National Advisory Committee on Immunization (NACI)

Process for Incorporating Economic Evidence into Federal Vaccine Recommendations Stakeholder Consultation

PROTECTING AND EMPOWERING CANADIANS TO IMPROVE THEIR HEALTH

Public Health Agency of Canada | Agence de la santé publique du Canada

Canada

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I. INTRODUCTION

The National Advisory Committee on Immunization (NACI) provides the Public Health Agency of Canada (PHAC) with ongoing and timely medical, scientific, and public health advice relating to immunization.

In addition to safety, efficacy, effectiveness, immunogenicity, and burden of illness, PHAC has expanded the mandate of NACI to include the systematic consideration of programmatic factors in developing evidence-based recommendations to facilitate timely decision-making for publicly funded vaccine programs at provincial and territorial levels. The additional factors to be systematically considered by NACI include: economics, ethics, equity, feasibility, and acceptability.

The NACI Economic Process outlines the process of determining when and how NACI incorporates economic evidence into its recommendations.

NACI is now seeking input on the draft Economic Process from stakeholders, including but not limited to:

- Provinces and territories
- The Canadian Immunization Committee
- Vaccine Safety Working Group
- The Council of the Chief Medical Officers of Health
- National Immunization Technical Advisory Groups (NITAGs)
- Provincial Immunization Technical Advisory Group (PITAGs)
- Health Technology Assessment Agencies
- Researchers
- Policy Makers
- Industry
- Other interested parties

The questionnaire has been prepared to make it easier for you to engage your colleagues in reviewing the Economic Process and convey your overall comments and position. The questionnaire addresses each section of the Economic Process and poses key questions for your feedback. All feedback received will be considered by the NACI Secretariat in their final review of the Economic Process before it is tabled for final approval by NACI and made publicly available.

The due date for this questionnaire can be found online.

If you have any questions, please contact the NACI Secretariat at phac.naci-ccni.aspc@canada.ca.

You must submit your answers online for your responses to be shared with the NACI Secretariat.

II. PRIVACY NOTICE

The personal information you provide to the Public Health Agency of Canada (PHAC) will be collected by the National Advisory Committee on Immunization under section 3 the Public Health Agency of Canada Act and handled in accordance with the Privacy Act.

Why are we collecting your personal information?

This personal information is being collected in order to facilitate following up with respondents should clarification be required for any responses given. Respondents will not be contacted for any other purpose and only if clarification is required.

Will we use or share your personal information for any other reason?

Except where required by law, your personal information will never be used for any other purpose other than the identified purpose.

What happens if you don't want to provide your personal information?

Should you choose to not provide your personal information, we will not be able to contact you in order to request response clarification if necessary. As such, your responses may not be interpreted as intended.

What are your rights?

You have the right to access and request a correction and/or notation to your personal information. You also have a right to complain to the Privacy Commissioner of Canada if you feel your personal information has been handled improperly. For more information about these rights, or about how we handle your personal information, you may contact us at phac.naci-ccni.aspc@canada.ca.

For more information:

The collection of your personal information is described in Info Source at infosource.gc.ca. Refer to the PHAC class of personal information Public Opinions.

III. INSTRUCTIONS FOR COMPLETING THE CONSULTATION

This consultation is organized into ten (10) modules:

- **Module A – Process for Incorporating Economic Evidence into Federal Vaccine Recommendations (Required)**
- **Module B – Supporting Tool #1: Prioritization Guide to Economic Evidence (Required)**
- Module C – Supporting Tool #2: Submission Criteria for Model-based Economic Evaluations (Optional)
- Module D – Supporting Tool #3: Presentation Template for Proposed Economic Evidence (Optional)
- Module E – Supporting Tool #4: Interim Guidelines for Economic Evaluation of Vaccines: Canada (Optional)
- Module F – Supporting Tool #5: Standard Operating Procedure on Reporting Economic Evaluations Of Vaccines (Optional)
- Module G – Supporting Tool #6: Standard Operating Procedure on Reporting Systematic Reviews of Economic Evaluations of Vaccines (Optional)
- Module H – Supporting Tool #7: Presentation Template for Presenting Economic Evaluations (Optional)
- Module I – Supporting Tool #8: Presentation Template for Presenting Systematic Reviews (Optional)
- **Module J – General Feedback (Required)**

Each module contains a summary of that particular process and its purpose.

Three (3) modules are required (modules A, B, and J) and the remaining modules are optional.

While your input is preferred for all modules, if you are unable to complete the entire consultation, we request that you focus your input on the modules that are most relevant to your organization or where you have the most expertise. Provide your responses in point form.

For provincial and territorial jurisdictions, federal/ provincial/ territorial groups, and other organizations (including industry), return only one completed consultation that summarizes your organization's position on the content of the draft Economic Process. Individuals are welcome to submit feedback as well.

Keep in mind that the final draft of the Economic Process will go through a comprehensive language edit, therefore, editorial comments are not necessary unless they are technically relevant or provide important context.

If you do not complete the consultation in one session, you may return to continue where you left off by accessing the consultation using the same computer or device you began the consultation with. Your responses should be saved up to the last page you clicked the forward arrow on.

You must press "Submit" at the end of the online questionnaire, for your responses to be shared with the NACI Secretariat.

IV. DEMOGRAPHIC QUESTIONS

1. Are you providing feedback on behalf of your organization?

- Yes
- No

a. What is the name of your organization?

b. Which of the following categories best describes your organization?

- National Immunization Technical Advisory Group (NITAG)
- Provincial Immunization Technical Advisory Group (PITAG)
- Health technology assessment agency
- Professional organization
- Academia
- Canadian provincial or territorial government
- Other level of Canadian government
- Government outside of Canada
- Consulting firm
- Industry with a vaccine product marketed in Canada/aiming to market in Canada
- Other, please specify:

2. Which of the following categories best describes your occupation?

- Health economist
- Epidemiologist/Data analyst
- Policy Analyst
- Healthcare provider
- Program evaluator
- Health promoter
- Supervisor/Manager
- Other, please specify:

3. Are you and/or your organization a direct end user of NACI recommendations?

- o Yes
- o No

a. If yes, will you and/or your organization directly use NACI's economic evidence?

- o Yes
- o No

b. If yes, for what purpose(s) will you and/or your organization use the economic evidence produced by NACI?

4. Please provide the following contact information. This information is optional and will only be used by the Secretariat to NACI to contact you if clarification is required.

a) Name:

b) Email:

c) Telephone:

V CONSULTATION QUESTIONS

V.1 Module A — Process for Incorporating Economic Evidence into Federal Vaccine Recommendations (Required)

The *Process* provides information related to the types of economic evidence commonly used for decision-making, the NACI workplan, and a high level outline of how NACI proposes to incorporate economic evidence into its vaccine recommendations.

5. Please indicate the extent to which you agree with the following statement: The Overview of Economic Process is clear.

- Strongly agree
- Somewhat agree
- Neither agree nor disagree
- Somewhat disagree
- Strongly disagree

6. In what ways could the Overview of Economic Process be changed to be clearer?

Economic Process in Detail

The *Economic Process in Detail* describes each step of the process and is comprised of a series of supporting tools to facilitate the Economic Process. These tools together provide guidance on priority setting, guidance for submissions of economic evidence, as well as standard methods for economic evidence, and the structure for reporting and presenting this work.

Supporting Tools

Tool #1. Prioritization Guide to Economic Evidence
Tool #2. Submission Criteria for Model-based Economic Evaluations
Tool #3. Presentation Template for Proposed Economic Evidence
Tool #4. Interim Guidelines for Economic Evaluation of Vaccines: Canada
Tool #5. Standard Operating Procedure on Reporting Economic Evaluations Of Vaccines
Tool #6. Standard Operating Procedure on Reporting Systematic Reviews of Economic Evaluations of Vaccines
Tool #7. Presentation Template for Presenting Economic Evaluations
Tool #8. Presentation Template for Presenting Systematic Reviews of Economic Evaluations

V.2 Module B — Supporting Tool #1: Prioritization Guide to Economic Evidence (Required)

The ***Supporting Tool #1: Prioritization Guide to Economic Evidence*** is a qualitative tool used to assess the need and urgency for economic analyses and to guide NACI to determine if economic evidence is required for a workplan item (i.e. the planned work to be conducted within given fiscal year, determined by factors including emerging public health needs, new vaccines or indications, provincial or territorial concerns).

7. Please indicate the extent to which you agree with the following statements about the Prioritization Guide to Economic Evidence.

	Strongly agree	Somewhat agree	Neither agree or disagree	Somewhat disagree	Strongly disagree
a) The criteria (e.g., burden of disease, economic considerations) identified in the "Assess the need for economic evidence" table are complete.					
b) The sub-criteria in the "Assess the need for economic evidence" table sufficiently evaluate the associated criterion.					
c) Overall, the "Assess the need for economic evidence" table adequately assesses the need for economic analyses.					
d) The sub-criteria (e.g., availability of vaccine, P/T programmatic concerns) identified in the "Assess the urgency for economic evidence" table are complete.					
e) The sub-criteria identified in the "Assess the urgency for economic evidence" table sufficiently evaluate the associated criterion.					
f) Overall, the elements of the "Assess the urgency for economic evidence" table adequately assess the urgency for economic analyses.					

8. In what ways could the "Assess the need for economic evidence" table be changed to more adequately assess the need for economic analyses?

9. In what ways could the "Assess the urgency for economic evidence" table be changed to more adequately assess the urgency for economic analyses?

Modules C to I (Optional)

The following modules (C-I) are optional. Each module contains a summary of the particular document and its purpose.

You may either complete the module or skip to the next. The final module (J) is required for all respondents.

V.3 Module C — Supporting Tool #2: Submission Criteria for Model-based Economic Evaluations (Optional)

The purpose of the ***Supporting Tool #2: Submission Criteria for Model-based Economic Evaluations*** is to outline the mandatory standards for submitting an economic model to NACI.

10. Please indicate the extent to which you agree with the following statements about the *Submission Criteria for Model-based Economic Evaluations.*

	Strongly agree	Somewhat agree	Neither agree or disagree	Somewhat disagree	Strongly disagree
a) The submission criteria for model-based economic evaluations are clear.					
b) The submission criteria for model-based economic evaluations are comprehensive.					
c) The submission criteria for model-based economic evaluations are feasible.					

11. In what ways could the submission criteria be changed to be more clear, comprehensive, and/or feasible?

V.4 Module D — Supporting Tool #3: Presentation Template for Proposed Economic Evidence (Optional)

This tool will be used to present the proposed approach for gathering economic evidence to NACI.

12. Please provide any comments (e.g. relevance, clarity, comprehensiveness, format) on the *Supporting Tool #3: Presentation Template for Proposed Economic Evidence*.

V.5 Module E — Supporting Tool #4: Interim Guidelines for Economic Evaluation of Vaccines: Canada (Optional)

The purpose of the tool is to inform best practices for conducting de novo economic evaluations of vaccines in Canada.

13. Please provide any comments (e.g. relevance, clarity, comprehensiveness, format) on the Supporting Tool #4: Interim Guidelines for Economic Evaluation of Vaccines: Canada.

V.6 Module F — Supporting Tool #5: Standard Operating Procedure on Reporting Economic Evaluations of Vaccines (Optional)

The purpose of the tool is to provide guidance on how to report economic evaluations for NACI.

14. Please provide any comments (e.g. relevance, clarity, comprehensiveness, format) on the *Supporting Tool #5: Standard Operating Procedure on Reporting Economic Evaluations Of Vaccines*.

V.7 Module G — Supporting Tool #6: Standard Operating Procedure on Reporting Systematic Reviews of Economic Evaluations of Vaccines (Optional)

The purpose of the SOP is to provide guidance on how to conduct and report systematic reviews of economic evaluations to NACI.

15. Please provide any comments (e.g. relevance, clarity, comprehensiveness, format) on the *Supporting Tool #6: Standard Operating Procedure on Reporting Systematic Reviews of Economic Evaluations of Vaccines*.

V.8 Module H— Supporting Tool #7: Presentation Template for Presenting Economic Evaluations (Optional)

The purpose of the tool is to provide a template to ensure economic data presented to NACI are uniform in presentation, understandable, and of the highest quality.

16. Please provide any comments (e.g. relevance, clarity, comprehensiveness, format) on the *Supporting Tool #7: Presentation Template for Presenting Economic Evaluations*.

V.9 Module I— Supporting Tool #8: Presentation Template for Presenting Systematic Reviews (Optional)

The purpose of the tool is to ensure economic data presented to NACI are uniform in presentation, understandable, and of the highest quality.

17. Please provide any comments (e.g. relevance, clarity, comprehensiveness, format) on the *Supporting Tool #8: Presentation Template for Presenting Systematic Reviews*.

V.10 Module J — General Feedback (Required)

This section of the consultation is a space for overall comments on the Economic Process and its supporting tools.

18. Please indicate the extent to which you agree with the following statements:

	Strongly agree	Somewhat agree	Neither agree or disagree	Somewhat disagree	Strongly disagree
a) The Economic Process and supporting tools clearly describe an appropriate process for economic analyses conducted by NACI.					
b) The Economic Process meets my/my organization's need(s).					

19. Are there any information gaps or missing steps you see in the Economic Process? If yes, please elaborate.

20. Are there any additional tools or checklists that you would like to suggest to inform or include in the Economic Process? What information gap(s) would including this tool address? If available, please provide the tool as an electronic copy or a hyperlink on the online questionnaire.

21. Please provide any general comments on the Economic Process.

Thank You

In order for your feedback to be considered, you must enter your answers in the online questionnaire and click “Submit”.

Thank you for taking the time to complete this consultation.

Health Canada and the Public Health Agency of Canada have designed a new stakeholder registry that will help you stay informed of the latest consultations and participate in our engagement activities.

Link is available through the online questionnaire.

VI. PROCESS FOR INCORPORATING ECONOMIC EVIDENCE INTO FEDERAL VACCINE RECOMMENDATIONS

Stakeholder consultation feedback

The National Advisory Committee on Immunization (NACI) provides the Public Health Agency of Canada (PHAC) with ongoing and timely medical, scientific, and public health advice relating to immunization.

In addition to safety, efficacy, effectiveness, immunogenicity, and burden of illness, PHAC has expanded the mandate of NACI to include the systematic consideration of programmatic factors in developing evidence-based recommendations to facilitate timely decision-making for publicly funded vaccine programs at provincial and territorial levels. The additional factors to be systematically considered by NACI include: economics, ethics, equity, feasibility, and acceptability.

The NACI economic process outlines the process of determining when and how NACI incorporates economic evidence into its recommendations.

NACI is now seeking input on the draft economic process from stakeholders, including but not limited to:

- Provinces and territories
- The Canadian Immunization Committee (CIC)
- Vaccine Safety Working Group
- The Council of the Chief Medical Officers of Health
- National Immunization Technical Advisory Groups (NITAGs)
- Provincial Immunization Technical Advisory Group (PITAGs)
- Health Technology Assessment (HTA) agencies
- Researchers
- Policy makers
- Industry
- Other interested parties

The questionnaire has been prepared to make it easier for you to engage your colleagues in reviewing the economic process and convey your overall comments and position. The questionnaire addresses each section of the economic process in modules and poses key questions for your feedback. Modules A, B and J are mandatory, whereas Modules C through I are optional. Further instructions for completing the questionnaire are provided once you click on the button below.

All feedback received will be considered by the NACI Secretariat in their final review of the economic process before it is tabled for final approval through the NACI and made publicly available.

VI.1 Module A – Process for Incorporating Economic Evidence into Federal Vaccine Recommendations

DRAFT Economic Process

Preamble

The National Advisory Committee on Immunization (NACI) provides the Public Health Agency of Canada (PHAC) with ongoing and timely medical, scientific, and public health advice related to immunization. Through the work of working groups and with the support of a secretariat at the Public Health Agency of Canada, NACI makes recommendations on the use of human vaccines that are currently or newly approved in Canada.

Traditionally, NACI reviewed safety, efficacy, immunogenicity, effectiveness and burden of illness. PHAC has recently expanded this mandate to include the systematic consideration of programmatic factors—economics, ethics, equity, feasibility and vaccine acceptability—in developing evidence-based recommendations. This expanded mandate is to facilitate timely decision-making for publicly funded vaccine programs at provincial and territorial levels.

Over the coming years NACI is continuing to refine methodological approaches to include these programmatic factors. NACI statements will include varying degrees of programmatic analyses for public health programs.

The *NACI Economic Process* is a document that outlines when and how NACI incorporates economic evidence for vaccine recommendation. To inform the development of the *Process*, information was gleaned from Canadian and international health technology assessment agencies, the Vaccine Industry Committee (VIC), and other national immunization technical advisory groups (NITAGs) from several countries.

