Recommendations on Hepatitis C Screening for Adults (2017)

Canadian Task Force on Preventive Health Care (CTFPHC)

Putting Prevention into Practice

Canadian Task Force on Preventive Health Care
Groupe d'étude canadien sur les soins de santé préventifs

Use of Slide Deck

- These slides are made **available publicly** following the guideline's release as an educational support to assist with the dissemination, uptake and implementation of the guidelines into primary care practice
- Some or all of the slides in this slide deck may be used in educational contexts

Hepatitis C Working Group

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Systematic Reviews Conducted by:

- PHAC
- Canadian Agency for Drugs and Technologies in Health (CADTH)

Modelling Study Conducted by:

- Toronto Health Economics and Technology Assessment Collaborative (Dr William Wong* et al)

Overview of Webinar

- **Presentation**
  - Background on Hepatitis C Screening
  - Methods of the CTFPHC
  - Key Findings
  - Recommendation
  - Implementation Considerations
  - Conclusions
- **Questions and Answers**

Screening for Hepatitis C

BACKGROUND

Background – Hepatitis C in Canada

0.64% - 0.71% of Canadians have chronic hepatitis C virus (**HCV**) infection

44% of those may **be undiagnosed**

Not all people with chronic HCV infection will **develop cirrhosis** or **signs indicative of liver disease**

Those at higher risk for HCV include individuals who:

- **Inject drugs**
- Have been **incarcerated**
- **Blood transfusion,** organ transplant prior to 1992, in Canada
- Have travelled or resided in **endemic regions**

Background & Purpose of Hepatitis C Screening Guideline 2017

- **PHAC** and the College of Family Physicians of Canada (**CFPC**) recommend testing for hepatitis C in people at increased risk for HCV

- There is **no organized general population screening** for adults who are not otherwise at increased risk for HCV

- **Reasons for developing** this recommendation include:
  - **New treatments** for chronic HCV infection
  - **Conflicting messages with U.S. guideline producers**

- Recommendations are intended to provide clinicians and policy-makers with guidance on screening asymptomatic Canadian adults for HCV

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METHODS

Methods of the CTFPHC

- Independent panel of
  - Clinicians and methodologists
  - Expertise in prevention, primary care, literature synthesis, and critical appraisal
  - Application of evidence to practice and policy
- Hepatitis C Working Group
  - 6 CTFPHC members
  - Establish research questions and analytical framework
  - Expertise in hepatitis C (clinical experts specific to this guideline)

CTFPHC Review Process

- **Internal review process** involving:
  - Guideline working group, CTFPHC, and PHAC scientific officers
- **External review is undertaken at key stages**:
  - Protocol, systematic review, and guideline
- **External stakeholder and peer reviewer groups:**
  - Generalist and disease specific stakeholders
  - Federal and P/T stakeholders
  - Academic peer reviewers
- **CMAJ undertakes an independent peer review process** to review guidelines prior to publication

What 'Evidence' Does The CTFPHC Consider?

Direct Evidence

- **Screening Review (by CADTH)**
  - Benefits and harms of screening
  - Cost-effectiveness
  - Patient preferences and values
  - Screening test clinical validity

Indirect Evidence

- **Treatment Review (by PHAC)**
  - Benefits and harms of treatment
- **Modelling Study (by Wong et al.)**
  - Long term benefits of screening

- **Patient focus groups**: patient preferences and values related to key outcomes
- **Stakeholder survey:** Feasibility, Acceptability, Cost, and Equity (FACE) tool

Eligibility Criteria: Screening Review

Population: Asymptomatic, non-pregnant, treatment-naive adults ≥ 18 years with unknown liver enzyme values *(Exclusions: Post-transplant patients, patients with HIV, hemodialysis patients, patients with occupational exposure)*

