Integrating 2017 model-based estimates of hepatitis C virus (HCV) prevalence into the evaluation of HCV screening cost effectiveness

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The Team

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Overview

- Background
  - Why Modelling?
- Methods
  - Back-calculation Model
  - Cost-Effectiveness Model
- Results
- Discussion and Conclusion
Background
Hepatitis C: Natural History

- Around 75% progressing to chronicity
  - (Chronic hepatitis C (CHC))

- 10-20% of whom will silently progress to cirrhosis
  - at risk of dying prematurely of liver failure and/or liver cancer

- A recent disease burden study from Ontario ranked hepatitis C first among all infectious diseases
  - Managing CHC is difficult because it is often asymptomatic
  - Disease is often discovered when symptoms of late stage liver disease have become apparent and the prognosis is poor

- Complications may be reduced by offering treatment in a timely manner

Kwong et. al. (2012)
Treatment Access

- In 2015, access to treatment was restricted to severe patients only
- Since then, we have great improvement in terms of treatment access

<table>
<thead>
<tr>
<th>Program</th>
<th>Fibrosis restrictions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ontario</td>
<td>All restrictions removed by the end of 2018.</td>
</tr>
<tr>
<td>British Columbia</td>
<td>All restrictions removed by the end of 2018.</td>
</tr>
<tr>
<td>Newfoundland &amp; Labrador</td>
<td>F2</td>
</tr>
<tr>
<td>New Brunswick</td>
<td>F2</td>
</tr>
<tr>
<td>Nova Scotia</td>
<td>F2</td>
</tr>
<tr>
<td>Price Edward Island</td>
<td>No restrictions$^2$</td>
</tr>
<tr>
<td>Manitoba</td>
<td>F2</td>
</tr>
<tr>
<td>Alberta</td>
<td>F2</td>
</tr>
<tr>
<td>Quebec</td>
<td>All restrictions removed by the end of 2018.</td>
</tr>
<tr>
<td>Saskatchewan</td>
<td>F2</td>
</tr>
<tr>
<td>Nunavut</td>
<td>F2</td>
</tr>
<tr>
<td>Northwest territories</td>
<td>F2</td>
</tr>
<tr>
<td>Yukon</td>
<td>F2</td>
</tr>
</tbody>
</table>

Table refers to: Simeprevir, sofosbuvir, ledipasvir-sofosbuvir, partitaprevir-ritonavir-ombitasvir
Source: Marshall et al. (2016) with updates from Canadian Action treatment Council
HCV Screening

• Screening remains controversial in Canada
  • Currently screening is primarily done in primary care on individuals who present with an elevated risk and for those with chronic liver disease (though this is ‘case finding,’ not screening).
  • The most recent 2016 guidance from the Canadian Liver Foundation advocates birth cohort screening.
  • In April 2017 the Canadian Taskforce on Preventive Health Care issued the following screening recommendation:
    • ‘We recommend against screening for HCV in adults who are not at elevated risk.’
Why decision models?

- 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
Why HCV Modeling?

• “In the area of hepatitis C virus screening, where benefits occur decades into the future, modelling is the only practical option we have for fully incorporating all health and cost outcomes”

  Haines, Wong, Krahn (2017) CMAJ

• Works on HCV Modeling
  • CEA on treatment
    • CADTH Therapeutic review 2014, 2016
  • CEA on screening
    • PHAC 2014
    • CTFPHC 2016
What we have learned so far?

CEA: 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)

Wong et al (2017) CMAJ Open
What we have learned so far?

BIA: Sensitivity analysis

Budget-Impact between screening and not screening over time per 100,000 people for each sensitivity analysis

Prevalence Data

• Notifiable disease database
  • Canadian Notifiable Disease Surveillance System (CNDSS)

• Seroprevalence survey
  • Stat Can (Rotermann et al 2013: ~0.5%, undiagnosed: ~70% )
  • PHO (Bolotin et al 2018: ~1.6% – 1.8%)

• Modeling studies
  • PHAC (Remis et al 2007: ~0.78%, undiagnosed: ~20%)
  • PHAC (Trubnikov et al 2014: ~0.64%-0.71%, undiagnosed: 44%)
Objectives

1. Estimate the prevalence and the undiagnosed population
2. Re-estimate the cost-effectiveness of birth-cohort (baby-boomer) screening
3. Estimate the budget impact
METHODS
Step 1: Estimate the Prevalence: Problem Setup

- What we know about:
  - Diagnosis numbers: CNDSS; HCV-HCC
  - Treatment efficacy

- What we kind of know about:
  - CHC Natural history
  - Treatment rate

- What we want to find out:
  - Prevalence, undiagnosed proportion

- What we have:
  - Validated model used by PHAC, CADTH, CTFPHC
Advanced liver disease

From all F4 states

- Decompensation
- HCC

liver-transplant

post-transplant

CHC-related Death

From all states

CHC-unrelated Death
Back-Calculation Model

- Based on Bayesian methods (Markov chain Monte Carlo (MCMC))
- Use the observed occurrence of current HCV-related events to make inference about the HCV-incipience in the past that lead to them
Idea

Inputs: Guesses of unknown/uncertain parameters (e.g. hcv-incidence, hcv-prevalence, undiagnosed proportion)

Outputs: Estimates of HCC diagnosis numbers.

