Interpretation Guide – Health Economics

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Preamble

The National Advisory Committee on Immunization (NACI) Interpretation Guide – Health Economics is a document that outlines how to interpret common concepts related to **cost-utility analysis (CUA)**. The audiences of this Interpretation Guide are NACI and federal, provincial and territorial immunization program planners and decision-makers.

Opportunity cost

In the context of a fixed budget in the health system, opportunity cost is the benefits foregone as a consequence of adopting a new intervention and displacing an existing one.

Economic evaluation

Health economic analyses evaluate the inputs (called costs) required to create and sustain health programs, and the outcomes (health) of these programs. Outcomes can be valued in a few different ways. Depending on which outcomes are used, the economic evaluation is classified differently:

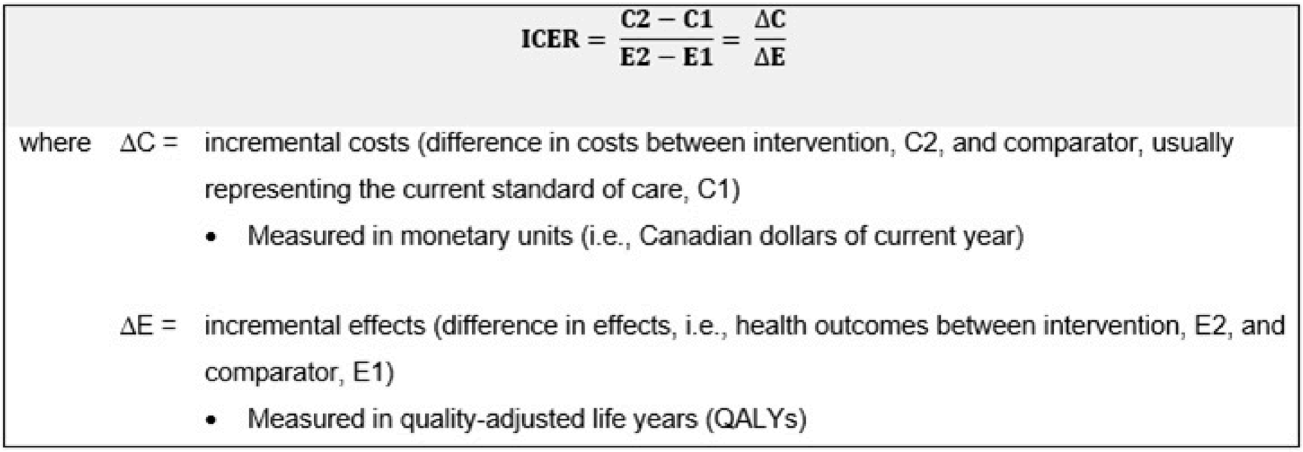
- Cost-utility analysis (CUA): Health outcomes are valued in **quality-adjusted life years (QALYs)** or another generic measure of health-related utility
- Cost-effectiveness analysis (CEA): Health outcomes are measured in natural units (e.g., cases averted)
- Cost-benefit analysis (CBA): Health outcomes are valued in monetary units.

CUA is the form of economic evaluation recommended by NACI as the reference case ("standard"), as outlined in the *NACI Guidelines for the Economic Evaluation of Vaccination Programs in Canada*. [1] CUA uses a generic outcome measure (QALYs) allowing decision-makers to make comparisons across different conditions and interventions.

Cost-utility analysis

- Assesses cost-effectiveness (or value for money)
    - Does not assess budget constraints. An intervention may be assessed to be cost-effective but not adopted because it is too expensive.
- Generates a summary measure called an **incremental cost-effectiveness ratio (ICER)**, sometimes called an incremental cost-utility ratio (ICUR) (Figure 1)
    - The ICER provides an estimate of the additional (incremental) cost for one additional unit of health outcome

Figure 1: Incremental cost-effectiveness ratio formula based on NACI recommendations to conduct a cost-utility analysis with outcomes expressed as quality-adjusted life-years.



$$\text{ICER} = \frac{\text{C2} - \text{C1}}{\text{E2} - \text{E1}} = \frac{\Delta\text{C}}{\Delta\text{E}}$$

where ΔC = incremental costs (difference in costs between intervention, C2, and comparator, usually representing the current standard of care, C1)

