



National Advisory Committee on Immunization (NACI): **Guidelines for the Economic Evaluation of Vaccination Programs in Canada**

October 17, 2023

NCCID webinar

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English



French



Land acknowledgements

We wish to acknowledge the land on which we work and live.

For thousands of years, Toronto has been the traditional territory of many nations including the Mississaugas of the Credit, the Anishnabeg, the Chippewa, the Haudenosaunee and the Wendat peoples.

Many of you are joining us from all over Turtle Island, a name many Indigenous peoples use for North America, and around the world. We encourage you to seek out whose ancestral lands you are on today.

<https://native-land.ca/>

Disclosure

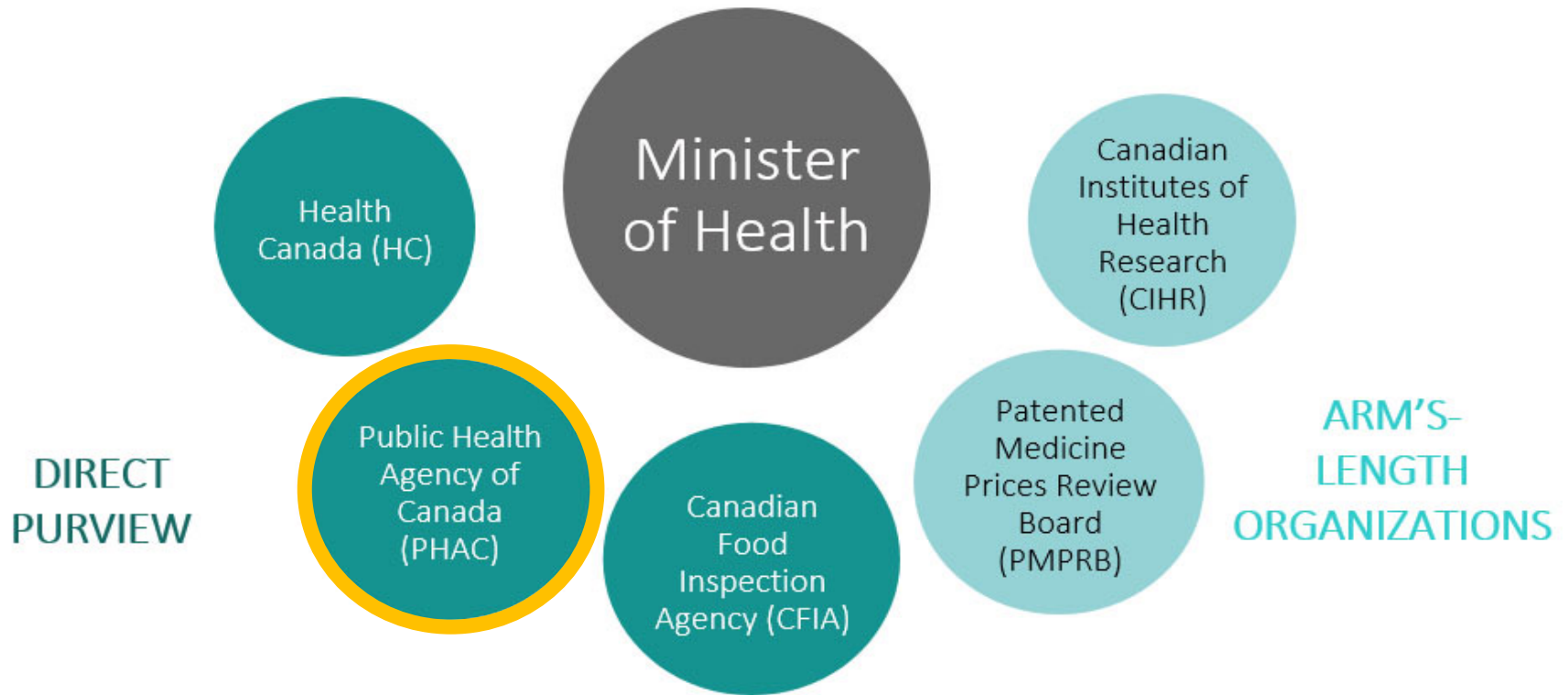
Dr. Beate Sander has no actual or potential conflict of interest in relation to this topic or presentation.

Man Wah Yeung has no actual or potential conflict of interest in relation to this topic or presentation.

Outline

- Overview of National Advisory Committee on Immunization (NACI)
- Overview of Economic Guidelines Task Group (EGTG)
- Guidelines for economic evaluation of vaccine programs in Canada
- Applications and next steps

Canada's federal health portfolio

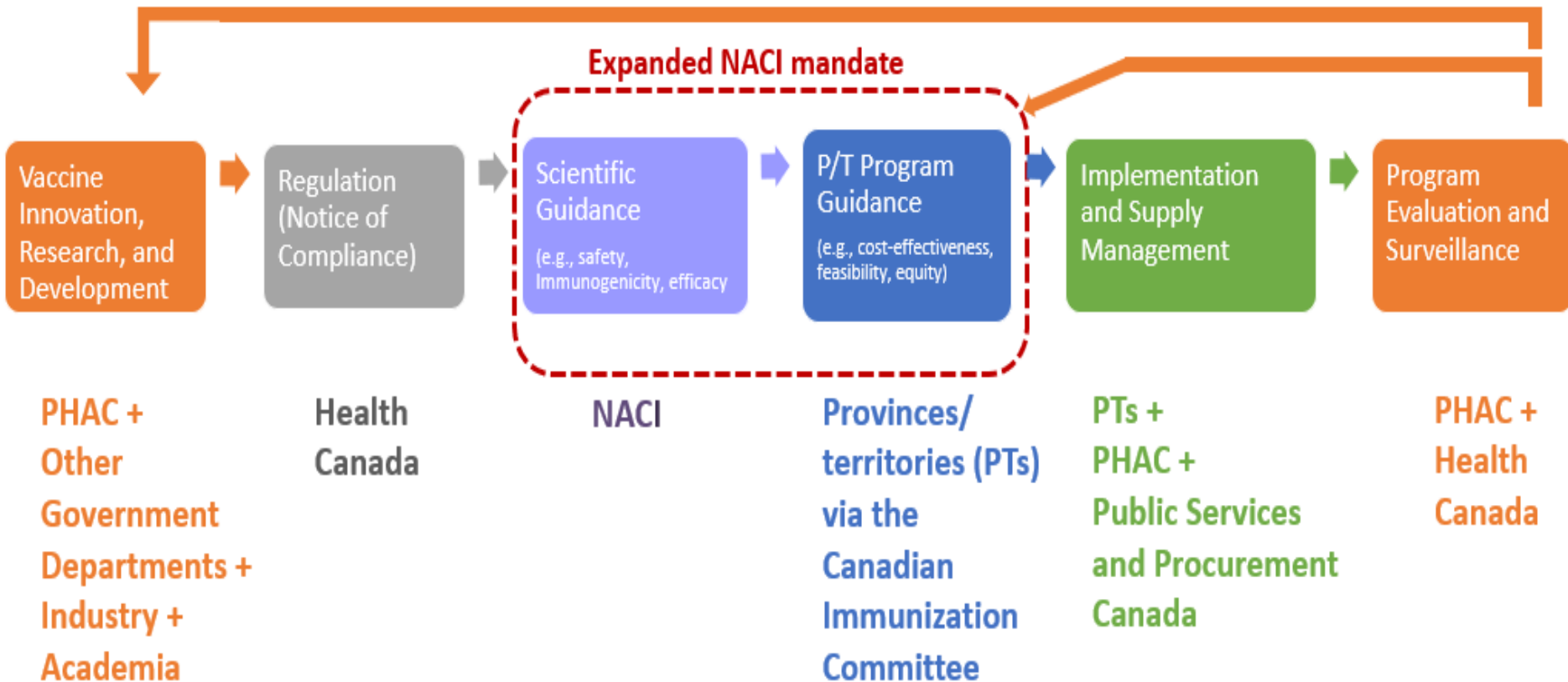


National Advisory Committee on Immunization (NACI): Structure and scope

- Established in 1964 by the Government of Canada (Health Canada)
- Provides public health advice relating to vaccines used for the prevention of disease and certain prophylactic agents for humans
- Comprised of Canadian experts in pediatric and adult infectious diseases, allergy/immunology, geriatrics, nursing, pharmacoeconomics, public health and preventive medicine, epidemiology, social sciences
- Scope has traditionally included recommendations based on safety, efficacy, immunogenicity, effectiveness and burden of illness
 - **As of 2019, NACI mandate is being gradually expanded to include programmatic factors, such as program feasibility and cost-effectiveness**
- Provinces/ territories (PTs) have discretion whether to accept NACI advice; Some PTs have own technical advisory groups and may complete complementary analyses
 - E.g. Comité sur l'immunisation du Québec (CIQ)
 - E.g. Alberta Advisory Committee on Immunization