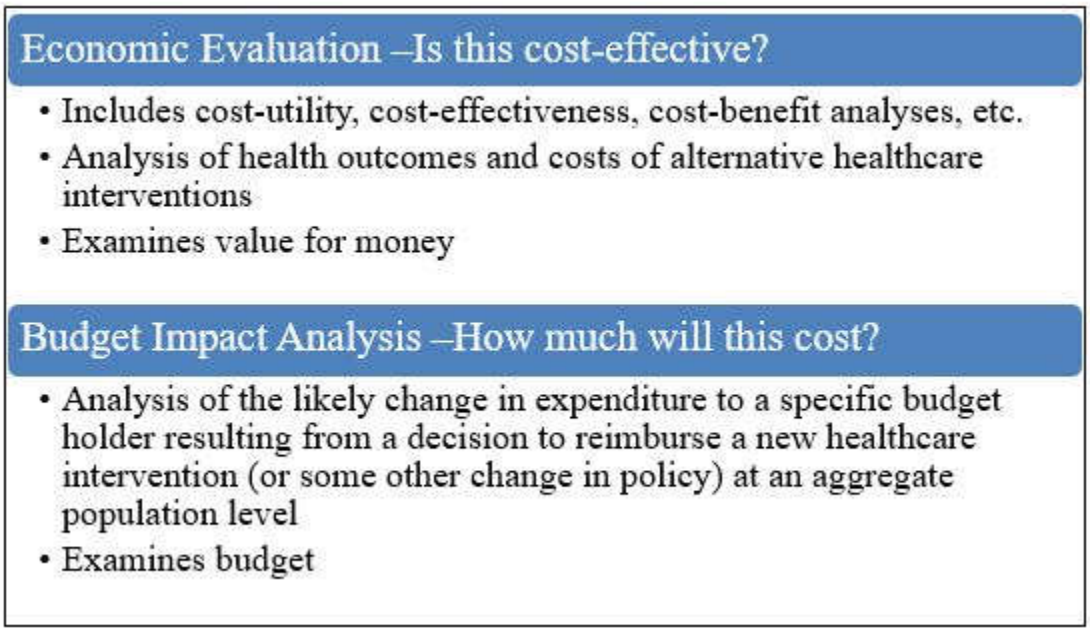
The stakeholder consultation seeks to obtain input from partners and stakeholders to ensure the most accurate and useful product.

Overview of Economic Process

Types of Economic Evidence

Two common types of economic evidence are economic evaluations and budget impact analyses (Figure 1). Systematic reviews (of economic evaluations), which are syntheses of existing cost-utility, cost-effectiveness, cost-benefit analyses, etc., are also increasingly used.

Figure 1. Two types of economic evidence commonly used in decision-making

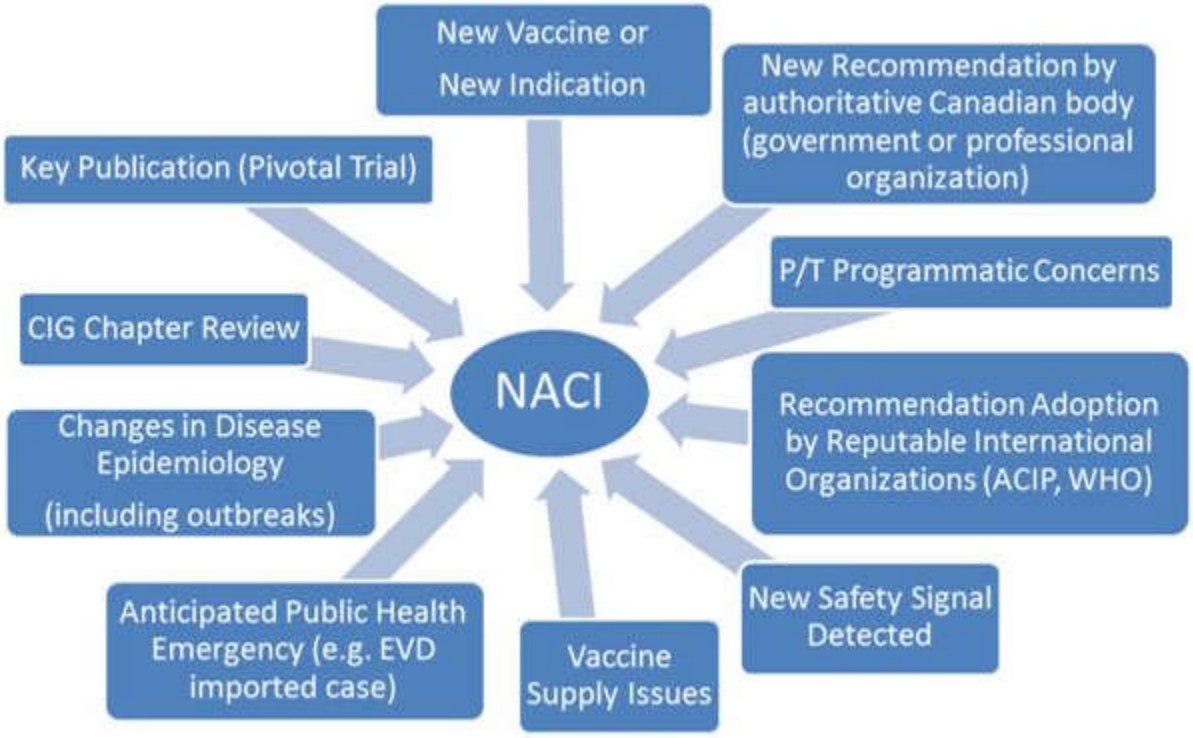


Based on feedback from the provinces and territories (P/Ts) the NACI economic analyses will bring considerations of cost-effectiveness into NACI guidance. Discussions about budget impact analyses will be re-visited by NACI at a later date. Therefore, in the remainder of this document, the term "economic evidence" refers to economic evaluations (de novo economic evaluations and systematic reviews of existing economic evaluations).

NACI Work plan

The NACI work plan consists of projects that have been prioritized for a given fiscal year. These projects will not necessarily be completed within the fiscal year. The work plan may be reassessed based on emerging public health needs. Figure 2 outlines possible triggers that may drive activation of Working Groups (WGs) and the development of new NACI guidance documents, or the adoption of new priorities.

Figure 2. Triggers that may determine the NACI work plan

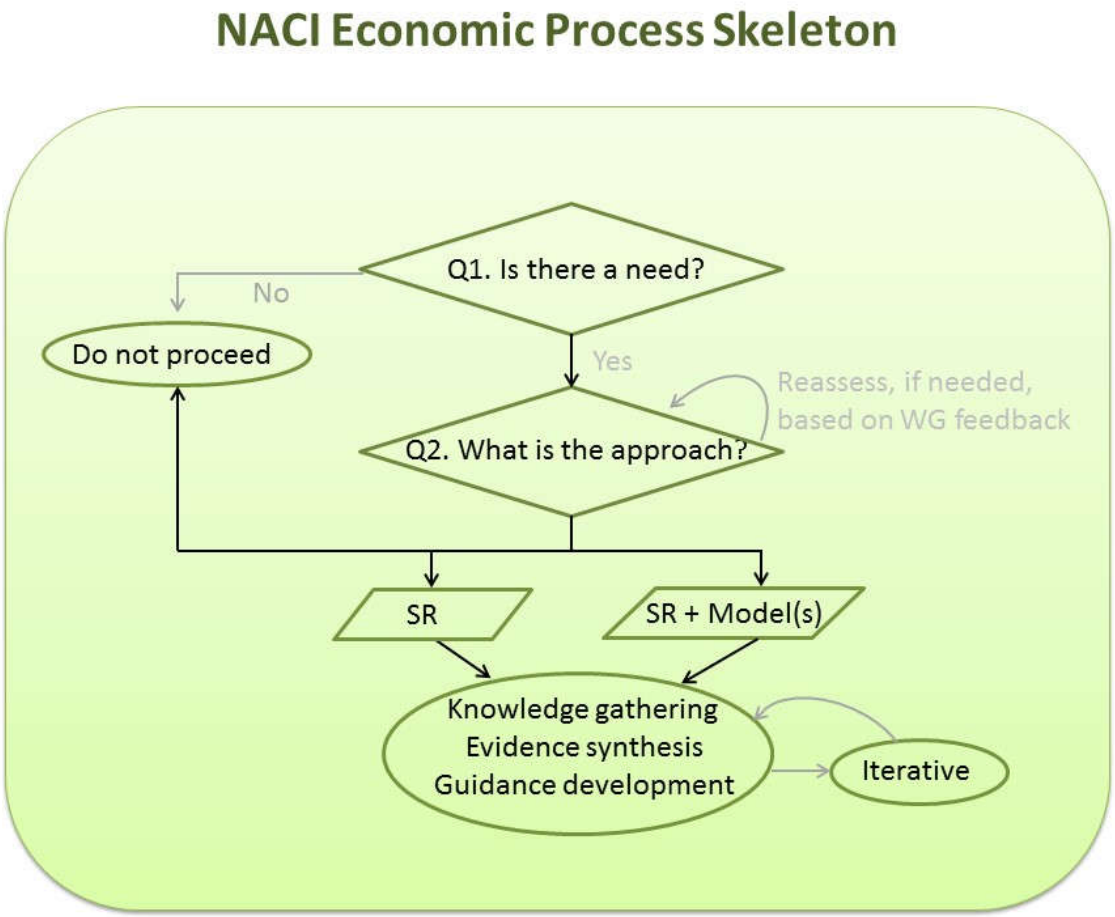


There are several expert WGs that draft products for NACI consideration and voting. WGs are comprised of NACI members and external experts. WGs may require the following evidence to inform NACI guidance:

1. Clinical evidence (including safety, efficacy, immunogenicity, effectiveness and burden of illness)
2. Ethics, Equity, Feasibility, Acceptability (EEFA) considerations
3. Economic evidence

Figure 3 outlines the process of determining when and how NACI incorporates economic evidence into its guidance. Please see each step in the "Economic Process in Detail" section.

Figure 3. Overview of the NACI Economic Process



Abbreviations: Q, question; SR, systematic review ; WG, working group

Economic Process in Detail

The *Economic Process* consists of three basic steps:

- Assessing need
- Determining the approach
- Knowledge gathering, evidence synthesis, guidance development

1. Assessing Need

Once a NACI work plan item has been identified, the first step of the Economic Process is to **determine if economic evidence is needed for NACI to make a vaccine recommendation**.

- The annual work plan is developed through a collaborative process between NACI and the P/Ts. This process consists of a survey and/or discussion with members of NACI and Canadian provinces and territories (e.g. Canadian Immunization Committee (CIC) and/or Council of Chief Medical Officers of Health (CCMOH)). Based on these priorities, a few key work plan items are selected each year for NACI to investigate.

Supporting tool #1: Economic prioritization tool

The *Economic Prioritization Tool* is a qualitative tool to assess need and urgency of generating/ synthesizing economic evidence for each policy question. The assessment is based on epidemiology, safety, economics and social values. There is no quantitative rating scale or weighting of the criteria assessed. Rather, the *Economic Prioritization Tool* is meant to provide structure and guidance to considering the need and urgency for economic evidence. The *Prioritization Tool* will be completed and deliberated upon by the WG Chair/ Vice Chair, the Secretariat (including at least one epidemiologist/ medical specialist, and one health economist), and if needed, additional WG subject matter experts.

- Once the NACI annual work plan has been finalized, the *Economic Prioritization Tool* will be applied to assess need and urgency.

If there is a need identified, then the work plan topic will move forward to the second step of the Economic Process (Section 2). Economic evidence will not be included for a work plan topic that does not have a sufficient need for it.

2. Determining the Approach

The second step of the Economic Process is to **determine the approach for generating economic evidence** for the work plan topic. This step will be informed by an environmental scan of the peer-reviewed literature, grey literature, and expert/ stakeholder input.

Several factors will be considered:

- Type of economic evidence base needed
- Timeliness of issuing NACI guidance
- Operational considerations

Below are three options of "information packages" to make up the economic evidence base for NACI decision-making:

- Systematic review
- Systematic review AND a de novo (i.e., purpose-built) or adapted model-based economic evaluation
- Systematic review AND a multi-model comparison

Note that all three options include a systematic review, where study quality will be appraised and data will be extracted from the included economic evaluations. In the second and third options, an additional de novo (or adapted) model and multi-model comparison will be included as part of the evidence base, respectively. These are described below. Once an approach has been decided upon, a *Presentation Template for Proposed Economic Evidence* is available to outline the rationale.

- **De Novo (or Adapted) Model-Based Economic Evaluation**: This refers to either a de novo (i.e., purpose-built) economic evaluation, or to an existing economic evaluation that will be updated or adapted for NACI's purposes.
    - Based on separate consultations with NACI, P/Ts, and the PHAC Public Health Ethics Consultative Group, an adapted model will not be based on a model developed by industry (i.e., developed by industry employees or by consultants sponsored by industry).

    - When determining which existing economic evaluation to update or adapt, many factors will be considered including: (i) ability to engage with the authors (i.e., willingness of authors to update/ adapt their work for NACI's needs); (ii) relevance of the economic evaluation to NACI needs in terms of the population, intervention, comparator, outcome, applicability (i.e., jurisdiction, recency, data sources); (iii) study quality; (iv) source(s) of study funding and the role of funders.
- **Multi-Model Comparison**: This refers to the comparison of two or more model-based economic evaluations. Model structures, inputs, assumptions and results will be assessed and compared.
    - One of the economic evaluations in a multi-model comparison will be a de novo/ adapted model.
    - The other economic evaluation(s) included may be developed/ funded by others such as academia, government, a recognized funding agency, and industry.
    - Relevant manufacturers will be invited to submit their economic models in the event that NACI seeks to conduct a multi-model comparison. If stakeholders choose to submit their economic model to NACI, please refer to the *Submission Criteria for Model-based Economic Evaluations*. Industry stakeholders can stay informed about NACI work plan topics on the NACI website

Supporting tool #2: Submission Criteria for Model-based Economic Evaluations

The *Submission Criteria for Model-based Economic Evaluations* outline the mandatory standards before submitting an economic model to NACI. The criteria include how to conduct and report the economic evaluation, software and run time requirements, as well as the submission of the model code.

Supporting tool #3: Submission Criteria for Model-based Economic Evaluations

The *Presentation Template for Proposed Economic Evidence* outlines the rationale for the approach proposed. Specifically, it outlines the results of the *Economic Prioritization Tool*, results of the environmental scan, and other considerations.

3. Knowledge Gathering, Evidence Synthesis, Guidance Development

The third step of the *Economic Process* is to gather knowledge, synthesize evidence and develop NACI guidance. The core work is to develop the project plan for the work plan topic; to generate and synthesize economic evidence; to review and discuss (within the WG) work plan items; and to draft an economic report that can be incorporated into NACI guidance. Five tools have been developed by NACI for conducting, reporting and presenting both economic evaluations and systematic reviews:

Supporting tool #4: Interim Guidelines for the Economic Evaluation of Vaccines: Canada

The purpose of the *Interim Guidelines for the Economic Evaluation of Vaccines* is to inform best practices for conducting economic evaluations of vaccines in Canada. This is to ensure the economic information is standardized, credible, and relevant for decision-makers in Canada's publicly funded health care system.

The *Interim Guidelines* are to be used while the official guidelines for economic evaluations are being developed by the NACI Economic Guidelines Task Group. The group was convened in January 2019 and consists of international experts who have expertise in economics, modelling, infectious diseases/vaccines, as well as experience on guideline development panels. In addition to having P/T representation in its membership, the Task Group will continue to seek further P/T feedback via CIC and CCMOH. Feedback from other stakeholders including industry, the Canadian research community, health technology assessment agencies and the public will be sought. Further information on the public consultation will be communicated when it becomes available. The official guidelines are outside the scope of this present public consultation process, which is on the *Economic Process*.

Supporting tool #5: Reporting Guidelines for Economic Evaluations of Vaccines: Canada

The purpose of the *Reporting Guidelines* is to provide guidance on reporting economic evaluations to NACI. Users include the Secretariat, contractors, and industry stakeholders submitting documentation to NACI as part of a multi-model comparison.

Supporting tool #6: Standard Operating Procedure (SOP) on Systematic Reviews of Economic Evaluations

The purpose of the *SOP on Systematic Reviews* is to provide guidance on conducting and reporting a systematic review of economic evaluations for NACI.

Supporting tool #7: Presentation Template for Presenting Economic Evaluations

The purpose of the *Template for Presenting Economic Evaluations* is to ensure economic evaluations presented to WGs and NACI are uniform in presentation, understandable, and of the highest quality.

Supporting tool #8: Presentation Template for Presenting Systematic Reviews

The purpose of the *Template for Presenting Systematic Reviews* is to ensure systematic reviews presented to WGs and NACI are uniform in presentation, understandable, and of the highest quality.

