Title: Cost-Effectiveness Modelling of Birth and Infant Dose Vaccination in Ontario from 2020 to 2050

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Appendix 1, as supplied by the authors. Appendix to: Biondi MJ, Estes C, Razavi-Shearer D, et al. Cost-effectiveness modelling of birth and infant dose vaccination against hepatitis B virus in Ontario from 2020 to 2050. *CMAJ Open* 2023. doi:10.9778/cmajo.20210284.

Appendix 1 - Supplementary Material

Methods

I. Literature search

The literature review was conducted by searching PubMed and Embase for peer-reviewed studies reported HBsAg prevalence using the terms: "[Ontario] AND [(hepatitis B) or HBV] AND [prevalence]" AND "[Ontario] AND ('prevalence'/exp OR prevalence) AND ('hepatitis B'/exp OR 'hepatitis B' OR 'HBV'/exp OR 'HBV')". Studies published between Jan 1, 1985, and March 1, 2020 and without language restrictions were assessed. Grey literature, ministry of health reports, conference presentations, local journals, and personal communications with local experts were included in the data review. Studies conducted in non-representative populations (e.g. blood donors, hemophiliacs, and patients on hemodialysis) were excluded. Per Delphi process protocol (Table 1S), two in-person meetings were held with Ontario experts who reviewed and approved epidemiologic inputs or provided improved data sources to finalize the model.

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HBV prevalence estimate

HBsAg prevalence in Ontario may vary by birth cohort due to changing vaccination policies and immigration over time (1). Therefore, 2016 HBsAg prevalence estimates based on recorded clinical data, adjusted based on two age distributions: reported cases by age group and population data for Ontario, with additional adjustment for the impact of immigration (2, 3). Among native-born Canadians, prevalence rates were modified to account for a declining prevalence in older Ontario residents (due to mortality rate and low infection rate). National surveillance data estimating a higher prevalence in men than women (13.2 vs. 9.6 per 100,000) (4), was applied to the distribution of cases by age group. While prevalence data do not exist for the immigrant population, estimated HBsAg prevalence based on Toronto data was considered in the baseline estimate for Ontario as a whole. For ten high prevalence countries with sizable immigrant populations (China, Hong Kong, India, Iran, Jamaica, Pakistan, Poland, Philippines, Sri Lanka, Vietnam) annual entrance data by age and sex were available from 1980-2016 (5). The Polaris Observatory has previously published country specific PRoGReSs Models for all ten of these countries (6). Utilizing these models and the annual country-specific entrance data by age and sex the estimated annual number of HBsAg+ immigrants by age, sex, and disease stage were added to the Ontario model. For years in which no published data were currently available (2017 onwards), the number of immigrants by country of birth and distribution by age and sex were assumed to remain constant into the future. It was estimated that 70% of cases in Ontario in 2017 were among first generation migrants.

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II. Scenario development: Additional criteria

In all scenarios, it was assumed that patients between ages 15-85, that had a high viral load or were cirrhotic, were eligible for treatment and that treatment efficacy was 90%. Prophylaxis coverage rates were varied in 3 waves (2021, 2022-2023, 2024-2050). Prevalence was also estimated for infants and 5-year-olds to assess the impact of intervention on disease outcomes in children.

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Appendix 1 - Table 1S. Delphi Process

