Incremental Cost-Effectiveness Analysis

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Learning Objectives and Outline

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Learning Objectives

- Differentiate between average & incremental CEA ratios
- Characterize decision problems by whether they are competing or non-competing
- Compute and interpret ICERs
- Practice ruling out “dominated” and “extendedly dominated” strategies
- Identify “high-value” versus “low value” care strategies, based on generally accepted cost-effectiveness thresholds

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Outline

1. Review of CEA ratio
2. Non-competing versus competing CEAs
3. Incremental CEA
4. Dominance & extended dominance
5. Comparators
6. CEA thresholds

Cost-Effectiveness Analysis

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Cost-Effectiveness Analysis

- Quantifies how to maximize the quality & quantity of life from among competing alternatives, given restricted resources
- It's an explicit measure of value for money
- A POPULATION-LEVEL decision-making tool

Cost-Effectiveness Analysis IS NOT

- Indiscriminate cost-cutting
- Downsizing
- For individual-level decision making
- The only tool for decision-making

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Cost-Effectiveness Analysis

Cost of Intervention

Cost of Alternative

Benefit of Intervention

Benefit of Alternative

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Cost-Effectiveness Analysis

Cost of Intervention

Cost of Alternative

Benefit of Intervention

Benefit of Alternative

Cost-Effectiveness Ratio

$$\frac{\text{Cost of Intervention} - \text{Cost of Alternative}}{\text{Benefit of Intervention} - \text{Benefit of Alternative}}$$

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Cost-Effectiveness Ratio

$$\frac{C_1 - C_0}{E_0 - E_1}$$

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Cost-Effectiveness Ratio

$$\frac{\Delta C}{\Delta E}$$

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Incremental Cost-Effectiveness Ratio

Most often used, since for most conditions there is already some available treatment.

- C_1: net present value of total lifetime costs of new treatment
- C_0: net present value of total lifetime costs of default treatment
- E_1: effectiveness of new treatment, measured in expected life expectancy, quality-adjusted life years (QALYs) or disability-adjusted life years (DALYs), or some decision-relevant health outcome.
- E_0: effectiveness of default treatment

$$\frac{C_1 - C_0 \quad (\Delta C)}{E_1 - E_0 \quad (\Delta E)}$$

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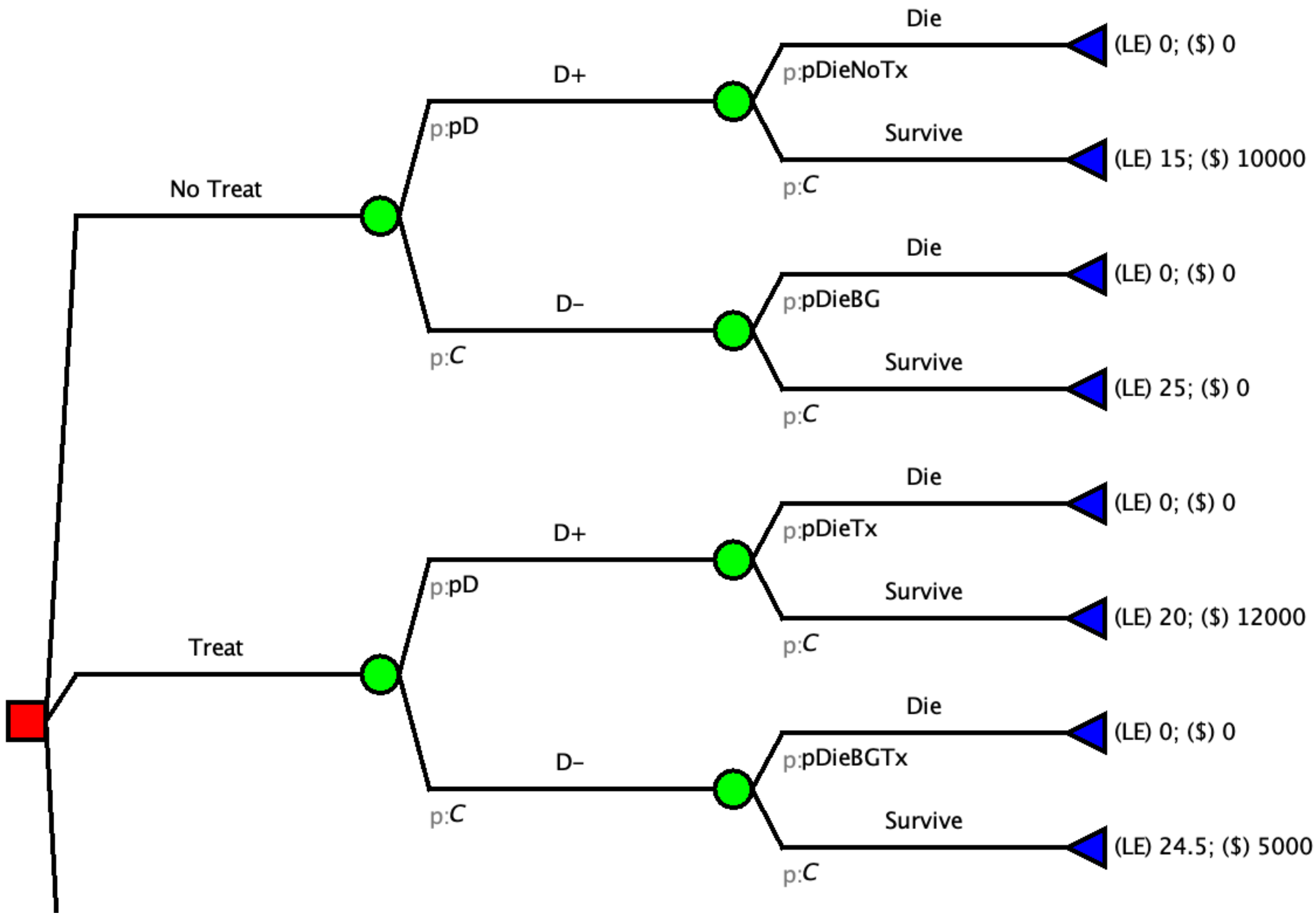
Neurologic Disease Decision Tree



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Outcomes

- C_{treat} = expected cost of treat everyone strategy.
- $C_{notreat}$ = expected cost of treat *no one* strategy.
- C_{biopsy} = expected cost of biopsy strategy.

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Outcomes

- C_{treat} = expected cost of treat everyone strategy.
- $C_{notreat}$ = expected cost of treat *no one* strategy.
- C_{biopsy} = expected cost of biopsy strategy.
- E_{treat} = expected life expectancy of treat everyone strategy.
- $E_{notreat}$ = expected expectancy of treat *no one* strategy.
- E_{biopsy} = expected expectancy of biopsy strategy.

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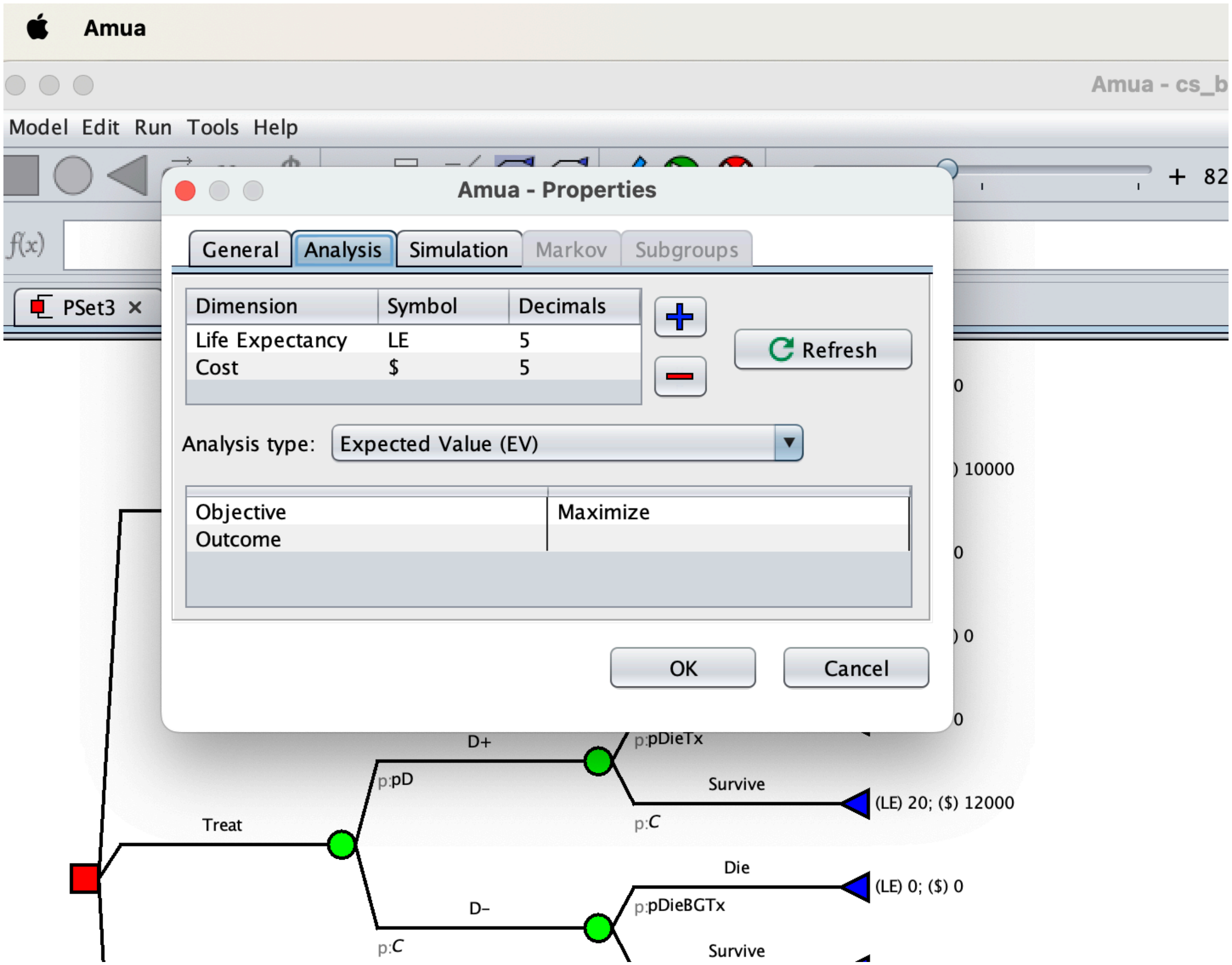
Outcomes in Amua



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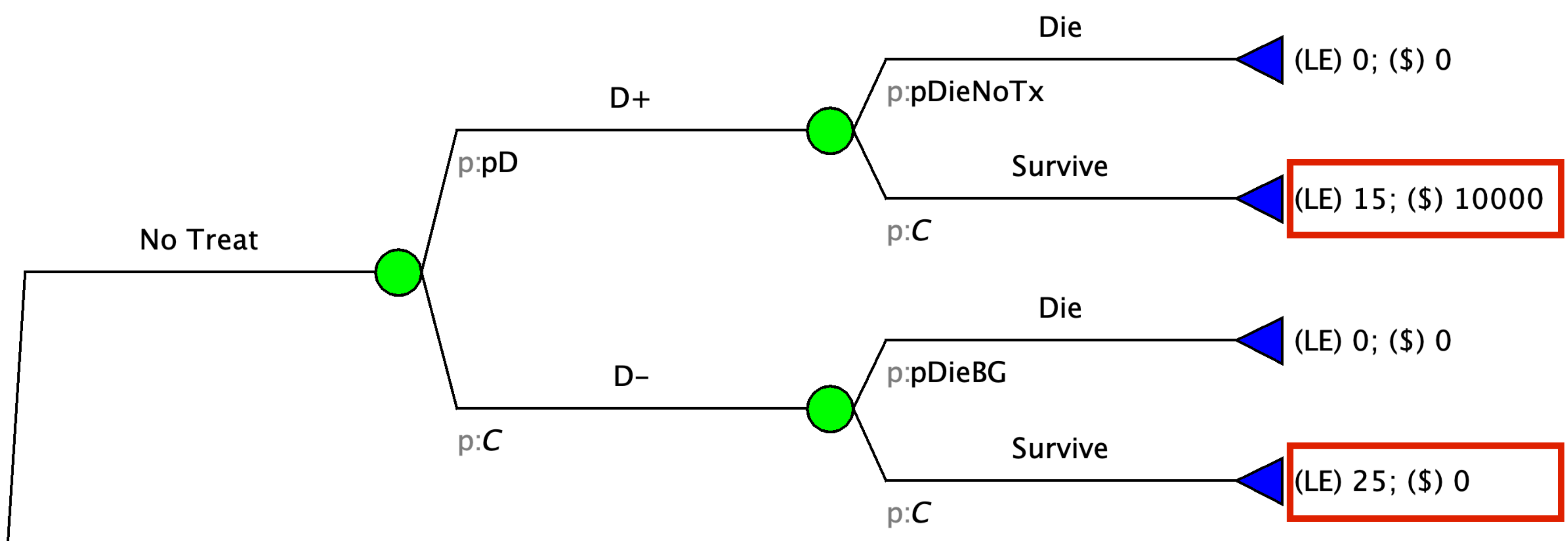
Treat All vs. Treat None

