (e.g., community, prison, rural, urban) • Geographic region	• Enhanced surveillance in Priority Populations • Use of routinely collected data	• BC Hepatitis Testers Cohort • I-Track Enhanced Surveillance System • Provincial and territorial prescription monitoring programs

Sub-Indicators and metrics

LABEL	INDICATOR	DEFINITION	NUMERATOR	DENOMINATOR	BREAKDOWN BY POPULATIONS	MEASUREMENT METHODS	EXAMPLES OF DATA SOURCES
Sub.P4a	OAT retention	Proportion of PWID retained in OAT	Number of PWID started on OAT and retained for 6/12 months	Number of eligible PWID and number who started OAT	• Type of medication (e.g., methadone, buprenorphine/ naloxone, slow-release oral morphine, injectables) • Setting (e.g., community, prison, rural, urban)	• Behavioural interviewing • Use of routinely collected data	• BC Hepatitis Testers Cohort • Provincial and territorial prescription monitoring programs • Provincial and territorial public drug benefit programs • Ongoing cohort studies (e.g. HEPCO, VIDUS/ARYS)

Continued on next page.

Sub.P4b	OAT quality	Proportion of PWID receiving high and low OAT dose	Number of PWID in OAT at a given point in time receiving high and low OAT doses	Number of PWID in OAT at a given point in time	• Type of medication (e.g., methadone, buprenorphine/ naloxone, slow-release oral morphine, injectables) • Setting (e.g., community, prison, rural, urban)	• Behavioural interviewing/ surveys • Use of routinely collected data	• BC Hepatitis Testers Cohort • Provincial and territorial prescription monitoring programs • Provincial and territorial public drug benefit programs • Ongoing cohort studies (e.g. HEPCO, VIDUS/ARYS)

1. Priority populations refers to those identified in this document

2. For HCV incidence, the denominator should include a measure of time (e.g., person-time)

3. Geographic region refers to distribution across provinces and territories

**To estimate the size of Priority populations, estimation methods are most commonly indirect, which are considered more suitable for "hard-to-reach" populations such as multi parameter evidence synthesis, capture-recapture and network scale-up methods.*

Table 9. Indicators and metrics for hepatitis C virus (HCV) testing and diagnosis

Key indicators and metrics to monitor and report progress

LABEL	INDICATOR	DEFINITION	NUMERATOR	DENOMINATOR	BREAKDOWN BY POPULATIONS	MEASUREMENT METHODS	EXAMPLES OF DATA SOURCES
T1	People living with HCV who have been diagnosed as HCV antibody positive and confirmed to have active infection	Proportion of people living with HCV who have been diagnosed with active infection	Number of persons with HCV who have been diagnosed with active infection (HCV RNA or HCV cAg)	Estimated number of persons living with HCV	• Age • Sex • Priority populations • Geographic region • Setting (e.g., community, prison, rural, urban)	• Use of linked administrative data to determine those who have received HCV testing and been diagnosed with active infection • Back-calculation from survey data collected from cohort studies or population-based surveys where people are asked about awareness of their HCV status (to estimate proportion diagnosed)	• British Columbia Hepatitis Testers Cohort (and other provincial linked datasets) • Notifiable disease surveillance system (federal or provinces and territories) • Cohort studies (e.g. VIDUS/ARYS, HEPCO) • I-Track Enhanced Surveillance System
T2	HCV testing	Testing for HCV antibody	Number of people who were tested for HCV antibodies during the reporting period (e.g. 1 year)	Population size	• Age • Sex • Priority populations • Geographic region • Setting (e.g., community, prison, rural, urban)	• Use of linked administrative data to determine those who have received HCV testing and been diagnosed with active infection • Survey data collected from cohort studies or population-based surveys where people are asked about HCV testing	• British Columbia Hepatitis Testers Cohort (and other provincial linked datasets) • Notifiable disease surveillance system (federal or provinces and territories) • Cohort studies (e.g. VIDUS/ARYS, HEPCO) • I-Track Enhanced Surveillance System

Continued on next page.

T3	Confirmation of active HCV infection	Testing for HCV RNA	Number of people with a positive HCV antibody test who have had undergone testing to confirm active infection (e.g, HCV RNA)	Number of people with a positive HCV antibody test	• Age • Sex • Priority populations • Geographic region • Setting (e.g., community, prison, rural, urban)	• Use of linked administrative data to determine those who have received HCV testing and diagnosed with active infection • Survey data collected from cohort studies or population-based surveys where people are asked about HCV testing	• British Columbia Hepatitis Testers Cohort (and other provincial linked datasets) • Notifiable disease surveillance system (federal or provinces and territories) • Cohort studies (e.g. VIDUS/ARYS, HEPCO) • I-Track Enhanced Surveillance System

Table 10. Indicators and metrics for hepatitis C virus (HCV) care and treatment

Key indicators and metrics to monitor and report progress

LABEL	INDICATOR	DEFINITION	NUMERATOR	DENOMINATOR	BREAKDOWN BY POPULATIONS	MEASUREMENT METHODS	EXAMPLES OF DATA SOURCES
C1	Proportion diagnosed* who are linked to care	Linked to care is defined as being assessed for care and treatment	Number with evidence of i) HCV care visit* ii) HCV genotype performed*	Total number of HCV RNA positive	• Age • Sex • Priority populations • Geographic region • Setting (e.g., community, prison, rural, urban)	• Laboratory data • Billing codes* • ICD codes	• Public health lab data • Administrative data*
C2	Proportion linked to care who are started on treatment	Treatment is defined as having a prescription filled for HCV DAA therapy**	i) Number of unique treatment prescriptions for DAA therapy per year ii) Number of filled prescriptions per patient	Total number of HCV RNA positive who are linked to care	• Age • Sex • Priority populations • Prescriber type (PCP vs specialist)	• Prescription data	• IMS Rogan prescription data • Drug benefit programs • Pharmaceutical sales data • Sentinel clinical sites***
C3	Proportion treated who are cured	Cure is defined as achieving SVR12 (the absence of detectable HCV RNA 12 weeks after completion of HCV treatment)****	Number who obtain SVR	Total number initiating treatment	• Age • Sex • Priority populations • Geographic region • Setting (e.g., community, prison, rural, urban) • Prescriber type (PCP vs specialist)	• HCV RNA laboratory data • Prescription data	• Public health lab data • Drug benefit programs • Treatment registries from sentinel clinical sites

Continued on next page.

C4	HCV Prevalence	Current number of people living with HCV in overall population or defined at-risk population	i) Number with confirmed HCV infection scaled up to account for estimated diagnosed fraction in general population ii) Number with confirmed HCV infection scaled up to account for estimated diagnosed fraction in specific at-risk population	i) Total Canadian population ii) Estimated population of risk group	• Age • Sex • Priority populations • Geographic region • Setting (e.g., community, prison, rural, urban)	• Laboratory data • Population data (census) • Estimates of size of at-risk populations (see Prevention section)	• Serosurvey • Canadian Health Measures survey • BC Hepatitis Testers Cohort • Notifiable Disease Surveillance System (federal and provincial and territorial) • Ongoing cohort studies (e.g. HEPCO, VIDUS/ARYS) • The Tracks Enhanced Surveillance System such as I-Track, M-Track, A-Track and Y-Track
C5	i) Number of liver transplants performed for HCV per year ii) Number of people listed for liver transplantation with HCV diagnosis	Liver transplantation with HCV listed as underlying medical condition	i) Number of liver transplants with HCV as indication per year ii) Total number of people listed for transplant with HCV as indication	NA	• Transplant indication (HCC vs liver failure) • Age • Sex • Priority populations • Geographic region • Setting (e.g., community, prison, rural, urban)	• Transplant registry	• Liver transplant programs
C6	Liver-related mortality	Death from liver cancer or decompensated cirrhosis related to HCV	Death from liver cancer or decompensated cirrhosis	i) Total liver-related deaths (HCV-attributable fraction) ii) Total with positive HCV antibody/HCV RNA (incidence among people with HCV)	• Age • Sex • Priority populations • Geographic region • Setting (e.g., community, prison, rural, urban)	Administrative health data linked with HCV laboratory data using validated codes for decompensated cirrhosis and liver cancer	• Administrative health data • Public health lab data • Cancer registry

Continued on next page.

Sub-indicators and metrics

LABEL	INDICATOR	DEFINITION	NUMERATOR	DENOMINATOR	BREAKDOWN BY POPULATIONS	MEASUREMENT METHODS	EXAMPLES OF DATA SOURCES
Sub.C1a	Time from diagnosis to linkage-to-care	Time interval between: i) HCV Ab positive or ii) HCV RNA positive to first clinic visit/HCV genotype or start of HCV treatment	Days from HCV Ab or HCV RNA + to first clinic visit/ genotype test performed or treatment initiated	Total number of HCV RNA positive	• Age • Sex • Priority populations • Geographic region • Setting (e.g., community, prison, rural, urban) • Prescriber type (PCP vs specialist)	• Laboratory data (Ab, HCV RNA, genotype) • Prescription data	• Administrative health data • Public health lab data • Sentinel clinical sites
Sub.C2a	Time from linkage to treatment	Time from first visit to HCV provider to first DAA prescription	Days from first HCV clinic visit to DAA prescription filled	Total number linked to care	• Age • Sex • Priority populations • Geographic region • Setting (e.g., community, prison, rural, urban) • Prescriber type (PCP vs specialist)	• Laboratory data • Billing codes* • ICD codes	• Administrative health data • Public health lab data • Sentinel clinical sites
Sub.C3a	Proportion remaining linked/ engaged	Engaged is defined as: a) Completed HCV therapy and post HCV treatment follow-up or b) If not treated, remaining in clinic care	a) Number who complete SVR assessment (e.g. HCV RNA 12 weeks post treatment completion)*** b) For those not treated, number with at least one HCV clinical care visit per year	a) Total number initiating HCV treatment b) Total in care not on treatment	• Age • Sex • Priority Populations • Geographic region • Setting (e.g., community, prison, rural, urban) • Prescriber type (PCP vs specialist)	• Laboratory data • Billing codes* • ICD codes • Prescription data	• Administrative health data • Sentinel clinical sites

Continued on next page.

