Cost-effectiveness analysis of hepatitis A vaccination in Canada using a dynamic model

GlaxoSmithKline — Andrea Anonychuk, MSc

University of Guelph — **Chris Bauch**, PhD

University Health Network, Achieving Global Impact — Maggie Hong Chen, MSc

Institut national de santé publique Québec — Bernard Duval, MD, MPH

Institut national de santé publique Québec — Vladimir Gilca, MD

University Health Network, Achieving Global Impact — Murray Krahn, MD, MSc

GlaxoSmithKline — Ba' Pham, MSc

University of Guelph — Arni S.R. Srinivasa Rao, PhD

GlaxoSmithKline — Andrea C. Tricco, MSc

CIHR IRSC

GlaxoSmithKline

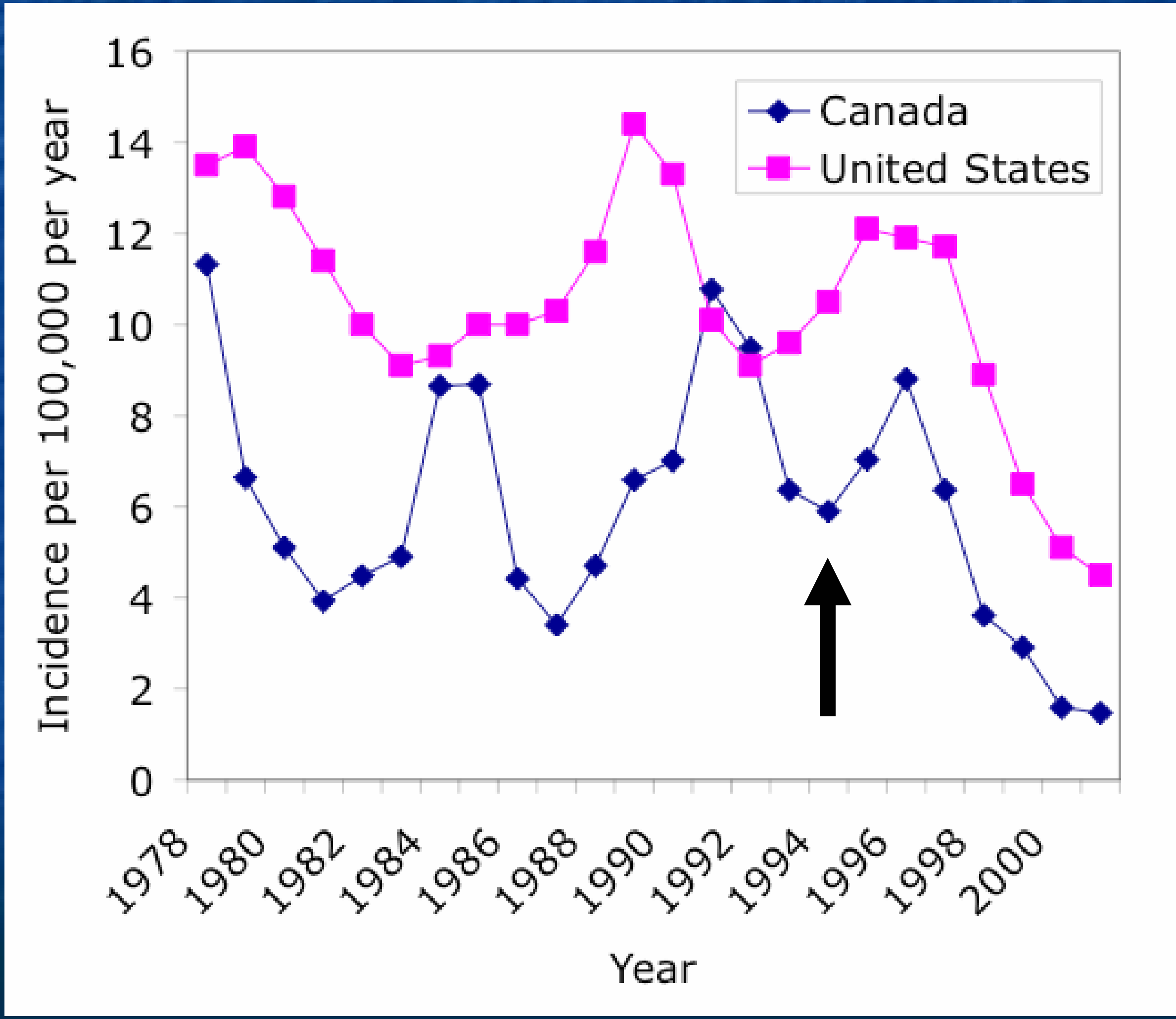
NSERC CRSNG

Global Hepatitis A Meeting, Miami, Florida, 1 December 2007

HAV epidemiology in Canada

- Hepatitis A virus (HAV) incidence is relatively low.
- Spread is primarily person-to-person (fecal-oral route) with very rare foodborne outbreaks.
- Vaccine licensed for use in Canada in 1994.
  - Average incidence 1980-1994: 6.3/100,000/yr
  - Average incidence 1995-2003: 3.8/100,000/yr
- Risk factors include MSM, IDUs, **travelers**.
- Vaccination in Canada is targeted toward high-risk groups.