Languages: English and French

	KQ1: Clinical Effectiveness	KQ2: Harms	KQ3: Cost-effectiveness	KQ4: Patient Preferences	KQ5: DTA
Outcomes	*Long-term outcomes*: Mortality due to HCV infection, morbidity due to HCV infection, HCC, liver transplantation, or quality of life. *Intermediate outcomes*: HCV transmission, virologic response, behavioural changes to improve health outcomes, or histological changes.	Overdiagnosis, overtreatment, false positives, false negatives, harms of follow-up tests (including biopsy), abuse or violence, or anxiety.	Cost-effectiveness analysis outcomes (e.g., ICER, ICUR, CBR) or budget impact analysis outcomes.	Willingness to be screened and factors considered in decisions to be screened.	DTA outcomes (e.g., sensitivity, specificity, positive predictive value, negative predictive value, likelihood ratio, diagnostic odds ratio, or AUC), detection rate, number needed to screen to detect 1 case.
Study Designs	RCTs, nonrandomized studies with a comparator group, or disease progression modelling studies	RCTs, nonrandomized studies with or without a comparator group, or disease-progression modelling studies	RCTs, economic evaluations, and economic modelling studies	Descriptive studies (surveys, qualitative) and mixed-methods studies	Cross-sectional

Eligibility Criteria: Treatment Review

Population: Asymptomatic, non-pregnant, treatment-naive adults ≥ 18 years with unknown liver enzyme values *(Exclusions: Post-transplant patients, patients with HIV, hemodialysis patients, patients with occupational exposure)*
Languages: English and French
Study Designs: Randomized or non-randomized, controlled or uncontrolled, intervention studies

	KQ6: Comparative Clinical Benefit of Treatments	KQ7: Harms Associated with Treatment
Outcomes	*Long-term outcomes*: Mortality (hepatic & all cause), Cirrhosis, Hepatocellular carcinoma, Hepatic decompensation, Need for liver transplantation, Quality of life (all scales reported) *Intermediate outcomes:* Reduced HCV transmission, Sustained virological response, Improvement in liver histology.	Withdrawal due to adverse events, Psychological adverse events, Neutropenia, Flu-like symptoms, Anemia, rash

How Does the CTFPHC Grade Evidence?

The "**GRADE**" System:

- **G**rading of **R**ecommendations, **A**ssessment, **D**evelopment & **E**valuation

1. Quality of Evidence

- Confidence that the available evidence **correctly reflects the true effect**

High, Moderate, Low, Very Low

2. Strength of Recommendation

- Quality of **supporting evidence**
- **Desirable and undesirable effects**
- **Values and preferences**
- **Resource use**

Strong, Weak

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KEY FINDINGS

Key Findings: Screening

CADTH Systematic Review

- **No studies of the clinical effectiveness of HCV screening** in the general population or in any other higher risk or higher prevalence subgroup (e.g. birth cohort, born from 1950 to 1975)

Wong et al.'s modelling Study

One time screening of 100,000 individuals not at elevated risk of HCV (0.2% prevalence)

Prevent 20 cases of hepatocellular carcinoma over a lifetime horizon

40 lives saved over a lifetime horizon

Key Findings: Treatment

The **PHAC review** ***(indirect evidence)*** found***:***

- **Treatment** with **new DAA-based regimens** achieved **higher SVR rate** than traditional regimens (Pegylated interferon) and **reduced the frequency of harms**
  - *Moderate quality evidence*

- **No difference in quality of life** or **all cause mortality** at 36-72 weeks post-treatment
  - *Very low quality evidence*

Patient Values and Preferences

CADTH Review (12 observational studies):

Decision to be screened for HCV

- Patient preference findings were **highly variable**
- Important decision-making concerns:
  - **Stigma**
  - **Access to care**

CTFPHC-Commissioned Survey and Focus groups (15 patients):

Reinforced CADTH findings

- **Equal value** placed on **benefits** and **harms** of screening
- **Reduced mortality** was perceived as a very important benefit
- Concerns were noted about **stigma** and **psychological adverse events** from positive screening test results

Resource Use

- Estimated **costs** (**Canadian population**):