Strategy: Treat No One



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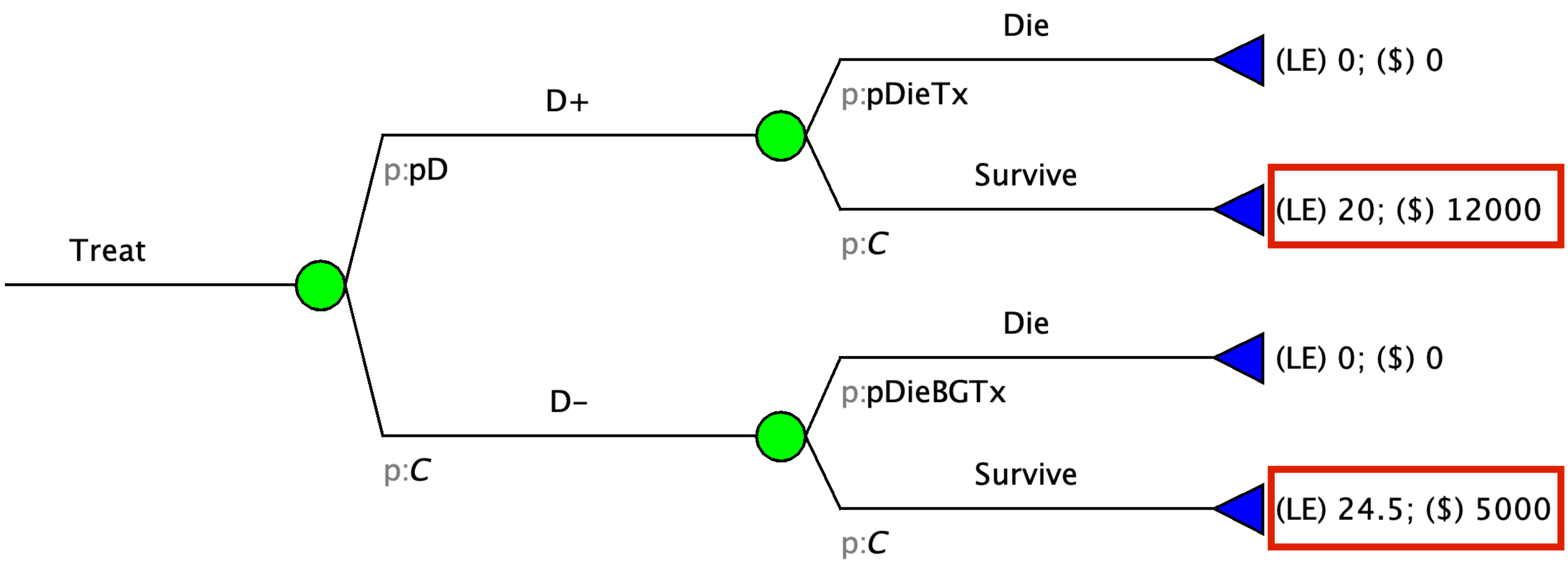
Treat All vs. Treat None

Strategy: Treat All



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Key Takeaways (For Now)

- Treatment yields *higher* life expectancy for those with disease, but comes at a cost.
- Treatment yields *lower* life expectancy for those without the disease, *and also* comes at a cost.
- Biopsy can help balance these two outcomes by better targeting treatment, but also comes with costs and risks.
- Incremental CEA provides a transparent framework for quantifying and weighing these considerations.

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Average Cost-Effectiveness Ratio

Special case where C_0 and E_0 are assumed to be zero.

- C_1: net present value of total lifetime costs of new treatment
- C_0: Assumed zero
- E_1: effectiveness of new treatment, measured in expected life expectancy, quality-adjusted life years (QALYs) or disability-adjusted life years (DALYs), or some decision-relevant health outcome.
- E_0: Assumed zero

$$
\begin{aligned}
ICER &= \frac{C_1 - 0}{E_1 - 0} \\
&= \frac{C_1}{E_1}
\end{aligned}
$$

Non-Competing vs. Competing CEAs

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Use of CEA in two situations

1. **Shopping Spree:** Decision problem has non-competing programs/interventions.

- Each program is compared to a null alternative; therefore, you're calculating an "average" cost-effectiveness ratio.

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Use of CEA in two situations

2. **Competing Choice:** Decision problem has competing programs/interventions for the same purpose; these choices are mutually exclusive.

- Two or more active alternatives in addition to the null option.
- You need to calculate an "incremental cost- effectiveness ratio", which gives us the added cost per unit of added benefit of an option, relative to the next less expensive choice

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Non-Competing (Shopping Spree) Decision Problem

How can we measure the relative priority of various health programs that compete for limited resources?

1. Cardiovascular disease program
2. Safe motherhood program
3. HIV prevention initiative
4. Child vaccination
5. Depression screening

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Assumptions

- Program alternatives are assumed to be independent
- Budget constraint is only limitation
- Neither the net cost nor the net effectiveness depend on what other programs are selected
- Programs are assumed to be divisible [programs can be partially implemented]

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Objectives: Shopping Spree Problem

- Maximize the total net effectiveness (health benefit) of the programs selected.
- Stay within budget.

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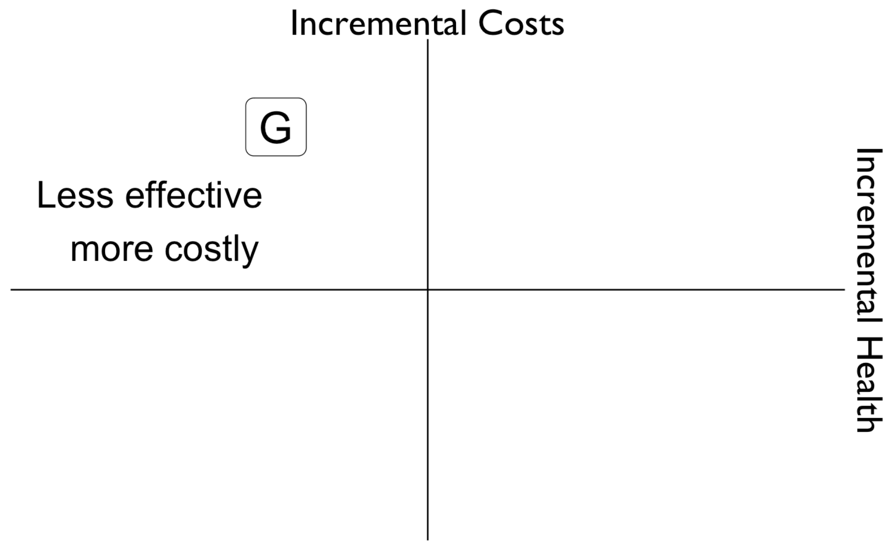
Shopping Spree Problem

Step 1: - Rule out programs that cost $ but have negative health effects
- Dominated by alternative of “no program”



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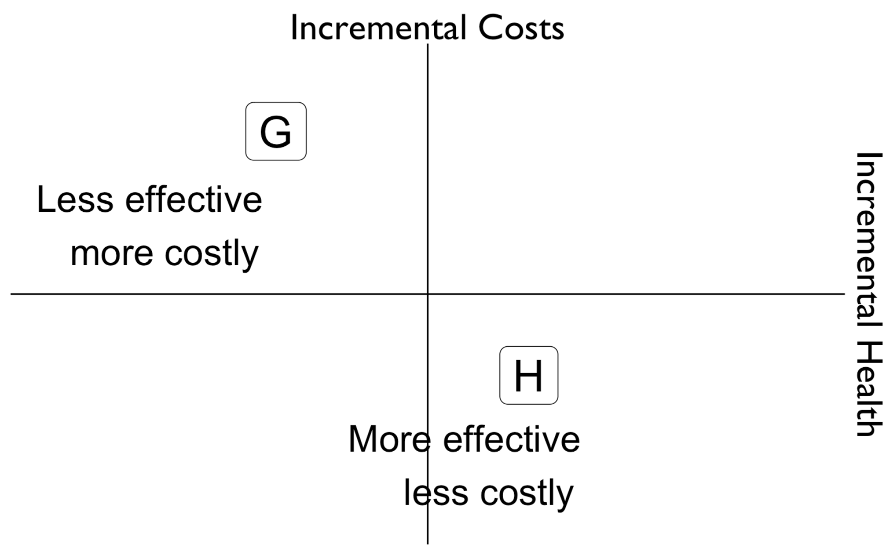
Shopping Spree Problem

Step 2:

- Select programs that are cost-saving & offer benefit; net savings can also be added to budget
- Cost-saving compared to alternative of no program



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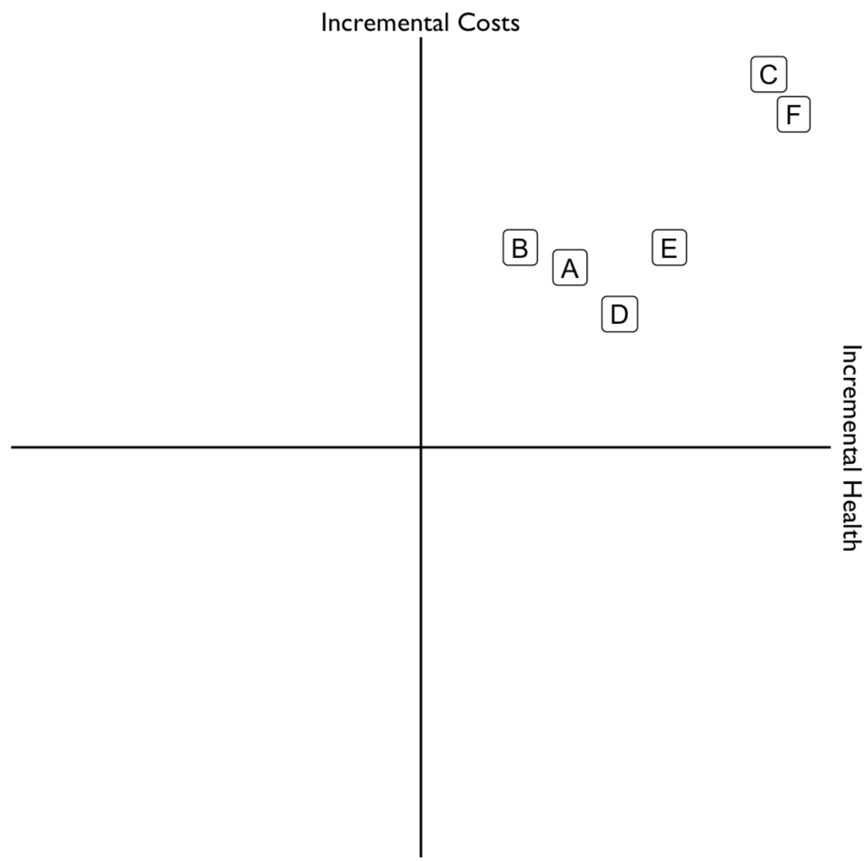
Shopping Spree Problem

Step 3:
- Rank other programs in ascending order by their cost-effectiveness ratio (lowest to highest)
- Programs are then selected from the LEAST to the MOST expensive until the budget is expended
- Final array of programs selected will depend on the budget constraint



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Shopping Spree Problem

Steps 1 & 2: Rule out dominated options & select cost-saving interventions

Program	Cost	QALYs	Status
A	27	30	
B	30	20	
C	56	70	
D	20	40	
E	30	50	
F	50	75	
G	**40**	**-30**	**Ruled Out**
H	**-20**	**20**	**Adopted**

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Shopping Spree Problem

- Initial budget: \$80
- Budget savings: \$20.
- Total budget: \$80 + \$20 = \$100

Program	Cost	QALYs	Status
A	27	30	
B	30	20	
C	56	70	
D	20	40	
E	30	50	
F	50	75	
G	**40**	**-30**	**Ruled Out**
H	**-20**	**20**	**Adopted**

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Shopping Spree Problem

- Calculate average cost-effectiveness ratio.

Program	Cost	QALYs	C/E
A	27	30	0.90
B	30	20	1.50
C	56	70	0.80
D	20	40	0.50
E	30	50	0.60
F	50	75	0.67

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Shopping Spree Problem

- Calculate average cost-effectiveness ratio.
- Sort (by C/E) in ascending order .