Closing Remarks

In summary, economic evidence may be one component of NACI guidance. Other components include clinical evidence (i.e., safety, efficacy, immunogenicity, effectiveness and burden of illness) as well as ethics, equity, feasibility, acceptability (EEFA) considerations. NACI guidance will be published on NACI's website with notifications to stakeholders, web subscribers, and typically with a notification in the Canada Communicable Disease Report (CCDR).

Abbreviations

ACIP
Advisory Committee on Immunization Practices (United States Centers for Disease Control and Prevention)

CADTH
Canadian Agency for Drugs and Technologies in Health

CCDR
Canada Communicable Disease Report

CCMOH
Council of Chief Medical Officers of Health

CIC
Canadian Immunization Committee

CIG
Canadian Immunization Guide

EFFA
Ethics, Equity, Feasibility, Acceptability

EVD
Ebola virus disease

NACI
National Advisory Committee on Immunization

NITAG
National Immunization Technical Advisory Groups

PHAC
Public Health Agency of Canada

P/Ts
Provinces and Territories

SOP
Standard Operating Procedure

WG
Working Group

WHO
World Health Organization

VI.2 Module B – Supporting Tool #1 - Prioritization Guide to Economic Evidence

Preamble

- Adapted from Health Quality Ontario's prioritization tool[1] and revised to meet specific needs of vaccine evaluations
- Multiple iterations of feedback from various stakeholders (i.e., Canadian Immunization Committee, NACI, NACI Economics Task Group) and from piloting within NACI Secretariat

For Users

- Purpose: Provide structure and guidance for assessing whether there is a need or urgency for economic evidence
- Tool is meant to be qualitative
- No quantitative rating or weighting of criteria
- Meant to be used for specific policy question (i.e., preferably with a PICO question defined)

The National Advisory Committee on Immunization's Prioritization Guide to Economic Evidence

- Date tool was used
- List of users and roles
- Policy question of interest

Table 1. Assess the need for economic evidence

Criteria	Sub criteria		Assessment				Rationale for Assessment
			High	Moderate	Low	Unknown	
Burden of disease	a)	Incidence/ prevalence (endemic levels), and potential for outbreaks	Moderate to high incidence/ prevalence, or moderate to high potential for outbreaks	Low incidence/ prevalence, or limited potential for outbreaks	Under eradication or no potential for outbreaks	Unknown	
	b)	Severity of disease (manifestations, sequelae)	Significant mortality or morbidity	Some mortality or morbidity	No expected impact on mortality or morbidity	Unknown	
	c)	Unmet health need (whether there are existing products available as standard of care for (sub)populations of interest, i.e., by age groups)	Significant unmet need	Some unmet need	No unmet need	Unknown	
	d)	Economic burden of disease (direct burden to health system)	Significant economic burden	Some economic burden	Low economic burden	Unknown	

Table 1. Assess the need for economic evidence

Criteria	Sub criteria		Assessment				Rationale for Assessment
			High	Moderate	Low	Unknown	
Proposed benefit and potential safety issues	a)	Effectiveness: potential to improve health outcomes *relative to existing* alternatives	Potential significant benefit	Some benefit	No benefit is expected, or inferior benefit is possible	Unknown	
	b)	Changing disease dynamics/ indirect effects of the program	Potential significant benefit	Some benefit	No benefit is expected	Unknown	
	c)	Potential burden due to safety issues (incidence, severity)	No safety concerns	Some safety concerns	Substantial safety concerns	Unknown	
Economic considerations	a)	Incremental costs to make vaccine available (cost per fully vaccinated individual, vaccine + vaccine delivery)	> $300	$100–$300	< $100	Unknown	
	b)	Potential budget impact (from implementing vaccine program)	Significant budget impact	Some budget impact	Low budget impact	Unknown	
	c)	Cost offsets to the health system (i.e., due to reduced healthcare visits, reduced morbidity/ mortality, reduced treatment costs, etc.)	Significant offsets expected	Some offsets expected	No offsets expected	Unknown	
Social value considerations	a)	Potential to impact on social values and equity (see EEFA)	Significant social values or equity issues	Some social values or equity issues	No remarkable impact on social values or equity	Unknown	

What is the need for economic evidence?: High/Moderate/Low

The main considerations for this decision were:

- 1st
- 2nd

Etc.

Table 2. Assess the urgency for economic evidence

Criteria	Sub criteria		Assessment				Rationale for Assessment
			High	Moderate	Low	High	
Urgency	a)	Canadian recommendation (e.g. CATMAT, CPS, SOGC, P/Ts)	≥3 organizations/ strong recommendation	1-2 organizations/ moderate recommendation	No organizations/ weak recommendation	Unknown	
	b)	Current availability of vaccine (publicly funded)	Widely available (≥3 provinces)	Some availability (1-2 provinces)	Limited or no availability	Unknown	
	c)	International recommendation (e.g., ACIP, JCVI, ATAGI)	Multiple international regions	One international region	None	Unknown	
	d)	P/T programmatic concerns	Strong demand / ≥ 3 provinces	Some demand / 1–2 provinces	None	Unknown	
	e)	Demand from stakeholders including the public, clinicians, manufacturers, etc.	Demand from multiple stakeholders / national stakeholder(s)	Demand from 1 stakeholder / provincial stakeholder(s)	None	Unknown	

What is the urgency for economic evidence?: High/Moderate/Low

The main considerations for this decision were:

- 1st
- 2nd

Etc.

Abbreviations: CATMAT, Committee to Advise on Tropical Medicine and Travel; CPS, Canadian Paediatric Society; SOGC, Society of Obstetricians and Gynaecologists of Canada; P/Ts, provinces and territories; ACIP, US Advisory Committee on Immunization Practices; JCVI, UK Joint Committee on Vaccination and Immunisation; ATAGI, Australian Technical Advisory Group on Immunisation

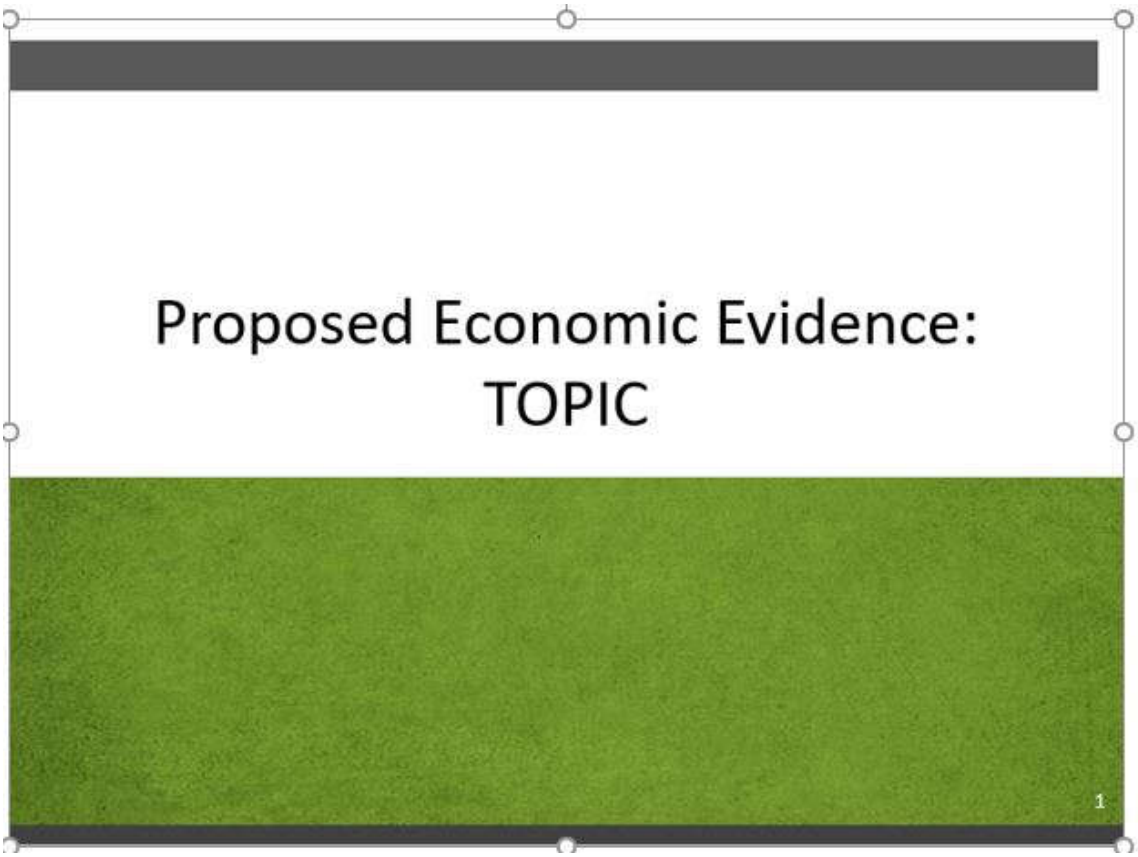
VI.3 Module C – Supporting Tool #2 - Submission Criteria for Model-based Economic Evaluations

For stakeholders submitting model-based economic evaluations to NACI, the following criteria must be met:

- Follow the *NACI Interim Guidelines for the Economic Evaluation of Vaccines*. This document will outline the requirements for conducting an economic evaluation including the required perspective, discount rate, comparator, etc.
- Follow the *NACI Reporting Guidelines for Economic Evaluations*. This document will outline the requirements for the report that should be submitted alongside the model-based economic evaluation.
- Provide full access to programming code (e.g., macros, VBA code). NACI must be able to vary individual parameters, view the calculations, and run the model to generate results. In other words, model must be fully unlocked and executable.
- Use the following software: Excel, TreeAge, R
    - Before using other specialized software, the submitter must contact NACI in advance to ensure the alternative software is acceptable. If acceptable, submitters will receive direction on how the model and software should be provided as part of the submission (e.g., licenses, software), which will be returned to the submitter at the end of the review process, at the submitter's expense.
- Provide basic user information on how to modify input parameters and run model.
- Ensure model run time is not excessive on a personal computer (i.e., cannot exceed over one business day or 8 hours on a standard computer)

Deviations from these requirements must be discussed with and accepted by NACI in advance of submission. Please contact phac.naci-ccni.aspc@canada.ca to provide complete details of the deviations from these requirements.

VI.4 Module D – Supporting Tool #3 - Presentation Template for Proposed Economic Evidence



Economic Prioritization Tool: Summary

- **Question:** [Workplan topic: PICO]

- **Need for economic evidence?** [High/Moderate/Low]
  - Reason(s)
  - Ex.) Burden of disease (e.g., incidence/ prevalence/ outbreaks, severity of disease, unmet need), proposed benefit and potential safety issues, economic considerations (incremental costs, budget impact, cost offsets), social value considerations

- **Urgency for economic evidence?** [High/Moderate/Low]
  - Reason(s)
  - Ex.) Canadian recommendations (e.g., CATMAT), current availability of vaccine, international recommendation (e.g., ACIP), PT programmatic concerns, demand from stakeholders

2

- **Environmental scan:**
  - Ex.) 1 existing Canadian model (CUA); Authors found the vaccine program to be cost-effective at $100 per QALY
  - 1 model from Chile (CUA); Population studied was broader than our population of interest; Authors found the vaccine program to be cost-saving
- **Considerations:**
  - Ex.) A relevant Canadian model exists. We are engaging with the authors to update the model
  - Ex.) Many economic models exist, including 5 Canadian studies relevant to our PICO. All studies conclude XYZ; hence, a new economic model may be redundant. A systematic review should be sufficient [OR] A multi-model comparison may help understand the heterogeneous results
  - Ex.) This is a new vaccine. An economic model is needed for decision-making.

[Topic]:
[A systematic review] OR [A systematic review + a PHAC model/ a multi-model comparison] is proposed for this topic.

OR

No economic evidence is proposed for this topic.

3

VI.5 Module E – Supporting Tool #4 - Interim Guidelines for the Economic Evaluation of Vaccines: Canada

Purpose

The purpose of these *Interim Guidelines* is to inform best practices for conducting de novo economic evaluations of vaccines in Canada. This is to ensure the economic information is standardized, credible, and relevant for decision-makers in Canada's publicly funded health care system.

Background

Traditionally, Canada's National Advisory Committee on Immunization (NACI) assessed vaccines based on clinical efficacy and safety. In 2016, NACI had expanded its mandate to address economic considerations, ethics, equity, feasibility and acceptability in its recommendations of vaccines.

Currently, guidelines for conducting economic evaluations exist in Canada for health technologies in general. The Canadian Agency for Drugs and Technologies in Health (CADTH) had published updated guidelines in 2016.Note de bas de page 1 Health technologies can refer to drugs, medical devices, diagnostics, and procedures, among others.

While recommendations found in the *CADTH Guidelines* are generally applicable to vaccines, a need for vaccine-specific guidelines was identified. This is based on the unique nature of vaccines and the infectious diseases they prevent.

Vaccine-specific guidelines are under development by the NACI Economic Guidelines Task Group. In their absence, these *Interim Guidelines* will be used by NACI for conducting economic evaluations. They are largely based on the CADTH Guidelines with modifications or additional commentary to highlight vaccine-specific nuances.

Guideline Statements

Please refer to the 15 guideline statements found in the *CADTH Guidelines*.[1] The *Interim Guidelines* follow CADTH recommendations unless otherwise indicated below. The letter "M" beside the interim statements below indicates modifications to the CADTH statement. The letter "A" indicates additional commentary, but no change to the CADTH statement. Modifications and additional commentary are presented in the subsequent section.

Table 3. Summary of differences between the NACI Interim Guidelines and the CADTH Guidelines

#	Topic	Change?	Statement
1	Decision Problem	-	
2	Types of Evaluations	-	
3	Target Population	-	
4	Comparators	-	
5	Perspective	M	CADTH: "In the reference case, the perspective should be that of the publicly funded health care payer. Where perspectives other than the reference case perspective are of interest to the decision-maker and could have a substantial impact on the results of the analysis, these should be included as additional non-reference case analyses." Interim: In the reference case, the perspective should be that of the publicly funded health care payer. **If indicated, the societal perspective may be included as an additional non-reference case analysis.**
6	Time Horizon	M	CADTH: "In the reference case, 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 condition and the likely impact of the intervention." Interim: In the reference case, the **individual-level** 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 condition and the likely impact of the intervention. **The population-level time horizon should not be defined prior to the analysis, as the model should be run until steady state is achieved.**
7	Discounting	A	
8	Modelling	M	CADTH: "The choice of modelling technique should be justified. The approach should be no more complex than is necessary to address the decision problem." Interim: The choice of modelling technique should be justified. The approach should be no more complex than is necessary to address the decision problem. **Researchers should consider transmission dynamics, as appropriate.**
9	Effectiveness	A	
10	Measurement and Valuation of Health	A	
11	Resource Use and Cost	A	
12	Analysis	M	CADTH: "In the reference case, expected values of costs and outcomes should be derived through probabilistic analysis, whereby all uncertain parameters are defined probabilistically." Interim: In the reference case **for static models**, expected values of costs and outcomes should be derived through probabilistic analysis, whereby all uncertain parameters are defined probabilistically.

Table 3. Summary of differences between the NACI Interim Guidelines and the CADTH Guidelines			
#	Topic	Change?	Statement
			For dynamic models, researchers should use their best judgement to determine if probabilistic analyses are appropriate (if at all). **For sensitivity analyses, researchers can consider deterministic analyses of parameter uncertainty (i.e., one-way, multi-way, or threshold analyses).**
13	Uncertainty	-	
14	Equity	-	
15	Reporting	-	
A = additional commentary, but no change to the CADTH statement; M = modifications to the CADTH statement; Abbreviation: CADTH = Canadian Agency for Drugs and Technologies in Health guidelines			

Modified Statements or Additional Commentary

5. Perspective

CADTH Statement(s):

"5.1 In the reference case, the perspective should be that of the publicly funded health care payer. The perspective of the economic evaluation should be related to the decision problem.
5.3 Where perspectives other than the reference case perspective are of interest to the decision-maker and could have a substantial impact on the results of the analysis, these should be included as additional non-reference case analyses."

NACI Commentary:

In the context of vaccines and infectious diseases, a societal perspective may be of particular interest to the decision-maker. The Advisory Committee on Immunization Practices (ACIP) in the United States recommend a societal perspective unless strong justification is provided for doing otherwise.[2] The perspective considers a broad range of health and non-health costs and effects.