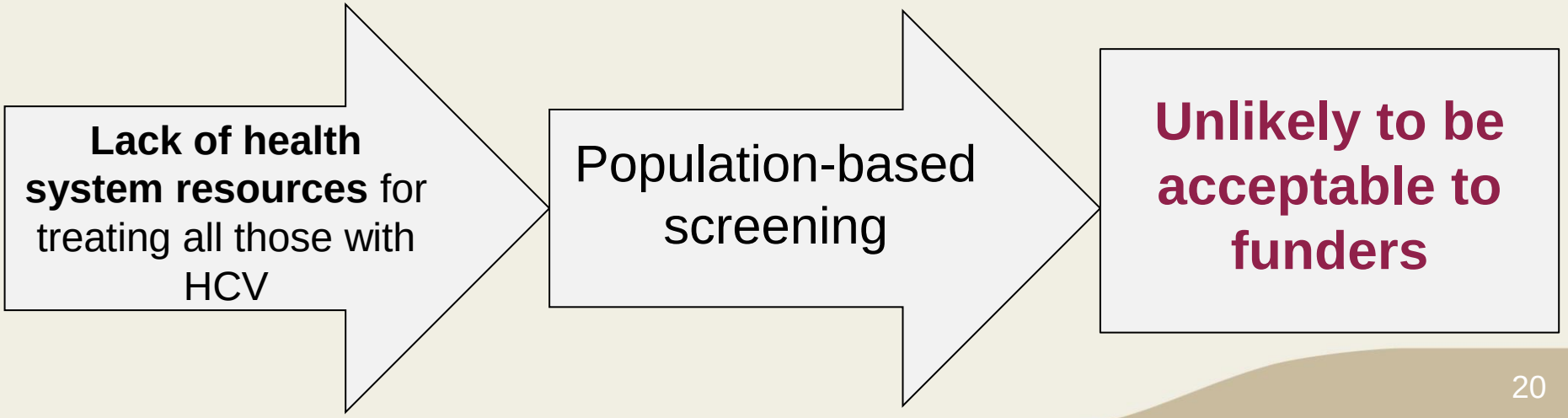
Over **$844 million for screening**

Approximately **$1.5 billion** to **screen and treat** with DAA-based regimens
(assuming 50% off drug list price)

- The CTFPHC places a relatively **higher value** on the**:**
  - **Very large impact that screening would have on healthcare budgets**
  - **Limit** on **funding** for health care **interventions supported by better evidence**

Feasibility, Acceptability and Equity

- Majority of individuals identified by screening would not qualify for treatment in Canada (asymptomatic, early stages of fibrosis, no comorbidities)
- A recommendation in favour of screening would **increase the number of people with known HCV who cannot access treatment**



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RECOMMENDATION

Hepatitis C 2017 Guideline: **Recommendation**

- For practitioners on preventive health screening in a primary care setting:

We recommend <u>against screening</u> for HCV in adults who are not at elevated risk

- ***Strong recommendation, very low quality evidence***

Overall Quality of Evidence

- **Overall quality of evidence** supporting this recommendation is **considered very low** (i.e. *highly uncertain*), given the:
  - Lack of direct evidence on screening for HCV in all groups of the population
  - Many assumptions required by the modelling study (several model parameters were based on expert opinion)

Rationale for Direction of Recommendation Against Screening

- ***Substantial uncertainty*** **remains about the effectiveness of screening** (benefits and harms) among adults **not at elevated risk** in Canada

CTFPHC Rationale

- This recommendation places a relatively lower value on:

1. Very low quality indirect evidence suggesting a potentially small benefit from screening

2. Low risk of household and sexual transmission of HCV among individuals not at elevated risk

3. Low risk of transmission through blood products given routine screening of blood and organs

4. Potential risk of developing end stage liver disease and transmitting the infection despite being asymptomatic

CTFPHC Rationale

- This recommendation places a relatively higher value on:

1. Anticipated increase in harm resulting from diagnosing and treating individuals who screen positive but would have never developed HCV related disease
2. False positives and false negatives
3. Very large impact that screening and treatment would have on health care budgets
4. Potential for screening to increase inequity
5. Unknown magnitude of benefit of treatment on reducing risk of transmission

Rationale for Strength of Recommendation Against Screening

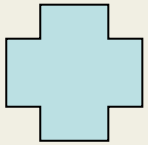
- We are **confident of the potential for harm** resulting from screening and treatment for HCV
  - Screening and treating people who would have never develop HCV related disease during their lifetime
  - Unnecessary anxiety, stigma

- We are **confident** that a recommendation to screen and treat those identified as HCV positive would **require substantial resources** to address **access to care and treatment restrictions**

Considerations for Re-Evaluating the CTFPHC 2017 Hep C Screening Guideline

- **Emergence** of new **evidence** to **support screening** the **general population**
  - Examining **long term consequences and** rates of **transmission**
- **Improved access to care** and **treatment** due to:

Significant reduction in drug prices, enabling treatment for *all* individuals with HCV



Successful roll out of a health-system wide treatment strategy

NOTE: Newer drugs will not trigger an update – high rates of SVR already assumed resulting from DAA treatment.