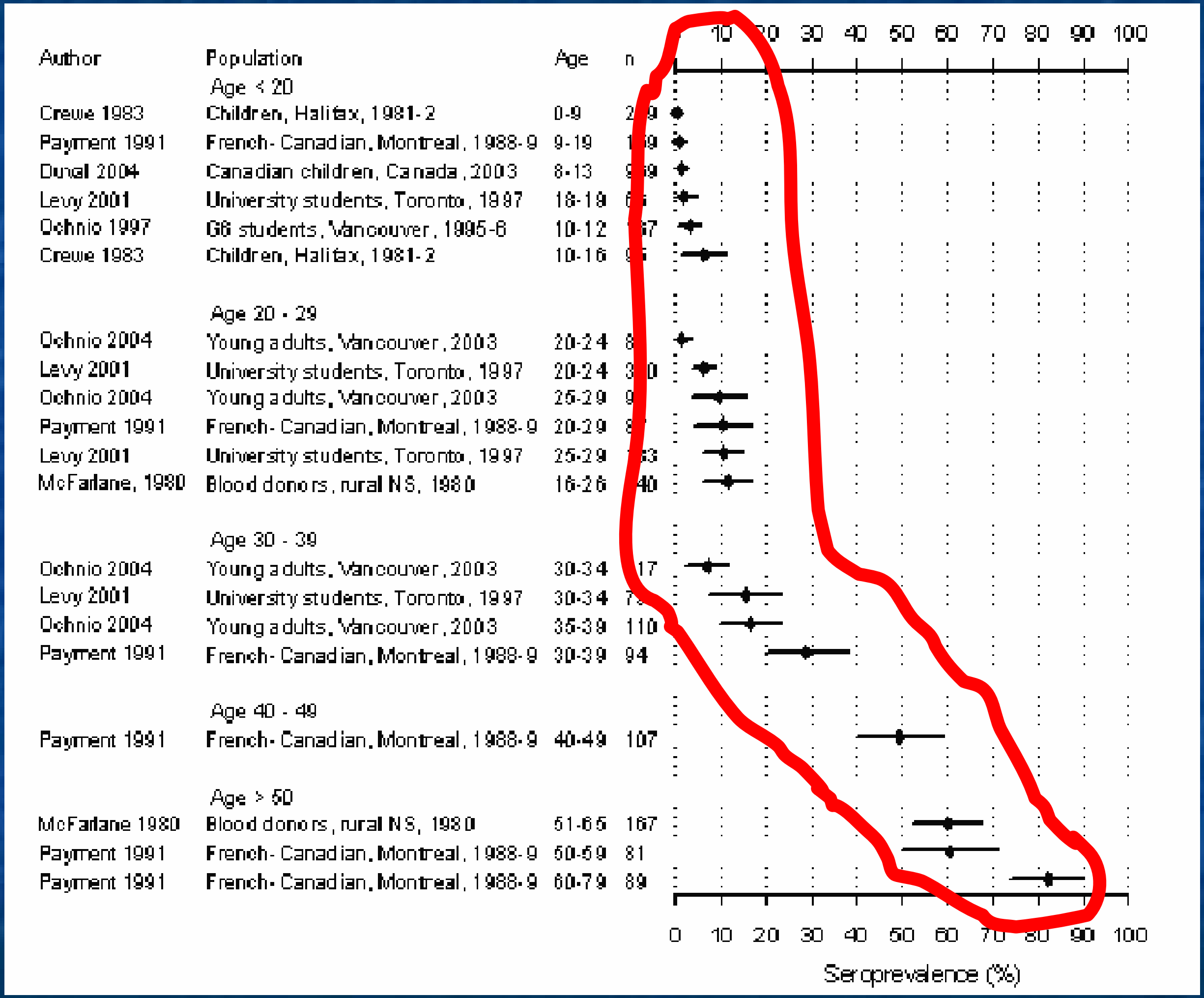
Hepatitis A epidemiology



- Average Canadian incidence 1980-94: 6.3/100,000/yr
- Average Canadian incidence 1995-03: 3.8/100,000/yr

Source: Health Canada
CDC

Hepatitis A epidemiology



Source: Pham et al 2005

Age

Seroprevalence

Research Rationale and Approach

- The cost-effectiveness and health outcomes of universal vaccination **relative to targeted vaccination, in a low incidence country,** are not currently known.
- **Research Questions**:
  - *What are the expected health outcomes under universal hepatitis A vaccination in Canada?*
  - *Which universal vaccination schedules are the most cost-effective?*
- We carried out a cost-utility analysis comparing universal vaccination to continuing the targeted policy.

Cost-utility methodology

- Assesses value for money.
- **Cost-effectiveness ratio**:
  increase in costs / gain in health units
- **Net Health Benefits, in health units:**
  (gain in health) - (increase in costs)/lambda
- **Net Health Benefits, in monetary units**:
  lambda*(gain in health) - (increase in costs)

Lambda = $50,000/QALY

Cost-utility methodology

- Costs measured in 2005 Canadian dollars.
- Both payer and societal perspectives used
  - Payer = costs to Ministry of Health
  - Societal = MOH costs + time costs + private sector costs.
- Health measured in QALYs = Quality Adjusted Life Years.

QALY and Utilities

- Health has dimensions of **quality** and **quantity**
- Utility is
  - Used to weight length of life;
  - A measure of patient preference for standardized health states;
  - Measured on a 0 to 1 scale.
- Example:
  - Life expectancy of 5 years, utility of 0.5 means 2.5 QALYs are accumulated.

Methods for collecting costing data

- A systematic review of data on Hepatitis A outcomes and costs was performed.
- Canadian data were used whenever possible
- Expert opinion and consensus used if no data available.

Vaccination Costs

- Costs of vaccination from the ministry perspective included:
  - Cost of vaccine (varied depending on strategy)
  - Cost of administration (ditto)
  - Cost of adverse events
- Societal costs included
  - Time costs due to getting vaccinated
  - Private sector vaccination
- Both proposed and current strategies were costed in this way.

Infection Costs

- Costs of infection from the ministry perspective included:
  - Physician visit
  - Outpatient clinic visits
  - Hospitalization
  - Diagnostic testing
  - Liver transplants
  - Public health interventions
- Additional infection costs from the societal perspective included:
  - Time costs (lost time at work due to acute infection and convalescence)
- Did **not** include home care or long-term care costs.