Sub.C3b	Build capacity and increase number of HCV providers	Number and type of provider prescribing HCV treatment	Number of unique providers who prescribe at least one HCV treatment	Total number of active providers and by specialty (e.g. GI/ hepatology/ ID-micro/GP/Addictions medicine)	• Prescriber type including specialty • Age • Sex • Geographic region • Setting (e.g., community, prison, rural, urban)	• Billing codes • ICD codes • Prescription data	• Administrative health data • Sentinel clinical sites
Sub.C5a	Hepatocellular carcinoma (HCC) surveillance for people with cirrhosis	Surveillance is defined as undergoing a liver ultrasound or other imaging (CT, MRI) or alpha fetoprotein (AFP) measurement	Number of ultrasounds/imaging or AFP measurements per year	Total number of patients with HCV-related cirrhosis	• Age • Sex • Priority populations • Geographic region • Setting (e.g., community, prison, rural, urban) • Prescriber type (PCP vs specialist)	• Billing codes • ICD codes • Laboratory data	• Administrative health data including laboratory data to calculate non-invasive measures of fibrosis • Sentinel clinical sites (more realistic)
Sub.C5b	HCV-related HCC	Diagnosis of HCC with positive HCV antibody and/or HCV RNA	Number of cases of HCC with positive HCV antibody and/or HCV RNA	i) Total HCCs (HCV-attributable fraction) ii) Total with positive HCV antibody/HCV RNA (incidence among people with HCV)	• Age • Sex • Priority populations	• Billing codes • ICD codes • Cancer registry data	• Cancer registry • Administrative health data • Sentinel clinical sites
Sub.C5c	HCV-related hospitalization	Hospitalization with a liver or HCV-related diagnostic code	Number of people with HCV or liver-related diagnostic code admitted to hospital	i) Total hospitalizations (HCV-attributable fraction) ii) Total with positive HCV antibody/HCV RNA (rate among people with HCV)	• Age • Sex • Priority Populations • Geographic region • Setting (e.g., community, prison, rural, urban)	• Billing codes • ICD codes	• Administrative health data • Public health lab data • Sentinel clinical sites

Continued on next page.

Sub.C6a	All-cause mortality	Death from any cause among people with HCV	Death from any cause	i) All deaths (HCV-attributable fraction) ii) Total with positive HCV antibody/HCV RNA (rate among people with HCV)	• Age • Sex • Priority populations • Geographic region • Setting (e.g., community, prison, rural, urban)	• Death certificates • Laboratory data	• Administrative health data • Public health lab data • Sentinel clinical sites

**Definition of HCV provider may be challenging as treatment expands outside of specialty clinics. Billing codes for HCV are often non-specific. Need for development of validated algorithms using laboratory data (e.g. genotype, liver diagnostic test, subsequent prescription etc.).*

***Measures the number of people who access treatment; it may not capture people intended to be treated who do not follow through (e.g. those given prescription that is never filled). The second measure (b) will give an estimate of whether treatment is completed by determining whether and over what time frame people renewed a prescription. The second outcome is also of interest and may be best tracked with "remain engaged".*

**** Sentinel clinical sites refers to sites where HCV care or care for those with HCV infection is provided including hospitals (tertiary care or community), community health centers, addiction services. Surveys of sentinel sites representing different clinical settings can provide estimates of relevant indicators in different clinical settings, different patient populations and by different provider types.*

***** May consider expanding cured population to those with undetectable HCV RNA more than 4 weeks after the end of treatment given the high correlation of SVR4 with SVR12 and the frequent occurrence of incomplete SVR12 HCV RNA testing*

APPENDIX 2: *BLUEPRINT* WRITING COMMITTEE AND WORKING GROUP MEMBERS

CanHepC has reunited **hepatitis C experts from all over Canada** including CanHepC researchers, representatives from community based organizations with wide representation including people with lived experience and affected populations, clinicians, healthcare workers and more.

Writing Committee members

- **Jason Altenberg**, Director of Programs and Services, South Riverdale Community Health Centre (SRCHC), Toronto
- **Lisa Barrett**, MD, PhD, Clinician Scientist, Infectious Diseases Nova Scotia Health Authority/ Dalhousie University
- **Julie Bruneau**, MD, MSc, Clinical researcher and Professor of Family and Emergency Medicine, Université de Montréal
- **Brian Conway**, MD, President and Medical Director of the Vancouver Infectious Diseases Centre
- **Curtis Cooper**, MD, Associate Professor of Medicine at the University of Ottawa, Director at The Ottawa Hospital Viral Hepatitis Program
- **Melisa Dickie**, MHSc, Associate Director, Hepatitis C Knowledge Exchange, CATIE, Canada's source for HIV and hepatitis C information
- **Laurie Edmiston**, Executive Director, CATIE, Canada's source for HIV and hepatitis C information
- **Jordan Feld (chairman)**, MD, R. Phelan Chair in Translational Liver Research, Toronto Centre for Liver Disease, Toronto General Hospital, University Health Network
- **Jason Grebely**, PhD, Professor and Researcher, Viral Hepatitis Clinical Research Program, the Kirby Institute, University of New South Wales and President of the International Network on Hepatitis in Substance Users
- **Naveed Zafar Janjua**, MD, MSc, PhD, Epidemiologist and Senior Scientist at the BC Centre for Disease Control and Clinical Associate Professor at the School of Population and Public Health, University of British Columbia
- **Lindsay Jennings**, Provincial Hep C Program Coordinator, Prisoners HIV/AIDS Support Action Network (PASAN)
- **Marina Klein**, MD, MSc, Clinical researcher and Professor of Medicine at McGill University in the Division of Infectious Diseases/Chronic Viral Illnesses
- **Alexandra King**, MD, Nipissing First Nation, Cameco Chair in Indigenous Health at the University of Saskatchewan
- **Mel Krajden**, MD, FRCPC, Medical Director, BC Centre for Disease Control Public Health Laboratory, Medical Head of Hepatitis Services, BC Centre for Disease Control, and Professor of Pathology and Laboratory Medicine at the University of British Columbia
- **Simon Ling**, MBChB, Head, Division of Gastroenterology, Hepatology and Nutrition, The Hospital for Sick Children, and Associate Professor, Department of Paediatrics, University of Toronto
- **Carrielynn Lund**, DRUM & SASH/CanHepC Coordinator, Canadian Aboriginal AIDS Network (CAAN)
- **Renée Masching**, Director of Research and Policy, Canadian Aboriginal AIDS Network (CAAN)
- **Naglaa H. Shoukry**, BPharm, PhD, Researcher and Professor of Medicine, Centre de Recherche du Centre Hospitalier de l'Université de Montréal (CRCHUM), and Director of CanHepC
- **Denise Thomas**, Nursing Faculty, Langara College and past-President of the Canadian Association of Hepatology Nurses

The Blueprint was reviewed by Liza Abraham and Mary Guyton (Canadian Association of Hepatology Nurses).

Working Group Members

The Writing Committee has been separated in **four working groups** (Priority populations, Prevention, Testing and diagnosis, Care and treatment) with additional members each responsible for **developing the background, objectives, targets and suggested activities** for their section.

Priority populations Working Group

- Jason Altenberg, South Riverdale Community Health Centre Toronto (SRCHC) (Co-Chair)
- Melisa Dickie, CATIE (Co-Chair)
- Naveed Zafar Janjua, BC Centre for Disease Control
- Lindsay Jennings, Prisoners HIV/AIDS Support Action Network
- Simon Ling, the Hospital for Sick Children
- Renée Masching, Canadian Aboriginal AIDS Network (CAAN)
- Karen Seto, Canadian Liver Foundation

The Priority populations section of the Blueprint was reviewed by Alexandra King (University of Saskatchewan); Carrielynn Lund (CAAN); Kate Mason (SRCHC); Laurel Challacombe, Christopher Hoy, Rivka Kushner, Tim Rogers, and Fozia Tanveer (CATIE); Sandra Ka Hon Chu (Canadian HIV/AIDS Legal Network); Ryan Peck and Meagan Johnston (HIV & AIDS Legal Clinic Ontario); Jordan Westfall past-President of the Canadian Association of People who Use Drugs.

Prevention Working Group

- Julie Bruneau, Université de Montréal (Co-Chair)
- Naveed Zafar Janjua, BC Centre for Disease Control (Co-Chair)
- Andreea Adelina Artenie, Université de Montréal
- Carrielynn Lund, Canadian Aboriginal AIDS Network
- Gerry Mugford, Memorial University of Newfoundland
- Élise Roy, Université de Sherbrooke
- Naglaa H. Shoukry, Université de Montréal
- Denise Thomas, Nursing Faculty, Langara College

Testing and diagnosis Working Group

- Mel Krajden, BC Centre for Disease Control (Co-Chair)
- Jason Grebely, The Kirby Institute, University of New South Wales (Co-Chair)
- Jordan Feld, Toronto General Hospital
- Jennifer van Gennip, Action Hepatitis Canada
- Tony Mazzulli, Sinai Health System and University Health Network
- Alexander Wong, University of Saskatchewan
- William W.L. Wong, School of Pharmacy, University of Waterloo

Care and treatment Working Group

- Curtis Cooper, The Ottawa Hospital (Co-Chair)
- Marina Klein, McGill University Health Centre (Co-Chair)
- Lisa Barrett, Dalhousie University
- Brian Conway, Vancouver Infectious Diseases Centre
- Alexandra King, University of Saskatchewan

Lead *Blueprint* writer

- Tracy Swan

Project management and editing

- Lorraine Fradette, CanHepC Project Manager, Centre de Recherche du Centre Hospitalier de l'Université de Montréal (CRCHUM)

Design and translation

- Valeria Saavedra, graphic design
- Jean Dussault and Josée Dussault, French translation

Funding:

The Canadian Network on Hepatitis C (CanHepC) is funded by a joint initiative of the Canadian Institutes of Health Research (NHC-142832) and the Public Health Agency of Canada. The funders had no role in the *Blueprint*'s design, development, and content. The views expressed in the *Blueprint* are those of the Blueprint Writing Committee and Working Groups and do not necessarily represent those of the funders.

Disclosures:

Liza Abraham is an advisor to AbbVie and Gilead.

Lisa Barrett is a consultant for AbbVie, Bristol Myer Squibb, Gilead, Merck, and ViiV; receives payment for lectures from AbbVie, Gilead and Merck; and develops presentations for AbbVie and Merck.

Julie Bruneau was an advisor for Gilead and Merck; and acted as steering committee member for and has received research grants from Gilead.

Brian Conway is an advisor - consultant for AbbVie, Merck and Gilead.

