Model-based Projection of Health and Economic Effects of Screening Hepatitis C: Informing on Screening Recommendations in Canada

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2016

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Overview

- Background
- Methods
- Decision Model
- Results
- Discussion and Conclusion
Background
Recent development of direct-acting antiviral agents (DAAs) has transformed hepatitis C virus (HCV) treatment, offering high cure rates with markedly improved tolerability.

While cost-effective, the high cost of DAAs seriously restrict treatment access. Since majority of infections are asymptomatic, hepatitis C screening remains to be a plausible strategy.

To assist the Canadian Task Force on Preventive Health Care in making screening recommendations, the objectives of this study is to examine the health and economics consequences of selective one-time hepatitis C screening programs under the current treatment patterns based on our published models.
Why decision models?

- Clinical trials may not be possible
- Mathematical simulation tools are often used in policy decision making
- Models provide a platform on which to integrate best evidence of effectiveness, safety, cost, and patient and public preferences that support rational decision making.
- For analyzing:
  - the potential impact of public health policies
  - obtaining information on the expected improvement in health with a given expenditure of resources
- Decision makers increasingly use such models to inform and interpret their decisions for adoption and reimbursement of new drugs, procedures, or programs of care
- Examples:
  - Agency for Healthcare Research (AHRQ)
    - MEDSIM, KIDSIM, and PUBSIM Models
  - Statistics Canada - Population health model (POHEM)
Decision models concept

- Efficacy data
- Safety data
- Cost data
- Demographic and Epidemiological data
- Patient and public preferences
- Resources constraints

Blackbox of decision models

Projected Outputs

Answer to the “what-if” type policy questions

Provide a platform to integrate the best evidence of effectiveness, safety, cost, and patient and public preferences
METHODS
Methods

- Cost-utility analysis, state transition model
- **Primary outcomes**: Cost, Quality adjusted life years (QALYs), Life Years (LY) with each strategy, incremental cost-effectiveness ratio (ICER)
- **Secondary outcomes**: population health outcomes (e.g. number of DC/HCC and liver death)
- **Target population**: Varied by scenarios
- **Perspective**: provincial Ministry of Health in Canada
- **Time Horizon**: Life-time, weekly cycle length.
- **Discount rate**: 5%
<table>
<thead>
<tr>
<th>Scenario</th>
<th>Definition* (as provided by PHAC)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Average-risk (i.e. adult general population)</td>
<td>Canadian-born, non-Aboriginal persons aged 14-79 who do not use injection drugs</td>
</tr>
<tr>
<td>2 Immigrant populations with high prevalence</td>
<td>Immigrants and refugees originating from intermediate and high HCV endemic countries, living in low HCV prevalence countries, such as Canada</td>
</tr>
<tr>
<td>3 Specific birth cohort (25 to 64 years of age)</td>
<td>Canadian Adults aged 25-64 in the general household population</td>
</tr>
<tr>
<td>4 Specific birth cohort (45-64 years of age)</td>
<td>Canadian adults aged 45-64 in the general household population</td>
</tr>
</tbody>
</table>
Strategies

(1) “No Screening, treat with DAA” if diagnosed
(2) “Screen and Treat with DAA”

• *“Case finding” strategy: Individuals are offered one-time screening for HCV infection through their primary care physician at a visit scheduled for another purpose.
  • Screening involves a blood test for HCV antibody.
  • All positive antibody tests will be followed by an HCV RNA test to confirm infection.
Screening Model

Start of simulation

HCV -

From all states

CHC-unrelated Death

Undiagnosed CHC

F0

F1

F2

F3

F4

diagnosed CHC

On treatment

F0

F1

F2

F3

F4

Advanced liver disease

Responding

F0-F3 SVR

Non-responding

F0

F1

F2

F3

F4

SVR

F4
Advanced liver disease

- From all F4 states
  - Decompensation
  - HCC
    - liver-transplant
    - post-transplant
  