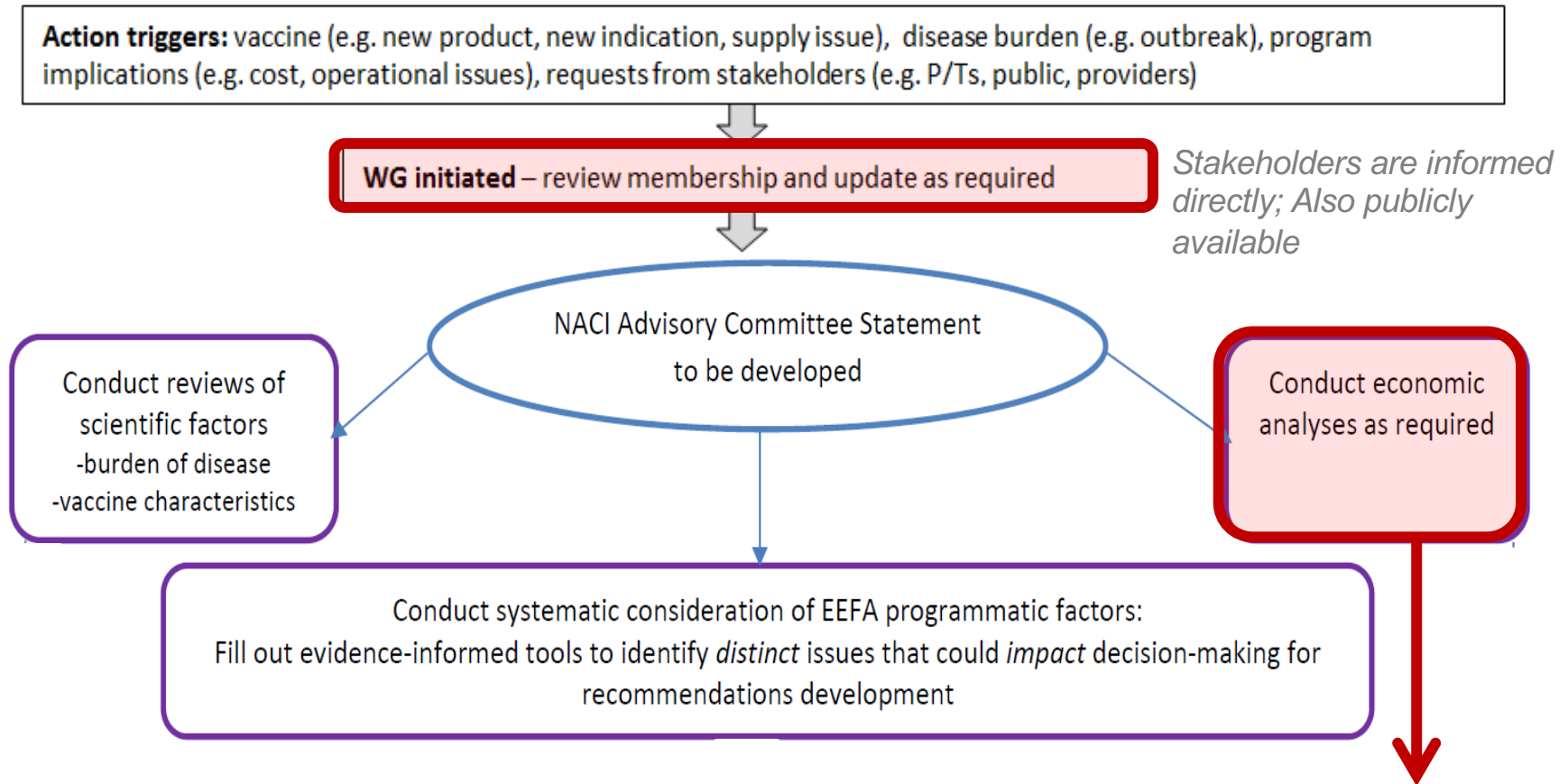


National Advisory Committee on Immunization (NACI): Structure and scope



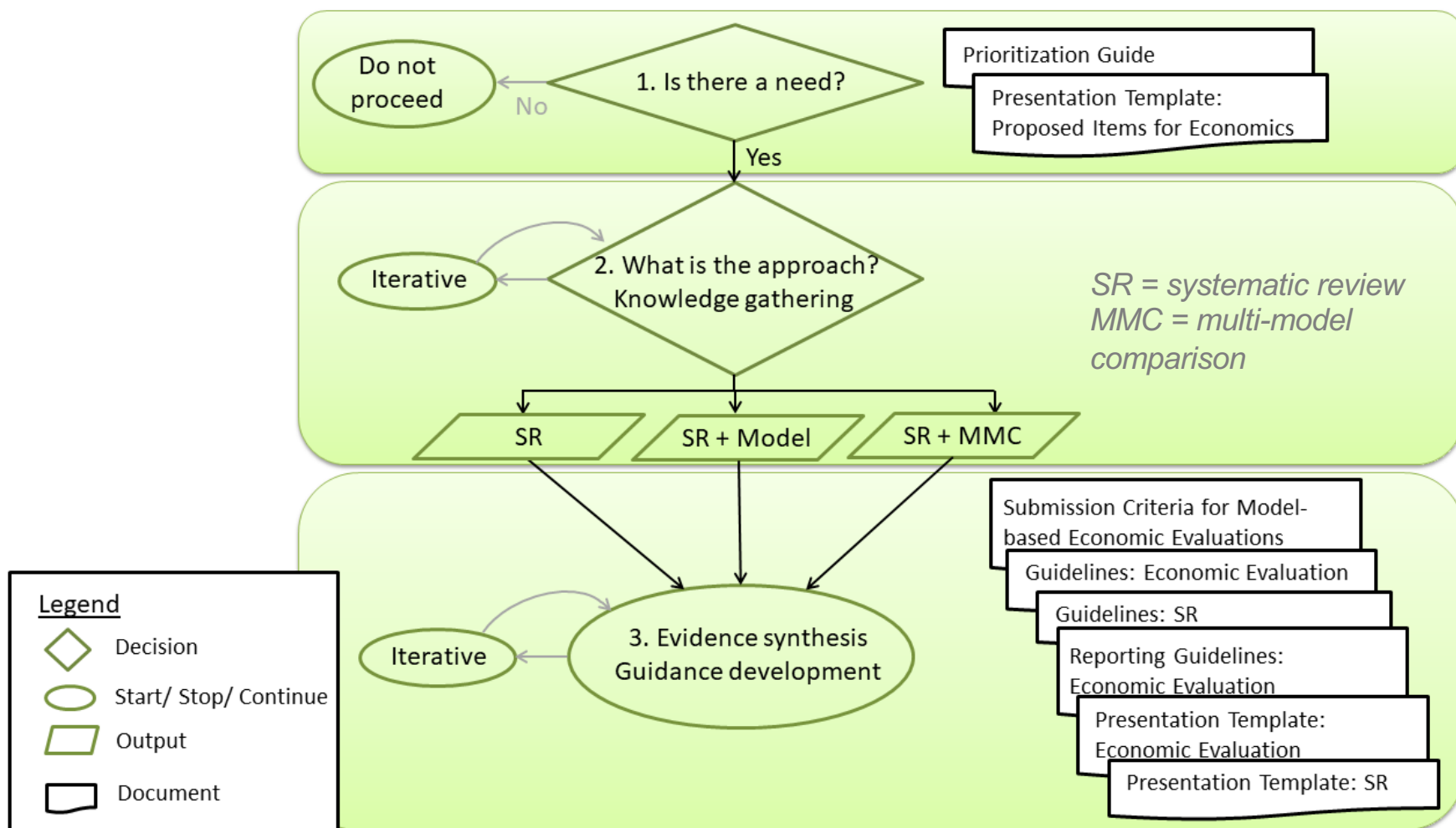
PHAC = Public Health Agency of Canada; PT = provinces/ territories