Curtis Cooper is a speaker and advisor for, and has received unrestricted program support from Gilead, Merck and AbbVie.

Jordan Feld has received research support from Abbott, Abbvie, Gilead, Janssen, and Wako/Fujifilm; and is a consultant for Abbott, Abbvie, Enanta, Gilead, and Roche.

Jason Grebely is an advisor for, has provided medical education to, and received research support from Cepheid, AbbVie, Gilead and Merck/MSD.

Marina Klein is a consultant for, and has received grant funding from Gilead and Merck.

Mel Krajden has received grant/contract funding paid to his institution from Hologic and Roche.

Simon Ling has received research support from Abbvie and Bristol Myers Squibb.

Tony Mazzuli has received grant/research support from Qvekka and bioMerieux; has received speaker honoraria from Merck and Verity Pharmaceuticals; and is a consultant/advisor for Cipher Pharmaceuticals, Merck, Microbix, Pfizer, Qvella, Roche, and Verity Pharmaceuticals.

Alexander Wong has received grant support from Gilead and Merck; and is advisor to AbbVie, Gilead, and Merck.

William W.L. Wong has received a research grant from the Canadian Liver Foundation.

None of these disclosures are related to this work.

RESOURCES

- WHO. Global Health Sector Strategy on Viral Hepatitis 2016-2021.
- WHO. Guidelines for the Care and Treatment of Persons Diagnosed with Chronic Hepatitis C Infection. 2018.
- WHO. Guidelines on Hepatitis B and C Testing. 2017.
- WHO. Monitoring and evaluation for viral hepatitis B and C: recommended indicators and framework. 2018.
- WHO. Manual for the development and assessment of national viral hepatitis plans: a provisional document. 2015.
- WHO. Combatting Hepatitis B and C to Reach Elimination by 2030. Advocacy Brief.

REFERENCES

1. Bolotin S, Feld JJ, Garber G, Wong WWL, Guerra FM, Mazzulli T. Population-based estimate of hepatitis C virus prevalence in Ontario, Canada. PLoS One [Online]. 2018 Jan 23 [Cited 2018 November 2];13(1):e0191184. Available from doi: 10.1371/journal.pone.0191184

2. Myers RP, Krajden M, Bilodeau M, et al. Burden of disease and cost of chronic hepatitis C virus infection in Canada. Can J Gastroenterol Hepatol [Online]. 2014 May [Cited 2018 September 1];28(5):243-50. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4049256/

3. Janjua NZ, Yu A, Kuo M, et al. Twin epidemics of new and prevalent hepatitis C infections in Canada: BC Hepatitis Testers Cohort. BMC Infectious Diseases [Online]. 2016 [Cited 2018 August 31];16:334. Available from: doi: 10.1186/s12879-016-1683-z

4. Krajden M, Cook D, Janjua N. Contextualizing Canada's hepatitis C virus epidemic. Can Liv Jour [Online]. December 1 2018 [Cited 2019 January 27];1(4); 218-30. Available from: https://doi.org/10.3138/canlivj.2018-0011

5. Public Health Agency of Canada. Hepatitis C in Canada: 2005-2010 Surveillance Report Ottawa: Centre for Communicable Diseases and Infection Control, Infectious Disease Prevention and Control Branch, Public Health Agency of Canada [Online]. 2011 [Cited 2018 August 31]. Available from: http://www.catie.ca/sites/default/files/1109-0139-Hep%20C%20Report-EN%20FINAL.pdf

6. Remis RS. A study to characterize the epidemiology of hepatitis C infection in Canada: Final Report. Public Health Agency of Canada [Online]. 2002 [Cited 2018 August 31]. Available from: http://publications.gc.ca/collections/collection_2009/aspc-phac/HP40-31-2008E.pdf

7. Wu H-X, Wu J, Wong T, et al. Enhanced surveillance of newly acquired hepatitis C virus infection in Canada, 1998 to 2004. Scand J Infect Dis [Online]. 2006 [Cited 2018 October 1];38:482-9. Available from: https://doi.org/10.1080/00365540500525161

8. Trubnikov M, Yan P, Archibald C. Estimated prevalence of hepatitis C virus infection in Canada, 2011. Public Health Agency of Canada. Canada Communicable Disease Report [Online]. 2014 December 18 [Cited 2018 August 31];40(19). Available from: http://www.phac-aspc.gc.ca/publicat/ccdr-rmtc/14vol40/dr-rm40-19/surveillance-b-eng.php

9. Trubnikov M, Yan P, Njihia J, Archibald C. Identifying and describing a cohort effect in the national database of reported cases of hepatitis C virus infection in Canada (1991-2010): an age-period-cohort analysis. CMAJ Open [Online]. 2014 Oct 1 [Cited 2018 November 17];2(4):E281-7. Available from doi: 10.9778/cmajo.20140041

10. Skeer MR, Ladin K, Wilkins LE, Landy DM, Stopka TJ. 'Hep C's like the common cold': understanding barriers along the HCV care continuum among young people who inject drugs. Drug Alcohol Depend [Online]. 2018 Sep 1 [Cited 2018 November 11];190:246-254. Available from doi: 10.1016/j.drugalcdep.2018.06.013

11. Treloar C, Rance J, Backmund M. Understanding barriers to hepatitis C virus care and stigmatization from a social perspective. Clin Infect Dis [Online]. 2013 Aug [Cited 2018 November 11];57 Suppl 2:S51-5. Available from doi: 10.1093/cid/cit263

12. Backus LI, Belperio PS, Shahoumian TA, Mole LA. Direct-acting antiviral sustained virologic response: Impact on mortality in patients without advanced liver disease. Hepatology [Online]. 2018 Jan 29 [Cited 2018 September 1]. Available from doi: 10.1002/hep.29811

13. Ioannou GN, Green PK, Berry K. HCV eradication induced by direct-acting antiviral agents reduces the risk of hepatocellular carcinoma. J Hepatol [Online]. 2017 Sep 5 [Cited 2018 September 1]. pii: S0168-8278(17)32273-0. Available from doi: 10.1016/j.jhep.2017.08.030

14. Nahon P, Bourcier V, Layese R, et al. Eradication of Hepatitis C Virus Infection in Patients With Cirrhosis Reduces Risk of Liver and Non-Liver Complications. Gastroenterology [Online]. 2017 Jan [Cited 2018 November 30]; 152 (1):142-156.e2. Available from doi: 10.1053/j.gastro.2016.09.009

15. Nuño Solinís R, Arratibel Ugarte P, Rojo A, Sanchez Gonzalez Y. Value of Treating All Stages of Chronic Hepatitis C: A Comprehensive Review of Clinical and Economic Evidence. Infect Dis Ther [Online]. 2016 Dec [Cited 2018 August 31]; 5(4):491-508. Available from: https://link.springer.com/article/10.1007%2Fs40121-016-0134-x

16. Saeed S, Moodie EE, Strumpf E, et al; Canadian Co-Infection Cohort Study Investigators. Real-World Impact of Direct Acting Antiviral Therapy on Health-Related Quality of Life in HIV/Hepatitis C Co-Infected Individuals. J Viral Hepat [Online]. 2018 Aug 23 [Cited 2018 September 2]. Available from doi: 10.1111/jvh.12985

17. Martin NK, Hickman M, Hutchinson SJ, Goldberg DJ, Vickerman P. Combination interventions to prevent HCV transmission among people who inject drugs: modeling the impact of antiviral treatment, needle and syringe programs, and opiate substitution therapy. Clin Infect Dis [Online]. 2013 Aug [Cited 2018 August 30];57 Suppl 2:S39-45. Available from doi: 10.1093/cid/cit296

18. Martin NK, Vickerman P, Grebely J, et al. Hepatitis C virus treatment for prevention among people who inject drugs: Modeling treatment scale-up in the age of direct-acting antivirals. Hepatol [Online]. 2013 Nov [Cited 2018 September 30]; 58(5):1598-609. Available from doi: 10.1002/hep.26431

19. Harris RJ, Martin NK, Rand E, et al. New treatments for hepatitis C virus (HCV): scope for preventing liver disease and HCV transmission in England. J Viral Hepat [Online]. 2016 Aug 23 [Cited 2018 September 30];(8):631-43. Available from doi: 10.1111/jvh.12529

20. Volkow ND, Frieden TR, Hyde PS, Cha SS. Medication-assisted therapies--tackling the opioid-overdose epidemic. N Engl J Med [Online]. 2014 May [Cited 2019 January 22]29; 370(22):2063-6. Available from doi: 10.1056/NEJMp1402780

21. World Health Organization. Global Health Sector Strategy on Viral Hepatitis. 2016-2021. [Online] Geneva; 2016 [Cited 2018 August 21]. Available from: http://apps.who.int/iris/bitstream/10665/246177/1/WHO-HIV-2016.06-eng.pdf?ua=1

22. Public Health Agency of Canada. Reducing the health impact of sexually transmitted and blood-borne infections in Canada by 2030: A pan-Canadian STBBI framework for action. [Online] July 9, 2018 [Cited 2018 August 12]. Available from: https://www.canada.ca/en/public-health/services/infectious-diseases/sexual-health-sexually-transmitted-infections/reports-publications/sexually-transmitted-blood-borne-infections-action-framework.html

23. The Lancet. Syndemics: health in context. Editorial [Online]. March 4 2017 [Cited 2018 August 31] 389; 10072. Available from doi: https://doi.org/10.1016/S0140-6736(17)30640-2

24. Willen SS, Knipper M, Abadía-Barrero CE, Davidovitch N. Syndemic vulnerability and the right to health. Lancet [Online]. 2017 Mar 4 [Cited 2018 August 31]; 389(10072):964-977. Available from doi: 10.1016/

S0140-6736(17)30261-1

25. World Health Organization. Global Hepatitis Report 2017 [Online]. Geneva; April 2017 [Cited 2018 September 1]. Available from: http://apps.who.int/iris/bitstream/handle/10665/255016/9789241565455-eng.pdf;jsessionid=8A81F371C37A624C2AD9D4BB79627B3E?sequence=1

26. World Health Organization. Monitoring and Evaluation for Viral Hepatitis B and C: Recommended Indicators and Framework. Technical Report [Online] Geneva; 2016 [Cited 2019 February 14]. Available from: https://apps.who.int/iris/bitstream/handle/10665/204790/9789241510288_eng.pdf?sequence=1

27. Hamadeh A, Haines A, Feng Z, Thien H, Janjua N, Krahn M, Wong WWL. Estimating the prevalence of chronic Hepatitis C infection in British Columbia and Ontario using mathematical modelling and health administrative data. Canadian Liver Meeting; 2019 May 24-26; Montreal, Canada.