Non-health costs include those to the[1]:

- Government payer: social services such as home help, meals on wheels,
- Private insurance: community-based services, nursing home care
- Patient and informal caregivers: out-of-pocket payments (e.g., copayments), cost of travel, paid caregivers, premiums paid to private insurers, patient's time spent for travel and receiving treatment
- Productivity costs: lost productivity due absenteeism from paid work or school, lost time at unpaid work (e.g., housework) by patient and informal caregiver, costs to employer to hire and train replacement worker

Non-health effects include[1,3]

Improved education attainment
- Increased work productivity
- Reduced household financial risk
- Increased attractiveness of tourism
- Information available to patients
- Reduction in criminal behaviour

Researchers should be careful not to double-count the non-health costs and effects.[4]

NACI Interim Statement:

In the reference case, the perspective should be that of the publicly funded health care payer. **If indicated, the societal perspective may be included as an additional non-reference case analysis.**

6. Time horizon

CADTH Statement(s):

"6.1 In the reference case, 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 condition and the likely impact of the intervention."

NACI Commentary:

In chronic diseases, an economic model follows individuals with the health condition of interest over a length of time, known as the time horizon. In infectious diseases, an economic model may follow (i) only those with infection, or (ii) those with and without infection, over a length of time. The former does not consider disease dynamics (i.e., transmission of pathogens between individuals or segments of populations). Hence, the time horizon of this type of infectious disease model may be thought of similarly to that of a chronic disease model. The time horizon here can be referred to as an individual-level time horizon. The latter infectious disease model considers disease dynamics. The time horizon here can be referred to as a population-/ program-level time horizon.

Individual-level time horizon: Length of time to follow a single cohort/ individuals. When choosing this time horizon, the researchers should consider:

- Duration of vaccine effectiveness[3]
- Reductions in chronic sequelae (e.g., deafness or neurological deficits after meningitis) due to the vaccine[3]
- Delayed disease outcomes (e.g., cervical cancer or decompensated liver disease) due to the vaccine[3]

A lifetime time horizon is often recommended if the vaccine is expected to impact survival or to provide benefits that persist for the remainder of a person's life.[5,6] However, a lifetime time horizon will almost always involve extrapolating data beyond the follow-up time of available clinical trials or observational studies. This adds uncertainty to the analysis. Short time horizons can be justified if the duration of effectiveness, and relevant costs and effects are captured within that time frame. For instance, a short time horizon is appropriate in the case of an acute infection that does not have long term sequelae.[6] Sensitivity analyses should be conducted for different time horizons.

Population-level time horizon: Length of time required to achieve herd immunity effects after the implementation of a vaccine program. In other words, this is the number of cohorts modelled. Usually, dynamic models simulate the epidemiology prior to the vaccine program (known as a run-in/ burn-in phase), the epidemiology after program implementation (known as an evaluation phase), and the epidemiology after estimates reach a plateau (i.e., when epidemiological estimates, such as disease outcomes, stabilize and no longer change over time).[5] This last phase is known as steady state. Researchers should let the model run

until steady state is achieved, which means the population-level time horizon should not be defined prior to the analysis.[5]

This time horizon can have a substantial impact on the results of a dynamic model.[7] Hence, the German Standing Committee on Vaccination (STIKO) recommends reporting cost-effectiveness results from the steady state phase, as well as from varying points of time before the steady-state.[8]

NACI Interim Statement:

In the reference case, the **individual-level** 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 condition and the likely impact of the intervention.

The population-level time horizon should not be defined prior to the analysis, as the model should be run until steady state is achieved.

7. Discounting

CADTH Statement(s):

"7.1 In the reference case, costs and outcomes that occur beyond one year should be discounted to present values at a rate of 1.5% per year.
7.2. The impact of uncertainty in the discount rate should be assessed by comparing the results of the reference case to those from non-reference case analyses, using discount rates of 0% and 3% per year."

NACI Commentary:

Unlike other curative therapies, the cost-effectiveness of vaccine programs is likely highly sensitive to discounting.[9] This is because benefits are not necessarily accrued immediately after vaccination. Rather, benefits are accrued over the longer term. For instance, a vaccine administered today can take effect after many years (i.e., avoid cervical cancer after human papilloma virus vaccination). Or, a vaccine that prevents premature death or chronic disability at early ages (i.e., polio, fatal rotavirus) can have benefits that last for the rest of the beneficiary's lifetime and beyond to future generations.[9] The cost-effectiveness of vaccine programs is highly sensitive to discounting distant benefits into present value because those benefits may be given little weight.

For this reason, some health economists argue that health effects should be discounted at a lower rate than costs (i.e., differential discounting).[9] However, some paradoxical situations can occur with differential discounting (known as the Keeler-Cretin paradox).[10] In brief, researchers may see the most cost-effective results if an intervention is postponed indefinitely into the future. Most guidelines recommend discounting costs and outcomes at the same rate.[9] One agency has suggested exploring lower discount rates in sensitivity analysis when the time horizon is over 30 years.[11] Others have suggested considering a non-constant (declining) discount rate.[9]

The methodological discussions on discounting will continue to evolve. The *Interim Guidelines* will follow the CADTH recommendations of using constant discount rates for both costs and effects at 1.5%, 0%, and 3%. Cost-effectiveness results discounted at 0% (also called undiscounted) and results discounted at 3% represent the range of possible results due to discounting. Cost-effectiveness results from differential discount rates and declining discount rates should fall within this range.

NACI Interim Statement:

No change to CADTH statement

8. Modelling

CADTH Statement(s):

"8.1 Model conceptualization and development should address the decision problem.
[p. 33 [Model conceptualization] involves the development of a model structure that is defined by specific states or events and the relationships among them that together constitute the clinical or care pathway for the condition of interest and the interventions being compared.]
8.4. The choice of modelling technique should be justified. The approach should be no more complex than is necessary to address the decision problem.
[p.34 There are many decision-modelling techniques available to researchers when conducting economic evaluations, including decision trees, cohort-level state-transition models (i.e., Markov models), patient-level state-transition models (i.e., microsimulations or first order Monte Carlo simulations), system dynamic models, discrete event simulation models, and agent-based models.]"

NACI Commentary:

Model Conceptualization: In infectious disease modelling, the natural history of infection and disease are commonly represented by the following model structures:

- SIS (susceptible-infectious- susceptible): Assumes no natural immunity
- SIR (susceptible-infectious-recovered): Assumes a host can only be infected once over the model time horizon
- SIRS (susceptible-infectious-recovered-susceptible): Assumes a host is protected from re-infection after recovering until natural immunity wanes
- SEIR (susceptible-exposed-infectious-recovered): Assumes a SIR model with an additional latency period where the host is infected but does not transmit infection

Modelling Technique: Modelling can predict the impact of vaccines on the disease epidemiology on the population-level rather than on the individual-level.[12] Models can be described by combinations of the following three model attributes[13]:

1. Static versus dynamic
    - Static model: Assumes a constant risk of infection (i.e., force of infection) in susceptible individuals. Although the transmissible nature of infectious diseases cannot be captured by static models, they may still be appropriate for modelling disease epidemiology in certain cases:
        - when vaccine coverage is low (which means the vaccine is unlikely to change the force of infection)[14]

- when the group targeted for vaccination does not impact overall transmission or prevent the circulation of the pathogen (which means the vaccine is unlikely to change the force of infection); (e.g., hepatitis A vaccination in travelers from low- to high-incidence countries)[14]

- when the vaccine does not produce "potential negative direct or indirect health effects (e.g., changes in the average age of those infected, serotype replacement, or changes in outbreak periodicity at different coverage rates")[3]

- when the decision-maker is only interested in a conservative estimate of cost-effectiveness for a vaccine compared to no intervention.[12] (For example, if a static model shows the vaccine is cost-effective, then a dynamic model will likely predict the vaccine is even more cost-effective. This is because the dynamic model can capture indirect protection via herd immunity and can predict a faster reduction in the number of infections)[12]

- Dynamic model: Assumes the risk of infection in susceptible individuals is a function of the proportion of the population infected. Common metrics for infection risk are the basic reproduction number and effective reproduction number. Dynamic models can account for indirect effects such as herd immunity, natural immunity, and age distribution shifts. There are various instances where dynamic models are appropriate for modelling disease epidemiology:

  - when the vaccine impacts disease transmission (e.g., "decreasing the proportion susceptible (e.g., mass vaccination), contact rates between individuals (e.g., closing schools during a pandemic), the duration of infectiousness, or the probability of transmission per act")[14]

  - when the vaccine induces selective pressures on that pathogen, allowing some types to gain a competitive advantage (i.e., strain replacement)[14]

  However, computational and data challenges remain for modelling complexities such as cross-protection (where protection against one pathogen type would offer some degree of protection against other types).[15] The World Health Organization has developed a flowchart to guide researchers in selecting a dynamic versus static model (see Figure 1 below)[15].

2. Deterministic versus stochastic

   - Deterministic model: Events occur in a pre-specified way set by the parameter values and initial model conditions.[13]

   - Stochastic model: Events in the model occur by chance.[13]

3. Population-based versus individual-based

   - Population-based model: Tracks groups. Individuals are assigned to compartments (also known as health states) and are assumed to be homogeneous in that health state. They transition to different health states based on parameter values at the aggregate level.

- Individual-based model: Tracks individuals. Individuals are modelled with their own patient characteristics, allowing for population heterogeneity to be captured. They transition to different compartments based on parameters values at the individual level and their history can be tracked. Individual-based models, by their nature, are stochastic (not deterministic).[13]

In infectious disease modelling, the following combinations of model attributes are common:

- Dynamic, stochastic, population-based: An example is the system dynamics model, where groups of individuals transition between health states based on differential equations

- Dynamic, stochastic, individual-based: Examples include the agent-based model and the discrete-event simulation, where individuals (not groups) transition between health states. The main difference between an agent-based model and a discrete-event simulation is that the modelling unit is individuals (also called agents) in the former, and is events in the latter.[16]

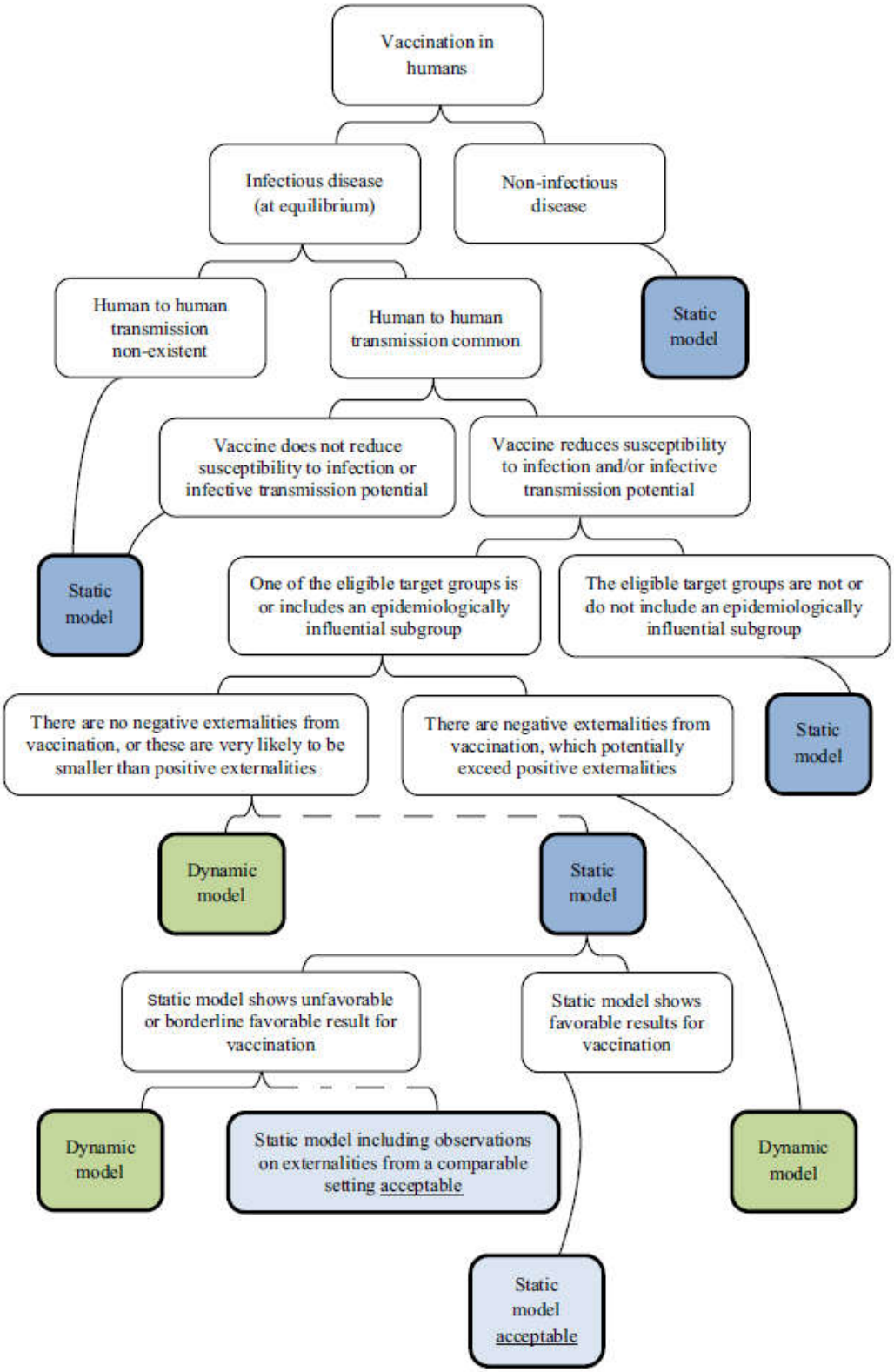
- Static, deterministic, population-based: Examples include decision trees, state-transition Markov models, or hybrids of the two.[13] These models are commonly seen in economic evaluations of chronic conditions

- Static, stochastic, individual-based: An example is the state-transition microsimulation

NACI Interim Statement:

The choice of modelling technique should be justified. The approach should be no more complex than is necessary to address the decision problem. **Researchers should consider transmission dynamics, as appropriate.**

Figure 4. World Health Organization flow chart15 for model choice adopted by Ultsch.5



9. Effectiveness

CADTH Statement(s):

"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.
9.3. Researchers should evaluate and justify the validity of any surrogate end points used for parameter estimation. Uncertainty in the association of the surrogate to the final clinical outcome should be reflected in the reference case probabilistic analysis. This uncertainty can also be explored through appropriate scenario analyses. The existence of multiple potential surrogates should be reflected in the analysis of uncertainty. When considering the use of biomarkers as surrogate end points, the researcher should evaluate and justify the validity of the biomarker and the degree to which the biomarker satisfies the criteria of a surrogate end point."

NACI Commentary:

Efficacy and effectiveness data of vaccines often come from randomized controlled trials and surveillance studies, respectively. When researchers use randomized controlled trial data, they should be aware that efficacy will be underestimated because indirect effects are not captured.[14] Trials recruit a small fraction of the population and thus do not experience a reduced force of infection.[14] Further, trials often assess surrogate end points such as immune response. Consequently, researchers need to extrapolate to hard end points such as mortality and morbidity.[14] Sensitivity analyses should be conducted for different assumptions for extrapolating future vaccine benefit (i.e., continuous treatment effect, one-time effect, rebound effect, etc.)[4] When researchers use surveillance study data, they should be aware that only individuals with sufficiently severe symptoms will present to the healthcare system for diagnosis and care.[14] Hence disease incidence may be underestimated and disease severity, hospitalization and case-fatality may be overestimated.[14]

For data on adverse events from immunization, researchers should be aware that adverse events may not be observed in clinical trials (due to their small size compared to a vaccination program). Signals should be considered in sensitivity analysis.

Other data required for building epidemiologic models include:

- Disease incidence and mortality[3]
- Vaccine coverage[3]
- Waning of immunity[3]
- Force of infection[3]
- Social contact matrices[3]
- Compliance with full schedules[15]

Interim Statement:

No change to CADTH statement

10. Measurement and Valuation of Health

CADTH Statement(s):

"10.1. In the reference case, the QALY should be used as the method for capturing the value of the effect of an intervention."

NACI Commentary:

In the vaccine literature, economic evaluations often value health using the metric, disability-adjusted life year (DALY) averted, but also the quality-adjusted life-year (QALY) gained. This choice appears to be based on historic reasons, rather than on inherent advantages of one over the other.[17] The World Health Organization had promoted the use of DALYs in their Global Burden of Disease study. Cost-per-DALY studies are more commonly used in low and lower-middle income countries, whereas cost-per-QALY studies are more commonly used in upper-middle income and high-income countries.[17] The *Interim Guidelines* will follow the CADTH recommendations of using the QALY metric.

Given that a societal perspective is often of interest in the context of vaccines, non-health effects should be valued where possible and appropriate (see Section 5: Perspective).

NACI Interim Statement:

No change to CADTH statement

11. Resource Use and Costs

CADTH Statement(s):

"11.1. In the reference case, researchers should systematically identify, measure, value, and report all relevant resources based on the perspective of the publicly funded health care payer. When a range of perspectives is relevant to the decision problem, researchers should classify resources and their associated costs in categories according to each perspective, reporting results separately for the reference case perspective and any additional non-reference case perspectives."

