Estimation of hepatitis C prevalence in Canada

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DISCLOSURE

This study was funded by the Canadian Liver Foundation
**AIM OF STUDY**

We wish to:  
Estimate prevalence of hepatitis C and size of undiagnosed population in Canada

...using:  
a recent hepatitis C natural history model

...and publicly available data for calibration:  
hepatitis C diagnosis data,  
liver cancer diagnosis data.

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**REASONS FOR STUDY**

**Economic reasons:** How much should we expect to spend treating the infected population?

**More importantly:** How much to invest in seeking out undiagnosed individuals, preventing advanced liver diseases.

**Concrete goal:** What and how much needs to be done to meet WHO 2030 elimination target?
OVERVIEW

- Previous work
- Review of natural history model
- Sources of uncertainty in model
- Model calibration approach
- Estimation results

Previous hepatitis C prevalence estimates for Canada
Study from 2014 refined model to include stages of liver fibrosis.

CHC Prevalence, 2011: 0.64-0.71%
Undiagnosed CHC, 2011: 44%

CHC Prevalence, 2007: 0.78%
Undiagnosed CHC, 2007: 20%

Why another study of hepatitis C prevalence?

- More recent data available
- Newer hepatitis C natural history model available
  - explicitly models treatment and SVR
- Bayesian MCMC calibration method:
  - takes into account model uncertainty
Countries with active screening programs estimate that around 44% of individuals infected with HCV are unaware. In Canada, 2007 study suggests that figure is 21%, despite no active screening program.

**A IM: ESTI MATE PREVALENCE USING 2015 MODEL**

- PHAC and Canadian Task force for CEA of screening (Wong et al., CMAJ, 2015, 2017)
- Used by CADTH for therapeutic review (Wong et al., CMAJ, 2017)
**How do model states evolve over time? (Mathematical View)**

Undiagnosed F0 (2013) = $\alpha \times $ New infections (2012) + $(1 - \beta - \gamma) \times $ Undiagnosed F0 (2012)

Diagnosed F0 cases (2012) = $\gamma \times $ Undiagnosed F0 (2012)

Can derive similar relations for entire model, relating states in year $t$ to states in year $t+1$

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**We have good knowledge of diagnosis numbers**

From public databases:
- Yearly liver cancer diagnoses
- Yearly hepatitis C diagnoses based on seroprevalence.
Model calibration via Metropolis-Hastings (MCMC) algorithm

**METROPOLIS-HASTINGS ALGORITHM USED TO CALIBRATE UNKNOWN PARAMETERS OF MODEL**

Think of model as a black box that takes guesses of unknown/uncertain parameters and returns estimates of diagnosis numbers.

Selectively accept guesses of unknown/uncertain parameters based on quality of model estimate’s fit to diagnosis data.
**Metropolis-Hastings Algorithm Calibrates Model for Each Birth Cohort Separately**

- Population divided into three birth cohorts:
  - Individuals born before 1945
  - Individuals born 1945-1964 (baby boomers)
  - Individuals born after 1945

- Data gathered for each cohort
  - Liver cancer diagnoses 1999-2013
  - Hepatitis C diagnosis (seroprevalence) 1999-2013

- Metropolis-Hastings algorithm calibrates each cohort’s parameters

- Calibrated model estimates quantities of interest
  - Prevalence of chronic hepatitis C
  - Undiagnosed proportion of chronic hepatitis C-infected population

**Calibration results**
CALIBRATION OF CANADA-WIDE COHORT OF INDIVIDUALS BORN BEFORE 1945

- Diagnosis data
- Estimate mean
- Estimate 95% CI bound

CALIBRATION OF CANADA-WIDE COHORT OF INDIVIDUALS BORN BETWEEN 1945-1964

- Diagnosis data
- Estimate mean
- Estimate 95% CI bound
CALIBRATION OF CANADA-WIDE COHORT OF INDIVIDUALS BORN AFTER 1964

Averages across Canada cohorts - PSA

ESTIMATES OF PREVALENCE AND UNDIAGNOSED CHC AVERAGED OVER CANADA-WIDE COHORTS

Averages across Canada cohorts - PSA
SENSITIVITY ANALYSIS – CANADA PREVALENCE

Sensitivity of Canada prevalence

-8 -6 -4 -2 0 2 4 6 8
% change in prevalence

No. new infections 1999-2013
SVR (PEG-INF)
Treatment (PEG-INF)
Diagnosis
Liver related death
Progression to DC
CHC progression
Progression to HCC
Liver transplant

S^+_prev +50% parameter perturbation
S^-_prev -50% parameter perturbation

SENSITIVITY ANALYSIS – CANADA UNDIAGNOSED CHC

Sensitivity of Canada undiagnosed CHC proportion

-20 -15 -10 -5 0 5 10 15 20 25
% change in undiagnosed CHC proportion

Diagnosis
No. new infections 1999-2013
SVR (PEG-INF)
CHC progression
Treatment (PEG-INF)
Liver related death
Progression to DC
Progression to HCC
Liver transplant

S^+_und +50% parameter perturbation
S^-_und -50% parameter perturbation
We have provided prevalence estimates based on a new model of hepatitis C natural history.

Our approach calibrates model using data integrated from different sources and explicitly handles model uncertainty.

Currently working on province-specific estimates using administrative data.

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