- Measured in monetary units (i.e., Canadian dollars of current year)

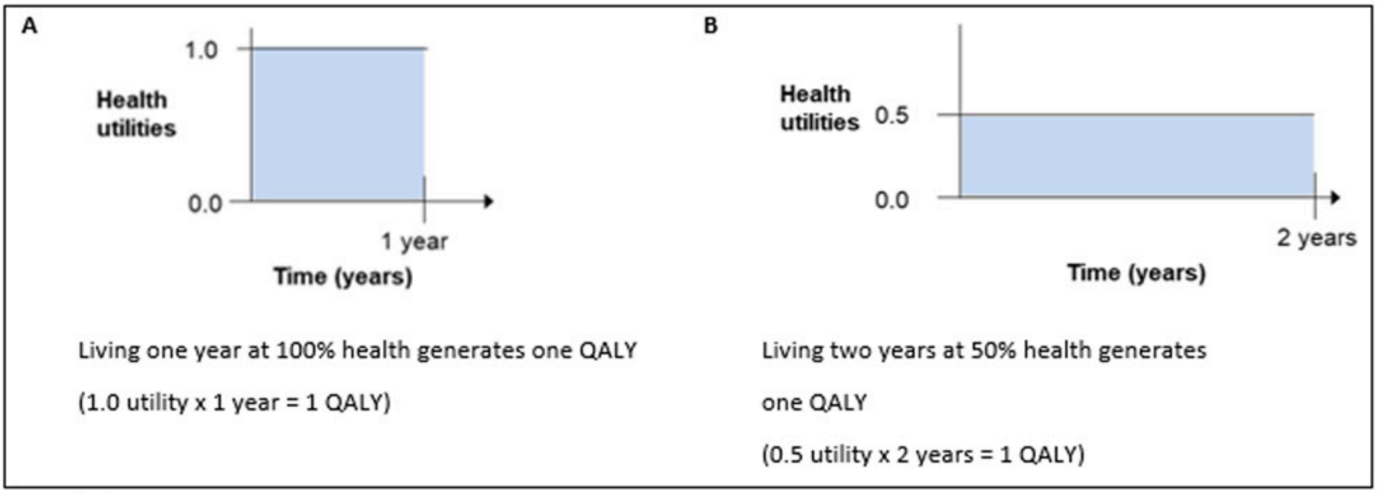
ΔE = incremental effects (difference in effects, i.e., health outcomes between intervention, E2, and comparator, E1)

- Measured in quality-adjusted life years (QALYs)

Quality-adjusted life year (QALY)

- QALY is a function of health-related quality of life (HRQoL) and quantity of life
- HRQoL is measured in health utilities, which:
    - Represent the strength of individuals' preferences for different health states
    - Are anchored at 0 and 1, representing HRQoL equivalent to being dead and equivalent to having perfect health, respectively
- See example in Figure 2, where both individuals A and B live an equivalent of one year in "perfect health" (i.e., 1 QALY)

Figure 2: Quality-adjusted life years of two individuals.



Living one year at 100% health generates one QALY

(1.0 utility x 1 year = 1 QALY)

Living two years at 50% health generates one QALY

(0.5 utility x 2 years = 1 QALY)

Cost-effectiveness plane

- The ICER formula can be represented graphically in a **cost-effectiveness plane** (Figure 3):
    - y-axis (vertical axis) = incremental costs (in dollars)

    - x-axis (horizontal axis) = incremental effects (often in QALYs)
    - Points on plane = interventions (A, B, C, D) or comparator (O), which is often the standard of care; the coordinates of the interventions (A, B, C, D) show the incremental costs and incremental effects compared to (O)
    - Slopes connecting interventions (A, B, C, D) to comparator (O) = ICERs comparing intervention (A to D) and comparator (O) (see Figure 4 for interpretations of ICERs falling in each quadrant)
    - Quadrants of plane can be labelled as I to IV, or by the directions of a compass.
- Note that the terms "**cost-saving**" and "**dominant**" are often incorrectly used interchangeably. Cost-saving refers to an intervention costing less than the comparator (hence, refers to quadrants III and IV collectively); whereas dominant refers to an intervention being less costly and more effective (hence, refers to quadrant IV exclusively).
- Quadrants III and I can both be used to calculate ICERs: cost (saved) per QALY (lost) in Quadrant III, and cost (expended) per QALY (gained) in Quadrant I (see section on "Cost-effectiveness thresholds"). While these ICERs should theoretically be treated similarly, the context of diminishing health to save money is quite different from the context of spending money to add health. This relates to opportunity costs, as the money saved would be used to invest in other interventions to, in theory, improve health. Similarly, the money spent would displace other interventions, but would, in theory, improve efficiency and resource allocation assuming the correct decision was made to adopt the intervention (see section on "Opportunity Costs").