Summary of strategies considered, and their costs

Strategy	Description	Cost per person vaccinated
Current policy	High-risk groups only	Ministry: $ 81 Society: $ 212
4+9	One dose at age 4 in a clinic with other scheduled vaccines. One dose at age 9 in a school setting by replacing a single HB vaccine dose with a combined HA/HB vaccine dose. Current policy is phased out in unvaccinated cohorts.	Ministry: $ 42.57 Society: $ 43.17
9+9	Two doses at age 9 in a school setting by replacing HB vaccine with combined HA/HB vaccine. Current policy is phased out in unvaccinated cohorts.	Ministry: $ 18.12 Society: $ 18.72

Summary of infection costs

Age Class	Direct Costs (ministry)	Time Costs	Direct + time costs (society)
0-4	$ 1,235	$ 598	$ 1,833
5-9	$ 1,235	$ 665	$ 1,900
10-19	$ 1,140	$ 729	$ 1,869
20-29	$ 1,163	$ 569	$ 1,732
30-39	$ 1,537	$ 1,446	$ 2,983
40-59	$ 1,923	$ 4,341	$ 6,264
60+	$ 1,556	$ 2,080	$ 3,636

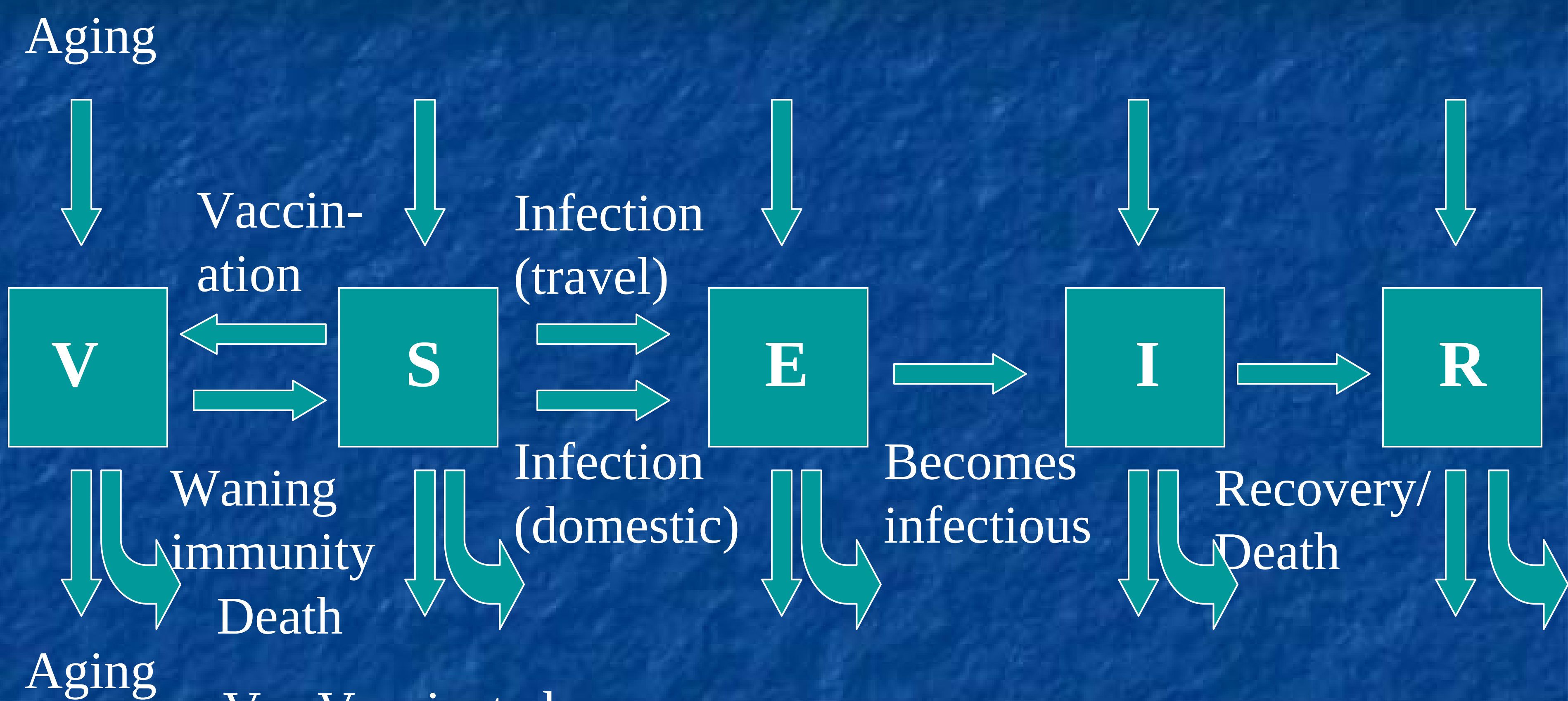
Need for dynamic model

- We also need to estimate how many cases and deaths would be averted by universal vaccination.
- Conventional analyses use **<u>cohort models</u>** which cannot capture herd immunity effects of vaccination.
- Instead we use **<u>dynamic models</u>** which capture herd immunity by modelling transmission mechanisms via computer simulation.

Dynamic model description

- Classify individuals according to:
  - Epidemiological status: susceptible (S), latent (E), infectious (I), recovered (R), vaccinated (V).
  - Age: 0-4, 5-9, 10-19, 20-29, 30-39, 40-59, 60+
- Age-dependence: probability of becoming infected, transmitting infection, developing jaundice, being vaccinated, etc.
- Calibrated using data on case reports, seroprevalence, clinical literature, demographics, vaccine coverage.