Program	Cost	QALYs	C/E
D	20	40	0.50
E	30	50	0.60
F	50	75	0.67
C	56	70	0.80
A	27	30	0.90
B	30	20	1.50

Shopping Spree Problem

- Calculate cumulative costs
- Determine what is adoptable based on global budget constraint ($100)
- Calculate cumulative effects (QALYs)

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Shopping Spree Problem

Budget: $100

Program	Cost	QALYs	C/E	Cumulative Cost	Cumulative QALYs
D	20	40	0.50	20	40
E	30	50	0.60	50	90
F	50	75	0.67	100	165
C	56	70	0.80	156	235
A	27	30	0.90	183	265
B	30	20	1.50	213	285

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Shopping Spree Problem

Budget: $100

Program	Cost	QALYs	C/E	Cumulative Cost	Cumulative QALYs
D	20	40	0.50	20	40
E	30	50	0.60	50	90
F	50	75	0.67	100	165
C	56	70	0.80	156	235
A	27	30	0.90	183	265
B	30	20	1.50	213	285

Budget	Adopted	Effect	Threshold
100	D, E, F, H	165	0.67

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Shopping Spree Problem

Budget: $150

Program	Cost	QALYs	C/E	Cumulative Cost	Cumulative QALYs
D	20	40	0.50	20	40
E	30	50	0.60	50	90
F	50	75	0.67	100	165
C	56	70	0.80	156	235
A	27	30	0.90	183	265
B	30	20	1.50	213	285

Budget	Adopted	Cost	Effect	Threshold	Remaining
150	D, E, F, H	100	165	0.67	50

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Shopping Spree Problem

Budget: $150

Program	Cost	QALYs	C/E	Cumulative Cost	Cumulative QALYs
D	20	40	0.50	20	40
E	30	50	0.60	50	90
F	50	75	0.67	100	165
C	56	70	0.80	156	235
A	27	30	0.90	183	265
B	30	20	1.50	213	285

Budget	Adopted	Cost	Effect	Threshold	Remaining
150	D, E, F, H	100	165	0.67	50

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Shopping Spree Problem

Budget: $150

Program	Cost	QALYs	C/E	Cumulative Cost	Cumulative QALYs
D	20	40	0.50	20	40
E	30	50	0.60	50	90
F	50	75	0.67	100	165
C (89.3%)	56	70	0.80	156	235
A	27	30	0.90	183	265
B	30	20	1.50	213	285

Budget	Adopted	Cost	Effect	Threshold	Remaining
150	D, E, F, C (89.3%), H	150	226.6	0.8	0

- $50 left but program C costs $56 (50/56 = 0.89)
- 0.89*70 QALYs of program C = 62.3 QALYs

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Summary: Shopping Spree Problem

- ✅ Maximize the total net effectiveness (health benefit)
- ✅ Stay within budget
- Can do the same with other objectives (e.g., Minimize costs, subject decision to ‘minimum benefit’ constraint, etc.)

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Use of CEA in two situations

1. **Shopping Spree**: Decision problem has non-competing programs/interventions.

Use of CEA in two situations

2. **Competing Choice:** Decision problem has competing programs/interventions for the same purpose; these choices are mutually exclusive.

Objectives: Competing Choice Problem

- Cannot implement more than one strategy at a time.
- Incremental cost-effectiveness ratio is below a pre-specified adoption threshold.

What's different?

Shopping Spree

1. Can select multiple programs
2. Different costs & effects associated with each
3. Requires calculation of an *Average Cost-Effectiveness Ratio*

Competing Choice

1. Programs are mutually exclusive.
2. Different costs & effects associated with each.
3. Requires calculation of an *Incremental Cost-Effectiveness Ratio* (ICER)

Incremental CEA

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1. Incremental CEA in Pictures

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1. Calculate incremental costs and effects

- Often, a strategy capturing current practice (‘status-quo’, ‘do nothing’, ‘natural history’) is defined.
- Costs and effects are then calculated for each strategy relative to the status-quo.
- Plot the difference in costs and effects with health effects on x-axis and cost effects on y-axis.

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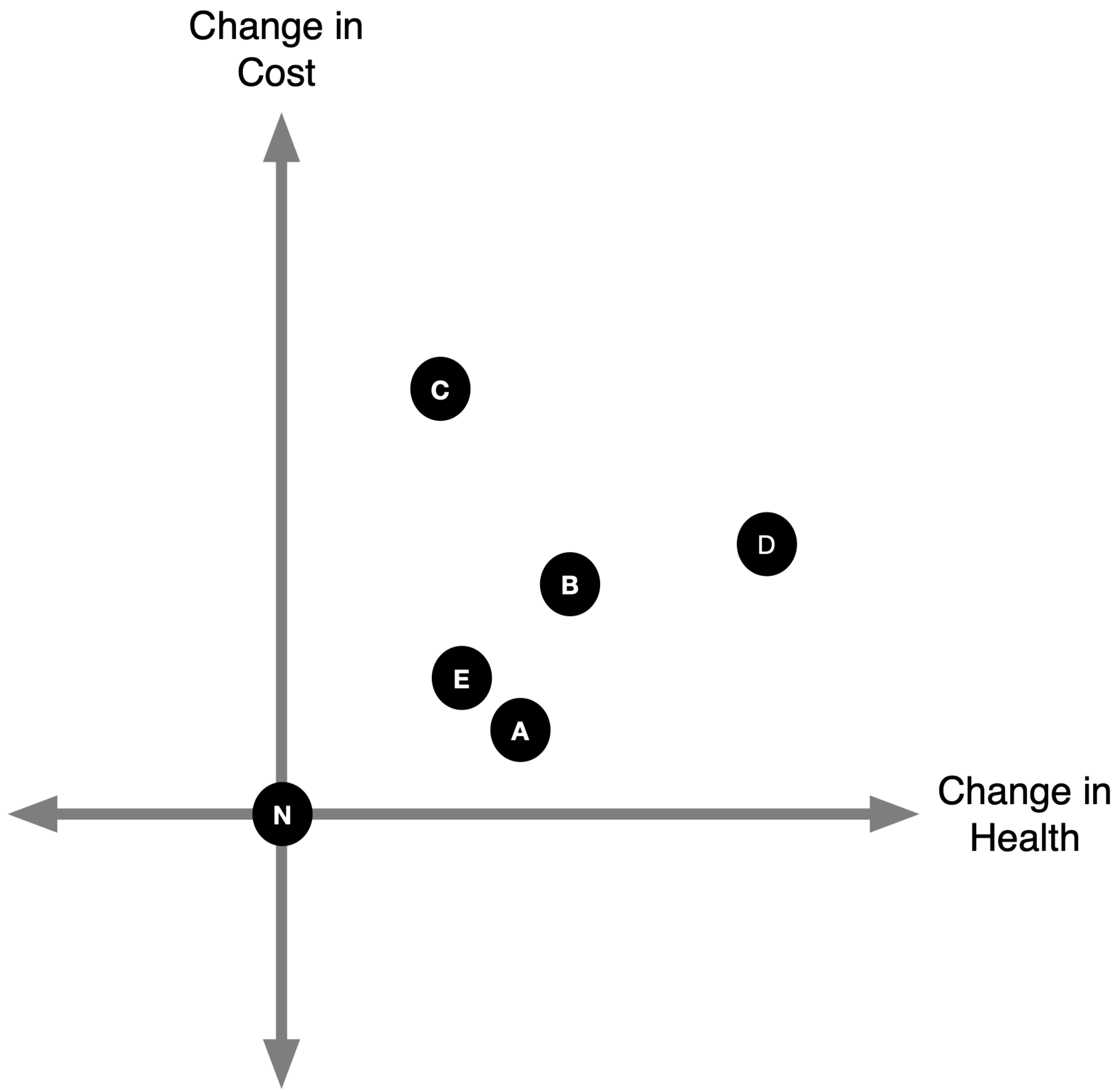
1. Calculate cost and effects



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Identify Dominated Strategies

- We can rule out any strategies that result in less health at higher cost.

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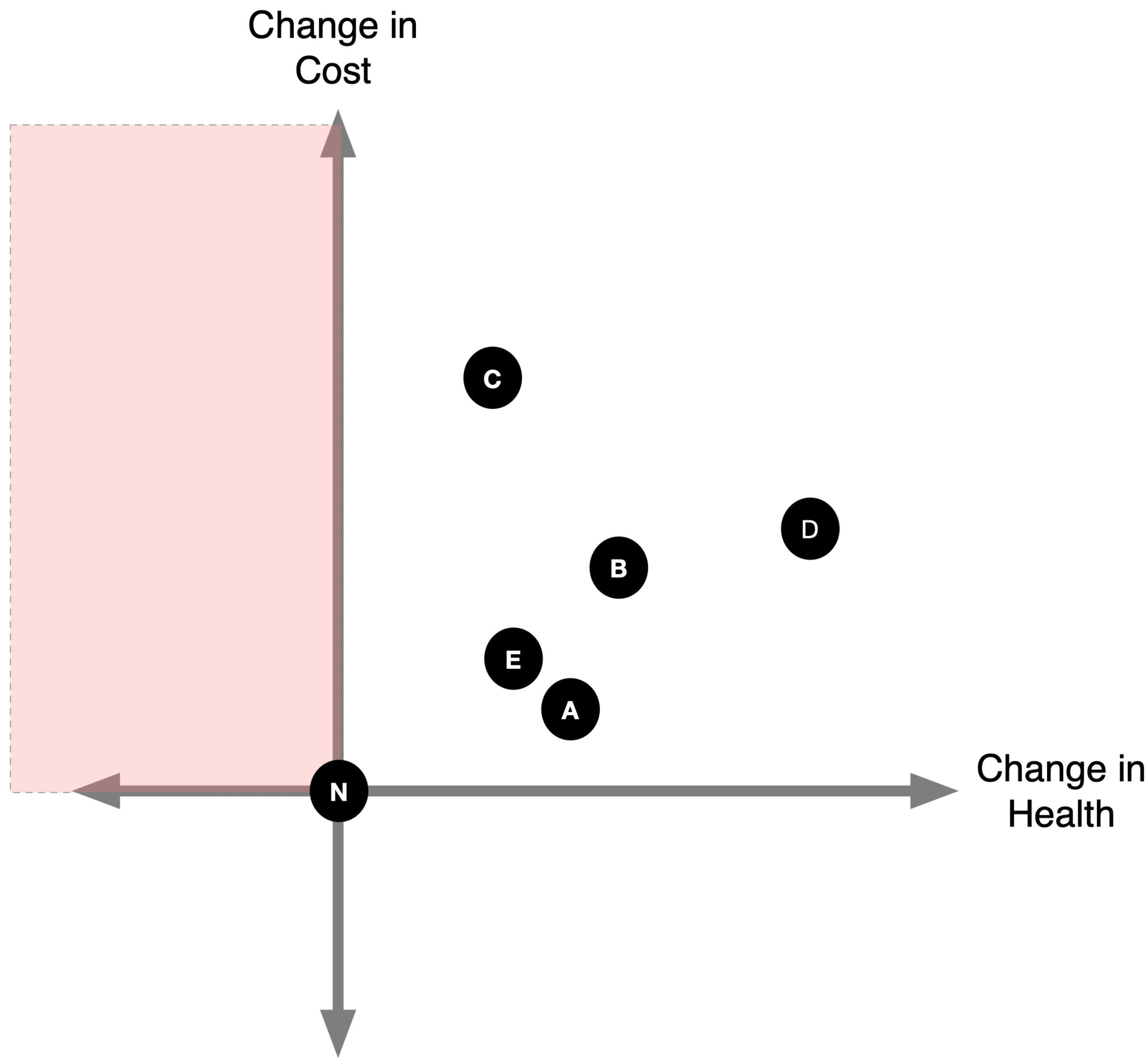
Identify Dominated Strategies



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Identify Dominated Strategies

- We can also rule out strategies where *some other competing strategy* results in more (or equal) health at lower (or equal) cost.
- This is known as “strong” dominance.