		Activities
Phase 1 – Data Gathering	1a	**Identify country experts who are willing to collaborate (March 2019)** • Experts were identified through HBV-related scientific contributions, or through referrals and recommendations from leading researchers. Panels consisted of hepatologists, gastroenterologists, virologists, infectious disease specialists, epidemiologists, health economists, health scientists and Ministry of Health representatives
	1b	**Literature Search (April 2019)** • Review the internal database for previously identified sources • Review online sources (MOH, WHO, etc.) to capture non-indexed sources • Run a literature search from 2013 forward to identify recent publications • Summarize input data available through the literature • Gather empirical data for new HCC cases, liver transplants (LT), percent of HCC and LT due to HBV, annual newly diagnosed, annual treated • Build draft model based on published data or extrapolate inputs from countries with data when data are missing (as a placeholder) • Schedule meeting with experts
Phase 2 – Country Meetings and Modeling	2a	**Expert Meeting 1 (2-3 hours) (October 2019)** • Provide a background on the project, model and methodology • Review data identified in Phase 1b and highlight gaps in data • Request data in local non-indexed journals, unpublished data and any other available data (e.g., hospital-level data) that can be used to fill the gaps • Gain agreement on countries that can used as for extrapolation when no local data are available
	2b	**Follow up with Experts Post Meeting 1 (October 2019-December 2019)** • Send minutes of the meeting and list of remaining action items to experts • Follow up with experts to collect missing data and get copies of publications in the local journals, unpublished data, relevant Ph.D. theses, government reports and raw hospital or registry-level data • Analyze raw data and send to experts for approval
	2c	**Disease Burden Modeling (December 2019-February 2020)** • Populate disease burden model with inputs and calibrate model to empirical data • Develop 2-3 scenarios to prepare for meeting 2, including a WHO target scenario (elimination by 2030) • Schedule second meeting • Develop a slide deck summarizing all inputs and associated data sources • Perform a final check of the model and slide deck and approve internally
	2d	**Expert Meeting 2 (2-3 hours) (February 2020)** • Review all inputs as well as data provided by experts since meeting 1 and results of analyses of any raw data provided • Gain agreement on all inputs to be used in the model • Update the model using any updated inputs • Run scenarios requested by experts (e.g., slow increase in the number of treated patients, disease control, WHO target) and review results and insights • Agree on final strategies that would be considered as part of a national strategy
Phase 3 – Follow-up Analyses	3a	**Follow-up Analyses (February 2020-June 2020)** • Update model as necessary and send results to experts • Provide support to address follow-up questions • Lock down inputs and outputs as approved • Run additional scenarios to support the development of a national strategy (e.g., economic impact, birth cohort screening and sources of transmission) • Report results to Polaris Observatory • Update analysis as new information becomes available (e.g., new national studies, updated treatment data)

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Appendix 1 - Table 2S. Vaccination Rate by Grade 7 – Ontario, 1994-2016.

Year	Value
1994-1995	86.6%
1995-1996	88.7%
1996-1997	93.6%
1997-1998	86.5%
1998-1999	85.9% *
1999-2000	85.2% *
2000-2001	84.6% *
2001-2002	83.9% *
2002-2003	83.3% *
2003-2004	82.6% *
2004-2005	82.0% *
2005-2006	81.3% *
2006-2007	80.7% *
2007-2008	80.0%
2008-2009	78.1%
2009-2010	74.2%
2010-2011	76.6%
2011-2012	86.6%
2012-2013	86.9%
2013-2014	71.7%
2014-2015	70.7%
2015-2016	69.9%

* Not reported, data linearly interpolated

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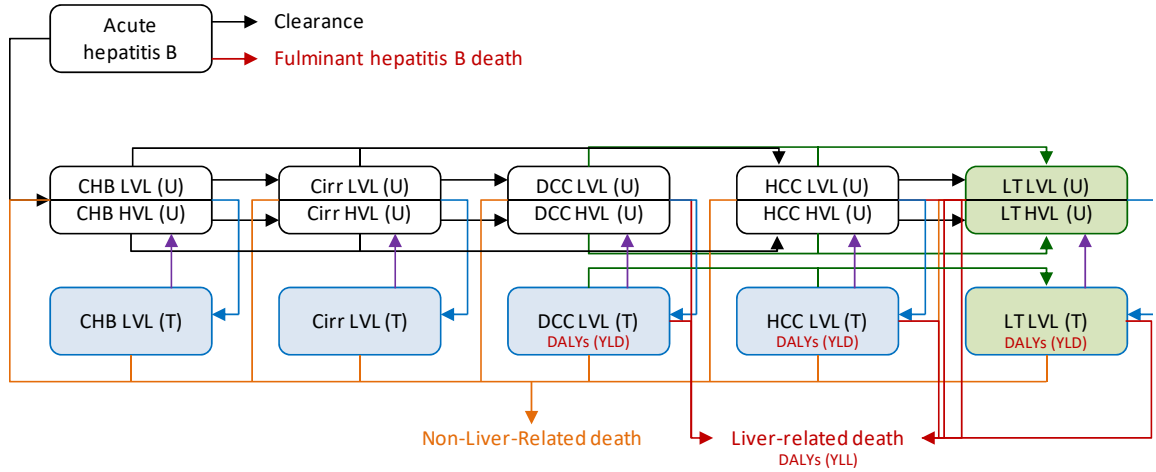
Appendix 1 - Figure 1S. Flow of disease progression of HBV