Figure 3: Cost-effectiveness plane.

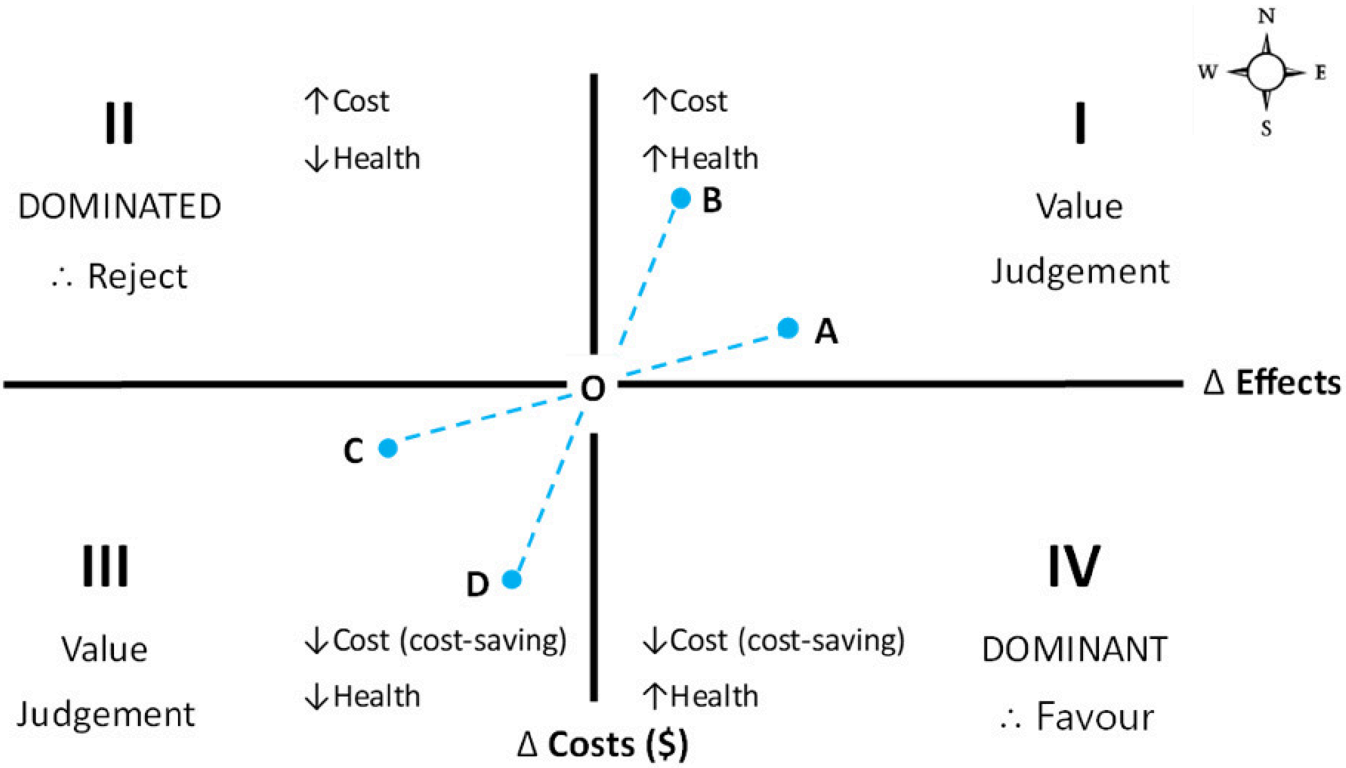