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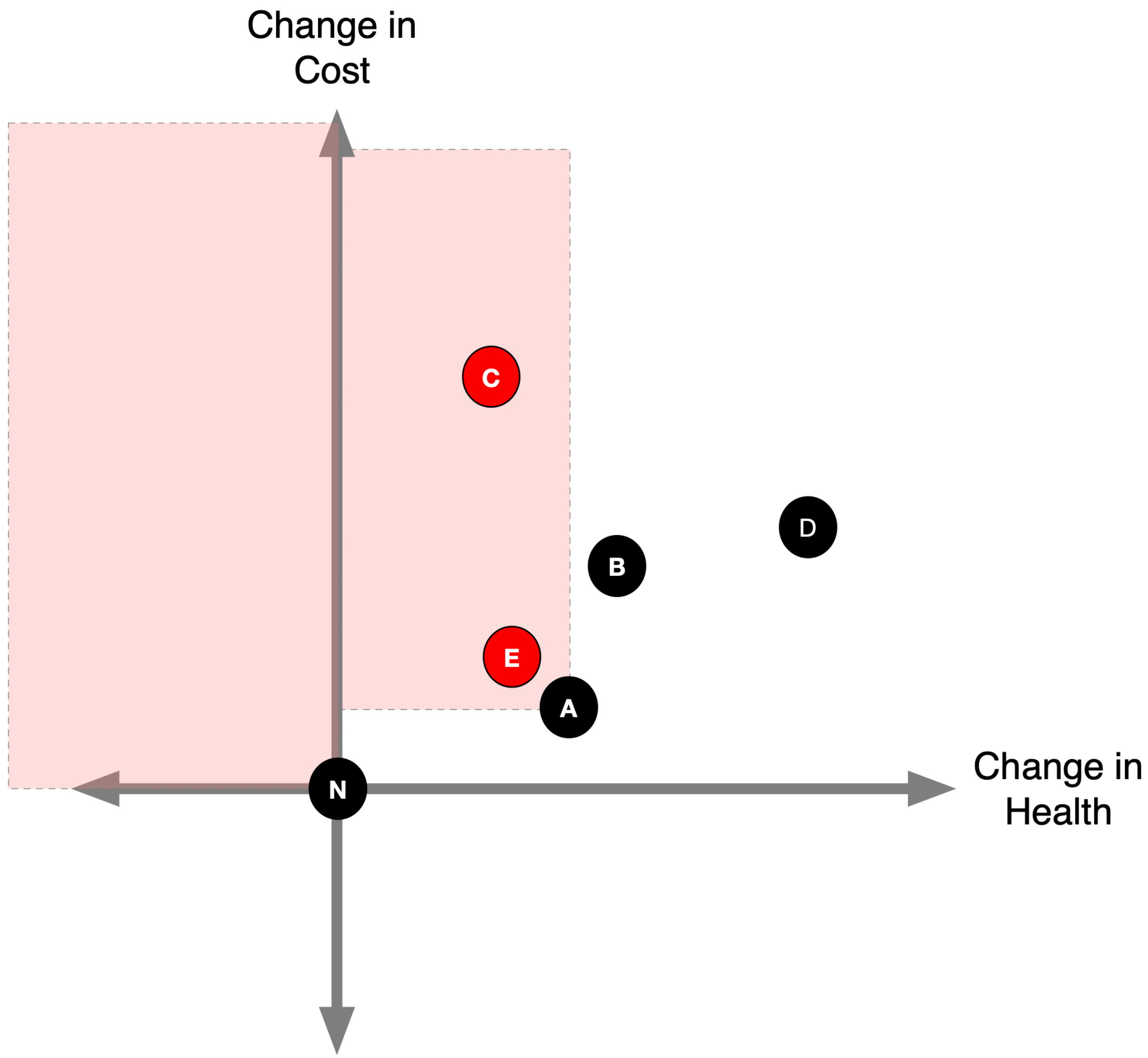
Identify Dominated Strategies



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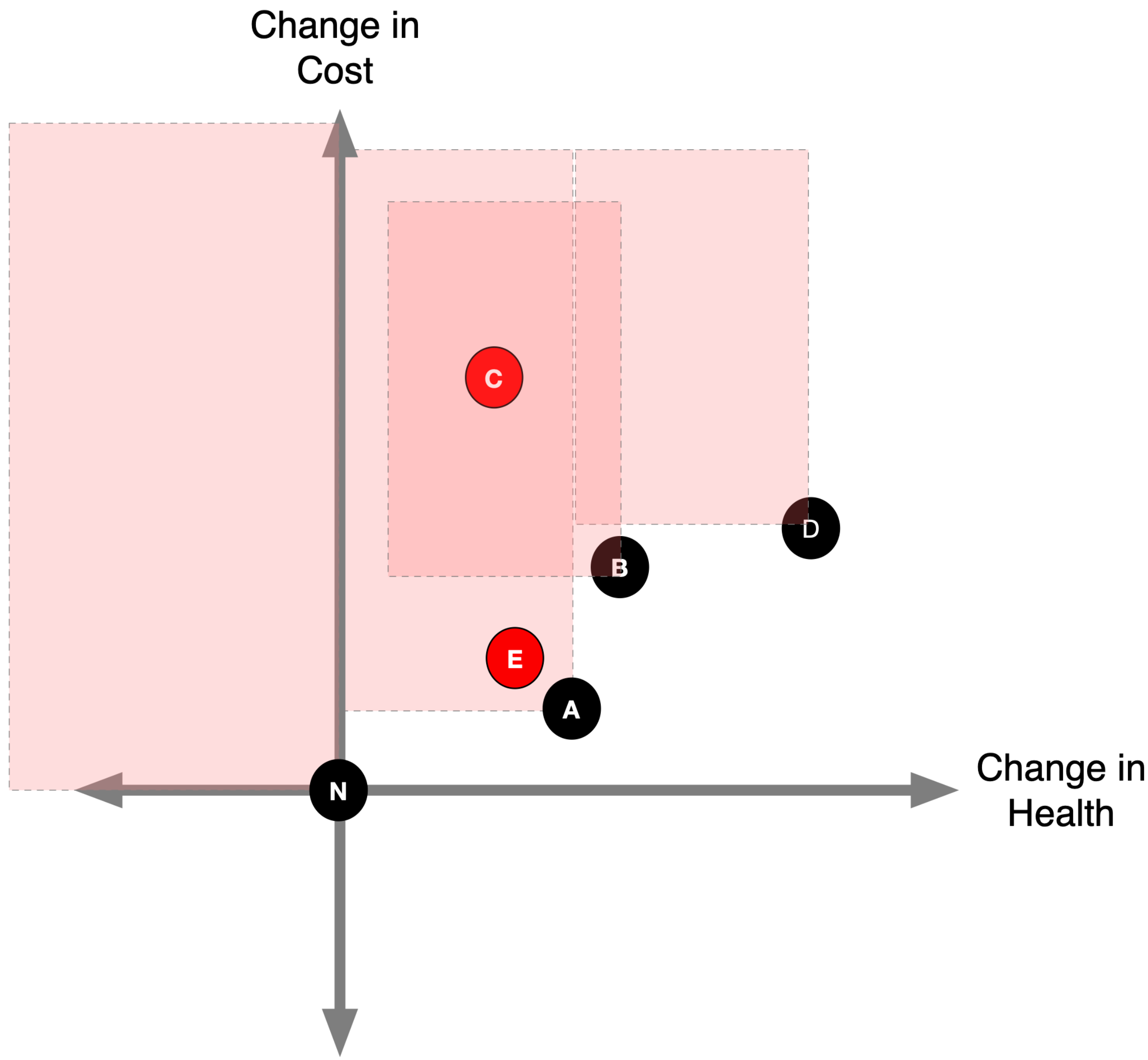
Identify Dominated Strategies



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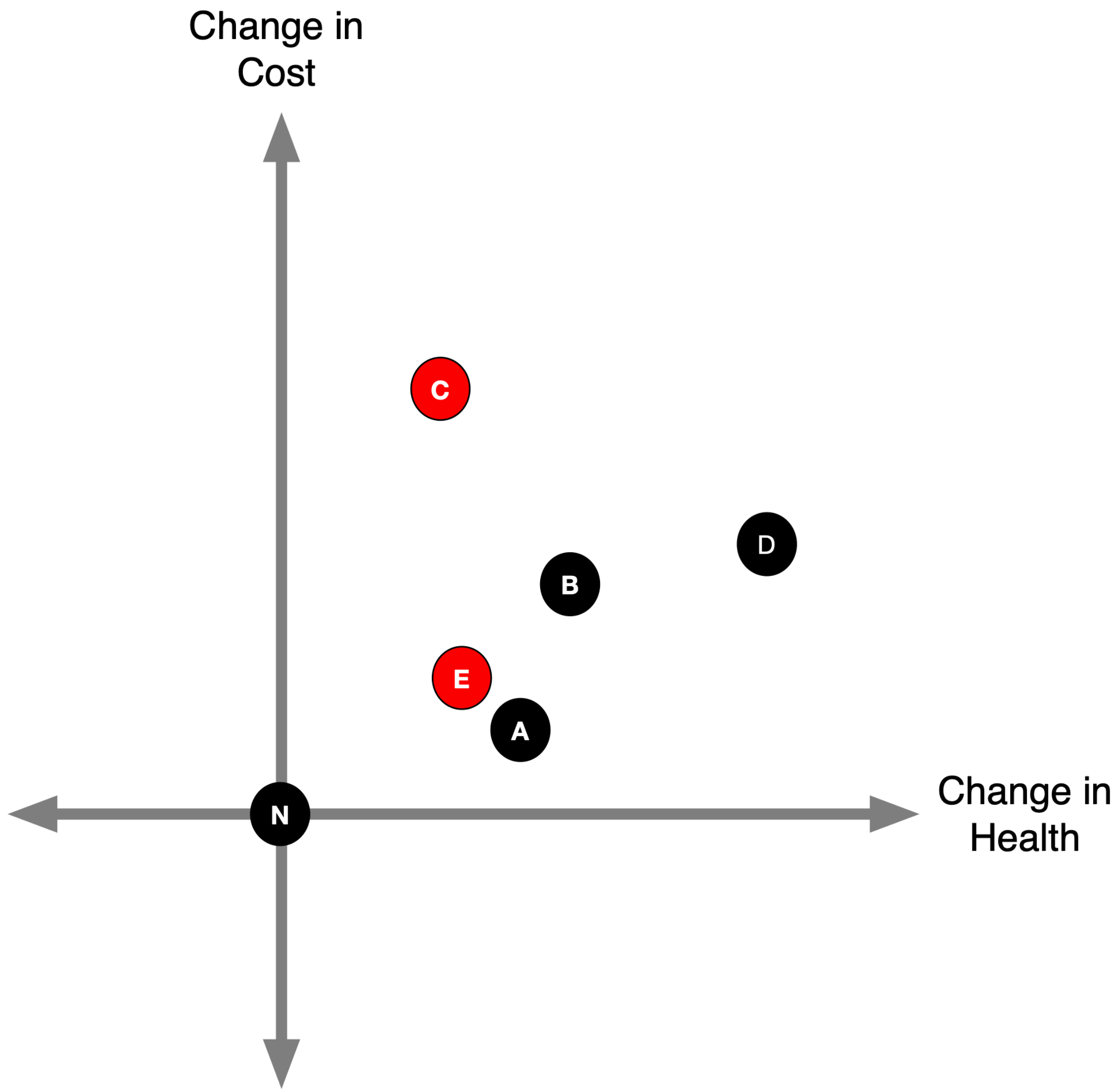
What about strategy B?



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Hybrid Strategies

- Suppose it is feasible to partially implement strategies **A** and **D**.
  - For example, we could implement **A** for 90% of the population and **D** for 10% of the population, or vice versa.

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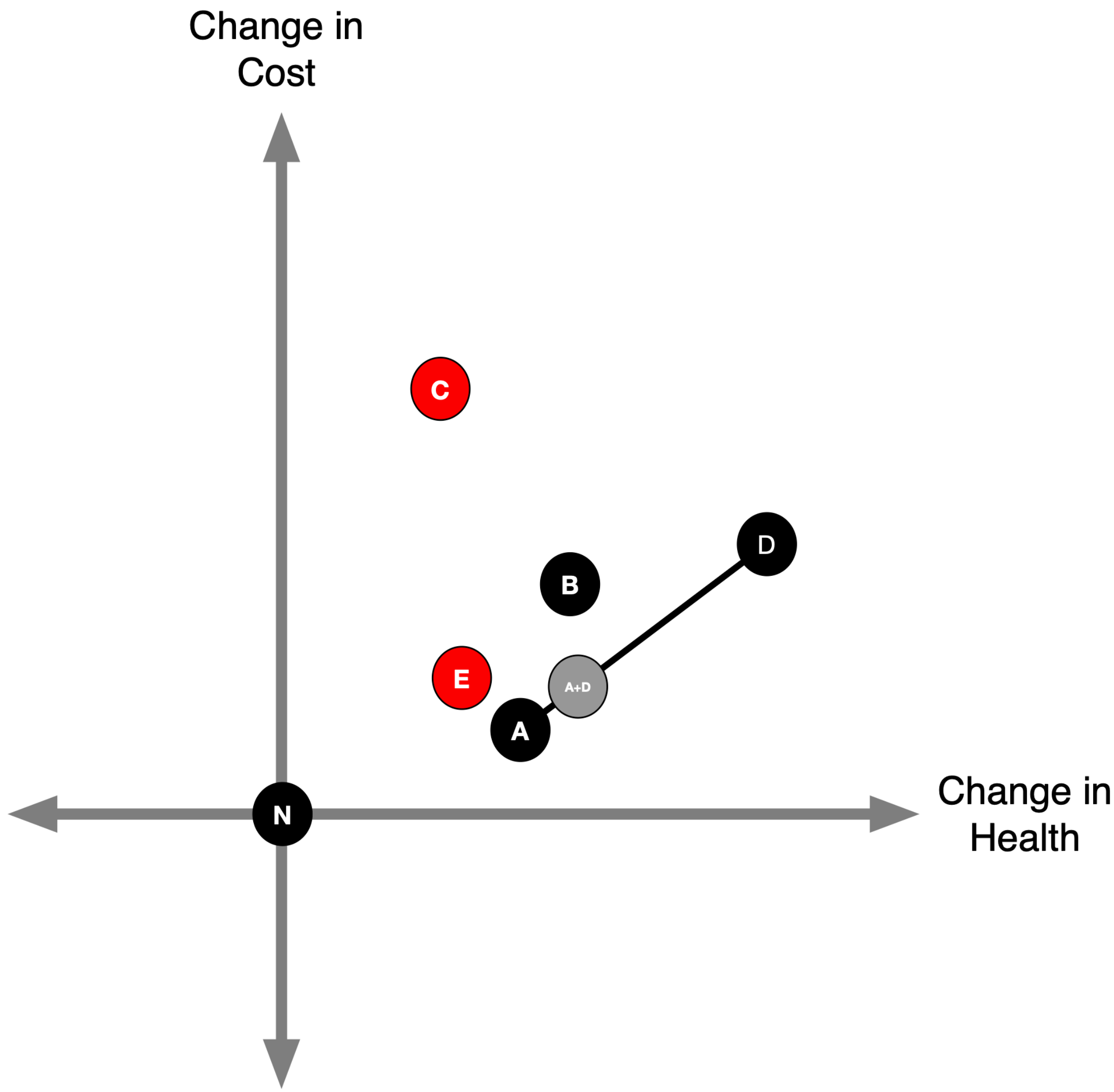
90% A, 10% D