CTFPHC Guideline vs. Other Recommendations

- Recommendation **aligns with** guidelines from:

World Health Organization

NICE
National Institute for Health and Care Excellence

SIGN

Immigration, Refugees and Citizenship Canada
Immigration, Réfugiés et Citoyenneté Canada

NSC UK National Screening Committee

GESA Gastroenterological Society of Australia

- Recommendation **partly aligns with** guidelines from:

CDC
Centers for Disease Control and Prevention

U.S. Preventive Services Task Force

  - ***Birth cohort screening recommendation based on indirect evidence***
  - US 'baby boomers' have ***4 times higher prevalence*** (3.25%) than Canada (0.8%)

Knowledge Gaps

- High quality, population-based prevalence data on chronic hepatitis C in Canada among the general population and in key sub-groups
- Trial data on the benefits and harms of screening in asymptomatic populations.
- Trial data on the benefits of earlier vs. later treatment (F0-F1 treatment vs. F2, F3 or F4)
- Evidence on the progression of chronic HCV to cirrhosis and to end-stage liver disease
- Evidence on the progression of disease despite SVR

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IMPLEMENTATION CONSIDERATIONS

Implementation Considerations

- More persons are diagnosed with chronic HCV in sub-groups such as the:

Indigenous populations (3% prevalence)

Cohort born from 1950 to 1975 (0.8% prevalence)

- **These populations have a higher proportion of individuals at higher risk** for HCV **due to risk behaviours**

If we account for subgroups of individuals at elevated risk due to risk behaviours

Prevalence in these groups **would be similar to the lower risk population**

Implementation Considerations

- Joint CFPC-PHAC guideline suggests HCV testing:

> "Anyone with **risk behaviours** for HCV, with **potential exposure** to HCV, and/or with **clinical clues** suspicious for HCV"

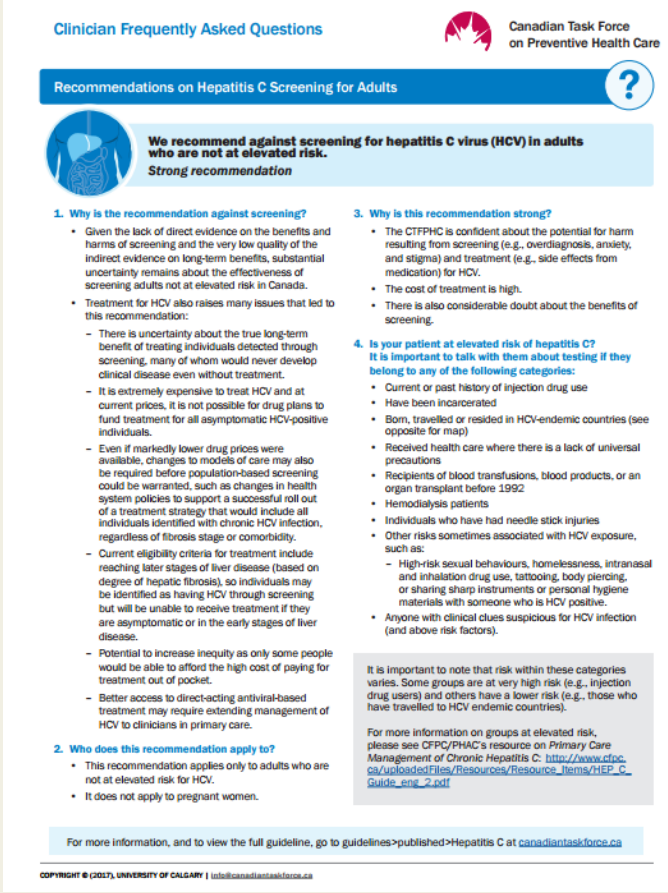
CTFPHC supports this recommendation

- Some immigrants are at increased risk for HCV due to a lack of standard precautions in their country of origin
  - E.g. medical or dental procedures with contaminated equipment
  - Not due to injection drug use or other higher risk behaviours