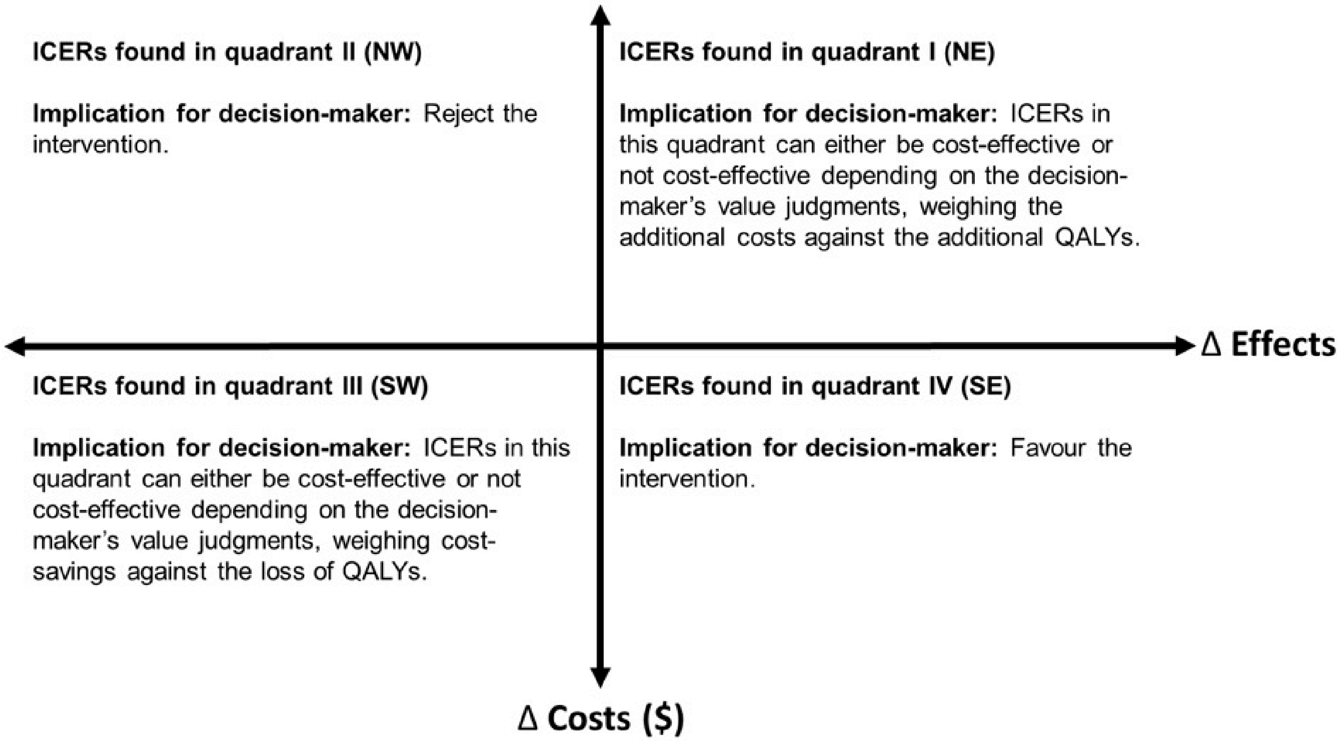