Snapshot of overall NACI process



EEFA = ethics, equity, feasibility, acceptability

NACI Economic process



Multi-model comparison

- Compare two or more models
 - One will be a de novo/ adapted model
 - Other(s) may be developed or funded by others (e.g., academia, government, a recognized funding agency, industry)
- Assess model structures, inputs, assumptions and results

Currently in piloting phase

Economic Guidelines Task Group (EGTG)

Time-limited task group: Jan 2019 – 2023

Mandate: Support of the expanded mandate; Develop guidelines for economic evaluations of vaccines in Canada

- Inform best practices
- Promote standardized and high-quality evidence for decision-making

Rationale:

- Existing guidelines are **not specific to Canada** (**World Health Organization** guidelines, 2nd ed., 2019 and **US Second Panel guidelines**, 2nd ed., 2017);
- Or are **not specific to vaccines** (**CADTH**, Canadian Agency for Drugs and Technologies in Health, 4th ed., 2017)

https://www.cadth.ca/sites/default/files/pdf/guidelines_for_the_economic_evaluation_of_health_technologies_canada_4th_ed.pdf
<https://apps.who.int/iris/bitstream/handle/10665/329389/WHO-IVB-19.10-eng.pdf>

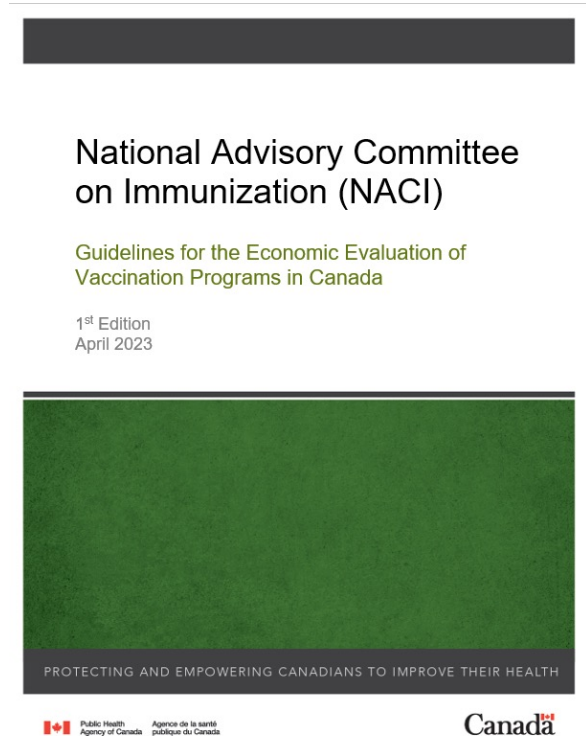
Economic Guidelines Task Group (EGTG)

Scope:

- Includes: Conducting and reporting of model-based economic evaluations
- Excludes: Budget impact analyses, decision-making processes

Target audience:

- Primary: Researchers (analysts conducting economic evaluations; mathematical modellers)
- Secondary: End-users of generated results (policy-makers and others)



Economic Guidelines Task Group (EGTG)



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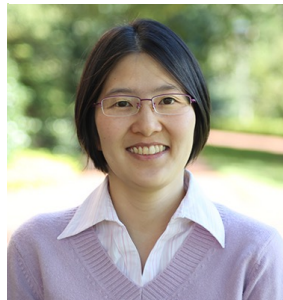
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Development process:

Outreach, consultations and review

- Chief Medical Officers of Health (CCMOH)
- Canadian Immunization Committee (CIC)
- Public Health Ethics Consultative Group (PHECG)
- Indigenous Services Canada (ISC)
- Canadian Indigenous Nurses Association (CINA)
- Indigenous Physicians Association of Canada (IPAC)
- NACI immunologists
- Sister task group, NACI Economics Task Group (ETG)
- Patented Medicine Prices Review Board (PMPRB)
- Academic peer-reviewers (Canadian and international)
- Public consultation via webinars and online survey (April – June 2022)
 - Various stakeholders including but not limited to industry, patient groups, economic guideline groups, health technology assessment agencies, general public

Vaccines vs. other health technologies

Vaccines can have broad impacts that are unique or are unusually large:

- Can affect both vaccinated and unvaccinated individuals
 - Via non-health spillovers and externalities
 - E.g., intergenerational effects
- Some externalities are vaccine-specific
 - E.g., herd/ community immunity, age-shifting of disease, serotype replacement, disease eradication
- Can have non-health impacts
 - E.g., productivity, consumption, education, environment

Hence, excluding broader impacts can undervalue vaccination programs

Chapters

1	Decision problem
2	Types of Evaluations
3	Study populations
4	Comparators
5	Perspectives
6	Time Horizon
7	Discounting
8	Modelling
9	Effectiveness
10	Measurement and Valuation of Health
11	Resource Use and Costs
12	Analysis
13	Uncertainty
14	Equity
15	Reporting

0	Foreword
0	Introduction
0	Abbreviations
0	Glossary
Appendix	Impact inventory table
Appendix	Reference case

Chapters to be highlighted today

1	Decision problem
2	Types of Evaluations
3	Study populations
4	Comparators
5	Perspectives
6	Time Horizon
7	Discounting
8	Modelling
9	Effectiveness
10	Measurement and Valuation of Health
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Recall:

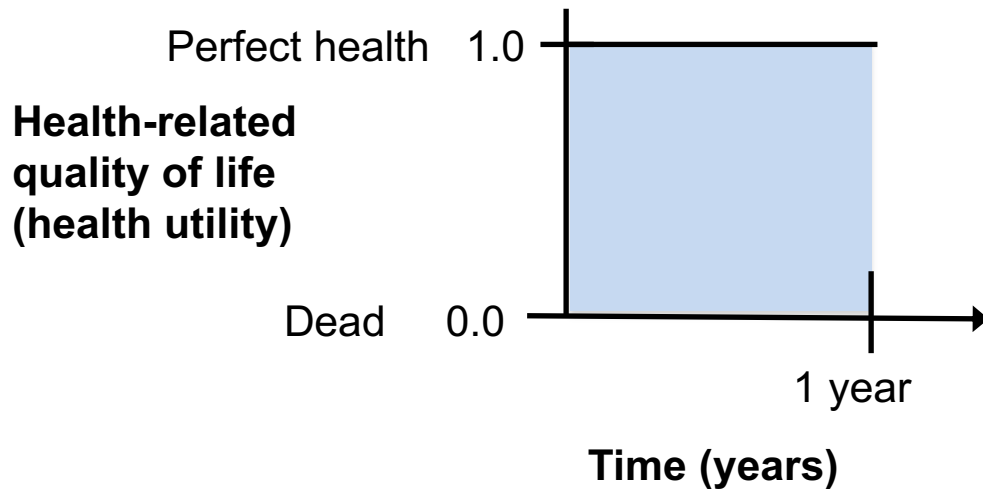
Types of Economic Evaluations (Drummond et al 2005*)