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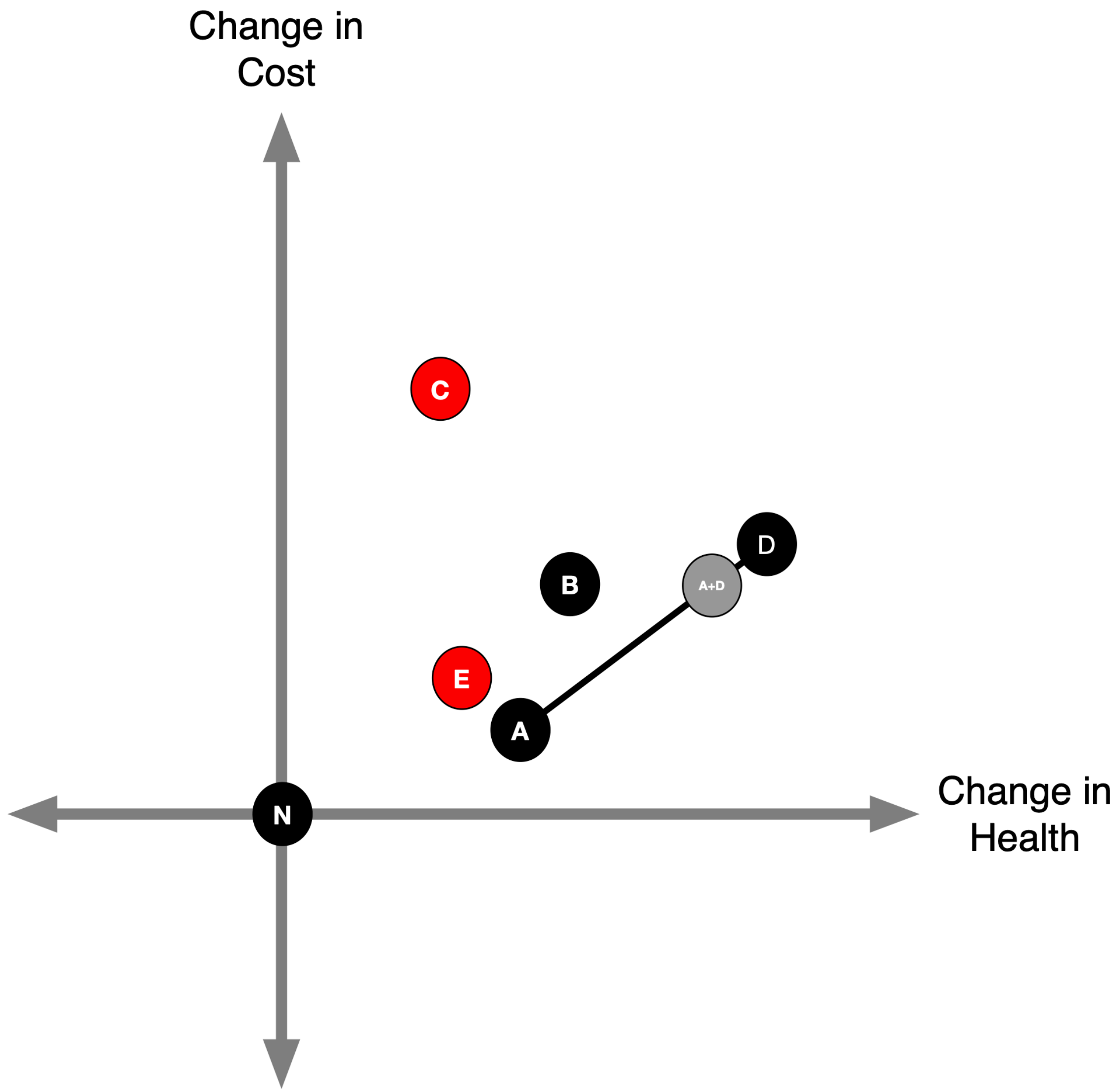
10% A, 90% D



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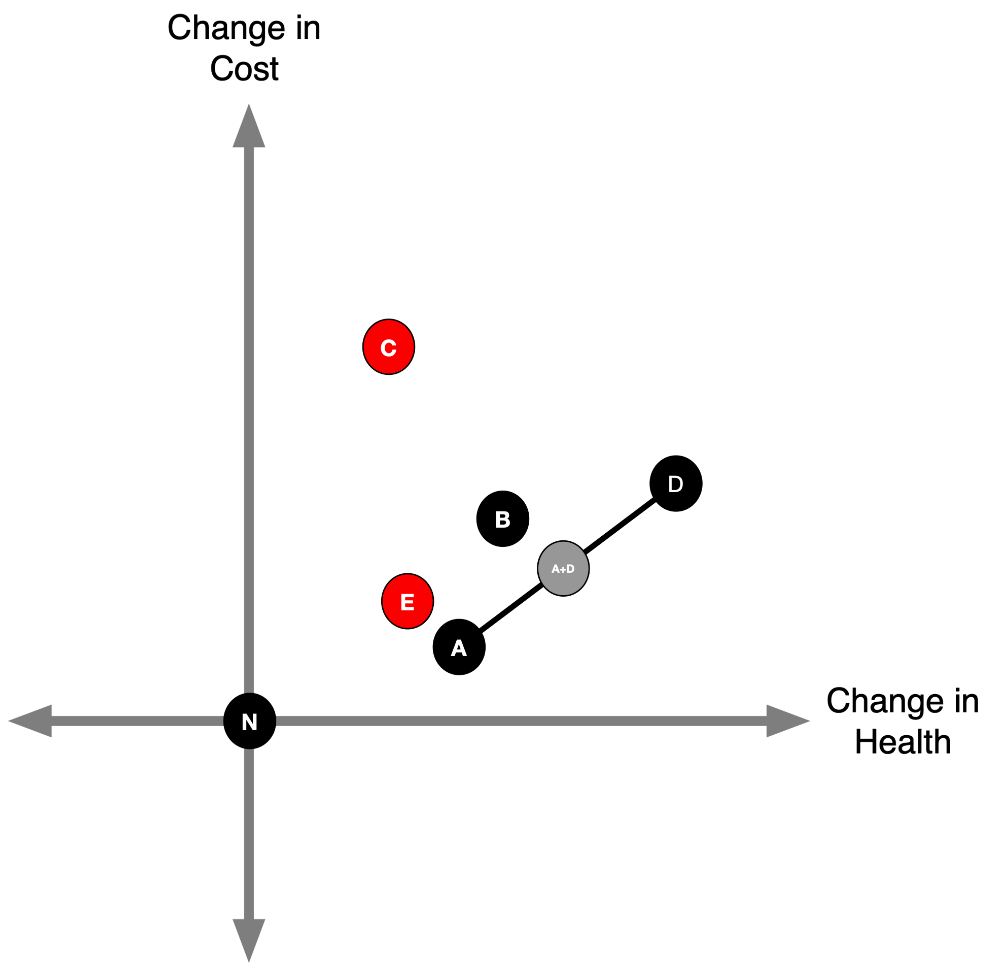
50% A, 50% D

- Can we make any statements about **B** now?



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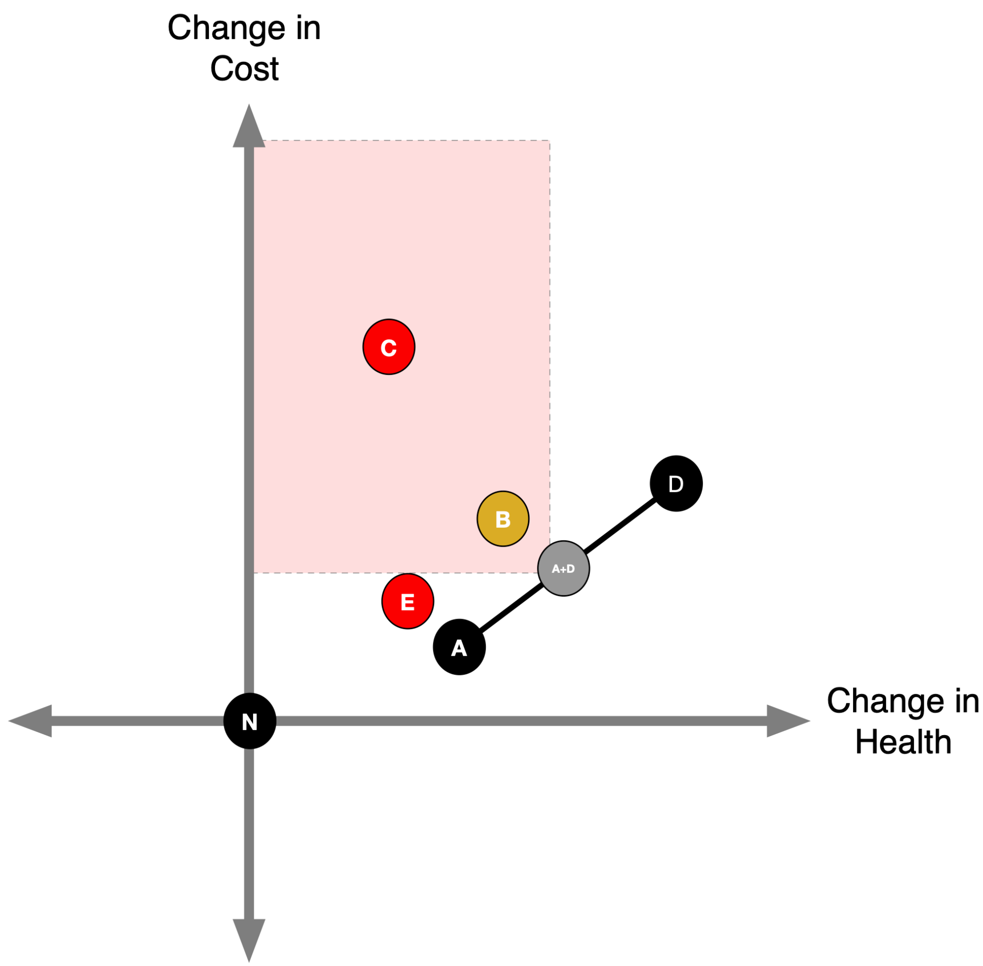
Extended (Weak) Dominance

- **B** is ruled out by extended ("weak") dominance.