28. Public Health Agency of Canada. Modelling the Incidence and Prevalence of Hepatitis C Infection and its Sequelae in Canada, 2007. Community Acquired Infections Division Centre for Communicable Diseases and Infection Control Infectious Disease and Emergency Preparedness Branch [Online] 2007 [Cited 2019 April 28]. Available from: https://www.canada.ca/content/dam/phac-aspc/migration/phac-aspc/sti-its-surv-epi/model/pdf/model07-eng.pdf

29. Gordon J, Bocking N, Pouteau K, et al. First Nations hepatitis C virus infections. Six-year retrospective study of on-reserve rates of newly reported infections in northwestern Ontario. Can Fam Physician [Online]. 2017 [Cited 2018 October 1]; 63:e488-e94. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5685465/

30. Spittal PM, Pearce ME, Chavoshi N, et al. The Cedar Project: high incidence of HCV infections in a longitudinal study of young Aboriginal people who use drugs in two Canadian cities. BMC Public Health [Online]. 2012 [Cited 2018 September 30]; 12: 632. 2. Available from doi: 10.1186/1471-2458-12-632

31. Public Health Agency of Canada. M-Track: Enhanced Surveillance of HIV, Sexually Transmitted and Blood-Borne Infections, and Associated Risk Behaviours among Men Who Have Sex with Men in Canada. Phase 1 report. Centre for Communicable Diseases and Infection Control, Infectious Disease and Prevention and Control Branch, Public Health Agency of Canada [Online]. 2011 [Cited 2018 October 1]. Available from: http://librarypdf.catie.ca/PDF/ATI-20000s/26403.pdf

32. Jacka B, Larney S, Degenhardt L, et al. Prevalence of injecting drug use and coverage of interventions to prevent HIV and hepatitis C virus among people who inject drugs in Canada. Am J Public Health; 2019. In Press.

33. Canadian Cancer Society's Advisory Committee on Cancer Statistics. Canadian Cancer Statistics 2017. Toronto, ON: Canadian Cancer Society [Online]. 2017 [Cited 2019 March 15]. Available at: cancer.ca/Canadian-CancerStatistics-2017-EN.pdf

34. Cacoub P, Comarmond C, Domont F, Savey L, Desbois AC, Saadoun D. Extrahepatic manifestations of chronic hepatitis C virus infection. Ther Adv Infect Dis [Online]. 2016 Feb [Cited 2018 August 23]; 3(1):3-14. Available from doi: 10.1177/2049936115585942

35. Cho HJ, Park E. Quality of Life of Chronic Hepatitis C Patients and Its Associated Factors. Osong Public Health Res Perspect [Online]. 2017 Apr [Cited 2018 November 11];8(2):124–129. Available from doi: 10.24171/j.phrp.2017.8.2.04

36. Strauss E, Dias Teixeira MC. Quality of life in hepatitis C. Liver Int [Online]. 2006 Sep [Cited 2018 November 12];26(7):755-65. Available from: https://onlinelibrary.wiley.com/doi/full/10.1111/j.1478-3231.2006.01331.x

37. Adinolfi LE, Nevola R, Rinaldi L, Romano C, Giordano M. Chronic Hepatitis C Virus Infection and Depression. Clin Liver Dis [Online]. 2017 Aug [Cited 2018 November 11];21(3):517-534. Available from doi: 10.1016/j.cld.2017.03.007

38. Crenshaw K. Demarginalizing the Intersection of Race and Sex: A Black Feminist Critique of Antidiscrimination Doctrine, Feminist Theory, and Antiracist Politics. University of Chicago Legal Forum [Online]. 1989 [Cited 2018 August 10];139–67. Available from: https://chicagounbound.uchicago.edu/cgi/viewcontent.cgi?article=1052&context=uclf

39. Hull M, Shafran S, Wong A, et al. CIHR Canadian HIV Trials Network Coinfection and Concurrent Diseases Core Research Group. Updated Canadian HIV/Hepatitis C Adult Guidelines for Management and Treatment. Can J Infect Dis Med Microbiol [Online]. 2016 [Cited 2018 November 11];2016: 4385643. Available from doi: 10.1155/2016/4385643

40. Jordan AE, Perlman DC, Neurer N, Smith DJ, Des Jarlais DC, Hagan H. Prevalence of hepatitis C virus infection among HIV+ men who have sex with men: a systematic review and meta-analysis. Int J STD AIDS [Online]. 2017 Feb [Cited 2018 November 12];28(2):145–159. Available from doi: 10.1177/0956462416630910

41. Saeed S, Strumpf EC, Moodie EEM, et al; the Canadian Co-Infection Cohort Study. Disparities in direct acting antivirals uptake in HIV-hepatitis C co-infected populations in Canada. J Int AIDS Soc [Online]. 2017 Nov [Cited 2018 November 14]; 20(3): e25013. Available from doi: 10.1002/jia2.25013

42. Thornton AC, Jose S, Bhagani S, et al; UK Collaborative HIV cohort (UK CHIC) steering committee. Hepatitis B, hepatitis C, and mortality among HIV-positive individuals. AIDS [Online]. 2017 Nov [Cited 2018 November 14]28;31(18):2525-2532. Available from doi: 10.1097/QAD.0000000000001646

43. Graham CS, Baden LR, Yu E, et al. Influence of human immunodeficiency virus infection on the course of hepatitis C virus infection: a meta-analysis. Clin Infect Dis [Online]. 2001 Aug 15 [Cited 2018 November 14];33(4):562-9. Available from: https://academic.oup.com/cid/article/33/4/562/278085

44. Falade-Nwulia O, Suarez-Cuervo C, Nelson DR, Fried MW, Segal JB, Sulkowski MS. Oral Direct-Acting Agent Therapy for Hepatitis C Virus Infection: A Systematic Review. Ann Intern Med [Online]. 2017 May 2 [Cited 2018 November 23];166(9):637-648. Available from doi: 10.7326/M16-2575

45. Feld JJ, Jacobson IM, Hézode C, et al; ASTRAL-1 Investigators. Sofosbuvir and Velpatasvir for HCV Genotype 1, 2, 4, 5, and 6 Infection. N Engl J Med [Online]. 2015 Dec 31 [Cited 2018 November 23];373(27):2599-607. Available from doi: 10.1056/NEJMoa1512610

46. Calleja JL, Crespo J, Rincón D, et al; Spanish Group for the Study of the Use of Direct-acting Drugs Hepatitis C Collaborating Group. Effectiveness, safety and clinical outcomes of direct-acting antiviral therapy in HCV genotype 1 infection: Results from a Spanish real-world cohort. J Hepatol [Online]. 2017 Jun [Cited 2018 November 23];66(6):1138-1148. Available from doi: 10.1016/j.jhep.2017.01.028

47. D'Ambrosio R, Pasulo L, Puoti M, et al; NAVIGATORE-Lombardia Study Group. Real-life effectiveness and safety of Glecaprevir/Pibrentasvir in 723 patients with chronic hepatitis C. J Hepatol [Online]. 2018 Nov 22 [Cited 2018 November 24]. pii: S0168-8278(18)32543-1. Available from doi: 10.1016/j.jhep.2018.11.011

48. Butt AA, Yan P, Shuaib A, Abou-Samra AB, Shaikh OS, Freiberg MS. Direct-acting Antiviral Therapy for HCV Infection is Associated with a Reduced Risk of Cardiovascular Disease Events. Gastroenterology [Online]. 2018 Nov 13 [Cited 2018 November 30]. pii: S0016-5085(18)35264-8. Available from doi: 10.1053/j.gastro.2018.11.022

49. Hum J, Jou JH, Green PK, et al. Improvement in Glycemic Control of Type 2 Diabetes After Successful

Treatment of Hepatitis C Virus. Diabetes Care [Online]. 2017 Sep [Cited 2018 December 1];40(9):1173-1180. Available from doi: 10.2337/dc17-0485

50. Cacoub P, Desbois AC, Comarmond C, Saadoun D. Impact of sustained virological response on the extrahepatic manifestations of chronic hepatitis C: a meta-analysis. Gut [Online]. 2018 Nov [Cited 2018 November 30];67(11):2025-2034. Available from doi: 10.1136/gutjnl-2018-316234

51. Schanzer D, Pogany L, Aho J, et al. Can we eliminate hepatitis C? Impact of availability of direct-acting antivirals for hepatitis C on Canadian hospitalization rates, 2012–2016. CCDR [Online]. 2018 July 5 [Cited 2018 August 26];Volume 44-7/8. Available from: https://www.canada.ca/en/public-health/services/reports-publications/canada-communicable-disease-report-ccdr/monthly-issue/2018-44/issue-7-8-july-5-2018/article-1-canadian-hospitalization-rates-hep-c.html

52. The Canadian Network on Hepatitis C Collaborators. Hepatitis C Virus Elimination in Canada is Achievable with Sustained Treatment Uptake. 2019. In preparation.