Figure 4: Interpretation of the cost-effectiveness plane.



ICERs found in quadrant II (NW)

Implication for decision-maker: Reject the intervention.

ICERs found in quadrant I (NE)

Implication for decision-maker: ICERs in this quadrant can either be cost-effective or not cost-effective depending on the decision-maker's value judgments, weighing the additional costs against the additional QALYs.

ICERs found in quadrant III (SW)

Implication for decision-maker: ICERs in this quadrant can either be cost-effective or not cost-effective depending on the decision-maker's value judgments, weighing cost-savings against the loss of QALYs.

ICERs found in quadrant IV (SE)

Implication for decision-maker: Favour the intervention.

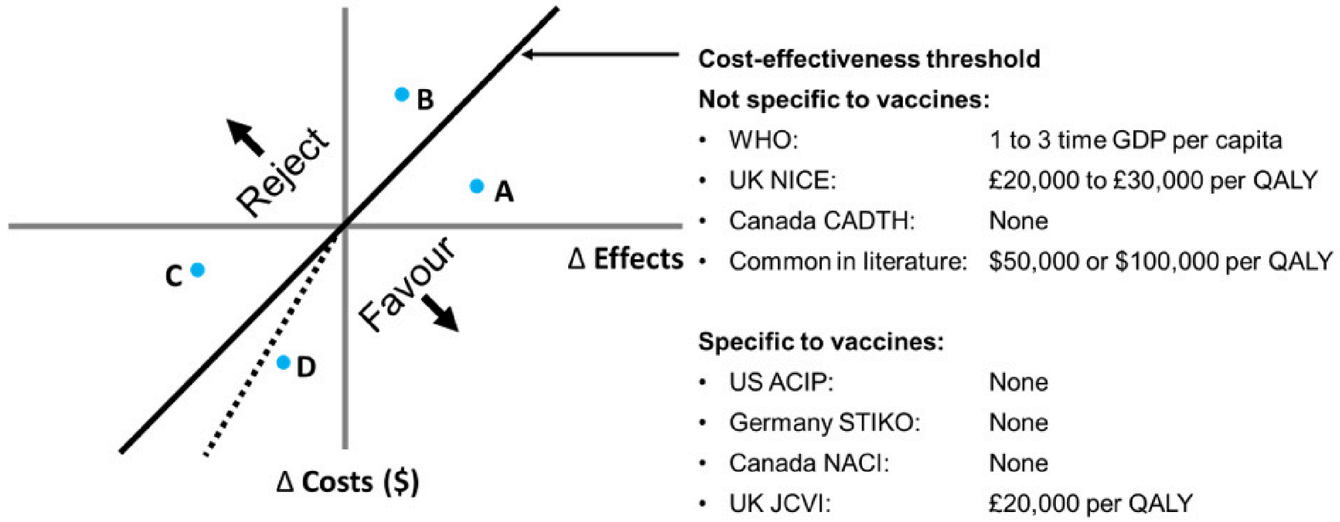
Cost-effectiveness thresholds

- Some international decision-makers use cost-effectiveness thresholds to support their value judgments of ICERs falling in quadrants I (NE) and III (SW) – that is, decision-makers compare if the ICERs are above or below

a threshold (interpretations are opposite for quadrants I and III as noted in Figure 3).
  - Canada and many other National Immunization Technical Advisory Groups (NITAGs) do not use explicit thresholds
  - In Canada, decisions to adopt or reject an intervention is not based on cost-effectiveness alone. NACI's decision framework accounts for efficacy, effectiveness, burden of disease, equity, ethics and other key public health decision criteria.
- Figure 5 is a graphical representation of a cost-effectiveness threshold on a cost-effectiveness plane
  - If decision-makers adopt interventions that are not cost-effective relative to the threshold, more cost-effective expenditures will be displaced
  - There are theoretical challenges of determining a threshold when using a societal perspective in an economic evaluation (which is one of the two perspectives that NACI recommends, the other being the publicly funded health system perspective)
    - The **opportunity cost** for the societal perspective is not known and there are no estimates in the literature
    - It is not appropriate to compare ICERs generated from a societal perspective to commonly used thresholds from a healthcare payer perspective.
  - There are theoretical challenges of adopting or rejecting interventions with ICERs that fall in quadrant III (SW)
    - Challenges include ethical considerations of accepting less effective interventions to save money, as well as inefficiency in resource allocation
    - Decision-makers may consider a steeper cost-effectiveness threshold in Quadrant III (SW) to account for people valuing health loss greater than the equivalent health gain.

Figure 5: Cost-effectiveness plane including cost-effectiveness thresholds. [2] [3] [4]

The solid line represents a cost-effectiveness threshold that does not change in Quadrant III (SW). The dotted line represents a cost-effectiveness threshold that becomes steeper in Quadrant III (SW). The steeper threshold accounts for people valuing health loss greater than the equivalent health gain. Given the explicit cost-effectiveness threshold depicted, decision-makers should adopt interventions A and D, and reject interventions B and C.