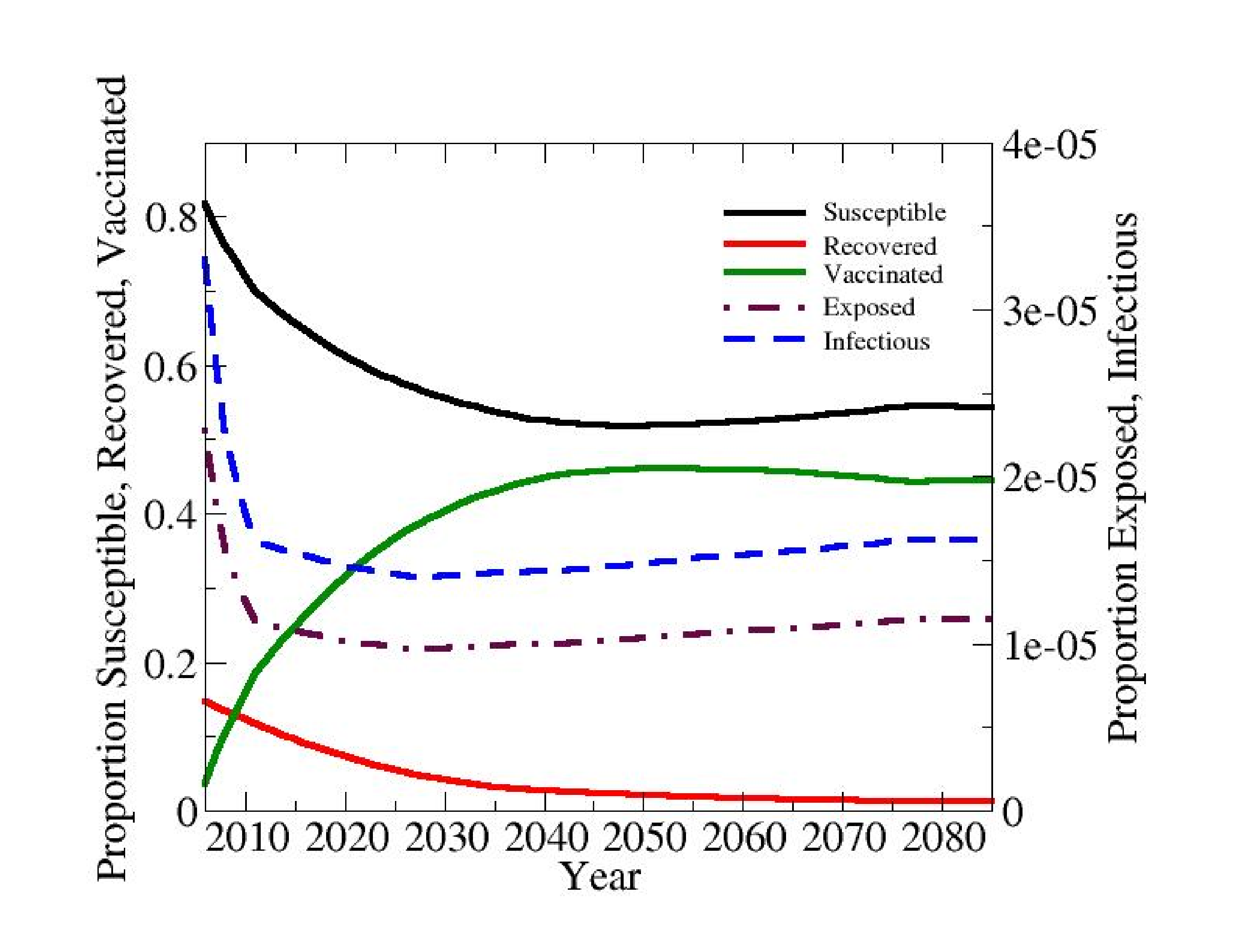
Dynamic model description