- CHC-related Death
  - From all states

- CHC-unrelated Death
## Key Data inputs

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prevalence</td>
<td>Provided by PHAC / CTFPHC (S1: 0.2%; S2: 1.9%; S3 0.4%-0.8%; S4: 0.8%)</td>
</tr>
<tr>
<td>Screening uptake</td>
<td>Provided by PHAC / CTFPHC</td>
</tr>
<tr>
<td>Treatment uptake</td>
<td>Provided by PHAC / CTFPHC</td>
</tr>
<tr>
<td>Fibrosis distribution</td>
<td>Provided by PHAC / CTFPHC</td>
</tr>
<tr>
<td>Fibrosis progression</td>
<td>Thein et al 2008 (meta-analysis)</td>
</tr>
<tr>
<td>Cirrhosis progression</td>
<td>van der Meer AJ et al. JAMA. 2012 (included Canadian patients)</td>
</tr>
<tr>
<td>Efficacy and safety</td>
<td>CADTH Therapeutic review (Wong et al. 2017)</td>
</tr>
<tr>
<td>All-cause treatment discontinuation</td>
<td>CADTH Therapeutic review (Wong et al. 2017)</td>
</tr>
<tr>
<td>Mortality</td>
<td>based on cancer registries and systematic review</td>
</tr>
<tr>
<td>Chronic Hepatitis C and liver-transplant related costs</td>
<td>Canadian costing studies (Krajden et al. 2010, Taylor et al. 2002)</td>
</tr>
<tr>
<td>Therapy Cost</td>
<td>CADTH CDR/Therapeutic review</td>
</tr>
<tr>
<td>Utilities</td>
<td>Canadian Study (Hsu et al. 2012)</td>
</tr>
</tbody>
</table>
Key Assumptions

- Treatment restriction for F0 and F1 CHC patients
- HCC and decompensated cirrhosis were assumed to occur only at F4
- One-time treatment was assumed
- Model assumed no other pre-existing conditions; e.g., HIV
- Model assumed no spontaneous remission
- Patients who discontinued treatment were assumed not to have achieved SVR
RESULTS
Health outcomes: Liver Death

Health events per 100,000 screened

- **S1**: Adult general population
- **S2**: Immigrant population with high prevalence
- **S3**: Birth cohort (25 – 64 years of age)
- **S4**: Birth cohort (45 – 64 years of age)
### CEA results

<table>
<thead>
<tr>
<th></th>
<th>Scenario 1</th>
<th>Scenario 2</th>
<th>Scenario 3</th>
<th>Scenario 4</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Incremental cost (per person)</strong></td>
<td>$102-$108</td>
<td>$619-$681</td>
<td>$261-$284</td>
<td>$304-$328</td>
</tr>
<tr>
<td><strong>Incremental QALY (per person)</strong></td>
<td>0.0020</td>
<td>0.0197</td>
<td>0.0080</td>
<td>0.0088</td>
</tr>
<tr>
<td><strong>ICER (compare with no screening)</strong></td>
<td>$50,490-$53,938</td>
<td>$31,468-$34,600</td>
<td>$32,712-$35,619</td>
<td>$34,614-$37,167</td>
</tr>
<tr>
<td><strong>Probabilistic sensitivity analysis</strong></td>
<td>% of cost-effectiveness (WTP:$50,000)</td>
<td>39.5%</td>
<td>63.2%</td>
<td>58.4%</td>
</tr>
</tbody>
</table>

**Scenario 1:** Adult general population  
**Scenario 2:** Immigrant population with high prevalence  
**Scenario 3:** birth cohort (25 – 64 years of age)  
**Scenario 4:** birth cohort (45 – 64 years of age)
CEA results by Age Range

ICER of screen and treat with DAA by screening age groups

<table>
<thead>
<tr>
<th>Age range</th>
<th>Scenario 1</th>
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<th>Scenario 4</th>
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</thead>
<tbody>
<tr>
<td>15-24</td>
<td>$49,940</td>
<td>$29,360</td>
<td>$40,590</td>
<td>$33,444</td>
</tr>
<tr>
<td>25-34</td>
<td>$54,617</td>
<td>$33,398</td>
<td>$30,202</td>
<td>$36,114</td>
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<tr>
<td>35-44</td>
<td>$40,162</td>
<td>$25,174</td>
<td>$30,836</td>
<td></td>
</tr>
<tr>
<td>45-54</td>
<td>$45,291</td>
<td>$28,732</td>
<td>$32,674</td>
<td></td>
</tr>
<tr>
<td>55-64</td>
<td>$51,965</td>
<td>$32,674</td>
<td>$34,252</td>
<td></td>
</tr>
<tr>
<td>65-74</td>
<td>$76,100</td>
<td>$52,935</td>
<td></td>
<td></td>
</tr>
<tr>
<td>75-79</td>
<td>$154,750</td>
<td>$111,307</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Scenario 1: Adult general population
Scenario 2: Immigrant population with high prevalence
Scenario 3: birth cohort (25 – 64 years of age)
Scenario 4: birth cohort (45 – 64 years of age)
One way sensitivity analysis