Cost-effectiveness threshold

Not specific to vaccines:

WHO:	1 to 3 time GDP per capita
UK NICE:	£20,000 to £30,000 per QALY
Canada CADTH:	None
Common in literature:	$50,000 or $100,000 per QALY

Specific to vaccines:

US ACIP:	None
Germany STIKO:	None
Canada NACI:	None
UK JCVI:	£20,000 per QALY

For the UK NICE threshold empirical evidence suggests threshold should be lower (best estimate: £12,936 per QALY). [6] For the UK JCVI threshold, the Consultation on the Cost-Effectiveness Methodology for Vaccination Programmes and Procurement Report recommended a lower threshold (£15,000), [7] which the UK government rejected. [8]

Sequential analysis

- When comparing **three or more** interventions, a **sequential analysis** is recommended
  - Compares an intervention with the next most costly intervention in sequence
  - Recall: ICERs compare two interventions (see Figure 1 formula)
  - Figure 6 describes the steps to calculate **sequential ICERs**
  - Tables 1 – 3 show the steps to calculate sequential ICERs with an example (adapted from CADTH 2017 Table 3) [9]

Figure 6: Steps to a sequential analysis when comparing three or more interventions

Step 1: Order interventions (3 or more) from least costly to most costly in table

Step 2: Calculate **delta cost** and **delta effect**, comparing to intervention listed directly above

Step 3: Remove any intervention that is more costly and less effective (i.e., **dominated**) than one directly above

Step 4: Calculate ratios, **delta cost** divided by **delta effect**, after the dominated interventions have been removed

Step 5: Remove any intervention whose sequential ICER is greater than the sequential ICER of the subsequent pair (i.e., intervention subjected to **extended dominance**, meaning the intervention will never be the optimal strategy regardless of the cost-effectiveness threshold)
Step 6: Recalculate ratios, **delta cost** divided by **delta effect**, after interventions subjected dominance have been removed to finalize sequential ICERs

Implication for decision-makers: The most cost-effective strategy is the intervention with the highest ICER that lies below the threshold, which is a different interpretation compared to quadrants I and III in the cost-effectiveness plane

Table 1: Example of calculating sequential ICERs in $ per QALY (Steps 1 – 3)

	Costs	QALYs	∆Costs	∆QALYs	Sequential ICER	Comment
Vaccine A	$3,000	4.00				
Vaccine B	$4,500	4.10	$1,500	0.10	15,000	
Vaccine C	$5,000	5.00	$500	0.90	556	
Vaccine D	$7,900	4.30	$2,900	**-0.70**	-4,143	Remove Vaccine D from analysis because it is more costly and less effective than C (i.e., D is dominated by C)
Vaccine E	$8,000	6.00	$100	1.70	59	
Vaccine F	$12,000	6.05	$4,000	0.05	80,000	
Vaccine G	$50,000	6.01	$38,000	**-0.04**	-950,000	Remove Vaccine G from analysis because it is more costly and less effective than F (i.e., G is dominated by F)

Table 2: Example of calculating sequential ICERs in $ per QALY (Steps 4 – 5)

	Costs	QALYs	∆Costs	∆QALYs	Sequential ICER	Comment

	Costs	QALYs	∆Costs	∆QALYs	Sequential ICER	Comment
Vaccine A	$3,000	4.00				
Vaccine B	$4,500	4.10	$1,500	0.10	**15,000**	Remove Vaccine B from analysis because its sequential ICER is greater than that of the next row (i.e., Vaccine B is subjected to extended dominance [*] through interventions A and C)
Vaccine C	$5,000	5.00	$500	0.90	556	
Vaccine E	$8,000	6.00	$3,000	1.00	3,000	
Vaccine F	$12,000	6.05	$4,000	0.05	80,000	

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[*] Extended dominance means that there is an alternative more effective and more costly than the intervention, but provides better value for money (lower ICER) than the intervention. In other words, the intervention will never be the optimal strategy regardless of the cost-effectiveness threshold.