Type of study	Measurement / valuation of costs in both alternatives	Measurement / valuation of outcomes
*Cost Effectiveness Analysis (CEA)	Monetary units	Natural units (e.g., life-years gained, cases averted, hospitalizations, etc.)
*Cost Utility Analysis (CUA)	Monetary units	Quality Adjusted Life Year (QALY)
*Cost Benefit Analysis (CBA)	Monetary units	Monetary units
Cost Minimisation Analysis (CMA)	Monetary units	Natural units (equal effectiveness)

Recall:

Quality-adjusted life year (QALY)

- Summary outcome measure used to quantify the effectiveness of an intervention
- Combine the impact of gains in quality of life and in quantity of life (i.e., life expectancy) associated with an intervention



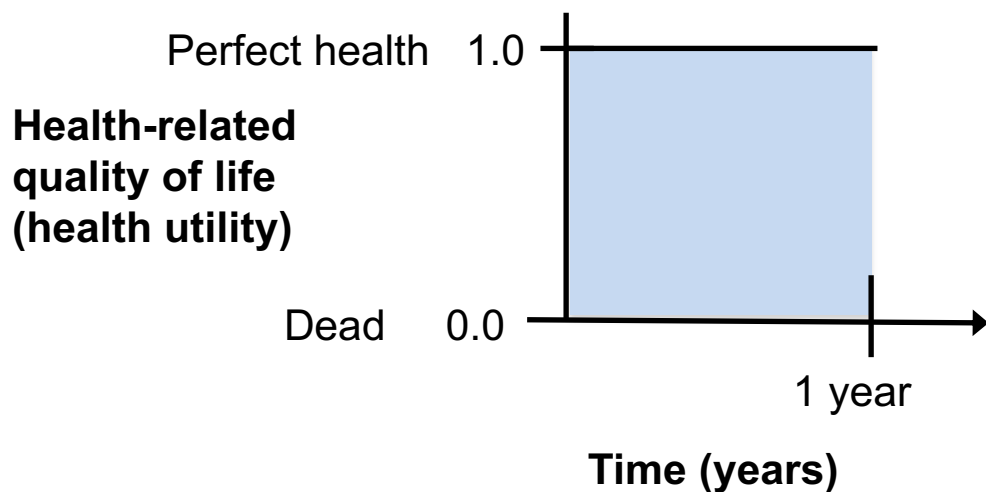
Health utilities are valued via:

- *Direct measures (e.g., standard gamble, time trade off)*
- *Indirect measures (e.g., EQ-5D, SF-6D)*

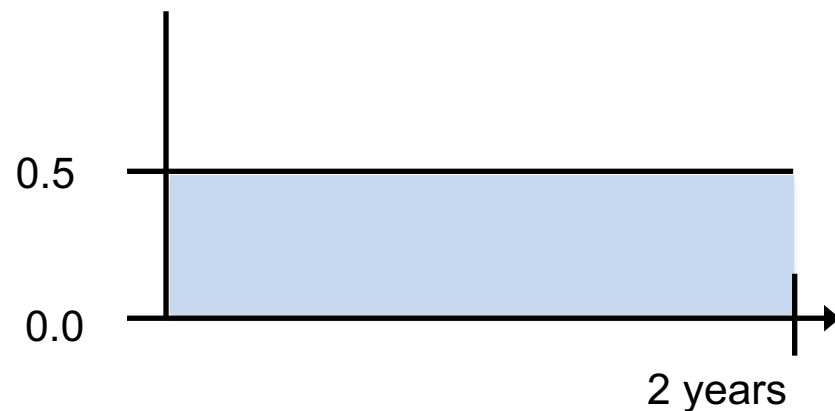
Recall:

Quality-adjusted life year (QALY)

- Summary outcome measure used to quantify the effectiveness of an intervention
- Combine the impact of gains in quality of life and in quantity of life (i.e., life expectancy) associated with an intervention



$$1.0 \text{ utility} \times 1 \text{ year} \\ = \mathbf{1 \text{ QALY}}$$



$$0.5 \text{ utility} \times 2 \text{ years} \\ = \mathbf{1 \text{ QALY}}$$

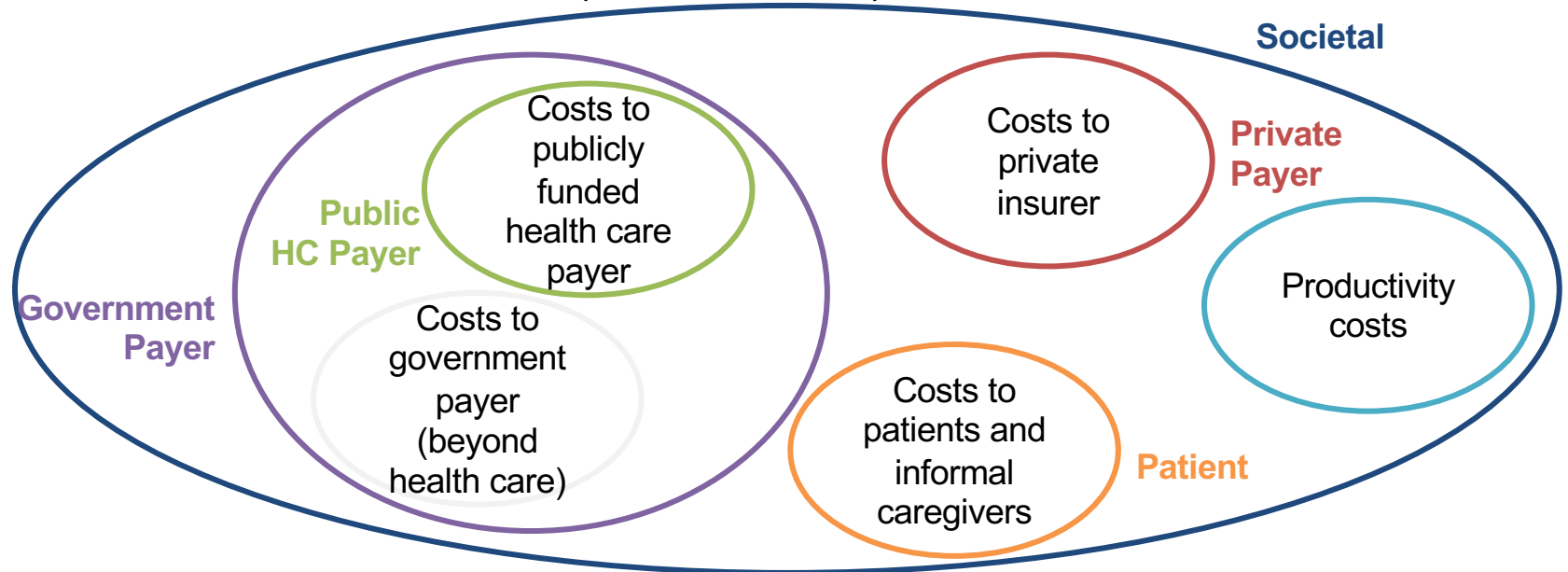
Guideline statements:

Chapter 2. Types of evaluations

1. In the reference cases, the economic evaluation should be a cost-utility analysis (CUA) with outcomes expressed as quality-adjusted life-years (QALYs). Any departure from this approach should be clearly justified. [CADTH Guideline Statement with amendment]
2. A cost-benefit analysis (CBA) may be used alongside the reference case CUAs in situations where the vaccination program may be compared to a non-health intervention.