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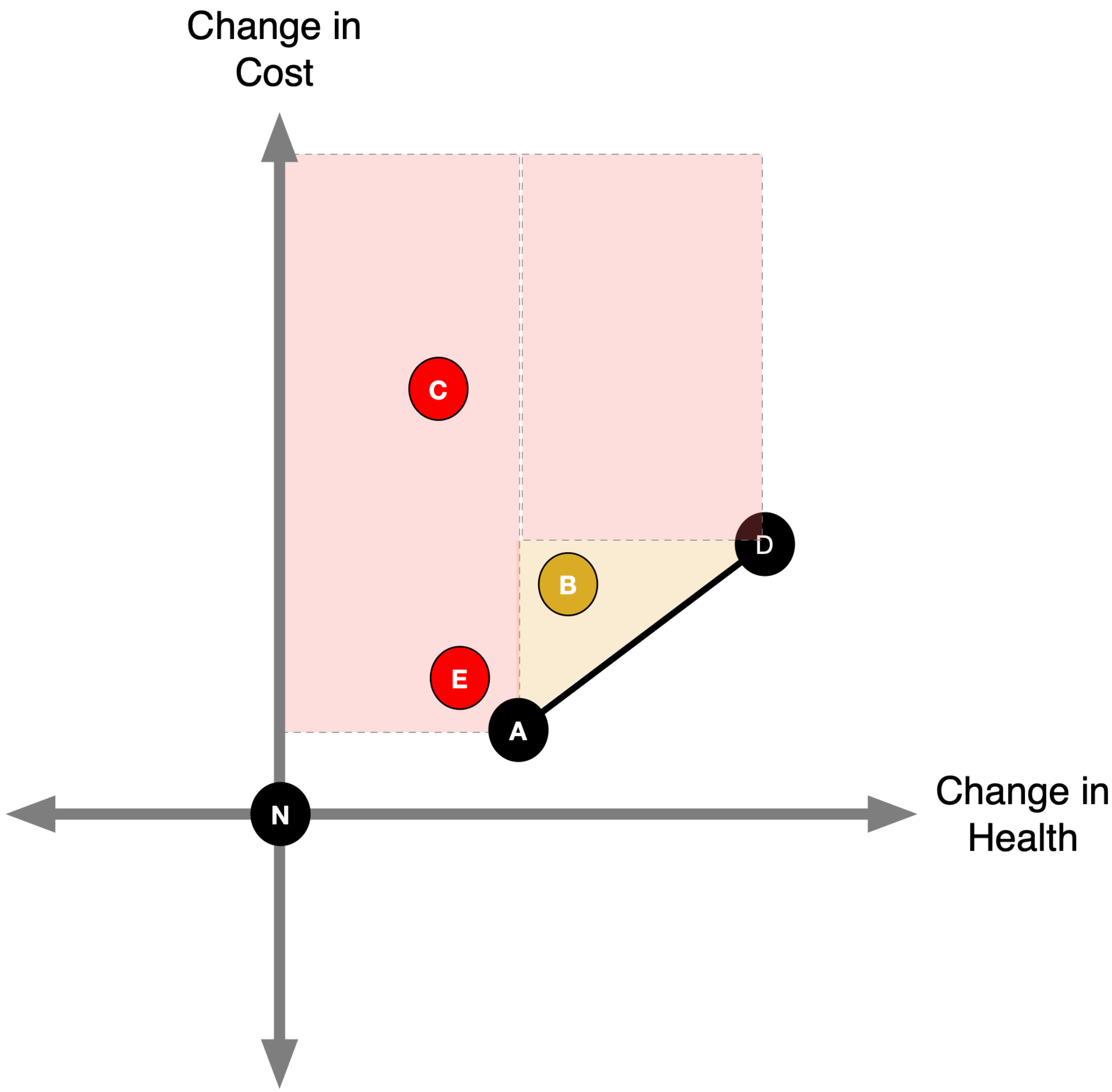
Extended (Weak) Dominance



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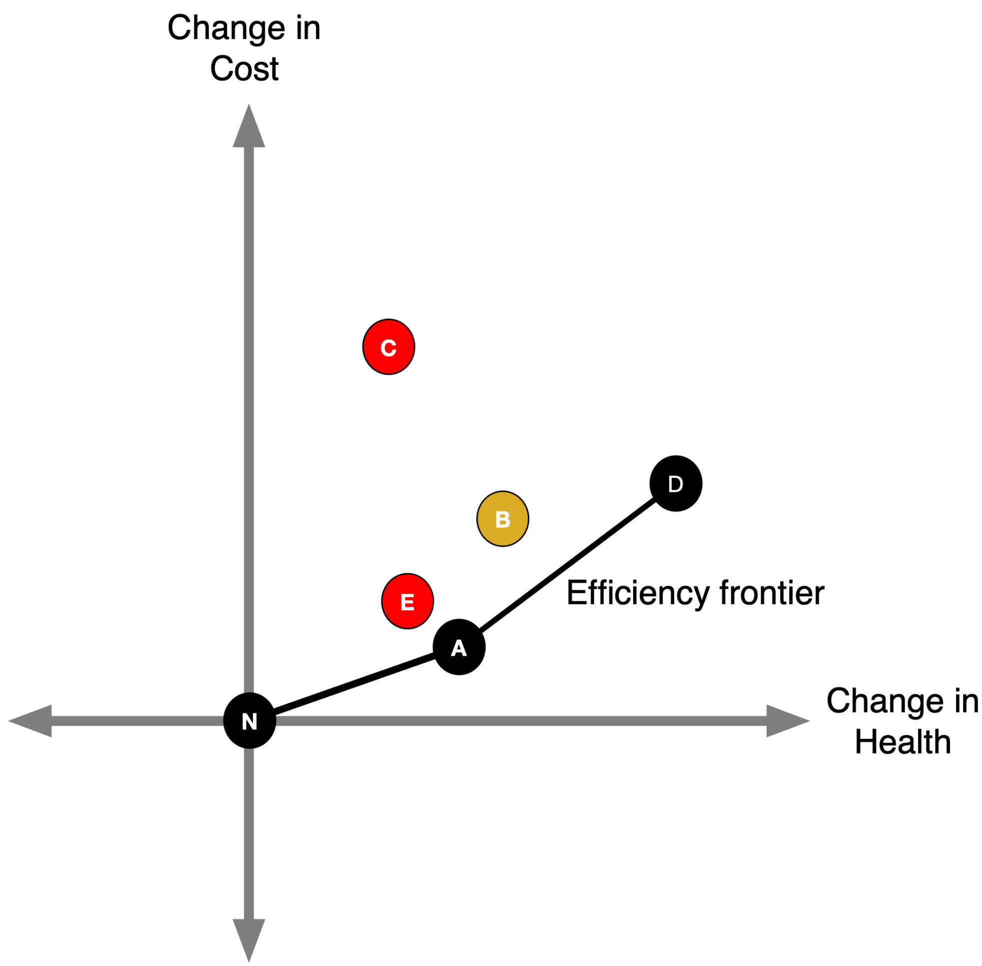
Efficiency Frontier

- The efficiency frontier is the set of non-dominated strategies.



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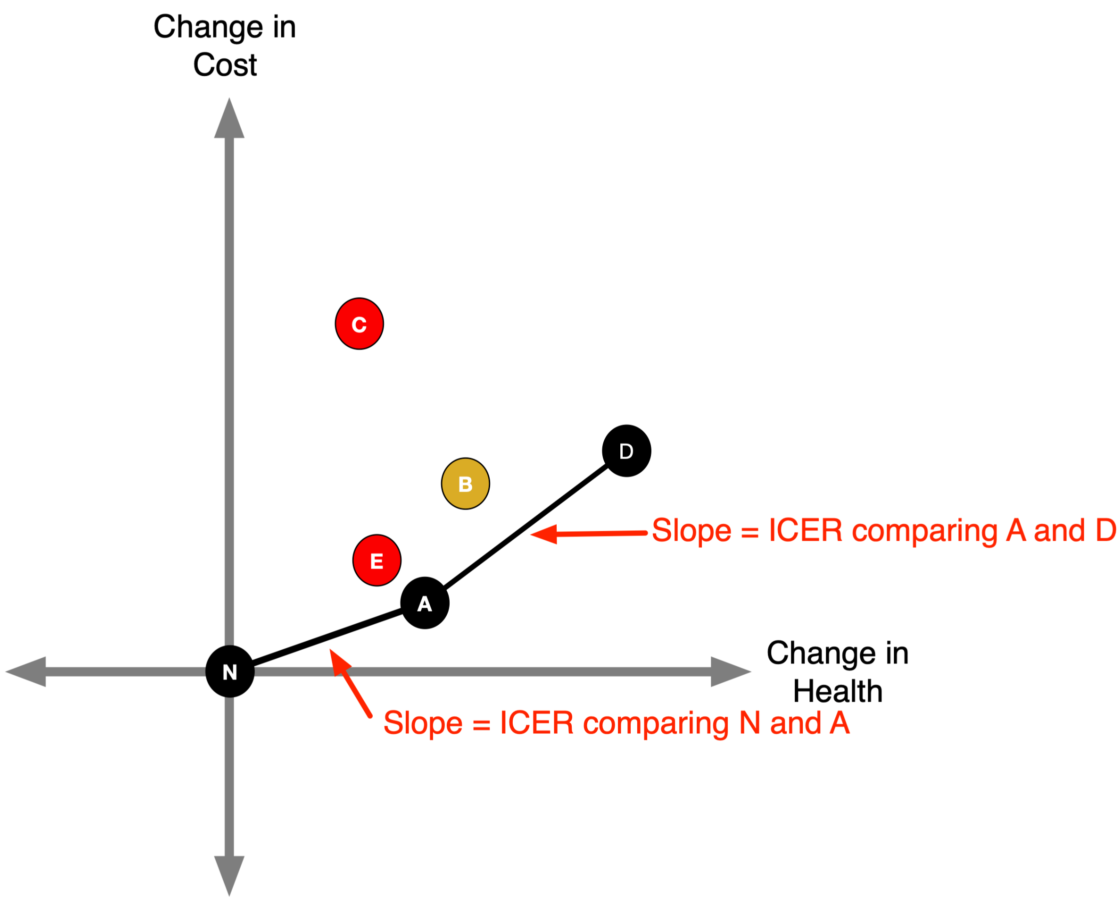
ICERs

- The slope of a line connecting two points is the incremental cost-effectiveness ratio comparing those strategies. More on this later!



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2. Incremental CEA in Tables

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Incremental CEA

Please note that the following example uses different strategies and values than the example used in the previous pictures!

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Incremental CEA

1. Calculate costs and effects for each strategy.
2. Sort table by costs in ascending order.[1]
3. Calculate ICER based on difference in costs and effects.
4. Determine dominated strategies (ICER<0).
5. Re-calculate ICERs after eliminating dominated strategies.
6. Determine strategies ruled out by extended dominance.
7. Re-calculate ICERs after ruling out all dominated strategies.
8. Repeat 5-7 as needed.

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Incremental CEA

1. Calculate costs and effects for each strategy.

Strategy	Cost	QALYs
A	16,453.99	17.332
D	24,504.08	17.491
C	33,443.25	17.580
B	21,456.58	17.409
E	43,331.68	17.491

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Incremental CEA

1. Calculate costs and effects for each strategy.

2. Sort table by costs in ascending order.[1]

Strategy	Cost	QALYs
A	16,454	17.332
B	21,457	17.409
D	24,504	17.491
C	33,443	17.580
E	43,332	17.491

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Incremental CEA

1. Calculate costs and effects for each strategy.
2. Sort table by costs in ascending order.[1]

3. Calculate ICER based on difference in costs and effects.

Strategy	Cost	dCost	QALYs	dQALYs	ICER
A	16,454		17.332		
B	21,457	5,003	17.409	0.077	64,974
D	24,504	3,048	17.491	0.082	37,171
C	33,443	8,939	17.580	0.088	101,580
E	43,332	9,888	17.491	-0.088	-112,364

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Incremental CEA

1. Calculate costs and effects for each strategy.
2. Sort table by costs in ascending order.[1]
3. Calculate ICER based on difference in costs and effects.

4. Determine dominated strategies (ICER<0)

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Determining Dominated Strategies

- Let’s take a look at our table.
- Notice that strategy E has a **negative** ICER. Why is this?
- Strategy E raises costs but lowers QALYs.
- Therefore, we’d be better off by selecting strategy C (we would get more health gain for less money…)

Strategy	Cost	dCost	QALYs	dQALYs	ICER
A	16,454		17.332		
B	21,457	5,003	17.409	0.077	64,974
D	24,504	3,048	17.491	0.082	37,171
C	33,443	8,939	17.580	0.088	101,580
E	**43,332**	**9,888**	**17.491**	**-0.088**	**-112,364**

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Determining Dominated Strategies

- **Strong dominance** refers to situations where one strategy is preferred over another on both costs and health effects (e.g., QALYs).
- When we identify a strongly dominated option, we remove it from the table and re-calculate ICERS based on the remaining strategies.

Strategy	Cost	dCost	QALYs	dQALYs	ICER	
A	16,454		17.332			
B	21,457	5,003	17.409	0.077	64,974	
D	24,504	3,048	17.491	0.082	37,171	
C	33,443	8,939	17.580	0.088	101,580	
E	**43,332**	**9,888**	**17.491**	**-0.088**	**-112,364**	**Dominated**

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A Brief Aside on Negative ICERs

- We want to rule out strategies that cost *more* but result in less health.
  - This implies a negative ICER.
- But what other scenario would result in a negative ICER?
  - Strategy adds health but reduces costs.
  - This is a great strategy!