NACI Commentary:

Direct costs for vaccine and infectious disease modelling may include[15]:

- Supplies (i.e., vaccine purchase, syringes, safety boxes)
- Program costs (i.e., labour, vaccine administration; note there may be cost variations across P/T's and across facility volumes)
- Public health costs (i.e., contact tracing, outbreak response)
- Disease surveillance
- Distribution system (i.e., transport and cold storage)
- Vaccine wastage and waste management
- Adverse events from immunization

Given that a societal perspective is often of interest in the context of vaccines, non-health costs should be valued where possible and appropriate (see Section 5: Perspective). Researchers should consider "any

potential spillover impacts beyond those individuals for whom the interventions are being targeted. For example, an intervention aimed at patients may have spillover impacts on informal caregivers due to changes in the level of care required by patients".[1]

Note that there may be significant variations in epidemiology (i.e., disease burden) and vaccine administration costs across P/T's. Researchers may consider using Canadian averages for both. Researchers may also consider using P/T-specific estimates for different scenarios to represent a range of possible cost-effectiveness results.

NACI Interim Statement:

No change to CADTH statement

12. Analysis

CADTH Statement(s):

"12.4. In the reference case, expected values of costs and outcomes should be derived through probabilistic analysis, whereby all uncertain parameters are defined probabilistically."

NACI Commentary:

Many current guidelines recommend conducting probabilistic analyses as part of sensitivity analysis.[3, 6, 15] The *CADTH Guidelines* appear singular, where they recommend conducting probabilistic analyses as the reference case rather than as sensitivity analysis.[1]

The International Society for Pharmacoeconomics and Outcomes Research (ISPOR) Task Force on dynamic modelling in 2012 did not include probabilistic sensitivity analysis as part of their best practice recommendations.[14] They noted methodological challenges for dynamic models, where "many of the parameters related to mixing and transmission are correlated and these correlations need to be preserved to ensure sensible models and reasonable fit to data".[14] A separate ISPOR Task Force on vaccines in 2018 recommended performing probabilistic sensitivity analysis to generate acceptability curves.[3]

NACI Interim Statement:

In the reference case **for static models**, expected values of costs and outcomes should be derived through probabilistic analysis, whereby all uncertain parameters are defined probabilistically.

For dynamic models, researchers should use their best judgement to determine if probabilistic analyses are appropriate (if at all).

For sensitivity analyses, researchers can consider deterministic analyses of parameter uncertainty (i.e., one-way, multi-way, or threshold analyses).

VI.6 Module F – Supporting Tool #5 - Standard Operating Procedure on Reporting Economic Evaluations of Vaccines

Purpose

The purpose of the standard operating procedure (SOP) is to provide guidance on how to report economic evaluations to NACI.

Development of SOP

We conducted an environmental scan of the grey literature to identify guidance on how to report economic evaluations. We searched the following:

- CADTH "Grey Matters: a practical tool for searching health-related grey literature"— This is a comprehensive list of Canadian and international HTA agencies
- Google search engine
- EQUATOR Network –This is an online database of reporting guidelines
- NITAGs

We reviewed relevant reporting guidelines and consolidated elements for minimum standard reporting:

- Consolidated Health Economic Evaluation Reporting Standards (CHEERS)[18]
- CADTH Methods for the Economic Evaluation of Health Technologies – Section 15 on Reporting[1]
- WHO guide for standardization of economic evaluations of immunization programmes[19]
- WWORTH SOP for Economic Evaluation[20],
- HIQA – Guidelines for the Economic Evaluation of Health Technologies in Ireland (2018) [21]
- EUNETHA – European Network for Health Technology Assessment[22]
- Developing NICE guidelines: the Manual – Approaches to bespoke economic evaluation[23]
- Belgian guidelines for economic evaluations and budget impact analyses: 2nd Ed.[24]
- Health Quality Ontario (HQO) – Health Technology Assessment Methods and Process Guide[25]
- Haute Autorité de Santé (HAS) – Choices in Methods for Economic Evaluation (2012)[26]
- Guideline for Economic Evaluations in Healthcare – Zorginstituut Netherlands (2016)[27]
- Methods for Health Economic Evaluation of Vaccines and Immunization Decision Frameworks: A Consensus Framework from a European Vaccine Economics Community[5]
- Economic evaluation using decision analytical modelling: design, conduct, analysis, and reporting[28]
- Increasing the generalizability of economic evaluations: recommendations for the design, analysis, and reporting of studies[29]
- Good Research Practices for Cost-Effectiveness Analysis Alongside Clinical Trials: The ISPOR RCT-CEA Task Force Report[30]
- Economic evaluation alongside randomised controlled trials: design, conduct, analysis, and reporting[31]
- U.S. Advisory Committee on Immunization Practices (ACIP) Handbook for Developing Evidence-based Recommendations[32]
- Modelling methods for predicting epidemiological and health economic effects of vaccinations - Guidance for analyses to be presented to the German Standing Committee on Vaccination (STIKO)[8]
- Peter J. Neumann, Theodore G. Ganiats, Louise B. Russell. Cost-Effectiveness in health and medicine. New York Oxford University Press. 2017[33]

Below, we provide guidance in the form of a checklist, as well as provide standard templates for tables/ figures when reporting to NACI. The recommended content can appear in the main report or technical appendix.

Reporting Guidelines - Checklist

Table 4. Reporting Guidelines - Checklist

Section	Recommendation on How to Report
1. Title	• Identify the study as an economic evaluation, or use more specific terms, such as "cost-effectiveness analysis" or "cost-utility analysis", and describe the interventions being compared and the condition of interest.[18]
2. Executive Summary	• Provide structured summary with the objectives (in the PICO format), perspective, context, methods (including the study design and the inputs), results (including the reference case and uncertainty analyses that drive the results), and conclusions.[18] • Use plain language, and define jargon or technical terms that may be unfamiliar to the reader or user.[1]
3. Background and Decision Problem	• The study question should be well defined, stated in an answerable form and relevant to the decision the target audience is facing.[19] Ex.) What is the cost-effectiveness of routinely vaccinating age group XX against Disease Y, using vaccine Z, using three doses given once per year over three consecutive years compared to the current approach of A?[32] • Specify the interventions, setting, perspective, costs, outcomes, time horizon and target population for the evaluation. [1]

4. Target Population and Subgroups	• Identify the population(s) for which the interventions are to be used.[1] Identify individuals whose health is directly or indirectly affected by the interventions studied.[26]
	• Describe the following characteristics or other characteristics: [25]
	  ○ Demographics (e.g., age, sex, socioeconomic status)
	  ○ Specific condition
	  ○ Disease severity
	  ○ Comorbidities
	  ○ Risk factors
	• Include the reasons why subgroups were chosen (if any).[18]

5. Interventions and Comparators	• List and clearly describe all interventions included in the analysis, including the comparator(s). Identify the time frame of the interventions.[33]
	
	Ex.) The most relevant comparison for new vaccines is usually current practice. If existing practice itself appears to be cost-ineffective compared to other available options, the analyst should include other relevant alternatives into the analysis, such as a best available alternative, a viable low-cost alternative or a do-nothing option.[19]
	• All health care-relevant preventive or curative comparators in the therapeutic indication of the respective vaccination should be considered in the development of the model. If they are not included, the reasons for their exclusion should be given.[8]
	
	Ex.) Preventive or curative comparisons may include:[8]
	
	  ○ No vaccination versus vaccination
	  ○ A screening program versus vaccination
	  ○ Existing vaccination strategy versus a new vaccination strategy for the same disease
	• Discuss the rationale for inclusion or exclusion of interventions.[32]
	
	Ex.) For example, the authors of an analysis of vaccination of adults against pertussis would discuss the rationale for inclusion or exclusion of a selective strategy of vaccinating care providers of young infants.[32]

Table 4. Reporting Guidelines - Checklist	
Section	Recommendation on How to Report
6. Study Perspective	• Identify whether the analysis uses the Reference Case perspectives (please see NACI Interim Guidelines on Conducting Economic Evaluations) and any alternative perspectives presented.[33] • Describe the study perspective and relate it to the costs and outcomes to be evaluated.[18]
7. Time Horizon	• The time frame and analytic horizon should be clearly stated and justified. Describe how their respective durations are contingent on the type of vaccine evaluated, the intervention and target population, and thus the type of model developed.[19] • In infectious disease economic modelling, there can be two time horizons (i) Individual-level time horizon—Length of time to follow a single cohort/ individuals, (ii) Population-level time horizon— Length of time required to achieve herd immunity effects after the implementation of a vaccine program. Both time horizons should be described.
8. Discount Rate	• Identify whether the analysis uses the Reference Case discount rate (please see NACI Interim Guidelines on Conducting Economic Evaluations). • Describe any alternative discounting methods used in sensitivity analyses. Report the choice of the discount rate(s) used for costs and outcomes and say why it is/they are appropriate.[18]
9. Choice of Health Outcomes	• Health outcomes must be clearly identified and justified (e.g., deaths, hospitalizations, outpatient visits, quality-adjusted life-years). Authors must ensure that health outcomes are relevant to the perspective and disease.[18], [22] • Provide any standardized case definitions for clinical outcomes.[5]
10. Measurement of Effectiveness	• Describe fully the methods used to identify the included studies and synthesize clinical effectiveness data.[18] Describe the types of data used to derive inputs for the analysis (e.g., primary data, secondary data from the published literature, administrative data, unpublished data).[33] • Report routine vaccination coverage, non-compliance, vaccine efficacy, adverse events from immunization.[19] Describe and distinguish between vaccine-induced protection through degree of protection or take. The degree of protection is the vaccine-induced protection in individuals who are completely vaccinated. Take is the percentage of completely vaccinated individuals with full protection (e.g. 50% of the completely vaccinated individuals have 100% protection).[8] • Describe any negative vaccine effects, both at an individual level (i.e. adverse events) and at a population level (i.e. replacement or age shift) and how they were included in the analysis.[8] If they were not included, the reasons for this should be given. • The quality of all sources needs to be assessed and reported.[22]
11. Measurement and Valuation of Preference-based Outcomes	• If applicable, describe the population and methods used to elicit preferences for outcomes.[18] • Identify if all relevant health outcomes are based on the Reference Case perspective. Identify if health preferences reflect the general Canadian population.[1]
12. Resource Use and Costs	• A summary should be provided of the expected resource use and unit costs for each alternative. This should include specifying the assumptions behind calculations of costs.[19] • Describe the approaches and data sources to estimate the use of resources associated with the model health status. Describe the primary or secondary research methods for valuing each item of the resources in terms of cost units. Describe any adjustment done to approximate opportunity costs.[18] • Present values and data sources in tabular form.[32] • Describe if data used reflect the Canadian context/ jurisdiction(s) of interest.[1] Describe the potential for variations in resource use both between and within jurisdictions.[1]

Table 4. Reporting Guidelines - Checklist	
Section	Recommendation on How to Report
	• Describe both medical and non-medical costs or resource use in the clinical processes of the intervention over the short and long term.[30] • If applicable, describe costs borne by other sectors of the society, e.g. indirect costs in an additional analysis when relevant.[22] Ex.) Indirect costs of carers, sick pay, productivity loss[22]
13. Currency, price, date and conversion	• Costs should be reported in local currency units, ideally using the most recent year as the base-year.[19] • Describe the methods to adjust estimated unit costs to the year of reported costs, if necessary (i.e., health care component of the Statistics Canada Consumer Price Index[25]). Describe the methods to convert the costs into a common currency and exchange rate.[18]
14. Modelling	• Describe - and give reasons for - the specific type of analytical decision model used.[1] If applicable, describe why was a dynamic model not used?[5] • If the epidemiological model was developed separately from the economic model, include a description of the model. Describe and justify model components such as the model being stochastic versus deterministic, individual-based versus population-based, etc. The authors must include a schematic diagram illustrating the model. Annotation in such a diagram must be done without use of mathematical notation. Authors are directed to ensure that such schematic diagrams can be readily understood without extensive reading of the main text (i.e., can "stand alone").[32] • Report the time step used in the epidemiologic model. "Time step" refers to the time associated with the probabilities used in the model. For example, if the authors use probabilities of death per unit population per year, then the de facto time step of such a model would be one year. Probabilities, and time step, can be in almost any unit of time. The total number of time steps must match the time frame of the economic model unless a specific explanation is given. Authors should note that it is insufficient merely to reference another source (e.g., reference a previously published paper).[32]
15. Study Parameters	• Report and justify the sources of information used for input parameters. Provide the input values for study parameters with reference to the sources of information in a table. Report the probability distributions for all parameters, if applicable.[1] • Report disease incidence, vaccine effectiveness, duration of immunity.[32] • Report parameters for infectious disease epidemiology: 1) The reproduction number; 2) Incidence and the force of infection; 3) Impact of vaccination.[1] • Split cost by vaccine-related intervention and downstream costs (i.e., disease treatment). • Report waning, or different scenarios for vaccine waning if it is not well understood[5] Report vaccine coverage (varied between desirable and undesirable levels).[5]
16. Assumptions	• The scope, structure, and assumptions should be clearly described and justified. The model should be validated, including an assessment of the face validity of the model structure, assumptions, data, and results.[1] Ex.) Vaccine-related assumptions can include: • Adequate supply of vaccine.[32] • Waning vaccine immunity.[5] • Wastage rate of vaccine (i.e., sum of vaccines discarded, lost, damaged or destroyed).[19] • Assumptions when a vaccine has not yet been developed or data on vaccine efficacy are not in the public domain.[19] • Method of delivery of the vaccine (i.e., school-based, clinic-based) • Compliance, uptake rate, acceptability

Table 4. Reporting Guidelines - Checklist	
Section	Recommendation on How to Report
	• Different immunization strategies (i.e., phased implementation versus simultaneous; schedule of vaccination, catch-up program) Other assumptions can include: • Assumptions on eligibility criteria • Assumptions necessary to transfer cost data when they are applied from other countries.[21] • Assumptions on how many infections are medically attended • Assumptions on how disease affects different subpopulations • Assumptions on how costs differ across subpopulations
17. Characterizing Heterogeneity	• Describe any subgroup analyses performed for all subgroups (pre-defined or ad hoc).[27] • If applicable, report the differences in cost, outcomes or cost-effectiveness that can be explained by variations between subgroups of patients with different baseline characteristics or other variabilities observed in effects that are not reducible by more information.[1] • If data sources come from multinational trials, describe any methods to address inter-country differences in population characteristics and treatment patterns.[30]

18. Characterizing Uncertainty	• Present sensitivity analyses in a clearly identified section, complete with relevant tables and graphs. The ranges and sources of the values used in the sensitivity analyses must be clearly reported.[32]
	• Authors shall, whenever possible, present a list of "most influential" variables as identified through sensitivity analysis.[32]
	• Report sensitivity analyses, including:
	  ○ One-way sensitivity analyses of the following variables: discount rate, vaccination effectiveness (where unknown or uncertain), incidence of disease (including complication rates where relevant), case fatality rates and vaccine price.[19] A tornado diagram is a useful way to present the results.[21]
	  ▪ Two-way sensitivity analyses. In particular, for vaccine cost and vaccine effectiveness.
	  ○ Threshold analyses.[32]
	  ○ Scenario analyses: Various relevant perspectives, best- and worst-case scenarios, etc.[29]
	  ○ Probabilistic sensitivity analyses (PSA), if applicable.[5] Present the results using the scatter plot on the cost-effectiveness plane.[21]

19. Analytical Methods	• The type of evaluation used must be specified (e.g., cost-benefit, cost-effectiveness, or cost-utility analysis). The summary measure must be defined/ identified.[32] • Describe all analytical methods supporting the evaluation. This could include methods for dealing with skewed, missing, or censored data; extrapolation methods; methods for pooling data; approaches to validate or make adjustments (such as half cycle corrections) to a model.[1] • Identify if ICERs are calculated between two interventions or calculated sequentially.
20. Validation and Calibration	• Provide details on the process for validating the model. Where details of the exercise are relevant for inclusion, consider including this as an appendix to the economic evaluation.[1] • Provide details on model calibration methods.[5] Calibration should be distinguished from other sources of parameter estimation, which involve separate processes from the model itself and do not consider the overall similarity of the model outputs to the external data.[1]

Table 4. Reporting Guidelines - Checklist	
Section	Recommendation on How to Report

21. Incremental Costs and Outcomes	• Report clinical outcomes: number of cases, number of deaths, LYs, QALYs, costs and ICER's or net monetary/ health benefit (including the cost-effectiveness threshold used for the net benefit calculation).
	• For each intervention, report the mean values for the main categories of estimated costs and outcomes of interest, as well as the mean differences between the comparator groups. If applicable, report the ICERs.[18]
	• Cumulative results should be reported at various time points over a model's construed decision horizon, including a longitudinal view up to the end of the defined time horizon of the model.[5]
	• Report results from sensitivity/ scenario analyses, such as:
	  ○ Various relevant perspectives
	  ○ Best- and worst-case scenarios, etc.[5]
	• Report results in tabular form, in a cost-effectiveness plane, in a cost-effectiveness acceptability curve (CEACs), where applicable.