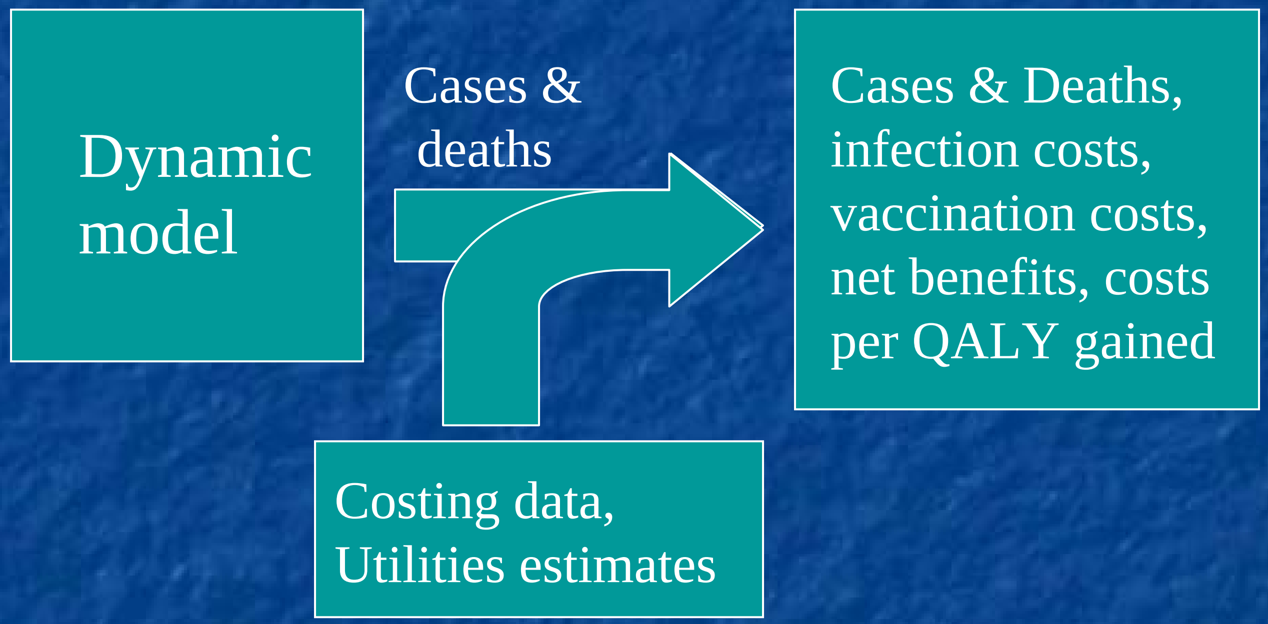
V = Vaccinated
S = Susceptible
E = Infected but not yet infectious