Systematically setup the guesses
Key Calibration Data

- HCC Data

- CNDSS
Step 2: CEA

- Cost-utility analysis, state transition model
- **Primary outcomes**: Cost, Quality adjusted life years (QALYs), with each strategy, incremental cost-effectiveness ratio (ICER)
- **Target population**: birth cohort (45-64 years of age)
- **Perspective**: provincial Ministry of Health in Canada
- **Time Horizon**: Life-time, weekly cycle length.
- **Discount rate**: 1.5%

Wong et al (2017) CMAJ Open
Step 2: 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.

Wong et al (2017) CMAJ Open
Key Assumptions

- No 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

Wong et al (2017) CMAJ Open
Step 3: BIA

- Budget Impact analysis, state transition model
- **Primary outcomes**: Budget impacted between no screening and screening
- **Target population**: Ontario birth cohort (1945-1964)
- **Perspective**: provincial Ministry of Health in Canada
- **Time Horizon**: up to 2030 (WHO target)
- **Discount rate**: 1.5%

RESULTS
Prevalence Estimate

Inputs: Guesses of unknown/uncertain parameters (e.g. hcv-incidence, hcv-prevalence, undiagnosed proportion)
Outputs: Estimates of HCC diagnosis numbers.

Systematically setup the guesses
1.30% (95% CI: 1.19% - 1.43%)

30.4% (95% CI: 27.2% - 33.3%)
## CEA results

<table>
<thead>
<tr>
<th></th>
<th>2016*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prevalence Used</td>
<td>0.8% (Stat Can)</td>
</tr>
<tr>
<td>Proportion of unaware</td>
<td>69.5% (Stat Can)</td>
</tr>
<tr>
<td>Per person cost increased</td>
<td>$304-$328</td>
</tr>
<tr>
<td>Per person QALY gained</td>
<td>0.0088</td>
</tr>
<tr>
<td>ICER (compare with no screening)</td>
<td>$34,614-$37,167</td>
</tr>
<tr>
<td>Probabilistic sensitivity analysis</td>
<td>58.1%</td>
</tr>
</tbody>
</table>

*2016: CTFHPC report (Wong et al 2017 CMAJ Open)

^2017: updated discount rate, and treatment restriction (Wong 2017 CADTH Sym))

^^2018: updated prevalence and undiagnosed population
### BIA results Snapshot

<table>
<thead>
<tr>
<th>Year</th>
<th>Budget-Impact for Ontario (C$ millions)*</th>
<th>New Budget-Impact for Ontario (C$ millions)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2018</td>
<td>$260.02</td>
<td>$202.22</td>
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<tr>
<td>2019</td>
<td>$423.58</td>
<td>$307.36</td>
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<tr>
<td>2020</td>
<td>$491.13</td>
<td>$356.61</td>
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<tr>
<td>2021</td>
<td>$551.14</td>
<td>$399.41</td>
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<tr>
<td>2022</td>
<td>$603.94</td>
<td>$437.76</td>
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<tr>
<td>2023</td>
<td>$654.75</td>
<td>$474.86</td>
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<tr>
<td>2024</td>
<td>$703.88</td>
<td>$510.99</td>
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<td>2024</td>
<td>$751.78</td>
<td>$546.56</td>
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<tr>
<td>2025</td>
<td>$799.26</td>
<td>$582.37</td>
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<tr>
<td>2026</td>
<td>$848.14</td>
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<td>2027</td>
<td>$858.00</td>
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<td>2028</td>
<td>$853.38</td>
<td>$621.75</td>
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<tr>
<td>2029</td>
<td>$849.03</td>
<td>$618.68</td>
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<tr>
<td>2030</td>
<td>$845.22</td>
<td>$615.99</td>
</tr>
</tbody>
</table>

Budget-Impact between screening and not screening over time per 100,000 people for each sensitivity analysis

DISCUSSION & Conclusion
Limitations

• Back-calculation Model
  • Model did not consider infectious disease dynamics
  • Based on only on limited HCC data

• CEA and BIA
  • 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
Conclusion

- Prevalence and undiagnosed estimates have a big impact on CEA and BIA
- The screening strategies are likely to be cost-effective for baby-boomer cohort.
- Early recognition and linkage of infected individuals to care, treatment can save and prolong the lives of CHC-infected patients
- Is it affordable? (616 million)
- Beside cost-effectiveness and budget impact, screening program will also need to consider the effects of screening on stigma, and health equity
Time is ticking

ICER of screen and treat with DAA by screening age groups

<table>
<thead>
<tr>
<th>Age range</th>
<th>Scenario 1</th>
<th>Scenario 2</th>
<th>Scenario 3</th>
<th>Scenario 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>15-24</td>
<td>$49,940</td>
<td>$29,360</td>
<td>$40,590</td>
<td>$33,444</td>
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<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>$33,444</td>
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<tr>
<td>45-54</td>
<td>$45,291</td>
<td>$28,732</td>
<td>$34,252</td>
<td>$36,114</td>
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<td>55-64</td>
<td>$51,965</td>
<td>$32,674</td>
<td>$40,000</td>
<td>$40,000</td>
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<tr>
<td>65-74</td>
<td>$76,100</td>
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<td>$60,000</td>
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<tr>
<td>75-79</td>
<td>$154,750</td>
<td>$111,307</td>
<td>$80,000</td>
<td>$80,000</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)
What’s next?

• More evidences are needed in order to update the recommendation
• Incorporating administrative data to further refine the prevalence and undiagnosed estimates
• Stay tuned …