53. Broady TR, Cama E, Brener L, Hopwood M, de Wit J, Treloar C. Responding to a national policy need: development of a stigma indicator for bloodborne viruses and sexually transmissible infections. Aust N Z J Public Health [Online]. 2018 Sep 10 [Cited 2018 November 29];42(6): 513-515. Available from doi: 10.1111/1753-6405.12809

54. Brener L, Von Hippel W, Kippax S, Preacher KJ. The role of physician and nurse attitudes in the health care of injecting drug users. Subst Use Misuse [Online]. 2010 Jun [Cited 2018 November 29];45(7-8):1007-18. Available from doi: 10.3109/10826081003659543

55. Hatzenbuehler ML. Structural stigma and health inequalities: Research evidence and implications for psychological science. Am Psychol [Online]. 2016 [Cited 2019 January 31];71(8):742-51. Available from doi: 10.1037/amp0000068

56. Pascoe EA, Richman LS. Perceived discrimination and health: A meta-analytic review. Psychol Bull [Online]. 2009 [Cited 2019 January 31];135(4):531-54. Available from doi: 10.1037/a0016059

57. von Hippel C, Brener L, Horwitz R. Implicit and explicit internalized stigma: Relationship with risky behaviors, psychosocial functioning and healthcare access among people who inject drugs. Addict Behav [Online]. 2018 [Cited 2019 January 31];76:305-11. Available from doi: 10.1016/j.addbeh.2017.08.036

58. Dowsett LE, Coward S, Lorenzetti DL, MacKean G, Clement F. Living with Hepatitis C Virus: A Systematic Review and Narrative Synthesis of Qualitative Literature. Can J Gastroenterol Hepatol [Online]. 2017 [Cited 2018 November 27];2017:3268650. Available from doi: 10.1155/2017/3268650

59. Brener L, Cama E, Hull P, Treloar C. Evaluation of an online injecting drug use stigma intervention targeted at health providers in New South Wales, Australia. Health Psychol Open [Online]. 2017 May 16 [Cited 2018 November 27];4(1). Available from doi: 10.1177/2055102917707180

60. Livingston JD, Milne T, Fang ML, Amari E. The effectiveness of interventions for reducing stigma related to substance use disorders: a systematic review. Addiction [Online]. 2012 Jan [Cited 2018 November 27];107(1):39-50. Available from doi: 10.1111/j.1360-0443.2011.03601.x

61. Dickie M, Fish S. Risks, realities and responses: Hepatitis C re-infection among people who inject drugs and HIV-positive MSM. CATIE [Online]. 2018 [Cited 2018 August 22]. Available from: https://www.catie.ca/en/pif/spring-2018/risks-realities-and-responses-hepatitis-c-re-infection-among-people-who-inject-drugs#bios

62. Fayeed S, King A, King M, et al. In the eyes of Indigenous people in Canada: exposing the underlying

colonial etiology of hepatitis C and the imperative for trauma-informed care. CanLivJ [Online]. 2018 [Cited 2019 30 April];1(3): 115-129. Available from doi: 10.3138/canlivj.2018-0009

63. CATIE. Windows of Opportunity: Integrated Hepatitis C Programming Approaches for Priority Populations. [Online] 2015 [Cited 2018 July 19]. Available from: http://www.catie.ca/en/windows-opportunity/3/3-4/3-4-1

64. Bombay A, Matheson K, Anisman H. The intergenerational effects of Indian Residential Schools: Implications for the concept of historical trauma. Transcult Psychiatry [Online]. 2014 [Cited 2019 January 30];51(3):320-338. Available from https://doi.org/10.1177/1363461513503380

65. Truth and Reconciliation Commission of Canada. Honouring the Truth, Reconciling for the Future: Summary of the Final Report of the Truth and Reconciliation Commission of Canada. [Online] April 3 2014 [Cited 2019 January 30]. Available from: http://publications.gc.ca/pub?id=9.800288&sl=0

66. Kouyoumdjian F, Schuler A, Matheson F. Health Status of Prisoners in Canada. Can Fam Physician [Online]. 2016 Mar [Cited 2019 January 31];62(3):215–222. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4984599/

67. Hoornenborg E, Achterbergh RCA, Schim van der Loeff MF, et al; Amsterdam PrEP Project team in the HIV Transmission Elimination Amsterdam Initiative, MOSAIC study group. MSM starting preexposure prophylaxis are at risk of hepatitis C virus infection. AIDS [Online]. 2017 Jul [Cited 2018 August 31];31(11):1603-10. Available from doi: 10.1097/QAD.0000000000001522

68. Price JC, McKinney JE, Crouch PC, et al. Sexually Acquired Hepatitis C Infection in HIV-uninfected Men Who Have Sex with Men Using Pre-exposure Prophylaxis Against HIV. J Infect Dis [Online]. 2018 Nov 20 [Cited 2018 November 22];219(9):1373-1376. Available from doi: 10.1093/infdis/jiy670

69. Midgard H, Weir A, Palmateer N, et al. HCV epidemiology in high-risk groups and the risk of reinfection. Journal of Hepatology [Online]. 2016 [Cited 2018 August 31];65:S33–S45. Available from: https://www.journal-of-hepatology.eu/article/S0168-8278(16)30336-1/fulltext

70. Prevention Access Campaign and Undetectable = Untransmittable. [Online] 2017 [Cited 2018 August 29]. Available from: https://www.preventionaccess.org/

71. Joy JB, McCloskey RM, Nguyen T, et al. Phylogenetic estimation of the temporal spread of hepatitis C genotype 1a in North America: a retrospective phylogenetic study. The Lancet Infectious Diseases [Online]. 2016 [Cited 2018 August 31];16(6):698-702. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5245154/

72. Rotermann M, Langlois K, Andonov A, Trubnikov M. Seroprevalence of hepatitis B and C virus infections: Results from the 2007 to 2009 and 2009 to 2011 Canadian Health Measures Survey. Health Rep [Online]. 2013 Nov [Cited 2018 October 21];24(11):3-13. Available from https://www.statcan.gc.ca/pub/82-003-x/2013011/article/11876-eng.pdf

73. Smith BD, Morgan RL, Beckett GA, Falck-Ytter Y, Holtzman D, Ward JW. Hepatitis C Virus Testing of Persons Born During 1945–1965: Recommendations From the Centers for Disease Control and Prevention. Ann Intern Med [Online]. 2012 [Cited 2018 August 31];157:817–822. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5777166/

74. Yutin I, Low-Beer D, Bergeri Isabel, et al. Viral Hepatitis Strategic Information to Achieve Elimination by 2030: Key Elements for HIV Program Managers. JMIR Public Health Surveill [Online]. 2017 Dec 15 [Cited 2019 February 7];3(4):e91. Available from doi: 10.2196/publichealth.7370

75. Janjua NZ, Kuo M, Yu A, et al. The Population Level Cascade of Care for Hepatitis C in British Columbia, Canada: The BC Hepatitis Testers Cohort (BC-HTC). EBioMedicine [Online]. 2016 Oct [Cited 2018 September 30];12:189-195. Available from: doi: 10.1016/j.ebiom.2016.08.035

76. Bruneau J, Arruda N, Zang G, Jutras-Aswad D, Roy É. The evolving drug epidemic of prescription opioid injection and its association with HCV transmission among people who inject drugs in Montréal, Canada. Addiction [Online]. 2019 Feb [Cited 2019 January 22];114(2):366-373. Available from doi: 10.1111/add.14487

77. Bach P, Walton G, Hayashi K, et al. Benzodiazepine Use and Hepatitis C Seroconversion in a Cohort of Persons Who Inject Drugs. Am J Public Health [Online]. 2016 Jun [Cited 2019 January 22];106(6):1067-72. Available from doi: 10.2105/AJPH.2016.303090

78. Wilson DP, Donald B, Shattock AJ, Wilson D, Fraser-Hurt N. The cost-effectiveness of harm reduction. Int J Drug Policy [Online]. 2015 Feb 26 [Cited 2018 September 29];26;Suppl 1:S5-11. Available from doi: 10.1016/j.drugpo.2014.11.007

79. World Health Organization. Guidelines for the Screening, Care and Treatment of Persons with Hepatitis C. [Online] Geneva; 2014 [Cited 2018 November 5]. Available from: http://apps.who.int/iris/bitstream/handle/10665/111747/9789241548755_eng.pdf?sequence=1

80. Platt L, Minozzi S, Reed J, 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 [Online]. 2018 Mar [Cited 2018 August 31];113(3): 545–563. Available from: doi: 10.1111/add.14012

81. Martin NK, Vickerman P, Dore GJ, et al; STOP HCV-Consortium. Prioritization of HCV treatment in the direct-acting antiviral era: An economic evaluation. J Hepatol [Online]. 2016 Jul [Cited 2019 February 14];65(1):17-25. Available from doi: 10.1016/j.jhep.2016.02.007

82. Zelenev A, Li J, Mazhnaya A, Basu S, Altice FL. Hepatitis C virus treatment as prevention in an extended network of people who inject drugs in the USA: a modelling study. Lancet Infect Dis [Online]. 2018 Feb [Cited 2018 November 5];18(2):215-224. Available from doi: 10.1016/S1473-3099(17)30676-X

83. Law JLM, Logan M, Wong J, et al. Role of the E2 Hypervariable Region (HVR1) in the Immunogenicity of a Recombinant Hepatitis C Virus Vaccine. J Virol [Online]. 2018 May [Cited 2018 August 31]14;92(11). pii: e02141-17. Available from doi: 10.1128/JVI.02141-17

84. Shoukry NH. Hepatitis C Vaccines, Antibodies, and T Cells. Front Immunol [Online]. 2018 Jun [Cited 2018 August 31];28;9:1480. Available from doi: 10.3389/fimmu.2018.01480

85. Bartenschlager R, Baumert TF, Bukh J, et al. Critical challenges and emerging opportunities in hepatitis C virus research in an era of potent antiviral therapy: Considerations for scientists and funding agencies. Virus Res [Online]. 2018 Mar 15 [Cited 2018 October 1];248:53-62. Available from doi: 10.1016/j.virusres.2018.02.016

86. Freedman H, Logan MR, Law JL, Houghton M. Structure and Function of the Hepatitis C Virus Envelope Glycoproteins E1 and E2: Antiviral and Vaccine Targets. ACS Infect Dis [Online]. 2016 Nov 11 [Cited 2018 October 1];2(11):749-762. Available from: https://www.ncbi.nlm.nih.gov/pubmed/27933781

87. Wong JA, Bhat R, Hockman D, et al. Recombinant hepatitis C virus envelope glycoprotein vaccine elicits antibodies targeting multiple epitopes on the envelope glycoproteins associated with broad cross-neutralization. J Virol [Online]. 2014 Dec [Cited 2018 October 1];88(24):14278-88. Available from doi: 10.1128/JVI.01911-14

88. Law JL, Chen C, Wong J, et al. A hepatitis C virus (HCV) vaccine comprising envelope glycoproteins gpE1/gpE2 derived from a single isolate elicits broad cross-genotype neutralizing antibodies in humans. PLoS One [Online]. 2013 [Cited 2018 October 1];8(3):e59776.Available from doi: 10.1371/journal.pone.0059776

89. Major M, Gutfraind A, Shekhtman L. Modeling of patient virus titers suggests that availability of a vaccine could reduce hepatitis C virus transmission among injecting drug users. Sci Transl Med [Online]. 2018 Jul 11 [Cited 2018 November 17];10(449). pii: eaao4496. Available from doi: 10.1126/scitranslmed.aao4496