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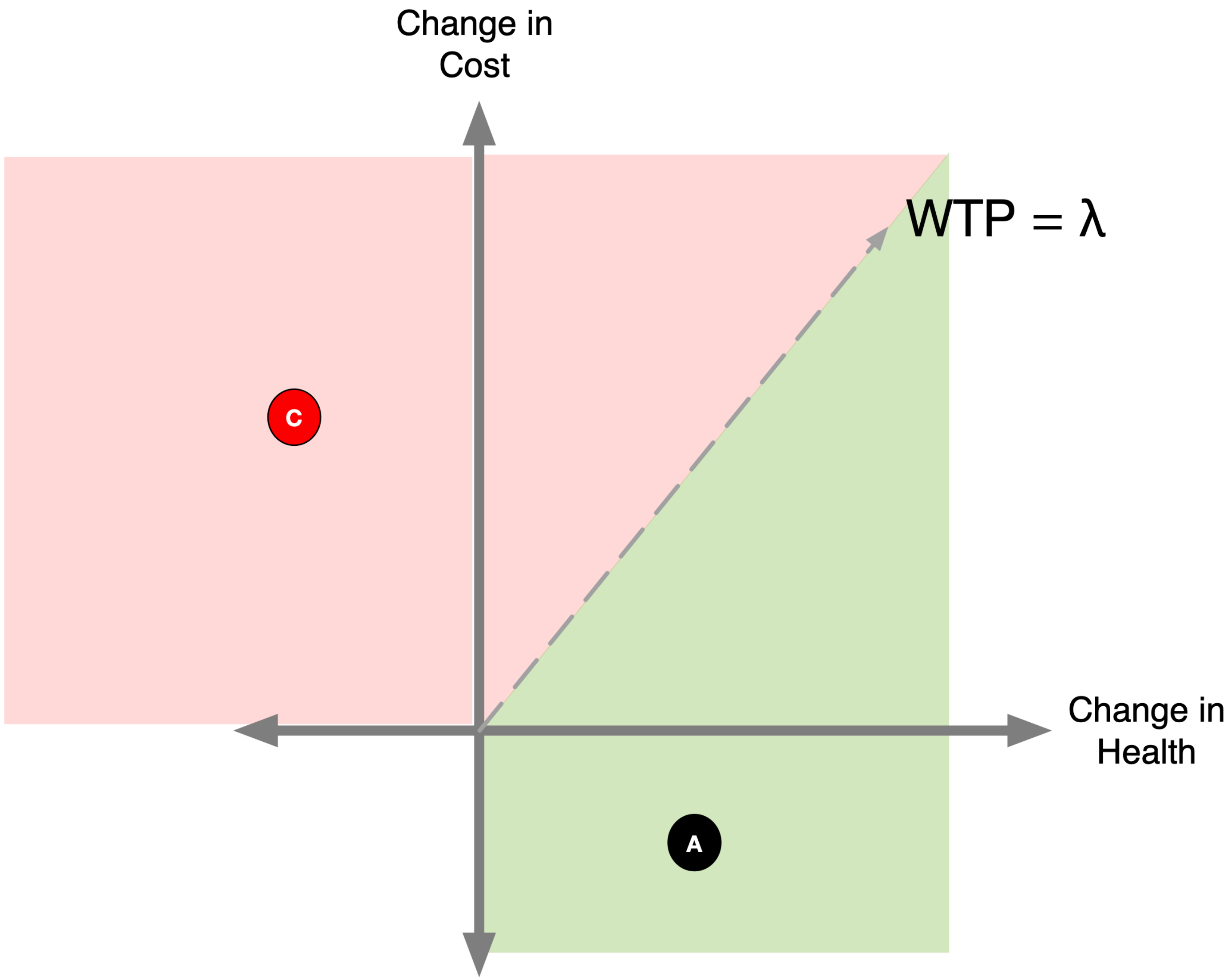
Both Strategies Have a Negative ICER



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A Brief Aside on Negative ICERs

- For this reason, it is poor practice to report negative ICERs.
- Be careful when deleting a strategy becuase it has a negative ICER!
  - It may be a great strategy!

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Incremental CEA

1. Calculate costs and effects for each strategy.
2. Sort table by costs in ascending order.[1]
3. Calculate ICER based on difference in costs and effects.
4. Determine dominated strategies (ICER<0)

Strategy	Cost	dCost	QALYs	dQALYs	ICER	
A	16,454		17.332			
B	21,457	5,003	17.409	0.077	64,974	
D	24,504	3,048	17.491	0.082	37,171	
C	33,443	8,939	17.580	0.088	101,580	
E	**43,332**	**9,888**	**17.491**	**-0.088**	**-112,364**	**Dominated**

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Incremental CEA

1. Calculate costs and effects for each strategy.
2. Sort table by costs in ascending order.[1]
3. Calculate ICER based on difference in costs and effects.
4. Determine dominated strategies (ICER<0).

5. Re-calculate ICERs after eliminating dominated strategies.

Strategy	Cost	dCost	QALYs	dQALYs	ICER	
A	16,454		17.332			
B	21,457	5,003	17.409	0.077	64,974	
D	24,504	3,048	17.491	0.082	37,171	
C	33,443	8,939	17.580	0.088	101,580	
E	**43,332**		**17.491**		**-112,364**	**Dominated**

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Incremental CEA

1. Calculate costs and effects for each strategy.
2. Sort table by costs in ascending order.[1]
3. Calculate ICER based on difference in costs and effects.
4. Determine dominated strategies (ICER<0).
5. Re-calculate ICERs after eliminating dominated strategies.

Strategy	Cost	dCost	QALYs	dQALYs	ICER
A	16,454		17.332		
B	21,457	5,003	17.409	0.077	64,974
D	24,504	3,048	17.491	0.082	37,171
C	33,443	8,939	17.580	0.088	101,580
E	43,332		17.491		

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Determining Dominated Strategies

- We're not quite done yet
- Notice something odd about strategy B?
- Its ICER is **higher** than the next most costly alternative (strategy D)

Strategy	Cost	dCost	QALYs	dQALYs	ICER
A	16,454		17.332		
B	**21,457**	**5,003**	**17.409**	**0.077**	**64,974**
D	24,504	3,048	17.491	0.082	37,171
C	33,443	8,939	17.580	0.088	101,580
E	43,332		17.491		

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Determining Dominated Strategies

- A telltale sign of extended dominance in a (sorted) CEA table is a strategy with a higher ICER than the next most expensive option.

Strategy	Cost	dCost	QALYs	dQALYs	ICER	
A	16,454		17.332			
B	**21,457**	**5,003**	**17.409**	**0.077**	**64,974**	**Dominated (Extended)**
D	24,504	3,048	17.491	0.082	37,171	
C	33,443	8,939	17.580	0.088	101,580	
E	**43,332**		**17.491**			**Dominated**

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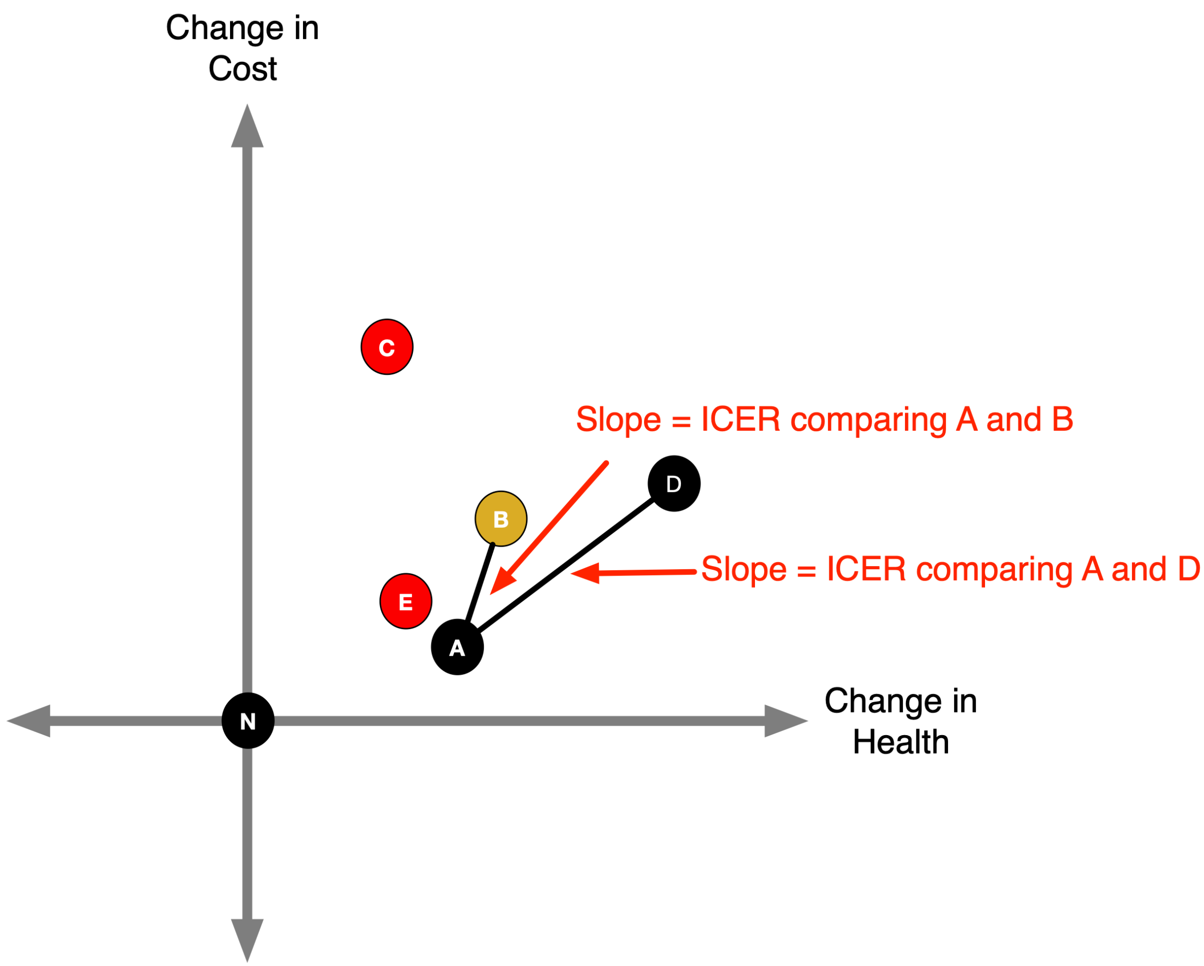
Determining Dominated Strategies

- You can see this in the pictures as well ....



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Incremental CEA

1. Calculate costs and effects for each strategy.
2. Sort table by costs in ascending order.[1]
3. Calculate ICER based on difference in costs and effects.
4. Determine dominated strategies (ICER<0).
5. Re-calculate ICERs after eliminating dominated strategies.

6. Determine strategies ruled out by extended dominance.

Strategy	Cost	dCost	QALYs	dQALYs	ICER	
A	16,454		17.332			
B	**21,457**	**5,003**	**17.409**	**0.077**	**64,974**	**Dominated (Extended)**
D	24,504	3,048	17.491	0.082	37,171	
C	33,443	8,939	17.580	0.088	101,580	
E	**43,332**		**17.491**			**Dominated**

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Incremental CEA

7. Re-calculate ICERs after ruling out all dominated strategies.

Strategy	Cost	dCost	QALYs	dQALYs	ICER	
A	16,454		17.332			
D	24,504	8,050	17.491	0.159	50,629	
C	33,443	8,939	17.580	0.088	101,580	
E	**43,332**		**17.491**			**Dominated**
B	**21,457**		**17.409**			**Dominated (Extended)**

- Strategy D is more expensive than Strategy B, but Strategy D is gaining health MORE EFFICIENTLY than Strategy B

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In-class practice: DALYs

Nine different prophylaxis to prevent someone with HIV from acquiring opportunistic infections related to AIDS

Strategy	Cost	DALYs
No prophylaxis	40,288	9.50
TMP-SMX	44,786	6.94
TMP-SMX, azithromycin	45,944	6.46
TMP-SMX, fluconazole	47,046	6.49
TMP-SMX, azithromycin, fluconazole	48,596	5.90
TMP-SMX, ganciclovir	54,628	6.30
TMP-SMX, azithromycin, ganciclovir	56,812	5.67
TMP-SMX, fluconazole, ganciclovir	58,082	5.70
TMP-SMX, azithromycin, fluconazole, ganciclovir	61,119	4.88

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Calculate Incremental Costs and DALYs Averted

Strategy	Cost	Incremental Cost	DALYs	DALYs Averted
No prophylaxis	40,288	0	9.50	0.00
TMP-SMX	44,786	4,498	6.94	2.56
TMP-SMX, azithromycin	45,944	1,158	6.46	0.48
TMP-SMX, fluconazole	47,046	1,102	6.49	-0.03
TMP-SMX, azithromycin, fluconazole	48,596	1,550	5.90	0.59
TMP-SMX, ganciclovir	54,628	6,032	6.30	-0.40
TMP-SMX, azithromycin, ganciclovir	56,812	2,184	5.67	0.63
TMP-SMX, fluconazole, ganciclovir	58,082	1,270	5.70	-0.03
TMP-SMX, azithromycin, fluconazole, ganciclovir	61,119	3,037	4.88	0.82

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Calculate incremental costs per DALY averted.