Recall: Perspective

→ Determines which costs (and outcomes) to include in economic evaluation



Adapted from the Health Technology Assessment Institute
(Toronto Health Economics and Technology Assessment Collaborative, THETA)

Guideline statements: Chapter 5. Perspectives

1. Two reference case analyses should be presented as part of the economic evaluation of vaccination programs: one conducted from the publicly funded **health system perspective**, and the other conducted from the **societal perspective**.
2. “Both costs and outcomes should be consistent with the stated perspective.” [CADTH Guideline Statement]

“Health system” = both healthcare clinical services and Public Health

Comparison to other major guidelines on economic evaluations

Guidelines	Jurisdiction	Type of health intervention	Recommendation on perspective
WHO, 2019	Low-, middle- or high-income economies	Vaccines	“Should reflect national guidelines about the reference case for health economic evaluation. If these do not exist, then analyses should adopt the perspective of society ”
2 nd Panel on Cost-Effectiveness in Health and Medicine, 2016	US	Health technologies in general	Healthcare sector perspective AND societal perspective
1 st Panel, 1996	US	Health technologies in general	Societal perspective
CADTH, 2017	Canada	Health technologies in general	Publicly funded health care payer

Appendix: Impact inventory

Purpose: Provide a comprehensive list of health and non-health impacts;
Have researchers explicitly indicate which impacts are included vs. excluded

Impacts include:

- Health outcomes (individual, population; vaccine recipient, caregiver)
- Health system costs (healthcare costs and public health costs; costs funded and unfunded by the system)
- Direct out-of-pocket costs
- Losses in productivity (e.g., paid work, unpaid work, caregiver, macroeconomic consequences)
- Consumption (e.g., future individual non-medical, household)
- Education, Social services and community services, Environment, Other areas (e.g., legal, criminal, housing)

Area of Impact	Definitions/Examples	Included in Reference Case?		Comments
		Publicly funded health system perspective	Societal perspective	
<i>Health</i>				
Health outcomes	Individual health outcomes for persons intended for vaccination			
	Mortality	<input type="checkbox"/>	<input type="checkbox"/>	
	Health-related quality of life	<input type="checkbox"/>	<input type="checkbox"/>	
	Safety (i.e., adverse events)	<input type="checkbox"/>	<input type="checkbox"/>	
	Health impacts not captured by QALYs	<input type="checkbox"/>	<input type="checkbox"/>	
	Individual health outcomes for informal caregivers			
	Health-related quality of life	<input type="checkbox"/>	<input type="checkbox"/>	
	Population health outcomes			
	Incidence of infection and disease in vaccinated and unvaccinated individuals	<input type="checkbox"/>	<input type="checkbox"/>	
	Changes in age distribution of individuals who develop infection and disease	<input type="checkbox"/>	<input type="checkbox"/>	
Emergence of new diseases related to variations of the pathogen (i.e., serotypes, serogroups, strains) or unrelated pathogens that may replace the one(s) targeted by the vaccine	<input type="checkbox"/>	<input type="checkbox"/>		
Disease eradication	<input type="checkbox"/>	<input type="checkbox"/>		

Excerpt

Highlights:

Chapter 8. Modelling

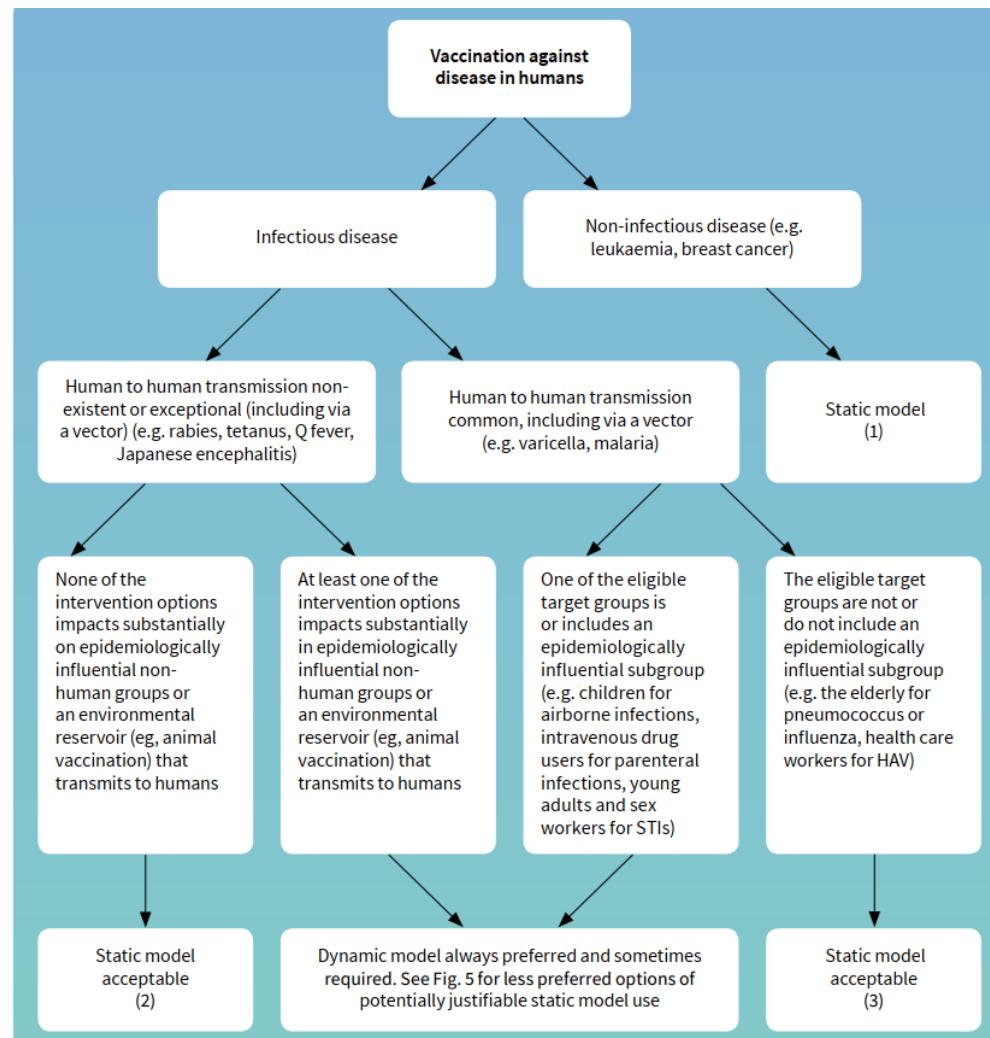
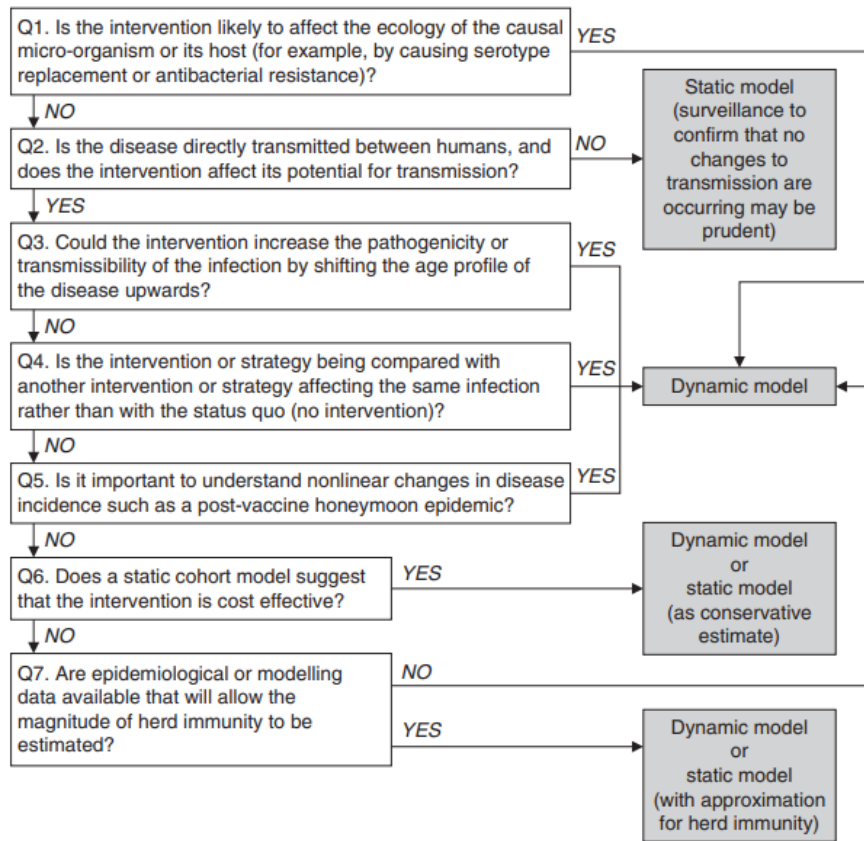
- Use **dynamic models** when there are externalities, e.g.,:
 - Prevention of human-to-human transmission of infection
 - Age-shifting of disease
 - Serotype replacement
- Can use **static models** under certain circumstances, e.g.,:
 - No human-to-human transmission (e.g., tetanus or rabies).
 - Intended group for vaccination is not epidemiologically influential with respect to transmission (e.g., hepatitis A vaccination of healthcare workers, influenza or pneumococcal vaccination in the elderly)
 - Individual is already a “host” (e.g., some pneumococcal strains; varicella zoster virus where herpes zoster (shingles) can occur later in life due to reactivation of latent infection that follows primary varicella (chickenpox) infection)
 - When a vaccination program is demonstrated to be cost-effective, and a dynamic model would only serve to reinforce this conclusion by accounting for infections prevented through indirect protection or secondary transmission
 - When there are epidemiological or modelling data available that will allow estimation of the magnitude of community immunity or secondary transmission in the same or very similar setting