Legend: CHB — chronic hepatitis B; Cirr — compensated cirrhosis; DCC — decompensated cirrhosis; HCC — hepatocellular carcinoma; LT — liver transplant; LVL — low-viral load; HVL — high-viral load; U — untreated/non-responder; T — treatment responder; DALYs (YLD) — disability-adjusted life years (years lived with disability); DALYs (YLL) — disability-adjusted life years (years of life lost); black arrows — disease progression; orange arrows — non-liver-related death; red arrows — liver-related death; blue arrows — treatment response; purple arrows — treatment discontinuation; green arrows — liver transplantation

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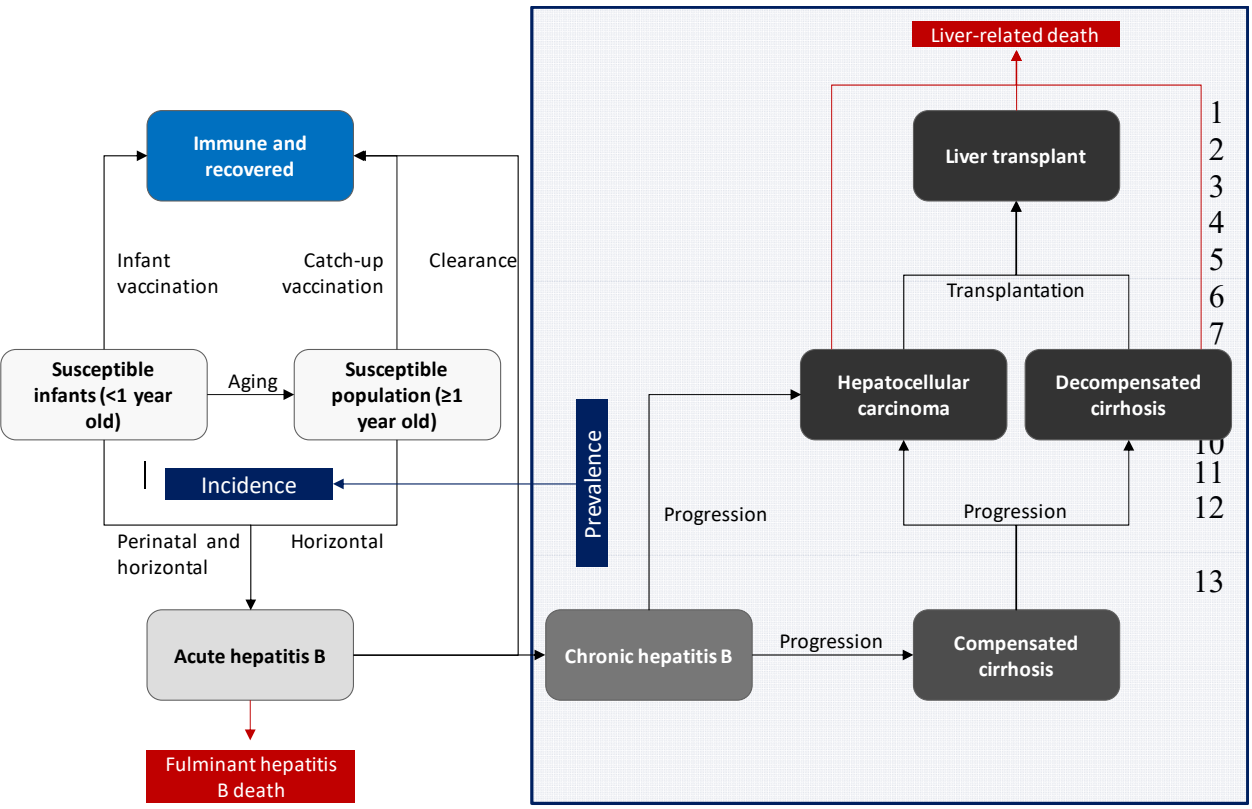

Appendix 1 - Figure 2S. Flow between populations in the model

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