90. Bruneau J, Roy E, Arruda N, Zang G, Jutras-Aswad D. The rising prevalence of prescription opioid injection and its association with hepatitis C incidence among street-drug users. Addiction [Online]. 2012 [Cited 2018 October 5];107(7):1318-27. Available from doi: 10.1111/j.1360-0443.2012.03803.x

91. Shrestha R, Karki P, Altice FL, et al. Correlates of willingness to initiate pre-exposure prophylaxis and anticipation of practicing safer drug- and sex-related behaviors among high-risk drug users on methadone treatment. Drug Alcohol Depend [Online]. 2017 Apr 1 [Cited 2018 August 31];173:107-16. Available from: doi: 10.1016/j.drugalcdep.2016.12.023

92. Roy E, Arruda N, Bruneau J, Jutras-Aswad D. Epidemiology of Injection Drug Use: New Trends and Prominent Issues. Can J Psychiatry [Online]. 2016 Mar [Cited 2018 August 15];61(3):136–144. Available from doi: 10.1177/0706743716632503

93. Ha S, Totten S, Pogany L, Wu J, Gale-Rowe M. Hepatitis C in Canada and the importance of risk-based screening. Can Comm Dis Rep [Online]. 2016 [Cited 2018 August 31];42(3):57-62. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5864411/

94. Jin F, Matthews GV, Grulich AE. Sexual transmission of hepatitis C virus among gay and bisexual men: a systematic review. Sexual health [Online]. 2017 [Cited 2018 August 31];14(1):28-41. Available from doi: 10.1071/SH16141

95. Terrault NA, Dodge JL, Murphy EL, et al. Sexual transmission of hepatitis C virus among monogamous heterosexual couples: the HCV partners study. Hepatology [Online]. 2013 Mar [Cited 2018 December 1];57(3):881-9. Available from doi: 10.1002/hep.26164

96. Falade-Nwulia O, Sulkowski MS, Merkow A, Latkin C, Mehta SH. Understanding and addressing hepatitis C re-infection in the oral direct-acting antiviral era. J Viral Hepat [Online]. 2018 Mar [Cited 2018 August 31];25(3):220-7. Available from doi: 10.1111/jvh.12859

97. Ingiliz P, Martin TC, Rodger A, et al; NEAT study group. HCV re-infection incidence and spontaneous clearance rates in HIV-positive men who have sex with men in Western Europe. J Hepatol [Online]. 2017 Feb [Cited 2018 August 31];66(2):282-7. Available from: doi: 10.1016/j.jhep.2016.09.004

98. Benova L, Mohamoud YA, Calvert C, Abu-Raddad LJ. Vertical transmission of hepatitis C virus: systematic review and meta-analysis. Clin Infect Dis [Online]. 2014 Jun 13 [Cited 2018 August 31];59(6):765-73. Available from: https://doi.org/10.1093/cid/ciu447

99. Roberts EA, Yeung L. Maternal-infant transmission of hepatitis C virus infection. Hepatology [Online]. 2002 Nov [Cited 2018 August 31];36(5 Suppl 1):S106-13. Available from doi: 10.1053/jhep.2002.36792

100. Robinson JL, Canadian Pediatric Society. Vertical transmission of hepatitis C virus: current knowledge and issues. Paediatr Child Health [Online]. 2008 [Cited 2018 August 31];13(6):529–534. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2532905/

101. Society for Maternal-Fetal Medicine, Hughes BL, Page CM, JKuller JA. Hepatitis C in pregnancy: screening,

treatment, and management. Society for Maternal-Fetal Medicine. Am J Obstet Gynecol [Online]. 2017 Nov [Cited 2018 August 31];217(5):B2-B12. Available from doi: 10.1016/j.ajog.2017.07.039

102. Yeung CY, Lee HC, Chan WT, Jiang CB, Chang SW, Chuang CK. Vertical transmission of hepatitis C virus: Current knowledge and perspectives. World J Hepatol [Online]. 2014 Sep 27 [Cited 2018 August 31];6(9):643-51. Available from doi: 10.4254/wjh.v6.i9.643

103. Werb D, Bluthenthal RN, Kolla G, et al. Preventing Injection Drug use Initiation: State of the Evidence and Opportunities for the Future. J Urban Health [Online]. 2018 February [Cited 2018 September 1];95(1):91-8.23. Available from doi: 10.1007/s11524-017-0192-8

104. Batchelder AW, Cockerham-Colas L, Peyser D, Reynoso SP, Soloway I, Litwin AH. Perceived benefits of the hepatitis C peer educators: a qualitative investigation. Harm Reduct J [Online]. 2017 Sep 29 [Cited 2018 November 14];14(1):67. Available from doi: 10.1186/s12954-017-0192-8

105. World Health Organization. Combating Hepatitis B and C to reach elimination by 2030. Advocacy brief. [Online] Geneva; 2016. [Cited 2018 August 26]. Available from: http://apps.who.int/iris/bitstream/10665/206453/1/WHO_HIV_2016.04_eng.pdf?ua=1

106. Walsh N, Verster A, Rodolph M, Akl EA. WHO guidance on the prevention of viral hepatitis B and C among people who inject drugs. Int J Drug Policy [Online]. 2014 May [Cited 2018 September 30];25(3):363-71. Available from doi: 10.1016/j.drugpo.2014.01.009

107. Trickey A, May MT, Hope V, et al. Usage of low dead space syringes and association with hepatitis C prevalence amongst people who inject drugs in the UK. Drug Alcohol Depend [Online]. 2018 Sep 15 [Cited 2018 September 30];192:118-124. Available from doi: 10.1016/j.drugalcdep.2018.07.041

108. Islam M, Wodak A, Conigrave KM. The effectiveness and safety of syringe vending machines as a component of needle syringe programmes in community settings. Int J Drug Policy [Online]. 2008 December [Cited 2018 September 1];19(6):436-41. Available from: https://www.ijdp.org/article/S0955-3959(07)00148-X/fulltext

109. WHO, UNODC, UNAIDS technical guide for countries to set targets for universal access to HIV prevention, treatment and care for injecting drug users – 2012 revision. [Online] Geneva; 2013 [Cited 2018 September 1]. Available from: http://apps.who.int/iris/bitstream/handle/10665/77969/9789241504379_eng.pdf?sequence=1

110. Gowing L, Farrell MF, Bornemann R, Sullivan LE, Ali R. Oral substitution treatment of injecting opioid users for prevention of HIV infection. Cochrane Database Syst Rev [Online]. 2011 Aug 10 [Cited 2019 April 16];(8):CD004145. Available from doi: 10.1002/14651858.CD004145.pub4

111. Ma J, Bao YP, Wang RJ, et al. Effects of medication-assisted treatment on mortality among opioids users: a systematic review and meta-analysis. Mol Psychatry [Online]. 2018 Jun 22 [Cited 2018 September 29]. Available from doi: 10.1038/s41380-018-0094-5

112. Public Health Agency of Canada. I-Track: Enhanced Surveillance of HIV, Hepatitis C and associated risk behaviours among people who inject drugs in Canada. Phase 3 (2010-2012). [Online] 2014 [Cited 2019 April 25]. Available from https://www.canada.ca/content/dam/phac-aspc/migration/phac-aspc/aids-sida/publication/reports/i-track-phase-3/assets/pdf/i-track-phase-3-eng.pdf

113. Public Health Agency of Canada. Supervised consumption sites: status of applications. [Online] 2018 August 29 [Cited 2018 September 1]. Available from: https://www.canada.ca/en/health-canada/services/substance-use/supervised-consumption-sites/status-application.html

114. Potier C, Laprevote V, Dubois-Arber F, Cottencin O, Rolland B. Supervised injection services: what has been demonstrated? A systematic literature review. Drug Alcohol Depend [Online]. 2014 December [Cited 2018 September 1];145:48-68. Available from doi: 10.1016/j.drugalcdep.2014.10.012

115. Westbrook RH, Dusheiko G. Natural history of hepatitis C. J Hepatol [Online]. 2014 Nov [Cited 2018 November 27];61(1 Suppl):S58-68. Available from doi: 10.1016/j.jhep.2014.07.012

116. Moyer VA; US Preventive Services Task Force. Screening for hepatitis C virus infection in adults: U.S. Preventive Services Task Force recommendation statement. Ann Intern Med [Online]. 2013 Sep 3 [Cited 2018 August 30];159(5):349-57. Available from doi: 10.7326/0003-4819-159-5-201309030-00672

117. World Health Organization. WHO guidelines on hepatitis B and C testing. [Online] Geneva; 2017 [Cited 2018 August 30]. Available from: http://apps.who.int/iris/bitstream/handle/10665/254621/9789241549981-eng.pdf?sequence=1

118. AASLD-IDSA. Recommendations for Testing, Managing, and Treating Hepatitis C. [Online] 2016. [Cited 2016 December 30]. Available from: http://www.hcvguidelines.org/

119. Bottero J, Brouard C, Roudot-Thoraval F, et al; Viral Hepatitis Testing Experts Group. 2014 French guidelines for hepatitis B and C screening: a combined targeted and mass testing strategy of chronic viruses namely HBV, HCV and HIV. Liver Int [Online]. 2016 Oct [Cited 2018 August 30];36(10):1442-9. Available from doi: 10.1111/liv.13135

120. Pawlotsky J-M, Negro F, Aghemo A, et al. EASL Recommendations on Treatment of Hepatitis C 2018. J Hepatol [Online]. 2018 Aug [Cited 2018 August 31];69(2):461-511. Available from: https://www.journal-of-hepatology.eu/article/S0168-8278(18)31968-8/pdf

121. Wong WWL, Erman A, Feld JJ, Krahn M. Model-based projection of health and economic effects of screening for hepatitis C in Canada. CMAJ Open [Online]. 2017 Aug 25 [Cited 2018 November 22];5(3):E662-E672. Available from doi: 10.9778/cmajo.20170048

122. Shah H, Bilodeau M, Burak KW, et al; Canadian Association for the Study of the Liver. The management of chronic hepatitis C: 2018 guideline update from the Canadian Association for the Study of the Liver. CMAJ [Online]. 2018 Jun 4 [Cited 2018 August 31];190(22):E677-E687. Available from doi: 10.1503/cmaj.170453

123. Grad R, Thombs BD, Tonelli M, et al; Canadian Task Force on Preventive Health Care. Recommendations on hepatitis C screening for adults. CMAJ [Online]. 2017 Apr 24 [Cited 2019 April 28];189(16):E594-E604. Available from doi: 10.1503/cmaj.161521

124. Cadieux G, Sachdeva H. Toward ending hepatitis C virus infection: What are the next steps? CMAJ [Online]. 2017 Apr 24 [Cited 2019 April 28];189(16): E583–E584. Available from doi: 10.1503/cmaj.170274

125. Wong WWL, Tu HA, Feld JJ, Wong T, Krahn M. Cost-effectiveness of screening for hepatitis C in Canada. CMAJ [Online]. 2015 Feb 17 [Cited 2019 April 28];187(3):E110-E121. Available from doi: 10.1503/cmaj.140711

126. Wong WWL, Haines A, Zangneh HF, Shah HS. Can we afford not to screen for hepatitis C virus in Canada? CanLivJ [Online]. Spring 2018 [Cited 2019 April 29];1(2):51-65. Available from: https://canlivj.utpjournals.press/doi/pdf/10.3138/canlivj.1.2.005

127. World Health Organization. Choosing Interventions that are Cost Effective (WHO-CHOICE). Geneva: WHO, 2005.

128. Laupacis A, Feeny D, Detsky AS, Tugwell PX. How attractive does a new technology have to be to warrant adoption and utilization? Tentative guidelines for using clinical and economic evaluations. CMAJ. 1992;146(4):473-81.