I = Infectious
R = Recovered

Dynamic Model Output



Summary of Methodology



Probabilistic uncertainty analysis applied

Univariate sensitivity analysis applied

Summary of Other Assumptions

- Under-reporting of symptomatic cases: 1:1.5 (*Mutsch et al CID 2006:42, Alter et al.Am J Epi 1987;125:133*)
- Discounting: 5% on costs and QALYs
- Waning immunity: 3.2/1.7/0.6% per year *(Jacobs et al Inf. Control & Hosp. Epi. 2004;25:563)*
- Efficacy: 97/100/100% *(Innis et al, JAMA 1994;271, Werzberger et al, NEJM 1992;327:453)*
- 80 years of vaccination: 2006-2085
- Compliance: 94% (child, school-based), 80% (child, clinic-based), 25% (adult, clinic-based)
- Targeted vaccination is phased out.
- Utility during acute HAV infection is taken to be 0.6 (Chodick et al. 2002, Arguedas et al. 2002).
- Transmission rates, current policy costs and coverage are constant after 2006.

Costs, cases, deaths (average discounted values)

Red = ministry, black = society

Strategy	Targeted Vaccine Costs, millions $	Universal Vaccine Costs, millions $	Infection Costs, millions $	Total Costs, millions $	Marginal Costs, millions $	Marginal QALYS
Current	7.44 ± 0.65 19.48 ± 1.77	0 0	0.45 ± 0.02 0.93 ± 0.05	7.89 ± 0.65 20.41 ± 1.77	0	0
4+9	5.94 ± 0.54 15.71 ± 1.47	3.41 ± 0.34 3.44 ± 0.34	0.24 ± 0.02 0.52 ± 0.04	9.59 ± 0.64 19.67 ± 1.51	1.69 ± 0.36 -0.74 ± 0.45	9.70 ± 0.59
9+9	5.94 ± 0.54 15.70 ± 1.46	1.59 ± 0.16 1.64 ± 0.17	0.36 ± 0.03 0.77 ± 0.06	7.88 ± 0.56 18.11 ± 1.48	-0.01 ± 0.18 -2.28 ± 0.33	3.69 ± 0.93

Strategy	Reported Cases	Deaths
Current	846	4.2
4+9	379	2.5
9+9	606	3.7

For 1980-1994 population values

Cost-utility results

Ministry perspective

Strategy	Costs per QALY Gained, $	Net Benefits, health units	Net Benefits, millions $
Current	N/a	N/a	N/a
9+9	- $46,000 ± $ 790,000	3.8 ± 3.0	0.2 ± 0.2
4+9	$ 175,000 ± $ 36,000	-24.2 ± 7.1	-1.2 ± 0.4

Society perspective

Strategy	Costs per QALY Gained, $	Net Benefits, health units	Net Benefits, millions $
Current	N/a	N/a	N/a
9+9	- $ 835,000 ± $4,333,000	49.4 ± 6.3	2.5 ± 0.3
4+9	- $77000 ± $48,000	24.5 ± 9.0	1.2 ± 0.5

Threshold for net benefits = $50,000

Special Case: ceasing targeted vaccination altogether in 2006

Ministry perspective

Strategy	Costs per QALY Gained, $	Net Benefits, health units	Net Benefits, millions $
9+9	53,600 ± 3,500	-1.5 ± 1.5	-0.1 ± 0.1
4+9	65,500 ± 8,600	-12.4 ± 6.8	-0.6 ± 0.3