Knowledge Translation (KT) Tools

- A KT tool is being developed to **help clinicians understand and implement** the hepatitis C screening guideline

- After the public release, this tool will be **freely available** for download in both **French** and **English** on the website: http://canadiantaskforce.ca



Clinician Frequently Asked Questions

Canadian Task Force on Preventive Health Care

Recommendations on Hepatitis C Screening for Adults

We recommend against screening for hepatitis C virus (HCV) in adults who are not at elevated risk.
Strong recommendation

1. Why is the recommendation against screening?

- Given the lack of direct evidence on the benefits and harms of screening and the very low quality of the indirect evidence on long-term benefits, substantial uncertainty remains about the effectiveness of screening adults not at elevated risk in Canada.
- Treatment for HCV also raises many issues that led to this recommendation:
  - There is uncertainty about the true long-term benefit of treating individuals detected through screening, many of whom would never develop clinical disease even without treatment.
  - It is extremely expensive to treat HCV and at current prices, it is not possible for drug plans to fund treatment for all asymptomatic HCV-positive individuals.
  - Even if markedly lower drug prices were available, changes to models of care may also be required before population-based screening could be warranted, such as changes in health system policies to support a successful roll out of a treatment strategy that would include all individuals identified with chronic HCV infection, regardless of fibrosis stage or comorbidity.
  - Current eligibility criteria for treatment include reaching later stages of liver disease (based on degree of hepatic fibrosis), so individuals may be identified as having HCV through screening but will be unable to receive treatment if they are asymptomatic or in the early stages of liver disease.
  - Potential to increase inequity as only some people would be able to afford the high cost of paying for treatment out of pocket.
  - Better access to direct-acting antiviral-based treatment may require extending management of HCV to clinicians in primary care.

2. Who does this recommendation apply to?

- This recommendation applies only to adults who are not at elevated risk for HCV.
- It does not apply to pregnant women.

3. Why is this recommendation strong?

- The CTFPHC is confident about the potential for harm resulting from screening (e.g., overdiagnosis, anxiety, and stigma) and treatment (e.g., side effects from medication) for HCV.
- The cost of treatment is high.
- There is also considerable doubt about the benefits of screening.

4. Is your patient at elevated risk of hepatitis C?
It is important to talk with them about testing if they belong to any of the following categories:

- Current or past history of injection drug use
- Have been incarcerated
- Born, travelled or resided in HCV-endemic countries (see opposite for map)
- Received health care where there is a lack of universal precautions
- Recipients of blood transfusions, blood products, or an organ transplant before 1992
- Hemodialysis patients
- Individuals who have had needle stick injuries
- Other risks sometimes associated with HCV exposure, such as:
  - High-risk sexual behaviours, homelessness, intranasal and inhalation drug use, tattooing, body piercing, or sharing sharp instruments or personal hygiene materials with someone who is HCV positive.
- Anyone with clinical clues suspicious for HCV infection (and above risk factors).

It is important to note that risk within these categories varies. Some groups are at very high risk (e.g., injection drug users) and others have a lower risk (e.g., those who have travelled to HCV endemic countries).

For more information on groups at elevated risk, please see CFPC/PHAC's resource on *Primary Care Management of Chronic Hepatitis C*: http://www.cfpc.ca/uploadedFiles/Resources/Resource_Items/HEP_C_Guide_eng_2.pdf

For more information, and to view the full guideline, go to guidelines>published>Hepatitis C at canadiantaskforce.ca

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CONCLUSIONS

Conclusions

- The CTFPHC recommends against screening adults not at elevated risk for HCV
  - In Canada, the prevalence of HCV is less than 1%
  - Direct evidence of the benefits and harms of screening for HCV is not available
- Not screening for HCV will focus our limited health care resources to test (and treat) individuals at elevated risk for HCV and to provide other medical interventions that are proven to be of benefit

More Information

For more information on the details of this guideline please see:

- Canadian Task Force for Preventive Health Care website: http://canadiantaskforce.ca

Questions & Answers

Thank you