129. Hamadeh A, Feng Z, Krahn M, Wong WW. A model-based framework for chronic hepatitis C prevalence estimation. PLoS One. 2019. Submitted.

130. Hamadeh A, Feng Z, Krahn M, Wong WWL. Estimation of Hepatitis C Prevalence in Canada Via a two-Stage back-calculation algorithm. Canadian Liver Meeting; 2018 February 9-11.Toronto (ON), Canada. Available from: https://canlivj.utpjournals.press/doi/pdf/10.3138/canlivj.1.issue-1

131. Alter MJ, Kruszon-Moran D, Nainan OV, et al. The prevalence of hepatitis C virus infection in the United States, 1988 through 1994. N Engl J Med [Online]. 1999 [Cited 2018 September 30];341:556-62. Available from: https://www.nejm.org/doi/10.1056/NEJM199908193410802?url_ver=Z39.88-2003&rfr_id=ori:rid:crossref.org&rfr_dat=cr_pub%3dwww.ncbi.nlm.nih.gov.

132. Mera J, Vellozzi C, Hariri S, et al. Identification and Clinical Management of Persons with Chronic Hepatitis C Virus Infection - Cherokee Nation, 2012-2015. Morb Mortal Wkly Rep [Online]. 2016 May 13 [Cited 2018 August 31];65(18):461-6. Available from: https://www.cdc.gov/mmwr/volumes/65/wr/mm6518a2.htm

133. Patel RC, Vellozzi C, Smith BD. Results of Hepatitis C Birth-Cohort Testing and Linkage to Care in Selected U.S. Sites, 2012-2014. Public Health Rep [Online]. 2016 May-Jun [Cited 2018 August 30];131(Suppl 2):12-9. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4853323/

134. Yehia BR, Schranz AJ, Umscheid CA, Lo Re V III. The treatment cascade for chronic hepatitis C virus infection in the United States: a systematic review and meta-analysis. PLOS One [Online]. 2014 Jul 2 [Cited 2018 August 3];9(7):e101554. Available from doi: 10.1371/journal.pone.0101554

135. Janjua NZ, Chapinal N, Yu A, et al. Prevention and care cascade for hepatitis C among people who inject drugs in British Columbia, Canada. J Viral Hep [Online]. 12 June 2018 [Cited 2019 January 27]; 25(S2):24-25. Available from https://doi.org/10.1111/jvh.33_12922

136. Zhou K, Fitzpatrick T, Walsh N, et al. Interventions to optimise the care continuum for chronic viral hepatitis: a systematic review and meta-analyses. Lancet Infect Dis [Online]. 2016 Dec [Cited 2018 August 31];16(12):1409-1422. Available from doi: 10.1016/S1473-3099(16)30208-0

137. Federman AD, Kil N, Kannry J, et al. An Electronic Health Record-based Intervention to Promote Hepatitis C Virus Testing Among Adults Born Between 1945 and 1965: A Cluster-randomized Trial. Med Care [Online]. 2017 Jun [Cited 2018 August 31];55(6):590-597. Available from doi: 10.1097/MLR.0000000000000715

138. Litwin AH, Smith BD, Drainoni ML, et al. Primary care-based interventions are associated with increases in hepatitis C virus testing for patients at risk. Dig Liver Dis [Online]. 2012 Jun [Cited 2018 August 31];44(6):497-503. Available from doi: 10.1016/j.dld.2011.12.014

139. Drainoni ML, Litwin AH, Smith BD, et al. Effectiveness of a risk screener in identifying hepatitis C virus in a primary care setting. Am J Public Health [Online]. 2012 Nov [Cited 2018 August 31];102(11):e115-21. Available from doi: 10.2105/AJPH.2012.300659

140. Konerman MA, Thomson M, Gray K, et al. Impact of an electronic health record alert in primary care on increasing hepatitis c screening and curative treatment for baby boomers. Hepatology [Online]. 2017 Dec [Cited 2018 September 2];66(6):1805-1813.Available from doi: 10.1002/hep.2936

141. Howes N, Lattimore S, Irving WL, Thomson BJ. Clinical Care Pathways for Patients With Hepatitis C: Reducing Critical Barriers to Effective Treatment. Open Forum Infect Dis [Online]. 2016 Jan 6 [Cited 2018 September 30];3(1):ofv218. Available from doi: 10.1093/ofid/ofv218

142. Kapadia SN, Marks KM. Hepatitis C Management Simplification From Test to Cure: A Framework for Primary Care Providers. Clin Ther [Online]. 2018 Aug [Cited 2018 November 14];40(8):1234-1245. Available from doi: 10.1016/j.clinthera.2018.05.010

143. Meyer JP, Moghimi Y, Marcus R, Lim JK, Litwin AH, Altice FL. Evidence-based interventions to enhance assessment, treatment, and adherence in the chronic Hepatitis C care continuum. Int J Drug Policy [Online]. 2015 Oct [Cited 2018 August 31];26(10):922-35. Available from doi: 10.1016/j.drugpo.2015.05.002

144. Hickman M, McDonald T, Judd A, et al. Increasing the uptake of hepatitis C virus testing among injecting drug users in specialist drug treatment and prison settings by using dried blood spots for diagnostic testing: a cluster randomized controlled trial. J Viral Hepat [Online]. 2008 Apr [Cited 2018 August 31];15(4):250-4. Available from: https://onlinelibrary.wiley.com/doi/abs/10.1111/j.1365-2893.2007.00937.x

145. Radley A, Melville K, Tait J, Stephens B, Evans JMM, Dillon JF. A quasi-experimental evaluation of dried blood spot testing through community pharmacies in the Tayside region of Scotland. Frontline Gastroenterol [Online]. 2017 Jul [Cited 2018 August 31];8(3):221-228. Available from doi: 10.1136/flgastro-2016-100776

146. Rosenberg SD, Goldberg RW, Dixon LB, et al. Assessing the STIRR model of best practices for blood-borne infections of clients with severe mental illness. Psychiatr Serv [Online]. 2010 Sep [Cited 2018 August 30];61(9):885-91. Available from doi: 10.1176/ps.2010.61.9.885

147. Bajis S, Dore GJ, Hajarizadeh B, Cunningham EB, Maher L, Grebely J. Interventions to enhance testing, linkage to care and treatment uptake for hepatitis C virus infection among people who inject drugs: A systematic review. Int J Drug Policy [Online]. 2017 Sep [Cited 2018 August 31];47:34-46. Available from doi: 10.1016/j.drugpo.2017.07.002

148. Aitken CK, Kerger M, Crofts N. Peer-delivered hepatitis C testing and counselling: a means of improving the health of injecting drug users. Drug Alcohol Rev [Online]. 2002 March [Cited 2018 August 31];21(1):33-7. Available from: https://onlinelibrary.wiley.com/doi/abs/10.1080/09595230220119327

149. Skipper C, Guy JM, Parkes J, Roderick P, Rosenberg WM. Evaluation of a prison outreach clinic for the diagnosis and prevention of hepatitis C: Implications for the national strategy. Gut [Online]. 2003 Oct [Cited 2018 August 31];52(10):1500-4. Available from: https://gut.bmj.com/content/52/10/1500.long

150. Brewer DD, Hagan H. Evaluation of a patient referral contact tracing programme for hepatitis B and C virus infection in drug injectors. Euro Surveill [Online]. 2009 Apr 9 [Cited 2019 November 3];14(14):5-9. Available from: https://www.eurosurveillance.org/content/10.2807/ese.14.14.19170-en

151. Callaghan M, Ford N, Schneider H. A systematic review of task- shifting for HIV treatment and care in Africa. Hum Resour Health [Online]. 2010 Mar 31 [Cited 2018 August 30];8:8. Available from doi: 10.1186/1478-4491-8-8

152. Seidman G, Atun R. Does task shifting yield cost savings and improve efficiency for health systems? A systematic review of evidence from low-income and middle-income countries. Hum Resour Health [Online]. 2017 Apr 13 [Cited 2018 August 30];15(1):29.Available from doi: 10.1186/s12960-017-0200-9

153. World Health Organization. Task shifting: rational redistribution of tasks among health workforce teams:

global recommendations and guidelines. [Online] Geneva; 2008 [Cited 2018 August 30]. Available from: http://www.who.int/healthsystems/TTR-TaskShifting.pdf

154. Grebely J, Applegate TL, Cunningham P, Feld JJ. Hepatitis C point-of-care diagnostics: in search of a single visit diagnosis. Expert Rev Mol Diagn [Online]. 2017 Dec [Cited 2018 September 2];17(12):1109-1115. Available from doi: 10.1080/14737159.2017.1400385

155. Grebely J, Lamoury FMJ, Hajarizadeh B, et al; LiveRLife Study Group. Evaluation of the Xpert HCV Viral Load point-of-care assay from venepuncture-collected and finger-stick capillary whole-blood samples: a cohort study. Lancet Gastroenterol Hepatol [Online]. 2017 Jul [Cited 2019 February 14];2(7):514-520. Available from doi: 10.1016/S2468-1253(17)30075-4