Highlights:

Chapter 8. Modelling

- Consider other model attributes:
 - Deterministic or stochastic
 - Aggregate level or individual level
 - Open or closed population

Consult published schematic diagrams to determine dynamic vs. static model



Left: Jit M., Brisson M. *Pharmacoeconomics*. 2011; 29(5): 371-86.

Right: WHO Guide for Standardization of Economic Evaluations of Immunization Programs: 2nd Ed. 2019.

Guideline statements: Chapter 14. Equity

1. **Researchers and decision-makers should work together** to establish which **equity dimensions and goals** should be included in the economic evaluation of the vaccination program being considered. Equity should be considered in the context of NACI's Ethics, Equity, Feasibility, and Acceptability (EEFA) framework.
2. Analyses that incorporate relevant equity concerns should accompany the reference case analysis (e.g., distributional cost-effectiveness analysis, extended cost-effectiveness analysis, or other emerging methods) and presented alongside the reference case.

1. Improving equity in access
2. Improving equity in uptake
3. Improving equity in health benefit related to health conditions addressed by the vaccination program
4. Reducing lifetime health inequities between groups
5. Reducing overall inequities (i.e., health and non-health related) between groups

Reference case [1]

Section	Guidance
Decision Problem	Specify the details of 1) the interventions to be compared; 2) the setting(s) in which they are to be compared; 3) the type of evaluation being conducted; 4) the perspectives from which the analysis is being carried out; 5) the costs and outcomes to be quantified in the analysis; 6) the time horizon over which the analysis is to be carried out; 7) and the population(s) for the evaluation.
Types of Evaluations	Conduct a cost-utility analysis (CUA) capturing health outcomes in terms of quality-adjusted life-years (QALYs).
Study Populations	Identify the population(s) in which the vaccination program will be used, and, when applicable, any populations that might experience externalities resulting from the vaccination program. Stratify analyses and report by subgroups when heterogeneities between groups of individuals may affect the results of the economic evaluation.
Comparators	Compare all relevant interventions, including other vaccination programs, screening interventions, medical and non-medical preventive interventions, and treatment-based approaches presently used in a Canadian context.
Perspective	Conduct two reference case analyses, one from the publicly funded health system perspective and one from the societal perspective.
Time Horizon	Select a time horizon that is long enough to capture all relevant differences in the future costs and outcomes associated with the interventions being compared.
Discounting	Discount costs and outcomes at a rate of 1.5% per year.
Measurement and Valuation of Health	Identify, measure, and value all relevant health outcomes based on the perspectives of the publicly funded health system and society. Use health preferences that reflect the general Canadian population. Obtain health preferences from an indirect method of measurement that is based on a generic classification system.
Resource Use and Costs	Identify, measure, and value all relevant resources and costs based on the perspective of the i) publicly funded health system, and ii) society. Estimate Canadian resources and costs using data that reflect the jurisdiction(s) of interest.

Reference case [2]

Analysis	<p>Derive expected values of costs and outcomes for both the publicly funded health system perspective and the societal perspective for each intervention through probabilistic analysis, incorporating potential correlation among parameters, whenever possible.</p> <p>Where distinct subgroups are identified within the study population, stratify analyses and report by subgroups.</p> <p>Calculate incremental costs, incremental effectiveness, and incremental cost-effectiveness ratios (ICERs) for both the publicly funded health system and societal perspective analyses. For evaluations with more than two comparators, calculate ICERs sequentially.</p>
Uncertainty	<p>Address methodological uncertainty by comparing the reference case results to those from a non-reference case analysis.</p> <p>Summarize decision uncertainty, using cost-effectiveness acceptability curves (CEACs) and cost-effectiveness acceptability frontiers (CEAFs), where possible.</p> <p>Use scenario analysis to address structural uncertainty.</p> <p>If a value-of-information analysis is undertaken, summarize the value of additional information using the expected value of perfect parameter information and the population expected value of perfect parameter information.</p>
Equity	<p>Consider whether there are inequities experienced by specific groups that could be improved by the vaccination program.</p> <p>Equity should be explored using methods such as distributional cost-effectiveness analysis and extended cost-effectiveness analysis. Any additional analyses should accompany the reference case analyses when applicable.</p>

Application and next steps

- To be used by NACI Secretariat for workplan items that require model-based economic evaluations
- Encourage use among health economists and mathematical modellers in academia, PTs, industry, etc.
 - NACI has a mechanism for accepting models for review as part of a multi-model comparison
- Next steps:
 - Worked example
 - Interpretation guide for decision-makers
 - List of commonly used societal costs and consequences
- Triggers for future revisions:
 - Methodological developments in the field of health economics (e.g., updates to CADTH guidelines); and/or
 - Identification of areas requiring updated guidance following periodic reviews by the NACI Secretariat

Acknowledgements

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Access Online



Guidelines
English



Guidelines
French

NACI Home Page > Methods and Process

SUPPLEMENTARY MATERIAL

Glossary

- **Quality-adjusted life-years (QALYs):** summary measure combining quality of life and in quantity of life
- **Cost-utility analysis (CUA) vs. cost-effectiveness analysis (CEA) vs. cost-benefit analysis (CBA) vs. cost-consequence analysis:** comparison of costs and consequences between interventions, where
 - consequences are expressed as QALYs (CUA)
 - consequences are expressed as natural units (CEA)
 - consequences are expressed in monetary terms (CBA)
 - costs and consequences are catalogued and disaggregated (CCA)
- **Incremental Cost-Effectiveness Ratio (ICER):** summary measure calculated by dividing the difference in total costs (incremental cost) by the difference in the chosen measure of health outcome or effect (incremental effect)
- **Reference case:** standard set of modelling assumptions

Impact Inventory [1]