Society perspective

Strategy	Costs per QALY Gained, $	Net Benefits, health units	Net Benefits, millions $
9+9	34,700 ± 3,500	6.6 ±1.8	0.3 ± 0.1
4+9	44,600 ± 8,700	4.4 ± 7.0	0.2 ± 0.4

Special Case: comparison with cohort model predictions

Ministry perspective, dynamic model

Strategy	Costs per QALY Gained, $	Net Benefits, health units	Net Benefits, millions $
9+9	- 46,000 ± 790,000	3.8 ± 3.0	0.2 ± 0.2
4+9	175,000 ± 36,000	-24.2 ± 7.1	-1.2 ± 0.4

Ministry perspective, cohort model

Strategy	Costs per QALY Gained, $	Net Benefits, health units	Net Benefits, millions $
9+9	-67,000 ± 2,673,000	1.8 ± 3.3	0.1 ± 0.2
4+9	467,000 ± 99,000	-32.1 ± 7.1	-1.6 ± 0.4

Sensitivity Analysis

- We studied the sensitivity of model predictions to variations in parameters, for 9+9 strategy:
  - rate of waning immunity (0% to 2% annual)
  - change in travel transmission rate over time (decline to 50%, climb to 150%)
  - under-reporting of symptomatic cases (1:1 to 1:3)
  - HAV mortality rate (± 50%)
  - Utility during acute HAV (± 50%)
  - universal vaccination costs (± 50%)
  - infection costs (± 50%)
  - costs of current policy (-20%,+40%)
  - efficacy of current policy in reducing incidence (1.7 to 3.3 per 100,000 per year with targeted alone)

Sensitivity Analysis

- The “9+9” strategy is cost-effective from ministry perspective as long as:
  - incremental cost of two doses of bivalent HA/HB vaccine versus two doses of monovalent HB vaccine is less than $21 (base case is $18).
  - long-term reported incidence under the current strategy remains above 2.2/100,000/year (base case is 3.3/100,000/year).
- Applies at a threshold of $50,000/QALY.

Conclusions

- Absolute QALY gains of implementing universal HA vaccination in Canada are small
  - 10-30 QALYs gained per year before discounting.
- However, a "9+9" strategy that replaces two doses of HB vaccine at age 9 with two doses of combined HA/HB vaccine appears to be economically attractive:
  - Cost-effective from ministry perspective, at $50,000/QALY threshold (positive net benefits).
  - Cost-saving from societal perspective.
- Using dynamic models instead of cohort models can make cost-effectiveness analyses of vaccination programmes more accurate.

Relevant publications

- C.T. Bauch, A.M. Anonychuk, B.Z. Pham, V. Gilca, B. Duval, M.D. Krahn. 'Cost-utility of universal hepatitis A vaccination in Canada'. ***Vaccine***, in press.
- R. Amariei, A.R. Willms, C.T. Bauch. 'The US and Canada as a coupled epidemiological system: an example from hepatitis A'. ***BMC Infectious Diseases***, accepted subject to revision.
- A.M. Anonychuk, A.C. Tricco, C.T. Bauch, B. Pham, V. Gilca, B. Duval, A. John-Baptiste, G. Woo and M. Krahn. 'Cost Effectiveness Analyses of Hepatitis A Vaccine: A Systematic Review to Explore the Effect of Methodological Quality on the Economic Attractiveness of Vaccination Strategies', ***Pharmacoeconomics***, in press.
- C.T. Bauch, A.S.R.S Rao, B. Pham, M Krahn, V. Gilca, B. Duval, M.H. Chen, A Tricco (2007). 'A dynamic model for assessing universal Hepatitis A vaccination in Canada' ***Vaccine*** 25:1719-1726.
- A.S.R.S. Rao, B. Pham, M. Chen, A. Tricco, V. Gilca, B. Duval, M. Krahn, C.T. Bauch (2006). 'Cohort effects in epidemic models: an example from Hepatitis A'. ***BMC Infectious Diseases*** 6: 174.