Recommendations on Hepatitis C Screening for Adults (2017)

Canadian Task Force on Preventive Health Care (CTFPHC)
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)

*non-voting member
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

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<thead>
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<tbody>
<tr>
<td><strong>Outcomes</strong></td>
<td>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.</td>
<td>Overdiagnosis, overtreatment, false positives, false negatives, harms of follow-up tests (including biopsy), abuse or violence, or anxiety.</td>
<td>Cost-effectiveness analysis outcomes (e.g., ICER, ICUR, CBR) or budget impact analysis outcomes.</td>
<td>Willingness to be screened and factors considered in decisions to be screened.</td>
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| 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

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>KQ6: Comparative Clinical Benefit of Treatments</th>
<th>KQ7: Harms Associated with Treatment</th>
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<td><em>Long-term outcomes:</em></td>
<td>Mortality (hepatic &amp; all cause), Cirrhosis, Hepatocellular carcinoma, Hepatic decompensation, Need for liver transplantation, Quality of life (all scales reported)</td>
<td>Withdrawal due to adverse events, Psychological adverse events, Neutropenia, Flu-like symptoms, Anemia, rash</td>
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<td><em>Intermediate outcomes:</em></td>
<td>Reduced HCV transmission, Sustained virological response, Improvement in liver histology.</td>
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How Does the CTFPHC Grade Evidence?

The “GRADE” System:
• Grading of Recommendations, Assessment, Development & Evaluation

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

Lack of health system resources for treating all those with HCV

Population-based screening

Unlikely to be acceptable to funders
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RECOMMENDATION
For practitioners on preventive health screening in a primary care setting:

We recommend **against** screening 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:
  
  ![Logos of NICE, SIGN, NSC, GESA]

• Recommendation **partly aligns with** guidelines from:
  
  ![Logos of CDC, US 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:

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<th>Indigenous populations (3% prevalence)</th>
<th>Cohort born from 1950 to 1975 (0.8% prevalence)</th>
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- **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
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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