Tornado Diagram: Screen and treat VS. no screening (Scenario 1)

- Prevalence
- CHC related Utilities
- Discount rate
- Cohort Fibrosis distribution
- Known to be CHC infected
- Advanced LD incidence in SVR cohort
- Therapy Efficiency
- Treatment uptake
- Cost of therapy
- Cost of screening
- F0/F1 Treatment Restriction
- Cost of CHC non-therapy
- Screening Uptake
- SVR Progression Assumption

ICER ($/QALY)

35000 40000 45000 50000 55000 60000 65000 70000 75000 80000
DISCUSSION & Conclusion
Limitations

• Model did not consider infectious disease dynamics
• We did not consider negotiated drug prices
• We did not consider every possible screening strategy. For example, we have not investigated the economic benefit of screening other high-risk groups such as emergency room or hospitalized populations, skin piercing practitioners, and low-income groups
• The CHC-related costs used was not fibrosis-specific, it may over estimate the cost of mild/no fibrosis and underestimate the cost of severe fibrosis
• The utilities of CHC patients who have late stage liver disease used by the model have a very small sample size, and may not cover the full spectrum of the severity of the disease
2016 Conclusion

- Our model suggests that some form of one-time hepatitis C screening and treatment program may be cost-effective for Canada.
- The screening strategies that are most likely to be cost-effective are those focusing on: immigrant populations with high prevalence (Scenario 2); a birth cohort aged 25 to 64 years (Scenario 3); and a birth cohort aged 45-64 years (Scenario 4).
- Canadian Task Force on Preventive Health Care Recommendation will be published soon.
What’s new in 2017?

• New treatments are available
• pan-Canadian Pharmaceutical Alliance (pCPA) has concluded successful negotiations with three drug manufacturers to help jurisdictions expand access to publicly funded medications for the treatment of chronic hepatitis C
  • No restriction is coming
  • New lower price
• CADTH has updated the “Guidelines for the Economic Evaluation of Health Technologies”
  • Discount rate updated to 1.5%
## 2017 Results Summary*

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<tr>
<td><strong>Incremental cost (per person)</strong></td>
<td>$120-$128</td>
<td>$763-$847</td>
<td>$317-$346</td>
<td>$359-$388</td>
</tr>
<tr>
<td><strong>Incremental QALY (per person)</strong></td>
<td>0.0052</td>
<td>0.0482</td>
<td>0.0178</td>
<td>0.0173</td>
</tr>
<tr>
<td><strong>ICER (compare with no screening)</strong></td>
<td>$23,123-$24,736</td>
<td>$15,821-$17,579</td>
<td>$17,780-$19,418</td>
<td>$20,754-$22,424</td>
</tr>
<tr>
<td><strong>2017 PSA Results</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>% of cost-effectiveness (WTP:$50,000)</td>
<td>63.3%</td>
<td>71.7%</td>
<td>74.2%</td>
<td>72.2%</td>
</tr>
<tr>
<td><strong>2016 PSA Results</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>% of cost-effectiveness (WTP:$50,000)</td>
<td>39.5%</td>
<td>63.2%</td>
<td>58.4%</td>
<td>58.1%</td>
</tr>
</tbody>
</table>

*Updated: Discount rate = 1.5%; no treatment restriction for F0 and F1 CHC
Scenario 1: Adult general population
Scenario 2: Immigrant population with high prevalence
Scenario 3: birth cohort (25 – 64 years of age)
Scenario 4: birth cohort (45 – 64 years of age)
Conclusion

• The screening strategies are most likely to be cost-effective for all scenarios.
• Early recognition and linkage of infected individuals to care, treatment can save and prolong the lives of CHC-infected patients
• Beside cost-effectiveness, screening program will also need to consider the aggregate health gains and budget impact of screening strategies, as well as the effects of screening on stigma, and health equity
What’s next?

• More evidences are needed in order to update the recommendation

• THETA / UW Hep C related Projects
  • Understanding the treatment benefits of novel antiviral agents for hepatitis C: quality of life, health utility, cost, and return to work
    • Funded by CIHR
  • Using economic modeling to estimate hepatitis C provincial and national drug plan expenditures in the next decade
    • Partnership with Canadian Liver Foundation

• Lots of other researches going on within the CanHepC network

• Stay tuned …