22. Limitations, Generalizability and Key Findings	• Study limitations must be discussed. Limitations shall include accuracy of any epidemiologic model and input data.[32] Explain how the limitations may impact the conclusions of an evaluation.[26] • Comment on the generalizability or relevance of results, and the validity of the data and model for the relevant jurisdictions and populations.[1] • Comment on regional differences in terms of disease epidemiology, population characteristics, clinical practice patterns, resource-use patterns, unit costs, and other factors of relevance. Where differences exist, discuss the impact on the results (expected direction and magnitude), and the conclusions.[1] • Summarize the key findings of the study and describe how they support the conclusions reached.[18]
23. Equity Considerations	• Indicate the distributional considerations (e.g., primary beneficiaries and those adversely affected).[1] • List other ethical and equity implications or issues; for example, are there likely to be variations in patients' access to the intervention due to geographic location or patient characteristics? Does the technology address the unmet needs of certain disadvantaged groups? Is the technology responsive to those with greatest need and for whom there is no alternative treatment (e.g., "rule of rescue")?[1] If applicable, comment on horizontal equity (equal treatment for people in equal circumstances); vertical equity (priority for people with worse problems); adequacy of demand; and public attitudes and wants.[19]
24. Sources of funding	• Describe how the study was funded and the role of the funder in the identification, design, conduction, and reporting of the analysis. Describe other non-monetary sources.[18]
25. Conflicts of Interest	• All authors shall include their affiliations. A separate section listing any potential conflicts of interest shall be included for each author. If there are no potential conflicts of interest, a statement to that effect must be included (e.g., Author A: No conflicts of interest).[32]

Reporting Guidelines - Templates for Tables/ Figures

Below are sample templates for your consideration:

Example Template 1: Table X. Summary of methods	
Type of analysis	**Cost-utility analysis**
Disease	Pneumococcal disease (pneumonia, otitis media, invasive pneumococcal disease)
Population	Infants (birth cohort)
Intervention	PCV13
Comparator(s)	No vaccine
Outcomes	Cases, deaths, DALYs/QALYs, cost
Perspective	Healthcare payer
Time horizon	Lifetime
Discounting	1.5%
Sensitivity analysis	Base case, scenarios, deterministic sensitivity analysis
Type of model	Single disease with multiple manifestations; decision tree

Example Template 2: Table X. Description of the variables used in a model				
Variable	**Description**	**Mean**	**Range/ Distribution & parameters (e.g. SD, 95% CI, α1, α2…)**	**Source**
Reference Case:				
A				
B				
Scenario Analysis:				
A				
B				
Abbreviations: SD = standard deviation; CI = confidence interval				

Example Template 3: Table X. Description of the cost variables used in a model				
Cost Variable	**Unit Cost**	**Number of units**	**Billing code/ Description**	**Source**
A				
B				
C				

Example Template 4: Table X. Results of an economic evaluation			
	Vaccine Program A	**Vaccine Program B**	**Vaccine Program C**
Clinical outcomes:			
LYs			
Cases averted			
Hospitalizations averted			
Deaths averted			
QALYs			
Costs:			
Vaccine-related			
Downstream			
Total			
Incremental Cost per QALY Gained (ICER):			
Versus Program A			
Sequential ICER			
If relevant, i.e., if the intervention is not dominated or dominant. *Consider reporting confidence intervals/ credibility intervals* Abbreviations: ICER = incremental cost-effectiveness ratio; QALY = quality-adjusted life-year			

Consider reporting other tables/ figures:

- Schematic of model structure
- Cost-effectiveness plane
- Cost-effectiveness acceptability curve
- Tornado diagram
- Two-way sensitivity analysis for vaccine cost and vaccine effectiveness

VI.7 Module G – Supporting Tool #6 - Standard Operating Procedure (SOP) for National Advisory Committee on immunization: Systematic Reviews of Economic Evaluations

Purpose

This standard operating procedure (SOP) outlines the steps that are needed to conduct a systematic review of economic evaluations for NACI

Introduction

The National Advisory Committee on Immunization (NACI) regularly produces recommendations, statements and updates related to the use of vaccines currently or newly approved for use in humans in Canada. The Centre for Immunization and Respiratory Infectious Diseases (CIRID) of the Public Health Agency of Canada (PHAC) provides direct support for this work. One form of this direct support is completion of economic evaluations and/ or systematic reviews of economic evaluations on various vaccines as a means of gathering evidence related to vaccines.

Search and development

1.1 Research Question, PICO (TS)

A systematic review of economic evaluations should be conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA[34]) guidelines. Research questions and objectives evaluating a systematic review of economic evaluations are defined and include the population, intervention, comparator(s), and outcome(s) of interest. Where relevant, research questions also address whether a specific timing or type of study and setting are of interest. (PICO (TS))

1.2 Inclusion and Exclusion criteria

Systematic review inclusion criteria should include: study population, intervention, language, dates included, countries and types of study; cost-utility analysis (CUA), cost-effectiveness analysis (CEA), cost-benefit analysis (CBA), as well as anything else relevant to the systematic review.

1.3 Register with PROSPERO

The systematic review of economic evaluations should be registered with PROSPERO during the initial stages of research development. PROSPERO[35] is an international database of registered systematic reviews in health and social care, welfare, public health, education, crime, justice, and international development, where there is a health related outcome. Features from the protocol are recorded and maintained as a permanent record. PROSPERO is produced by the Centre for Reviews and Dissemination and funded by the National Institute for Health Research (NIHR).

1.4 Develop Search Strategy

The search strategy should be developed with a research librarian (Health Canada) using medical subject headings (MeSH) and text words related to economic evaluations, cost-effectiveness, and the disease area. NACI strongly recommends the use of the Canadian Agency of Drugs and Technologies in Health (CADTH)

search filters for Economic Evaluations/Cost/Economic Models[36]. At the minimum, the following three recommended electronic databases should be searched: MEDLINE, EMBASE, and The Cochrane Library, which includes the Health Technology Assessment Database (HTA), the NHS Economic Evaluation Database (NHS EED) and the Database of Abstracts of Reviews of Effects (DARE). The Health Canada librarian can run the search and provide search results.

1.5 Grey Literature Search Strategy

NACI recommends the use of CADTH's search tool for grey literature that focuses on health technology assessments and economic evaluations[37]. (Please see Grey Literature Search Extraction Table 1). Also, please contact organizations directly for grey literature that is not publicly available.

1.6 Organize the References and Distiller SR

NACI recommends the use of Distiller SR[38] or equivalent software for managing and tracking screening; however Excel could be used as well. DistillerSR is systematic review software that manages, tracks, and streamlines the screening, data extraction, and reporting processes of systematic reviews and literature reviews.

1.7 Revise the proposed search strategy, inclusion/exclusion criteria, PICO (TS) and PROSPERO registration

The search strategy, study inclusion / exclusion criteria, PICO (TS) and registration with PROSPERO should be done in consultation with PHAC, working groups (WG) and in consultation with Health Canada librarians. Revise the proposed search strategy, inclusion/exclusion criteria, PICO (TS) and PROSPERO registration based on feedback from these groups.

Screening, data extraction and quality appraisals

2.1 Retrieve Abstracts and Relevant Literature

Retrieve abstracts and relevant literature from the Health Canada librarian search.

2.2 Conduct Abstract and Full Text Screen

Conduct abstract and full text screen based on the inclusion/exclusion criteria. At the beginning of the screening process, complete a reviewer calibration using a sample size of the total number of studies (suggestion of 5% or another reasonable number) between the two reviewers to ensure consistency. Two reviewers conduct title abstract level 1 screening and full text level 2 screening. Conflicts should be resolved through discussion, and if needed via a third reviewer.

2.3 Hand searching of bibliographies of included studies.

Hand search the bibliographies of included studies.

2.4 Complete Data Extraction Template

To complete the data extraction template, two extractors extract in duplicate and agree on the results. (Please see Data Extraction Table 1a, 1b and 1c. They can be merged into one table for extraction purposes). NACI

encourages proper documentation for data extraction. Data extraction forms are to be submitted to PHAC. This data may also be made available for public access.

2.5 Quality appraisal

For quality appraisal of the included studies, use The Joanna Briggs Institute Critical Appraisal Checklist for Economic Evaluations[39]. Two reviewers assess quality in duplicate and agree on assessment. Quality appraisal can be done in Distiller SR or Excel concurrently during data extraction or after data extraction. (See Data Extraction Table 2 and Report Figure 1)

Reviewers need to work with PHAC and the NACI WG to make the decision of whether to include or exclude low quality studies and to consider the appropriateness of excluding low quality studies. For instance, reviewers could report only the "best evidence" by including studies deemed high quality or acceptable and excluding unacceptable studies[40]. Reviewers can work with PHAC and NACI WG to determine the essential appraisal questions. Studies can be considered "high quality" if they satisfy essential appraisal questions and do not have any severe deficiencies. Studies can be considered "acceptable" if they satisfy essential appraisal questions, but have some minor deficiencies in other sections of the quality appraisal. Studies can be considered "unacceptable" if they have clear issues across essential questions in the quality appraisal. Screening out these low quality studies may prevent bias from being introduced into the final dataset and from potentially generating misleading results.

JBI does not include a summary score; however, the stacked bar graphs (Report Figure 1) may be able to provide a visual representation of the quality of the studies. Reviewers are to discuss with PHAC and the NACI WG if they want to use alternative/ additional quality appraisal tool(s) based on the research question.

2.6 Vaccine Model-specific appraisal

For the vaccine model-specific appraisal, use the World Health Organization (WHO) guide for standardization of economic evaluations of immunization programmes, chapter 6[15]. Two reviewers assess the quality in duplicate and agree on assessment. (See Data Extraction Table 3 and Report Figure 1).

Note: In appraising the model, the reviewers should also consider vaccine-specific items such as:

a. Herd immunity
b. Natural immunity
c. Supplies (i.e., vaccines, syringes, safety boxes)
d. Public health costs (i.e., contact tracing)
e. Disease surveillance
f. Distribution system (i.e., transport and cold storage)
g. Vaccine wastage and waste management

2.7 Applicability and Transferability appraisal

Transferability of ICERs: NACI recommends that an Applicability and Transferability tool be used to measure the fit to the Canadian context (see Data Extraction Table 3 and Report Figure 1):

a. Recommended tools are either Heyland's generalizability criteria
b. Or Antonanzas' transferability index[42] (formula is not necessary just use the checklist)
c. Or a combination of both

Summary and results

3.1 Inclusion of Studies

Reviewers should describe if they are reporting on all studies or if they are reporting on select studies based on their quality or on conflict of interest.

In terms of obtaining grey literature that is not publicly available, report which organizations were contacted, whether multiple attempts were made to contact them, and whether you were successful in obtaining the grey literature.

Reviewers can comment on publication bias.

Reviewers may also consider a stratified analysis where studies with conflicts of interest are excluded from analysis.

3.2 Summary

Prepare a summary of the included studies. Prepare a PRISMA Flow Diagram, track documents and synthesize the included studies for PHAC and the relevant NACI Working Group(s) for comment and feedback. The summary will focus on a high level synthesis of the literature retrieved and includes, but is not limited to, a summary of: (Use a version of Data Extraction Table 1a, 1b and 1c or Report Table 1)

- Location of study;
- Year of study;
- Population and subgroups;
- Age range/ gestational age;
- Health condition;
- Intervention/ comparator;
- Funding;
- Vaccine Coverage and duration of Protection
- Vaccine Schedule assessed;
- Study designs;
- Type of study design, analytic technique
- Study perspective;
- Time horizon, discount rate;
- Cost outcome;
- Effectiveness outcomes;
- Results, ICERs, Net health/ monetary benefit, reduction in hospitalization etc.;
- Influential parameters from Sensitivity Analysis, results from influential parameters;
- Stratified analysis excluding those with conflicts of interest (COIs)

3.3 Inflate the Incremental Cost- Effectiveness Ratios (ICER)

Inflate ICERs (or any monetary outcomes) to current Canadian dollars by converting the local currency to Canadian dollars using the Organization for Economic Co-operation and Development's (OECD) purchasing power parity rates, then the Bank of Canada's inflation rates. Note: Keep the unadjusted and adjusted ICERs for analysis purposes

3.4 Prepare evidence tables and any summary measures

Prepare evidence tables and any summary measures for all studies included in the review as per specifications of NACI methodology. (See Report Tables 1 – 3)

Update the literature review prior to preparation of report and update as per input from PHAC, relevant NACI WG(s) and if required, NACI. NACI encourages proper documentation for all evidence tables and summary measures. All evidence tables and summary measures are to be submitted to PHAC. This data may be made available for public access.

What's needed in the report

4.1 What's needed in the report?

1. Executive Summary/Abstract

2. Introduction

3. Detailed Technical Report Methods

   a. Methods – Search Strategy, PROSPERO registration number
   b. PICO(TS), Eligibility criteria (Inclusion / Exclusion criteria)
   c. Screening, data extraction, quality appraisal and vaccine model-specific appraisal.
   d. Critical appraisal/Planned analysis (subgroup analysis) and evidence synthesis (or descriptive reporting)
   e. Reviewers' conflicts of interest or funding source(s)

4. Results

   a. PRISMA Flow chart of studies screened and included, use of PRISMA guidelines[34].
   b. Summary/ Overview of studies included (Patient characteristics, study characteristics) (Report Table 1)
   c. Summary of Economic analytic technique, Model Structure if applicable, Perspective, Time horizon, Discount rate, Health outcomes measured, Cost outcomes measured and Vaccination cost.
   d. Main Results and Conclusions
      - Preference to have reviewers report both discounted and undiscounted results.
      - For all studies conducted in non-Canadian jurisdictions report the cost-effectiveness threshold of the country.

        Preference to have reviewers report unconverted ICERs and converted ICERs (in CAD and converted/inflated) in the results table. (Report Table 2 and 3)

      - Graphical representation of ICERs (e.g. scatterplot, or histogram) to illustrate cost-effectiveness in a cost-effectiveness plane or in relation to another variable (e.g. incidence of X, age of patients).
      - Canadian Results and Conclusions (Report Table 2 and/or 3)
        - Highlights of Canadian studies, summary of results
        - Summary of ICERs
        - Conclusions
        - Comparison of Canadian Studies

e. Description of Sensitivity Analysis/Scenario analysis (i.e., one-way, PSA, threshold analysis, etc. how methodological, parameter, and structural uncertainty were addressed). As well, report findings of sensitivity analysis and which variables the analysis were sensitive to.
f. Study Sponsorship and any potential impact on cost-effectiveness results. Stratified analysis excluding those with COIs. Reviewers could also provide a narrative summary on industry results versus other results.