Area of Impact	Definitions/Examples	Included in Reference Case?		Comments
		Publicly funded health system perspective	Societal perspective	
<i>Health</i>				
Health outcomes	Individual health outcomes for persons intended for vaccination			
	Mortality	<input type="checkbox"/>	<input type="checkbox"/>	
	Health-related quality of life	<input type="checkbox"/>	<input type="checkbox"/>	
	Safety (i.e., adverse events)	<input type="checkbox"/>	<input type="checkbox"/>	
	Health impacts not captured by QALYs	<input type="checkbox"/>	<input type="checkbox"/>	
	Individual health outcomes for informal caregivers			
	Health-related quality of life	<input type="checkbox"/>	<input type="checkbox"/>	
	Population health outcomes			
	Incidence of infection and disease in vaccinated and unvaccinated individuals	<input type="checkbox"/>	<input type="checkbox"/>	
	Changes in age distribution of individuals who develop infection and disease	<input type="checkbox"/>	<input type="checkbox"/>	
	Emergence of new diseases related to variations of the pathogen (i.e., serotypes, serogroups, strains) or unrelated pathogens that may replace the one(s) targeted by the vaccine	<input type="checkbox"/>	<input type="checkbox"/>	
	Disease eradication	<input type="checkbox"/>	<input type="checkbox"/>	

Impact Inventory [2]

Publicly funded health system costs	Healthcare costs			
	Publicly funded healthcare services (e.g., physician visits, diagnostic tests, drug treatment where applicable, hospitalization, formal caregiving, ^a rehabilitation in a facility or at home, ^a home care, ^a long-term care in nursing homes ^a)	<input type="checkbox"/>	<input type="checkbox"/>	
	Future related and unrelated healthcare costs	<input type="checkbox"/>	<input type="checkbox"/>	
	Public Health costs			
	Program-related costs (e.g., implementation, delivery and recurrent costs including Public Health campaigns and health promotion activities; transaction costs related to introduction of new vaccines or switching between vaccines; costs related to screening, diagnosis, and treatment of disease; epidemiological surveillance, contact tracing, investigation and management of outbreaks)	<input type="checkbox"/>	<input type="checkbox"/>	
	Intervention-related costs (e.g., cost of vaccine doses, distribution such as transportation and cold storage, administration including personnel, wastage and ancillary supplies)	<input type="checkbox"/>	<input type="checkbox"/>	
Healthcare costs NOT funded by the health system	Prescription medications (in some cases)	N/A	<input type="checkbox"/>	
	Formal caregiver services, ^a rehabilitation in a facility or at home, ^a home care, ^a long-term care in nursing homes ^a (in some cases)	N/A	<input type="checkbox"/>	
	Miscellaneous out-of-pocket costs (e.g., non-prescription medications)	N/A	<input type="checkbox"/>	
	Ancillary costs (e.g., private insurance copayments, dental care, vision care, assistive devices, physiotherapy, etc.)	N/A	<input type="checkbox"/>	

Impact Inventory [3]

<i>Non-Health</i>					
Direct out-of-pocket costs	Transportation costs	N/A	<input type="checkbox"/>		
	Accommodation costs	N/A	<input type="checkbox"/>		
Losses in productivity	Paid work				
	Time off work resulting from vaccine administration, treatment, illness, disability, or death	N/A	<input type="checkbox"/>		
	Presenteeism	N/A	<input type="checkbox"/>		
	Lifetime productivity consequences of childhood disease	N/A	<input type="checkbox"/>		
	Unpaid work				
	Time off work in informal labour market (e.g., volunteering, helping, mentoring) resulting from vaccine administration, treatment, illness, disability, or death	N/A	<input type="checkbox"/>		
	Uncompensated household production (e.g., cooking, cleaning, shopping, raising children, other tasks related to household management)	N/A	<input type="checkbox"/>		
	Informal caregiver productivity				
	Time off work resulting from caring for sick individuals, accompanying individuals to vaccine appointments	N/A	<input type="checkbox"/>		
	Caregiver presenteeism	N/A	<input type="checkbox"/>		
	Macroeconomic consequences				
	Labour supply shocks, widespread business closures	N/A	<input type="checkbox"/>		
	Consumption	Future individual non-medical consumption	N/A	<input type="checkbox"/>	
		Changes in household consumption	N/A	<input type="checkbox"/>	
Health impacts of consumption (e.g., associated with job loss)		N/A	<input type="checkbox"/>		

Impact Inventory [4]

Education	Level of educational achievement <u>as a result of</u> physical health, mental health, and cognition	N/A	<input type="checkbox"/>	
	Costs of special education needs <u>as a result of</u> illness/disability	N/A	<input type="checkbox"/>	
	Disruptions to learning outcomes (e.g., <u>as a result of</u> school-based vaccine delivery, pediatric disease and disability, or death/disability of a close family member)	N/A	<input type="checkbox"/>	
Social services and community services	Social services and community services (e.g., disability support, programs to improve access to vaccination programs for adults)	N/A	<input type="checkbox"/>	
	Child and Youth Services (e.g., awareness programs, family respite, programs to improve access to vaccination programs for children and youth)	N/A	<input type="checkbox"/>	
Environment	Environmental impact of vaccination programs and comparators from manufacturing, distribution, and implementation (e.g., antibiotic use)	N/A	<input type="checkbox"/>	
	Food and non-food waste	N/A	<input type="checkbox"/>	
	Carbon consumption	N/A	<input type="checkbox"/>	
Other Areas	Consider areas such as housing when applicable	N/A	<input type="checkbox"/>	

GUIDELINE STATEMENTS

1. Decision Problem

- 1.1 “The decision problem addressed by the economic evaluation should be clearly stated.” [CADTH Guideline Statement]
- 1.2 The decision problem statement should provide a comprehensive specification of the interventions to be compared, the setting(s) in which they are to be delivered, the perspectives of the evaluation, which costs and outcomes are to be considered (including externalities), the time horizon, and the population(s) for the evaluation (including populations directly and indirectly affected by the vaccination program). [CADTH Guideline Statement with amendment]

2. Types of Evaluations

- 2.1 In the reference cases, the economic evaluation should be a cost-utility analysis (CUA) with outcomes expressed as quality-adjusted life-years (QALYs). Any departure from this approach should be clearly justified. [CADTH Guideline Statement with amendment]
- 2.2 A cost-benefit analysis (CBA) may be used alongside the reference case CUAs in situations where the vaccination program may be compared to a non-health intervention.

3. Study Populations

- 3.1 Researchers should identify the population(s) intended for the vaccination program, the population(s) at risk for the disease of interest, and any populations that may be indirectly affected by the vaccination program, either through externalities or spillover effects.

- 3.2 Researchers should present an overall analysis that includes the costs and outcomes for all affected populations. When relevant, researchers should also summarize the results separately for each affected group (e.g., intended population, population experiencing externalities or spillover effects) that was included in the overall analysis.

- 3.3 Where there are factors that could lead to differences in costs and outcomes related to the vaccination program across affected populations, researchers should stratify analyses and report by subgroups. These factors could include demographic factors, behavioural factors, disease-related factors, and effectiveness of the vaccine or comparator(s).

4. Comparators

- 4.1 The choice of comparator(s) should be related to the scope of the decision problem. As such, the comparators should reflect the population(s) intended for the vaccination program and the jurisdiction for which the decision is being made. [CADTH Guideline Statement with amendment]

- 4.2 Researchers should consider both preventive and treatment-based approaches when selecting comparators for economic evaluations of vaccination programs. Preventive interventions could include vaccine-based measures, screening programs, preventive medication-based interventions, and preventive non-medical interventions.

5. Perspectives

- 5.1 Two reference case analyses should be presented as part of the economic evaluation of vaccination programs: one conducted from the publicly funded health system perspective, and the other conducted from the societal perspective.

- 5.2 “Both costs and outcomes should be consistent with the stated perspective.” [CADTH Guideline Statement]

6. Time Horizon

- 6.1 In the reference cases, the time horizon should be long enough to capture all relevant differences in the future costs and outcomes associated with the interventions being compared. Thus, the time horizon should be based on the infectious disease and the likely impact of the intervention. [CADTH Guideline Statement with amendment]

- 6.2 Researchers should justify their choice of time horizon. Where it spans a long period of time (i.e., multiple decades), researchers should report incremental costs, incremental effects and incremental cost-effectiveness ratio (ICER) estimates from various time points throughout the time horizon.