156. Chevaliez S, Poiteau L, Rosa I, et al. Prospective assessment of rapid diagnostic tests for the detection of antibodies to hepatitis C virus, a tool for improving access to care. Clin Microbiol Infect [Online]. 2016 May [Cited 2019 February 14];22(5):459.e1-6. Available from doi: 10.1016/j.cmi.2016.01.009

157. Cosmaro ML, Oldrini M, Rancilio L, et al. Facilitated access procedures for HIV and HCV testing in vulnerable groups. Infect [Online]. 2011 March [Cited 2018 August 31];39:S33. Available from: https://www.researchgate.net/publication/295669250_Facilitated_access_procedures_for_HIV_and_HCV_testing_in_vulnerable_groups

158. Remy AJ, Bouchkira H, Wenger H, Montabone S. New tools of screening viral hepatitis in real life: New french model of care. United European Gastroenterology Journal 2015 [Cited 2018 November 27]; 2 (Supl 1). Available from: https://www.ueg.eu/education/document/news-tools-of-screening-viral-hepatitis-in-real-life-new-french-model-of-care/121614/

159. Kiana G, Shahi R, Alimohammadi A, Raycraft T, Singh A, Conway B. Community pop-up clinic: a harm reduction strategy to engage hepatitis C virus infected injection drug users. J Hepatol [Online]. 2017 [Cited 2018 August 31];66 (1) S489. Available from doi.org/10.1016/S0168-8278(17)31371-5

160. Morano JP, Zelenev A, Lombard A, MarcusR, Gibson BA, Altice FL. Strategies for hepatitis C testing and linkage to care for vulnerable populations: point-of-care and standard HCV testing in a mobile medical clinic. J Community Health [Online]. 2014 Oct [Cited 2018 September 1];39(5):922-34. Available from doi: 10.1007/s10900-014-9932-9

161. Bottero J, Boyd A, Gozlan J, et al. Simultaneous Human Immunodeficiency Virus-Hepatitis B-Hepatitis C Point-of-Care Tests Improve Outcomes in Linkage-to-Care: Results of a Randomized Control Trial in Persons Without Healthcare Coverage. Open Forum Infect Dis [Online]. 2015 Oct [Cited 2018 September 1];2(4):ofv162. Available from doi: 10.1093/ofid/ofv162

162. Beckwith CG, Kurth AE, Bazerman LB, et al. A pilot study of rapid hepatitis C virus testing in the Rhode Island Department of Corrections. J Public Health (Oxf) [Online]. 2016 Mar [Cited 2018 September 1];38(1):130-7. Available from doi: 10.1093/pubmed/fdv023

163. Fonjungo PN, Boeras DI, Zeh C, Alexander H, Parekh BS, Nkengasong JN. Access and Quality of HIV-Related Point-of-Care Diagnostic Testing in Global Health Programs. Clin Infect Dis [Online]. 2016 Feb 1 [Cited 2018 August 30];62(3):369-374. Available from: doi: 10.1093/cid/civ866

164. Peeling RW, Boeras DI, Marinucci F, Easterbrook P, et al. The future of viral hepatitis testing: innovations in testing technologies and approaches. BMC Infect Dis [Online]. 2017 Nov 1 [Cited 2018 September 2];17(Suppl 1):699. Available from doi: 10.1186/s12879-017-2775-0

165. Pallarés C, Carvalho-Gomes Â, Hontangas V, et al. Performance of the OraQuick Hepatitis C virus antibody test in oral fluid and fingerstick blood before and after treatment-induced viral clearance. J Clin Virol

[Online]. 2018 May [Cited 2018 September 1];102:77-83. Available from doi: 10.1016/j.jcv.2018.02.016

166. Grebely J, Lamoury FMJ, Hajarizadeh B, Mowat Y et al; LiveRLife Study Group. Evaluation of the Xpert HCV Viral Load point-of-care assay from venepuncture-collected and finger-stick capillary whole-blood samples: a cohort study. Lancet Gastroenterol Hepatol [Online]. 2017 Jul [Cited 2018 September 1];2(7):514-520. Available from doi: 10.1016/S2468-1253(17)30075-4

167. Adinolfi LE, Nevola R, Lus G, et al. Chronic hepatitis C virus infection and neurological and psychiatric disorders: an overview. World J Gasterol [Online]. 2015 Feb 28 [Cited 2018 November 11];21(8):2269-80. Available from doi: 10.3748/wjg.v21.i8.2269

168. Su J, Brook RA, Kleinman NL, Corey-Lisle P. The impact of hepatitis C virus infection on work absence, productivity, and healthcare benefit costs. Hepatology [Online]. 2010 Aug [Cited 2018 November 24];52(2):436-42. Available from doi: 10.1002/hep.23726

169. Grebely J, Dalgard O, Conway B, et al; SIMPLIFY Study Group. Sofosbuvir and velpatasvir for hepatitis C virus infection in people with recent injection drug use (SIMPLIFY): an open-label, single-arm, phase 4, multicentre trial. Lancet Gastroenterol Hepatol [Online]. 2018 Mar [Cited 2019 April 23];3(3):153-161. Available from doi: 10.1016/S2468-1253(17)30404-1

170. Janjua NZ, Darvishian M, Wong S, et al; British Columbia Hepatitis Testers Cohort Team. Effectiveness of Ledipasvir/Sofosbuvir and Sofosbuvir/Velpatasvir in People Who Inject Drugs and/or Those in Opioid Agonist Therapy. Hepatol Commun [Online]. 2019 Jan 10 [Cited 2019 April 23];3(4):478-492. Available from doi: 10.1002/hep4.1307

171. World Health Organization. Guidelines for the Care and Treatment of Persons Diagnosed with Chronic Hepatitis C Infection. [Online] Geneva; 2018 [Cited 2018 September 2]. Available from: http://apps.who.int/iris/bitstream/handle/10665/273174/9789241550345-eng.pdf?ua=1

172. CATIE. Let's get the news out about hepatitis C treatment: Access is up and cure rates are high. [Online] Undated [Cited 2018 October 2]. Available from: https://www.catie.ca/en/printpdf/news/hepc-treatment-access-cure-rates-high

173. Arora S, Thornton K, Murata G, et al. Outcomes of treatment for hepatitis C virus infection by primary care providers. N Engl J Med [Online]. 2011 Jun 9 [Cited 2018 December 11];364(23):2199-207. Available from: 10.1056/NEJMoa1009370

174. Cooper CL, Hatashita H, Corsi DJ, Parmar P, Corrin R, Garber g. Direct-Acting Antiviral Therapy Outcomes in Canadian Chronic Hepatitis C Telemedicine Patients. Ann Hepatol [Online]. 2017 November-December [Cited 2018 December 11];16(6):874-880. Available from doi: 10.5604/01.3001.0010.5277

175. Janjua NZ, Islam N, Wong J, et al. Shift in disparities in hepatitis C treatment from interferon to DAA era: A population-based cohort study. J Viral Hepat [Online]. 2017 Aug [Cited 2019 February 14];24(8):624-630. Available from doi: 10.1111/jvh.12684

176. Bartlett SR, Chapinel N, Rossi C, Butt Z, Wong S, Yu A, Darvishian M, Gilbert M, Wong J, Binka M, Alvarez M, Tyndall MW, Krajden M, Janjua NZ. The population level care cascade for hepatitis C in British Columbia, Canada as of 2017: Impact of Direct Acting Antivirals. Liver International; 2018. Under review.

177. The Kirby Institute. Monitoring hepatitis C treatment uptake in Australia. Issue 9 [Online]. July 2018 [Cited 2018 November 19]. Available at https://kirby.unsw.edu.au/report/monitoring-hepatitis-c-treatment-uptake-australia-issue-9-july-2018.

178. Kattakuzhy S, Gross C, Emmanuel B, et al. Expansion of Treatment for Hepatitis C Virus Infection by Task

Shifting to Community-Based Nonspecialist Providers: A Nonrandomized Clinical Trial. Ann Intern Med [Online]. 2017 Sep 5 [Cited 2018 October 5];167(5):311-318. Available from doi: 10.7326/M17-0118

179. Read P, Lothian R, Chronister K, et al. Delivering direct acting antiviral therapy for hepatitis C to highly marginalised and current drug injecting populations in a targeted primary health care setting. Int J Drug Policy [Online]. 2017 Sep [Cited 2018 October 4];47:209-215. Available from doi: 10.1016/j.drugpo.2017.05.032

180. Norton BL, Fleming J, Bachhuber MA, et al. High HCV cure rates for people who use drugs treated with direct acting antiviral therapy at an urban primary care clinic. Int J Drug Policy [Online]. 2017 Sep [Cited 2018 November 30];47:196-201. Available from doi: 10.1016/j.drugpo.2017.07.021

181. Butner JL, Gupta N, Fabian C, Henry S, Shi JM, Tetrault JM. Onsite treatment of HCV infection with direct acting antivirals within an opioid treatment program. Subst Abuse Treat [Online]. 2017 Apr [Cited 2018] November 29];75:49-53. Available from doi: 10.1016/j.jsat.2016.12.014

182. Neuhaus M, Langbecker D, Caffery LJ, et al. Telementoring for hepatitis C treatment in correctional facilities. J Telemed Telecare [Online]. 2018 Dec [Cited 2018 November 28];24(10):690-696. Available from doi: 10.1177/1357633X18795361

183. Maasoumy B, Vermehren J. Diagnostics in hepatitis C: The end of response-guided therapy? J Hepatol [Online]. 2016 Oct [Cited 2018 September 2];65(1 Suppl):S67-S81. Available from doi: 10.1016/j.jhep.2016.07.023

184. Young J, Rossi C, Gill J, et al; Canadian Co-infection Cohort Investigators. Risk Factors for Hepatitis C Virus Reinfection After Sustained Virologic Response in Patients Coinfected With HIV. Clin Infect Dis [Online]. 2017 [Cited 2018 November 30];May 1;64(9):1154-1162. Available from doi: 10.1093/cid/cix126

185. Rossi C, Butt ZA, Wong S, et al. Hepatitis C virus reinfection after successful treatment with direct-acting antiviral therapy in a large population-based cohort. J Hepatol [Online]. 2018 Nov [Cited 2019 February 14];69(5):1007-1014. Available from doi: 10.1016/j.jhep.2018.07.025