5. Discussion/ Overall Conclusions

a. Brief summary of key findings
b. Limitations and strengths of the review
c. Transferability of ICERs: Recommend that an Applicability and Transferability tool be used to measure the fit to the Canadian context
    - Recommended tools are either Heyland's generalizability criteria
    - Or Antonanzas' transferability index (formula is not necessary just use the checklist)
    - Or a combination of both

(Please answer questions in excel, yes, no or unclear as well as an answer to justify your answer) (See Data Extraction Table 4)

4.2 Tables/ Figures/ Appendices

1. Full search strategy
2. PRISMA Flow chart
3. Grey Literature Search Extraction Table 1
4. Data Extraction Table: Characteristics to Review Studies; (Data Extraction Table 1a, 1b, 1c)

1. Report Table: Detailed Characteristics of Included Studies (examples: Author, year, perspective, study type, comparators, population, model type, time horizon, discount rate, cost-effectiveness threshold, included interventions and results); (Report Table 1 or combination of Data Extraction Table 1a, 1b, 1c)
2. Table/ Figure: Critical appraisal, Model appraisal and Transferability appraisal for individual studies (Data Extraction Table 2, 3 and 4) and as a summary figure (stacked bar charts); (Report Figure 1)
3. List/ Frequency history for the influential parameters from the sensitivity analysis
4. Additional graphical representation of ICERs (e.g. scatterplot, or histogram) to illustrate cost-effectiveness in a cost-effectiveness plane or in relation to another variable (e.g. incidence of X, age of patients). May consider adding additional graphs for subgroups of interest.
5. Cost-effectives results table (Report Table 2 and 3)
6. Stratified analysis excluding those with COIs. (Modified Report Table 2 or 3 for excluding industry studies or COIs)

Definitions

1. SOP: Standard operating procedure
2. NACI: The National Advisory Committee on Immunization
3. CIRID: The Centre for Immunization and Respiratory Infectious Diseases
4. PHAC: Public Health Agency of Canada
5. PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses
6. PICO (TS): Population, intervention, comparator(s), and outcome(s) of interest (specific timing or type of study and setting)
7. CUA: Cost-utility analysis

8. CEA: Cost-effectiveness analysis
9. CBA: Cost-benefit analysis
10. PROSPERO: International database of registered systematic reviews in health and social care, welfare, public health, education, crime, justice, and international development, where there is a health related outcome. Features from the protocol are recorded and maintained as a permanent record. PROSPERO is produced by the Centre for Reviews and Dissemination and funded by the National Institute for Health Research (NIHR).
11. HC: Health Canada
12. MeSH: Medical subject headings
13. CADTH: Canadian Agency of Drugs and Technologies in Health
14. HTA: Health Technology Assessment Database
15. NHS EED: NHS Economic Evaluation Database
16. DARE: Database of Abstracts of Reviews of Effects
17. DistillerSR is systematic review software that manages, tracks, and streamlines the screening, data extraction, and reporting processes of systematic reviews and literature reviews.
18. WG: Working groups
19. WHO: World Health Organization
20. ICER: Incremental Cost- Effectiveness Ratios
21. OECD: Organization for Economic Co-operation and Development
22. PSA: Probabilistic sensitivity analysis
23. ID: Identifier
24. AEFI: Adverse event following immunization
25. CE: Cost-effectiveness
26. GA: Gestational Age
27. QALY: Quality-adjusted life year
28. COI: Certificate of Insurance

Template for grey literature search strategy

All Tables are examples and items may be modified, added to or deleted based on your discretion and on your review. NACI encourages proper documentation for all evidence tables, figures and summary measures. They are to be submitted to PHAC. This data may be made available for public access.

Grey Literature Search Extraction Table 1:			
Resource/ Website	Search Terms	Number of Results Screened	Number of Results Retained

Templates for data extraction

All Tables are examples and items may be modified, added to or deleted based on your discretion and on your review.

NACI encourages proper documentation for data extraction. Data extraction forms are to be submitted to PHAC. This data may also be made available for public access.

Data Extraction Table 1a: Data Extraction Template 1

Author, Year	Age range/ Gestational age	Location of Study	Population and Subgroups	Characteristics of population and Setting	Health Condition	Intervention/ Comparator	Herd Effect	Vaccine Coverage and Duration of Protection	Funding / Funding Source
		(Country)					(Yes/ No)		(Yes/ No) and Source

(All tables can be broken up into more categories if needed)

* Optional Categories: Reference ID, Direct Vaccine Efficacy, Strain Coverage, Protection Against Carriage and Adverse event following immunization (AEFI)

Data Extraction Table 1b: Data Extraction Template 2

Author, Year	Analytic technique	Study design	Study perspective	Dosing schedule assessed	Time horizon and discount rate	Cost outcome	Cost of intervention	Effectiveness outcomes	Threshold used
	(e.g., CBA, CEA, CUA)	(e.g. decision analysis, Markov, etc.)			(Years, %)	(Currency, year)		($/ QALY, hospital admission avoided)	

(All tables can be broken up into more categories if needed)

* Optional Categories: Reference ID, Hospitalization Rate, Mortality Rate and Reduction in Hospitalization, Reduction in Mortality

Data Extraction Table 1c: Data Extraction Template 3

Author, Year	Results for CE or Health Outcomes	Results for CE or Health Outcomes Units	Results Context	Result Conclusion	Type of Sensitivity Analysis	Influential Parameters from SA	Results from Influential Parameters
	(absolute numbers, Cost/ QALY, reduction in hospitalization etc)	$/QALY		(Cost-effective or not?)	(e.g. 1-way, PSA)	(e.g. CE to not, and vice versa)	

(All tables can be broken up into more categories if needed)

* Optional Categories: Reference ID, Scenario Analysis and Results from Scenario Analysis

**Note tables can be used for Data Extraction or inclusion in report

Data Extraction Table 2: Quality Appraisal: Joanna Briggs Institute Checklist		
Author, Year	Yes/No/Unclear	Comments
Q1: Is there a well-defined question?		
Q2: Is there comprehensive description of alternatives?		
Q3: Are all important and relevant costs and outcomes for each alternative identified?		
Q4: Has clinical effectiveness been established?		
Q5: Are costs and outcomes measured accurately?		
Q6: Are costs and outcomes valued credibly?		
Q7: Are costs and outcomes adjusted for differential timing?		
Q8: Is there an incremental analysis of costs and consequences?		
Q9: Were sensitivity analyses conducted to investigate uncertainty in estimates of cost or consequences?		
Q10: Do study results include all issues of concern to users?		
Q11: Are the results generalizable to the setting of interest in the review?		

Data Extraction Table 3: Vaccine Model-specific appraisal: WHO guide for standardization of economic evaluations of immunization programs, chapter 6		
Author, Year	Yes/No/Unclear	Comments
Q1: Model structure and assumptions		
Q2: Model type		
Q3: Validation (i.e., verification, calibration)		
Q4: Vaccine Specific Considerations:		
a. Herd immunity		
b. Natural immunity		
c. Supplies (i.e., vaccines, syringes, safety boxes)		
d. Public health costs (i.e., contact tracing)		
e. Disease surveillance		
f. Distribution system (i.e., transport and cold storage)		
g. Vaccine wastage and waste management		

Questions for vaccine model-specific appraisal

1. Are the model structure and implicit or explicit assumptions clearly described?
2. Is the model type (static, dynamic or stochastic) clearly stated and justified in light of likely changes to the force of infection and the role of chance in the transmission process? Have the model's strengths and weaknesses been discussed?
3. Has the model been validated? If so, has it been validated in as many facets of validation as possible?
4. Vaccine Specific Considerations:
    a. Herd immunity
    b. Natural immunity
    c. Supplies (i.e., vaccines, syringes, safety boxes)
    d. Public health costs (i.e., contact tracing)
    e. Disease surveillance
    f. Distribution system (i.e., transport and cold storage)
    g. Vaccine wastage and waste management

Please answer questions in excel, yes, no or unclear as well as an answer to justify your answer for either Heyland's generalizability criteria or Antonanzas' transferability index (without formula) or a combination of both.

Example: **Heyland's Generalizability Criteria**

Data Extraction Table 4: Transferability appraisal		
Author, Year	Yes/No/Unclear	Comments
Q1: Clinical generalizability; patients described in the analysis similar to those patients you see in your own setting?		
Q2: Systems generalizability; viewpoint relevant to your clinical setting/situation?		
Q3: Intervention under study generalizable to your setting?		
Q4: Costing methods applicable		
Q4a: Unit price		
Q4b: Mix of resources consumed the same?		
Q4c: Average cost per patient, similar across systems?		
Q4d: Convert exchange rates across countries appropriately?		
Q5: Outcomes measured appropriate to your setting?		
Q5a: Method to measure the outcomes compatible		
Q5B: Preferences of your patients are the same as those preferences used in the analysis?		
Q6: Discount rate applicable to your setting?		

Templates for report: tables and figures

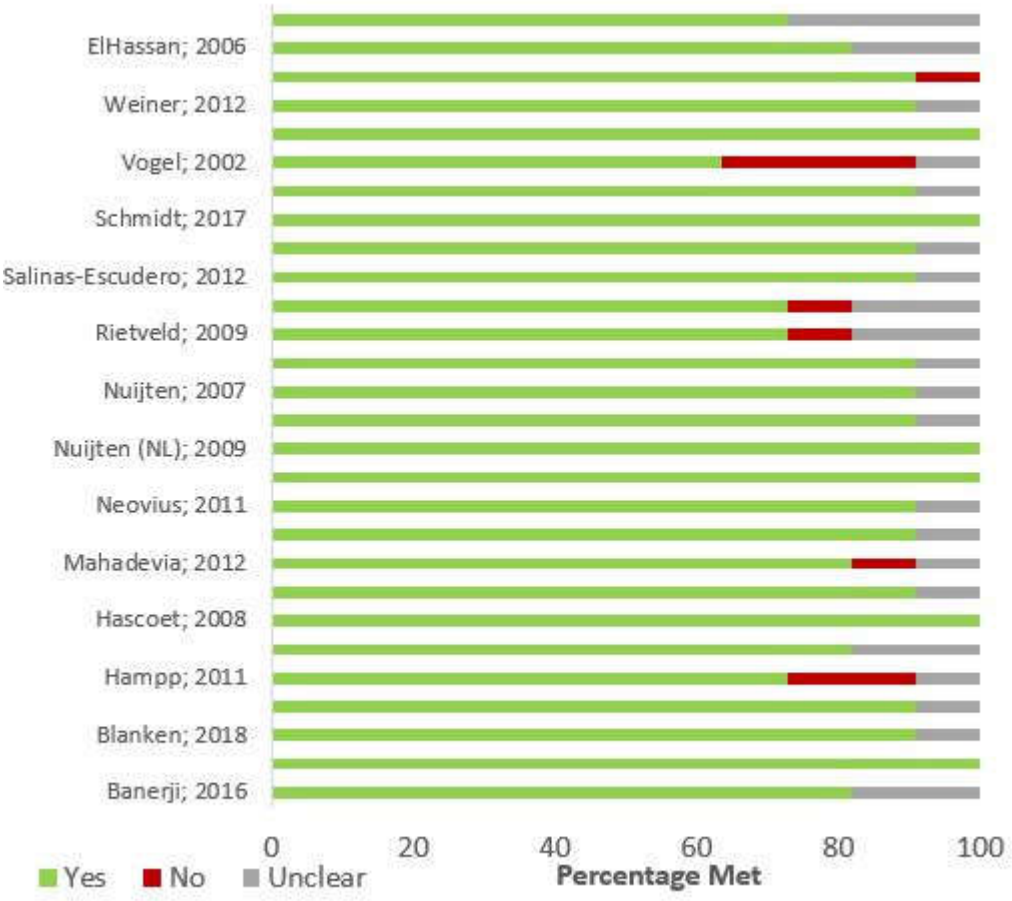
Please consider the following table/ figure templates when writing the NACI report. Items in the tables may be modified, added to or deleted based on your discretion and on your review. Formatting should be followed however.

NACI encourages proper documentation for all evidence tables, figures and summary measures. They are to be submitted to PHAC. This data may be made available for public access.

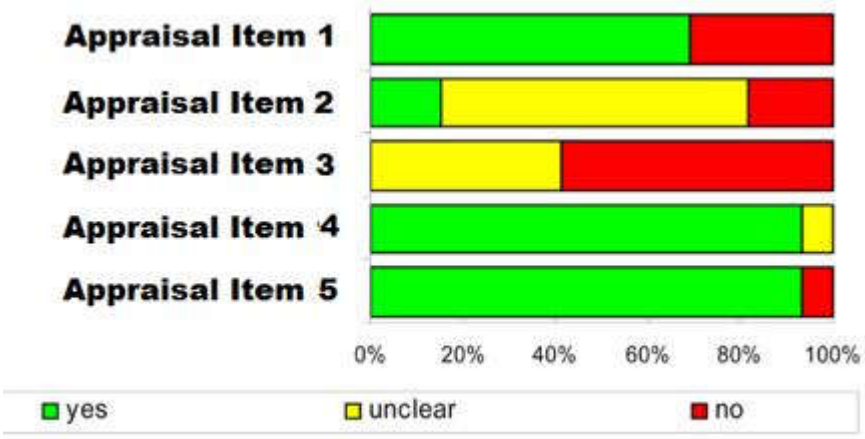
Report Table 1: Study Characteristics	
Health conditions reported	Number of studies*
Pre-term	
<=32 weeks GA	
32-35 weeks GA	
Health Conditions	
Other risk factors	
NR or healthy	
Country	**Number of studies**
US	
Canada	
UK etc.	
Age (months)	**Cumulative number of estimates from all studies***
< 3 months	
< 6 months	
< 12 months	
<24 months	
Not reported	
Outcomes	**Number of studies**
Cost per cases averted	
Cost per hospitalizations averted	
Cost per QALY	
Other	
Industry Sponsored	**Number of studies**
Yes	
No	
*Can exceed total n since some studies report multiple population, scenarios, and outcomes (Can add more outcomes of characteristics that are study specific)	

And /Or alternate option for Report Table 1: Study Characteristics								
Authors, Year	Country	Perspective	Analytic Technique	Study Design	Outcome Measure	Population	Time Horizon	Industry Funding
*Analytic Technique = CUA or CEA or CBA, Study Design = Markov model, piggyback trial, etc.								

Report Figure 1a. Quality Appraisal: Proportion of appraisal items met in each study
Vaccine Model-Specific Appraisal: Proportion of appraisal items met in each study
Transferability Appraisal: Proportion of criteria considered generalizable/ applicable in each study



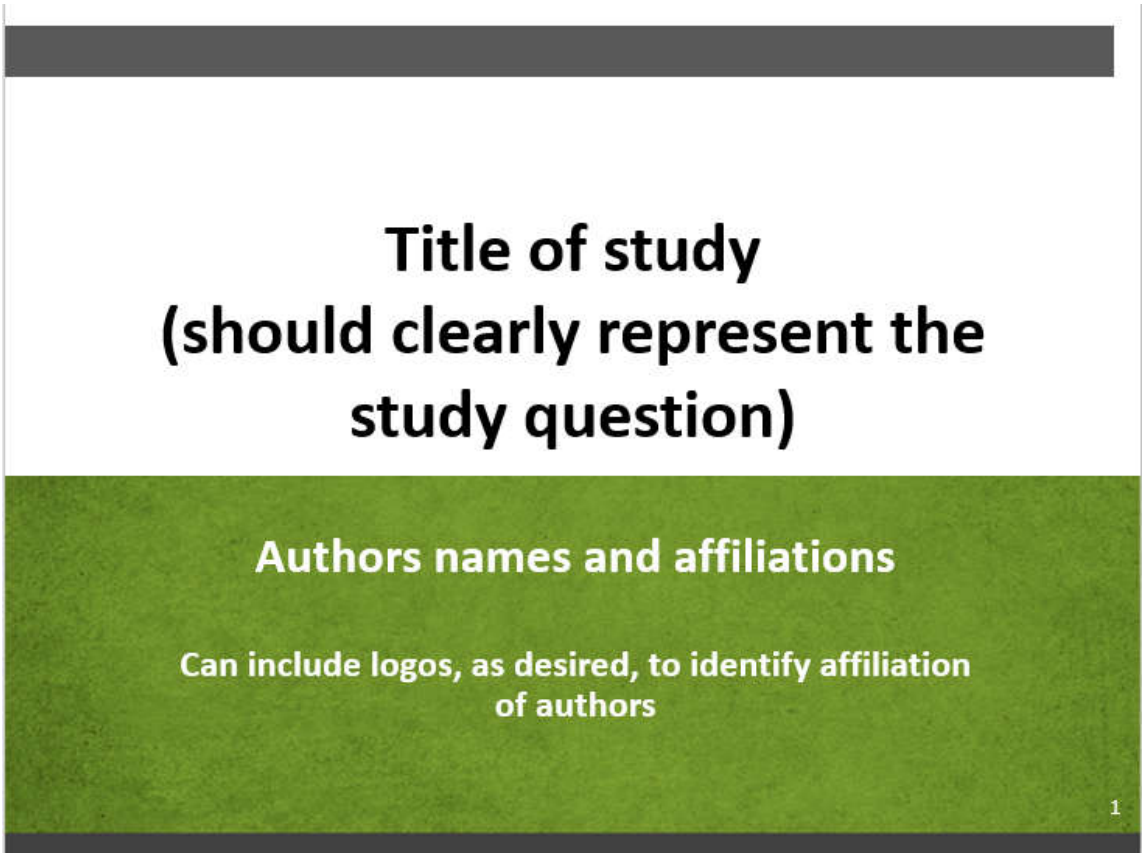
Report Figure 1b. Quality Appraisal: Proportion of appraisal items met in each study
Vaccine Model-Specific Appraisal: Proportion of appraisal items met in each study
Transferability Appraisal: Proportion of criteria considered generalizable/ applicable in each study



Report Table 2: Cost-Effectiveness (Payer perspective or Healthcare perspective or one table for each)							
	Health Conditions*						
	BPD	CHD	Healthy	Pre-term	Pre-term with BPD	Pre-term with risk factors	Other risk factors*
Number of estimates							
ICER (Minimum)							
ICER (Maximum)							
Proportion of estimates CE at $50,000/QALY							
Proportion of estimates CE at $100,000/QALY							
Proportion of estimates CE at $200,000/QALY							
*Health conditions that pertain to your Economic Systematic Review							

Report Table 3: Cost-effectiveness						
Study Author & Year	Condition	weeks GA	Perspective	ICER (Original)	Currency Year	ICER (2017 CAD per QALY)

VI.8 Module H – Supporting Tool #7 - Presentation Template for Presenting Economic Evaluations



Conflicts of Interest and Funding

- List any potential conflicts of interest for each author. If there are no potential conflicts of interest, a statement to that effect must be included (e.g., Author A: No conflicts of interest).
- Describe how the study was funded and the role of the funder in the identification, design, conduct, and reporting of the analysis. Describe other non-monetary sources.