7. Discounting

- 7.1 In the reference cases, costs and outcomes that occur beyond one year should be discounted to present values at a rate of 1.5% per year. [CADTH Guideline Statement with amendment]

- 7.2 “The impact of uncertainty in the discount rate should be assessed by comparing the results of the reference cases to those from non-reference case analyses, using discount rates of 0% and 3% per year.” [CADTH Guideline Statement]

8. Modelling

- 8.1 “Model conceptualization and development should address the decision problem.” [CADTH Guideline Statement]
- 8.2 Researchers should consider any existing well-constructed and validated models that appropriately capture the clinical or care pathway for the infectious disease of interest when conceptualizing their model. [CADTH Guideline Statement with amendment]
- 8.3 The model structure should reflect the natural history of disease, the clinical or care pathway, and account for susceptibility, infectiousness, immunity, morbidity and mortality related to the infection.
- 8.4 Relevant behavioural dynamics including contact patterns between individuals and behaviours related to infection prevention and control should be incorporated into the model where appropriate.
 - 8.5 Dynamic models should be considered in economic evaluations of vaccines that are associated with externalities such as prevention of human-to-human transmission of infection and age-shifting of disease.
 - 8.6 Other model attributes should be considered in the context of the decision problem such as whether the model is deterministic or stochastic, whether the population is modelled at the aggregate level or individual level, and whether the population is open or closed.
 - 8.7 Researchers should transparently report on model calibration and validation processes that were undertaken and on their results.

9. Effectiveness

- 9.1 A comprehensive search of the available data sources should be conducted to inform the estimates of effectiveness and harms associated with the interventions. Report the included studies and methods used to select or combine the data. Researchers should assess sources used for effectiveness based on their fitness for purpose, credibility, and consistency. Describe the trade-offs among these criteria and provide justification for the selected source(s). [CADTH Guideline Statement with amendment]
- 9.2 The following criteria should be considered when assessing estimates of vaccine effectiveness: vaccine effectiveness by dose and time (e.g., waning protection); pathogen variation-specific effectiveness (i.e., serotypes, serogroups, strains); and geographic and vaccine recipient factors that may affect effectiveness.
- 9.3 Researchers should ensure that immune biomarkers used as surrogate outcomes in studies of vaccine efficacy or effectiveness meet the criteria for correlates of protection.

10. Measurement and Valuation of Health

- 10.1 In both reference cases, the quality-adjusted life year (QALY) should be used as the method for valuing health outcomes.
- 10.2 “Health preferences should reflect the general Canadian population.” [CADTH Guideline Statement]
- 10.3 In the reference cases, researchers should use health preferences obtained from an indirect method of measurement that is based on a generic classification system (e.g., EuroQol 5-Dimensions questionnaire [EQ-5D], Health Utilities Index [HUI], Short Form 6-Dimensions [SF-6D], Child Health Utility 9-Dimensions [CHU9D], Assessment of Quality of Life [AQoL]). Researchers must justify where an indirect method is not used. [CADTH Guideline Statement with amendment]
- 10.4 A comprehensive search of the available data sources should be conducted to inform the health state utility values. Report the included studies and methods used to select or combine the data. Researchers should assess sources used for health state utility values based on their fitness for purpose, credibility, and consistency. Describe the trade-offs among these criteria and provide justification for the selected sources. [CADTH Guideline Statement with amendment]

11. Resource Use and Costs

- 11.1 For each reference case analysis, researchers should systematically identify, measure, value, and report all relevant resources consumed or saved as a result of the delivery or implementation of the vaccination program under consideration.
- 11.2 Where possible, researchers should value the consumption of relevant resources identified for all sectors in monetary terms. In situations where this is not possible, researchers should present the relevant resources that have been identified in the *Impact inventory table for economic evaluations of vaccination strategies* (Appendix I) for consideration by decision-makers.
- 11.3 Resource use, unit prices, and costs should be based on Canadian sources and reflect the jurisdiction(s) of interest (as specified in the decision problem).
[CADTH Guideline Statement with amendment]
 - 11.4 When valuing and monetizing resources, researchers should select data sources that most closely reflect the opportunity cost, given the perspective of the analysis. [CADTH Guideline Statement with amendment]
 - 11.5 A comprehensive search of the available data sources should be conducted to inform the resource use and cost values. Report the included studies and methods used to select or combine the data. Researchers should assess sources used for cost data based on their fitness for purpose, credibility, and consistency. Describe the trade-offs among these criteria and provide justification for the selected sources.

12. Analysis

- 12.1 Incremental costs, incremental effectiveness, incremental cost-effectiveness ratios (ICERs) and, where useful for interpretation, net monetary benefits, or net health benefits, should be calculated for both reference case analyses.
- 12.2 “For analyses with more than two interventions, a sequential analysis of cost-effectiveness should be conducted following standard rules for estimating ICERs, including the exclusion of dominated interventions.” [CADTH Guideline Statement]
- 12.3 The expected values of costs and outcomes, where possible, should be generated probabilistically to reflect the overall uncertainty in the model parameters.

13. Uncertainty

- 13.1 Researchers should address parameter uncertainty using a probabilistic reference case analysis, where possible, as well as deterministic sensitivity analyses.

- 13.2 “Methodological uncertainty should be explored by comparing the reference case results to those from a non-reference case analysis that deviates from the recommended methods in order to examine the impact of methodological differences.” [CADTH Guideline Statement]

- 13.3 Cost-effectiveness acceptability curves (CEACs) and cost-effectiveness acceptability frontiers (CEAFs) should be used to represent the uncertainty in the estimates of costs and outcomes when these estimates have been generated probabilistically. [CADTH Guideline Statement with amendment]

- 13.4 When the decision problem includes the option of commissioning or conducting future research, value-of-information analysis may be helpful to characterize the value of these options and design future research, and may be included in the reference case analyses. [CADTH Guideline Statement with amendment]

- 13.5 Scenario analyses should be used to assess structural uncertainty. [CADTH Guideline Statement with amendment]

14. Equity

- 14.1 Researchers and decision-makers should work together to establish which equity dimensions and goals should be included in the economic evaluation of the vaccination program considered. Equity dimensions should be considered in the context of NACI's Ethics, Equity, Feasibility, and Acceptability (EEFA) framework.

- 14.2 Analyses that incorporate relevant equity concerns should accompany the reference case analyses (e.g., distributional cost-effectiveness analysis, extended cost-effectiveness analysis, or other emerging methods), and presented alongside the reference cases.

15. Reporting

- 15.1 “The economic evaluation should be reported in a transparent and detailed manner with enough information to enable the reader or user (e.g., decision-maker) to critically assess the evaluation.” [CADTH Guideline Statement with amendment]
- 15.2 “A summary of the evaluation written in non-technical language should be included.” [CADTH Guideline Statement]
- 15.3 “Results of the economic evaluation should be presented in graphical or visual form, in addition to tabular presentation.” [CADTH Guideline Statement]
- 15.4 “Details and/ or documents describing quality assurance processes and results for the economic evaluation should be provided. An electronic copy of the model should be made available for review with accompanying documentation in adequate detail to facilitate understanding of the model, what it does, and how it works.” [CADTH Guideline Statement]
- 15.5 “Funding and reporting relationships for the evaluation should be described, and any conflicts of interest disclosed.” [CADTH Guideline Statement]
- 15.6 Researchers should use NACI’s Guidelines for Reporting Economic Evaluations of Vaccination Programs in Canada (supplemental document) and complete the *Impact inventory table for economic evaluations of vaccination strategies* (Appendix 1).