Table 3: Example of calculating sequential ICERs in $ per QALY (Step 6)

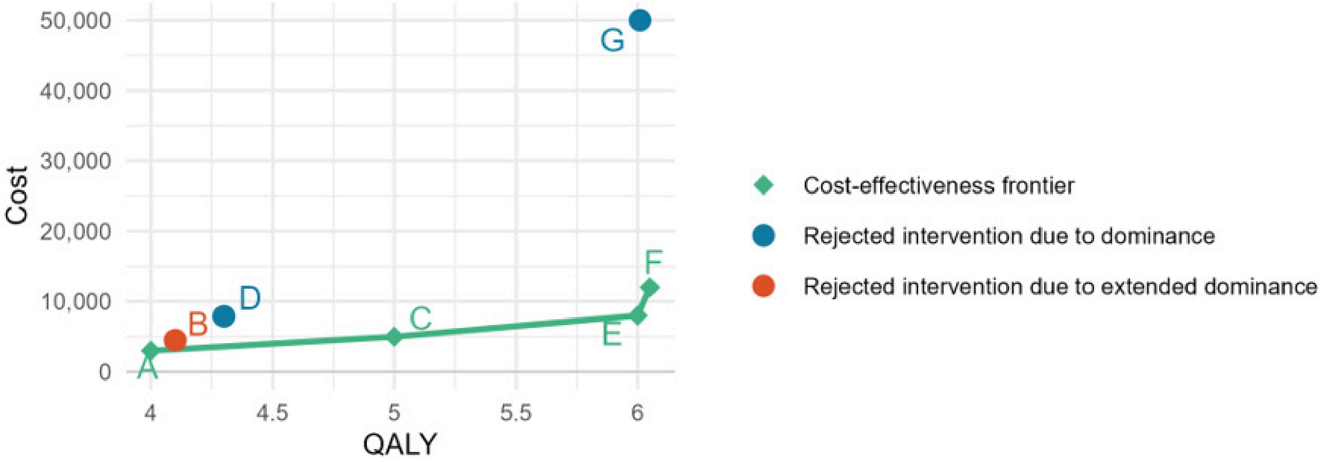
	Costs	QALYs	∆Costs	∆QALYs	Sequential ICER	Comment
Vaccine A	$3,000	4.00				**Implication**: If the decision-maker uses an explicit cost-effectiveness threshold of $50,000 per QALY, then the most cost-effective intervention is E. If the threshold is $100,000 per QALY, then the most cost-effective intervention is F.
Vaccine C	$5,000	5.00	$2,000	1.00	2,000	
Vaccine E	$8,000	6.00	$3,000	1.00	3,000	
Vaccine F	$12,000	6.05	$4,000	0.05	80,000	

Cost-effectiveness frontier

- A sequential analysis comparing three or more interventions can be graphically represented by a **cost-effectiveness frontier** (Figure 7)
    - y-axis (vertical axis) = mean costs

    - x-axis (horizontal axis) = mean effects
        - Note that the axes are mean effects and costs, not incremental effects and costs like in the cost-effectiveness plane in Figure 3
    - Point = intervention
    - Frontier = line linking the interventions that are not dominated
- **Interpretation**:
    - Any interventions above and to the left of the frontier are more costly and less effective than existing interventions (i.e., Vaccines D and G in Figure 7)
    - Any interventions below and to the right of the frontier are less costly and more effective than existing intervention; hence, the new intervention would redefine the frontier
- **Implication for decision-maker**: Interventions above and to the left of the frontier can be rejected; interventions located on the frontier can be considered efficient, existing interventions; interventions below and to the right of the frontier can be favoured (and should subsequently redefine the frontier with its inclusion).

Figure 7: Cost-effectiveness frontier (in green) based on the sequential analysis example from Table 3.



Further readings

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Abbreviations

ACIP	Advisory Committee on Immunization Practices
CADTH	Canadian Agency for Drugs and Technologies in Health
CUA	Cost-utility analysis
CBA	Cost-benefit analysis
CEA	Cost-effectiveness analysis
CUA	Cost-utility analysis
HRQoL	Health-related quality of life
ICER	Incremental cost-effectiveness ratio
JCVI	Joint Committee on Vaccination and Immunisation
NACI	National Advisory Committee on Immunization
NICE	National Institute for Health and Clinical Excellence
NITAG	National Immunization Technical Advisory Group
QALY	Quality-adjusted life year
STIKO	Standing Committee on Vaccination
WHO	World Health Organization

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