2

Decision Problem

- The study question should be well defined, stated in an answerable form and relevant to the decision the target audience is facing.

- For example: What is the cost-effectiveness of routinely vaccinating age group XX against Disease Y, using vaccine Z compared to the current approach of A?

3

Methods

4

Methods: PICO

- Statement to specify the **interventions** included, including the **comparator(s)**. Justify the comparator
- Statement to identify the **population(s) (including subgroups)** directly or indirectly affected by the interventions studied. Describe:
  - Demographics (e.g., age, sex, socioeconomic status), specific condition, disease severity, comorbidities, risk factors, etc.
- Statement to specify **health outcomes** measured (e.g., cases, deaths, hospitalizations, outpatient visits, quality-adjusted life-years)

5

Methods: Study Design

- Statement of **setting, perspective, cost categories and outcomes**
- Statement of **time frame and analytic horizon** should be clearly stated. Describe how their respective durations are contingent on the type of vaccine evaluated, the intervention and target population, and thus the type of model developed
- Statement of **discount rate** used

6

Methods: Economic Model

- Specify **analytic method**
  - Identify **summary measure**
    - This could be presented as a word equation such as
      - Cost per case averted = etc., etc.
- Simple statement of economic model
- **Schematic of model structure**
- Describe - and give reasons for - the specific type of analytical decision model used. If applicable, describe why was a dynamic model not used?

7

Methods: Dynamic Model

- If the dynamic model was developed separately from the economic model, use this slide
- Specify type of dynamic model used (i.e., SIR)
- Describe model (i.e., how long does it take to reach herd immunity, minimum vaccine coverage to reach herd immunity, etc.)
- Show a **schematic diagram with suitable annotation**
  - Annotation in such a diagram must be done without use of mathematical notation. Authors are directed to ensure that such schematic diagrams can be readily understood without extensive reading of the main text

8

Methods: Key Assumptions

- Statement on key assumptions. They may include:
  - Adequate supply of vaccine
  - Waning vaccine immunity
  - Wastage of vaccine (i.e., sum of vaccines discarded, lost, damaged or destroyed)
  - Assumptions when a vaccine has not yet been developed or data on vaccine efficacy are not in the public domain
  - Assumptions necessary to transfer cost data when they are applied from other countries
  - Assumptions on how many infections are medically attended
  - Assumptions on how disease affects different subpopulations
  - Assumptions on how costs differ across subpopulations

9

Reference Case: Key Inputs

Variable	Description	Mean	Range/ Distribution	Source
	May have >1 of these slides Inputs that should always be presented include • Disease incidence • Vaccine effectiveness • Duration of immunity • Vaccine coverage • Cost (split by vaccine-related intervention and downstream costs i.e., disease treatment)			

10

Methods: Sensitivity Analyses

- Description of what sensitivity analyses were conducted
  - Type *(i.e., probabilistic, two-way SA for vaccine cost and vaccine effectiveness, threshold analyses, scenario analyses for relevant perspectives, best- and worst-case)*
  - Variables included
  - Ranges/ distributions and data sources

11

Summary of Methods

Table X: Summary of methods	
Type of analysis	Cost-utility analysis
Disease	Pneumococcal disease (pneumonia, otitis media, invasive pneumococcal disease)
Population	Infants (birth cohort)
Intervention	PCV13
Comparator(s)	No vaccine
Outcomes	Cases, deaths, DALYs/QALYs, cost
Perspective	Healthcare payer
Time horizon	Lifetime
Discounting	1.5%
Sensitivity analysis	Base case, scenarios, deterministic sensitivity analysis
Type of model	Single disease with multiple manifestations; decision tree

12

Results

13

Results

- Present:
  1. Health outcomes
  2. Costs
  3. Summary measure(s) - combining health outcomes and costs
- These could be presented in either a table or a graph. *(See sample table in the next slide. Also see SOP for recommended tables and figures)*

14

Table X: Results of an economic evaluation			
	Vaccine Program A	Vaccine Program B	Vaccine Program C
Clinical outcomes:			
LYs			
Cases averted			
Hospitalizations averted			
Deaths averted			
QALYs			
Costs:			
Vaccine-related			
Downstream			
Total			
Incremental Cost per QALY Gained (ICER):			
Versus Program A			
Sequential ICER			

Results: Additional Results

- 1-2 tables and/or graphs presenting some additional results *(See SOP for recommended tables and figures)*

16

Results: Sensitivity Analyses

- 1-2 slides presenting tables or graphs showing results from sensitivity analyses

17

Results: Influential Variables

- List/table/graph of influential variables (typically 3-5) *(See SOP for recommended tables and figures)*
  - Include how they might change results

18

Limitations and Generalizability

- List of important limitations and how they may impact the conclusions
- Comment on generalizability *(i.e., regional differences in terms of disease epidemiology, population characteristics, clinical practice patterns, resource-use patterns, unit costs, and other factors of relevance. Where differences exist, discuss the impact on the results (expected direction and magnitude), and the conclusions.)*

19

Key Findings

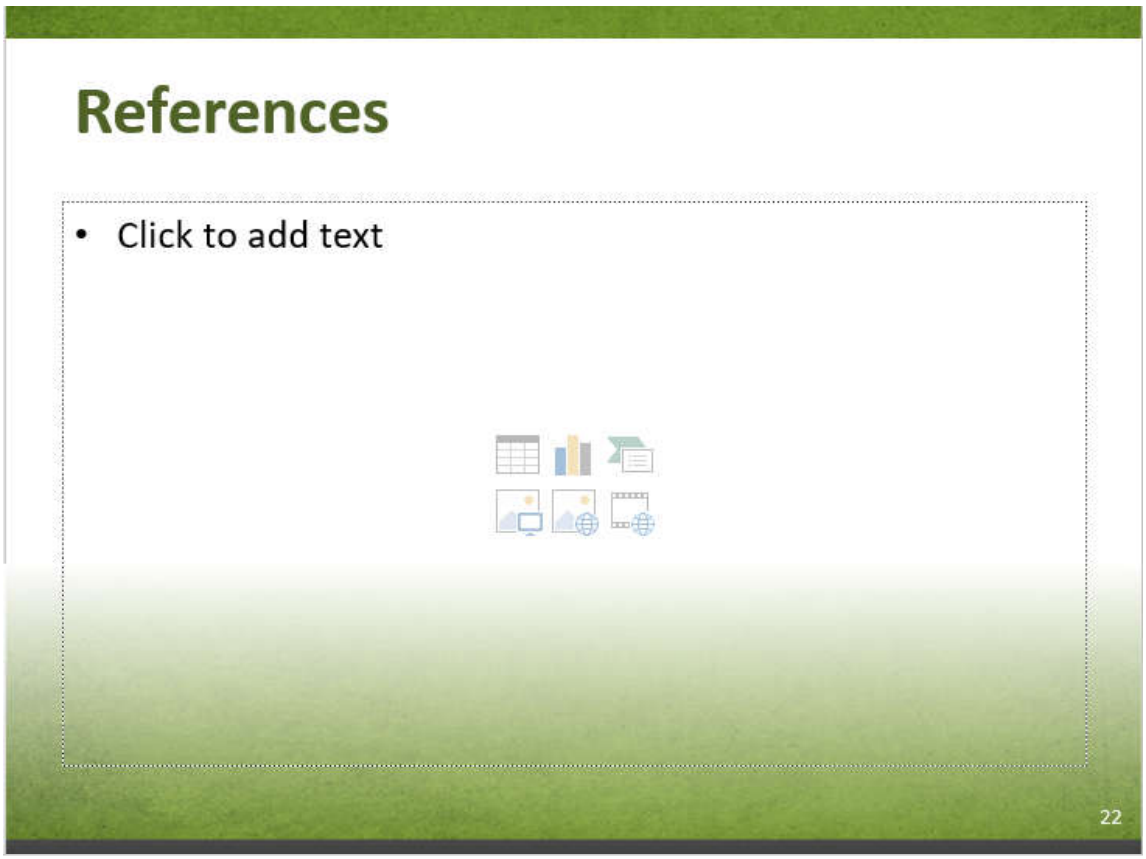
- Summarize the key findings of the study

20

Relation to Other Studies

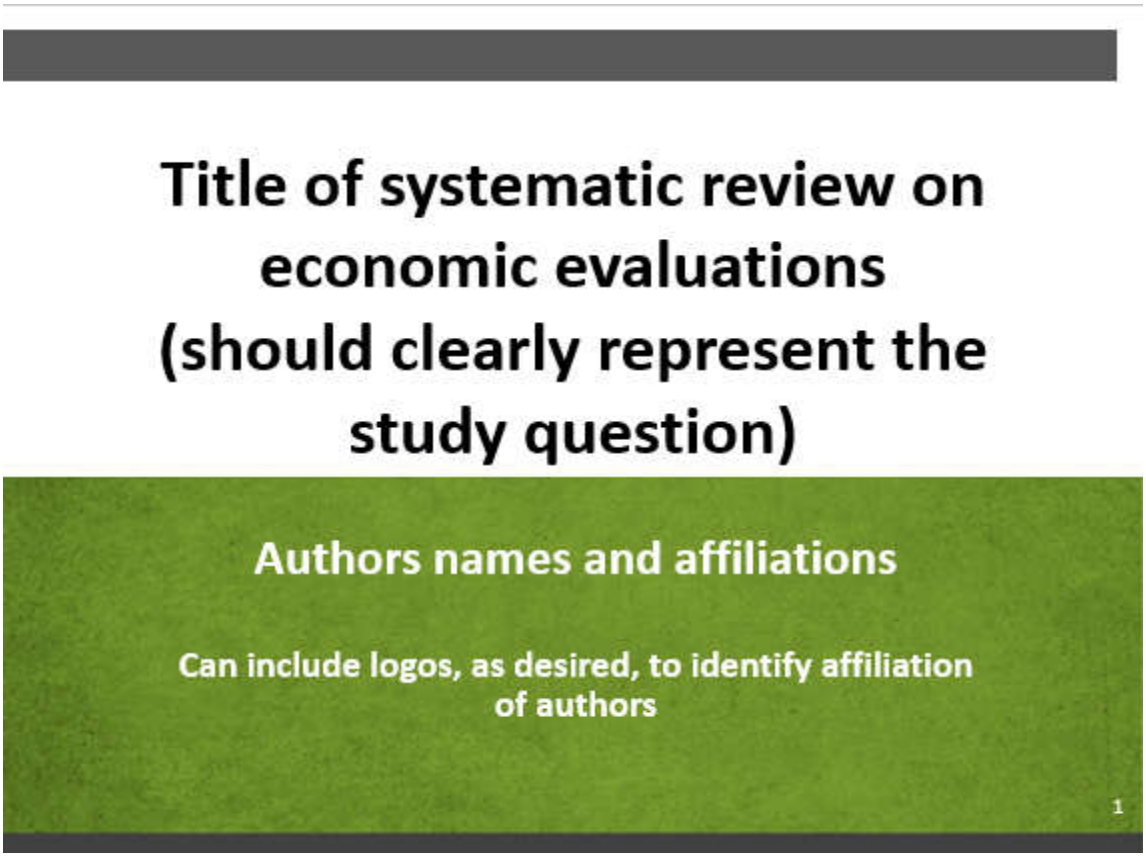
- If appropriate, compare results to results from other studies, including a fulsome discussion on comparability, differences, and significance. Could be presented as a list or table.

21



Supplementary Material

VI.9 Module I – Supporting Tool #8 - Presentation Template for Presenting Systematic Reviews



Conflicts of Interest and Funding

- List any potential conflicts of interest for each author. If there are no potential conflicts of interest, a statement to that effect must be included (e.g., Author A: No conflicts of interest).
- Describe how the study was funded and the role of the funder in the identification, design, conduct, and reporting of the analysis. Describe other non-monetary sources.

2

Research Question

- Define PICO (TS)
  - Where relevant, address type of study and setting are of interest

3

Methods [Please keep to 1 – 2 slides]

Search Strategy:

- State time frame searched & rationale for it (if applicable)

Inclusion and Exclusion Criteria:

- Please list

Reporting:

- Outcomes are reported in CAD [index year]

If any methods diverged from the NACI SOP, please briefly describe here (in terms of the search strategy, appraisal tools used, etc.)

4

PRISMA Flow Diagram

- This slide marks the beginning of the "Results" section
- Please provide diagram

5

Overview of Included Studies (N =)

Study Characteristics

- Countries/ jurisdictions (n =)
- Model-based (n =) versus Non-model-based (n =)
- Studies funded by industry (n =)
- Years of publication
- Etc.

Patient Characteristics

- Relevance to PICO of interest (i.e., age, health condition, comparator, etc.)

6

I. Overview of Non-Model Studies (N =) [such as trial-based studies, studies based on admin data, etc.]

- Comparators
- Perspective
- Types of sensitivity analysis
- Sample size(s)
- Time horizon(s)
- Choice of effectiveness outcomes/ intermediate outcomes
- Analysis: comment on protocol driven care vs. clinical practice; how missing/ censored/ skewed data were handled
- Etc.

7

II. Overview of Economic Models (N =)

- Types of models (i.e., Markov, agent-based, etc.)
  - Comment on model structure, if possible (i.e., what were the health states)
- Perspective(s) used
- Time horizon(s) used
- Types of sensitivity analyses conducted
- Assessment of study quality
- Etc.

8

II. Economic Models
Key Model Parameters

- Provide the average and range of some key model parameters
  - Mandatory variables to report: vaccine cost, vaccine effectiveness, epidemiology (i.e., incidence)
  - Influential parameters
  - Etc.
- For face validity

9

Summary of Results

- Report clinical outcomes, cost outcomes, and ICER outcomes in graphical or tabular form
  - Consider disaggregating outcomes
  - Specify if the ICERs are sequential or against a reference case (specify comparator)
- Consider presenting key parameters (i.e., vaccine price, vaccine effectiveness, epidemiology) alongside results
- Consider presenting sensitivity analyses (i.e., deterministic, probabilistic)
- See SOP example tables (i.e., Report Table 2 and 3; as well as following 2 slides)

10

Example Results Table #1

Incremental Cost-effectiveness Ratios	
Number of estimates	
ICER (Minimum)	
ICER (Maximum)	
Proportion of estimates that are cost-saving	
Proportion of estimates CE at $50,000/QALY	
Proportion of estimates CE at $100,000/QALY	

11

Example Results Table #2

Author, Year	Study 1	Study 2
Population		
Intervention		
Comparator		
Clinical Outcomes		
Cost Outcomes		
ICER *(specify if sequential or against a reference case)*		

12

Stratified Results

- Present results by industry vs. public health agency vs. recognized funding agency
- May consider presenting by study perspective, i.e., healthcare vs. societal
- May consider presenting by poor quality vs. not
- May provide range of results or brief description

13

Canadian Studies (N =)

- State key findings
- Compare results to non-Canadian studies
- Industry funding (n =)
- Discuss study quality and applicability to PICO of interest

14

Key Findings and Discussion

- What is the take-home message for decision-makers?
  - Consider reporting on results of studies most relevant to decision-makers (i.e., highest quality studies, high quality Canadian studies)
  - Consider
  - Avoid stating policy implications and any references to explicit or implicit cost-effectiveness thresholds. Policy implications are the responsibility of NACI
  - For example, reviewers may not say "Based on the SR, the intervention appears to be cost-effective". Reviewers may say "Most included studies (N = 9) concluded that the intervention is cost-effective based on their respective regional thresholds used"
- Was there a consensus among studies? Were the studies too heterogeneous?
- Recap: List the most **influential parameters** reported by included studies
- Recap: Comment on study quality

15

Strengths and Limitations

- Of the included studies (i.e., Were disease dynamics appropriately captured? Were the data sources appropriate?)
- Of the systematic review itself

16

Generalizability

- Comment on generalizability *(i.e., regional differences in terms of disease epidemiology, population characteristics, clinical practice patterns, resource-use patterns, unit costs, and other factors of relevance. Where differences exist, discuss the impact on the results (expected direction and magnitude), and the conclusions.)*
  - *Key parameters to discuss are vaccine price, vaccine effectiveness, and epidemiology*
- Consider using the Transferability Tools to guide your discussion

17

References

- Click to add text

18

Supplementary Material

19

VII. REFERENCES

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