Strategy	Incremental Cost	DALYs Averted	Incremental Cost per DALY Averted
No prophylaxis	0	0.00	
TMP-SMX	4,498	2.56	1,757
TMP-SMX, azithromycin	1,158	0.48	2,413
TMP-SMX, fluconazole	1,102	-0.03	-36,733
TMP-SMX, azithromycin, fluconazole	1,550	0.59	2,627
TMP-SMX, ganciclovir	6,032	-0.40	-15,080
TMP-SMX, azithromycin, ganciclovir	2,184	0.63	3,467
TMP-SMX, fluconazole, ganciclovir	1,270	-0.03	-42,333
TMP-SMX, azithromycin, fluconazole, ganciclovir	3,037	0.82	3,704

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Determine dominated strategies

Strategy	Incremental Cost	DALYs Averted	Incremental Cost per DALY Averted	Status
No prophylaxis	0	0.00		
TMP-SMX	4,498	2.56	1,757	
TMP-SMX, azithromycin	1,158	0.48	2,413	
TMP-SMX, fluconazole	**1,102**	**-0.03**	**-36,733**	**Dominated (Strong)**
TMP-SMX, azithromycin, fluconazole	1,550	0.59	2,627	
TMP-SMX, ganciclovir	**6,032**	**-0.40**	**-15,080**	**Dominated (Strong)**
TMP-SMX, azithromycin, ganciclovir	2,184	0.63	3,467	
TMP-SMX, fluconazole, ganciclovir	**1,270**	**-0.03**	**-42,333**	**Dominated (Strong)**
TMP-SMX, azithromycin, fluconazole, ganciclovir	3,037	0.82	3,704	

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Remove dominated strategies and recalculate

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Determine dominated strategies

Strategy	Cost	Incremental Cost	DALYs	DALYs Averted
No prophylaxis	40,288	0	9.50	0.00
TMP-SMX	44,786	4,498	6.94	2.56
TMP-SMX, azithromycin	45,944	1,158	6.46	0.48
TMP-SMX, azithromycin, fluconazole	48,596	2,652	5.90	0.56
TMP-SMX, azithromycin, ganciclovir	56,812	8,216	5.67	0.23
TMP-SMX, azithromycin, fluconazole, ganciclovir	61,119	4,307	4.88	0.79

Determine dominated strategies

Strategy	Incremental Cost	DALYs Averted	Incremental Cost per DALY Averted	Status
No prophylaxis	0	0.00		
TMP-SMX	4,498	2.56	1,757	
TMP-SMX, azithromycin	1,158	0.48	2,413	
TMP-SMX, azithromycin, fluconazole	2,652	0.56	4,736	
TMP-SMX, azithromycin, ganciclovir	**8,216**	**0.23**	**35,722**	**Dominated (Extended)**
TMP-SMX, azithromycin, fluconazole, ganciclovir	4,307	0.79	5,452	

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Remove dominated strategies and recalculate

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Determine dominated strategies

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Determine dominated strategies

Strategy	Cost	Incremental Cost	DALYs	DALYs Averted
No prophylaxis	40,288	0	9.50	0.00
TMP-SMX	44,786	4,498	6.94	2.56
TMP-SMX, azithromycin	45,944	1,158	6.46	0.48
TMP-SMX, azithromycin, fluconazole	48,596	2,652	5.90	0.56
TMP-SMX, azithromycin, fluconazole, ganciclovir	61,119	12,523	4.88	1.02

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Determine dominated strategies

Strategy	Incremental Cost	DALYs Averted	Incremental Cost per DALY Averted	Status
No prophylaxis	0	0.00		
TMP-SMX	4,498	2.56	1,757	
TMP-SMX, azithromycin	1,158	0.48	2,413	
TMP-SMX, azithromycin, fluconazole	2,652	0.56	4,736	
TMP-SMX, azithromycin, fluconazole, ganciclovir	12,523	1.02	12,277	

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Final Table

Strategy	Incremental Cost	DALYs Averted	Incremental Cost per DALY Averted	Status
No prophylaxis	0	0.00		
TMP-SMX	4,498	2.56	1,757	
TMP-SMX, azithromycin	1,158	0.48	2,413	
TMP-SMX, azithromycin, fluconazole	2,652	0.56	4,736	
TMP-SMX, azithromycin, fluconazole, ganciclovir	12,523	1.02	12,277	
TMP-SMX, fluconazole	**1,102**	**-0.03**		**Dominated (Strong)**
TMP-SMX, ganciclovir	**6,032**	**-0.40**		**Dominated (Strong)**
TMP-SMX, fluconazole, ganciclovir	**1,270**	**-0.03**		**Dominated (Strong)**
TMP-SMX, azithromycin, ganciclovir	**8,216**	**0.23**		**Dominated (Extended)**

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A note on COMPARATORS

4.7 COMPARATORS

Selection of one or more appropriate comparator interventions is crucial in a CEA (**Recommendations 9–10**). In theory, if study resources were unlimited, the ideal approach would be to identify all possible intervention variations applicable to the particular problem and all possible comparator interventions and their variations, including a "do-nothing" option. Costs and effects would be gathered on all of these interventions. Incremental cost-effectiveness would be used to analyze the results and to present the findings to the decision makers (see Chapter 13).

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A note on COMPARATORS

at a minimum, Reference Case analyses from the healthcare sector and societal perspectives should compare the intervention to relevant alternatives and to the existing practice for addressing the health problem (the status quo), which may itself be variable between locations, healthcare settings, and clinicians. The question being addressed is, "What is the cost-effectiveness of replacing existing practice with the new intervention or relevant alternatives?" If the comparators included in the analysis do not include existing practice, the results can be deceptive. For example, if a new drug treatment for hypertension is compared to "no treatment," or to an expensive and not very effective alternative, the analysis will overstate the new drug's cost-effectiveness. That is, the comparison would not reflect the true value of an incremental change in practice.

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Where to draw the line?

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CEA Thresholds

- So now we have our ICERs, but how do we make a decision?
- We must define a **threshold** (λ), or an ICER value that determines whether or not we implement a given strategy.
  - Also known as "willingness-to-pay" (WTP) threshold.

CEA Thresholds

What are common thresholds and how are they determined?

- In high income countries, common thresholds are \$50,000/QALY, \$100,000/QALY, and \$100,000/QALY.
- In LMICs, 0.5-3x per capita gross domestic product (GDP) per DALY averted.
- More on this in a few minutes.

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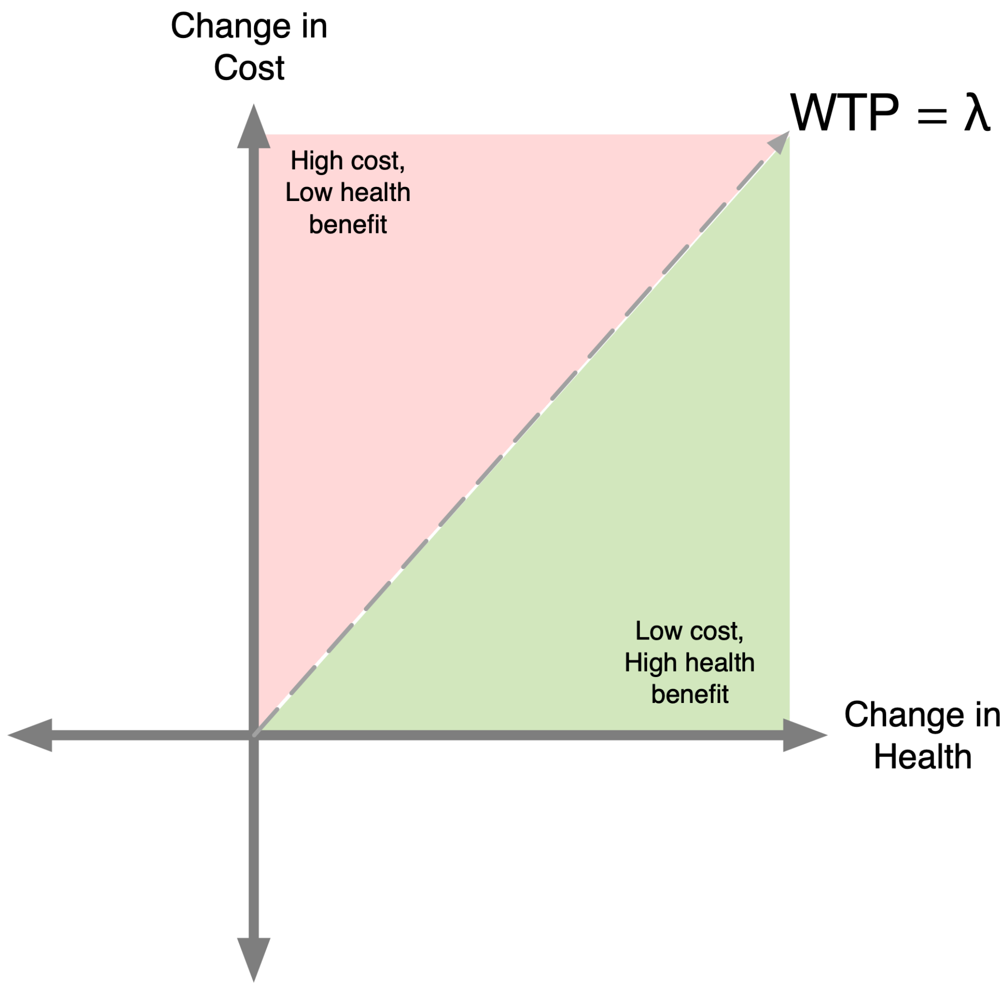
How do CEA Thresholds Guide Decisionmaking?



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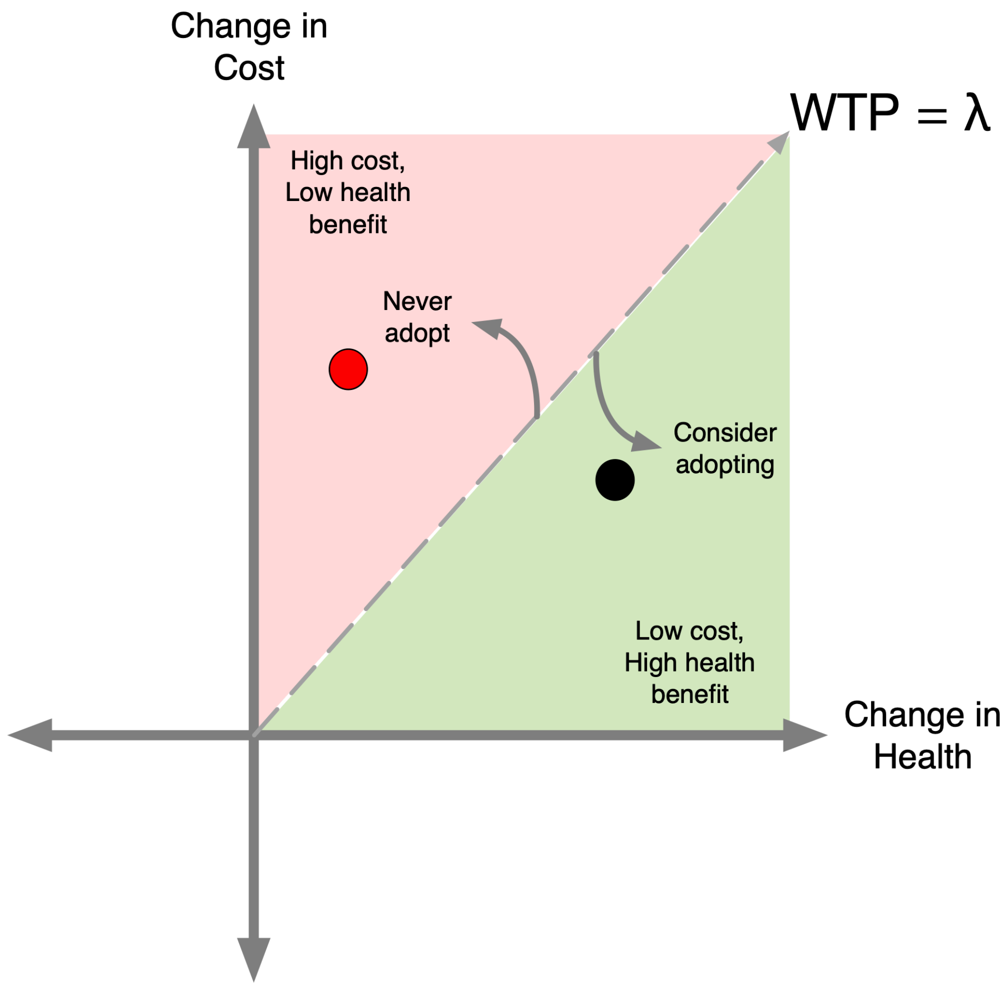
How do CEA Thresholds Guide Decisionmaking?



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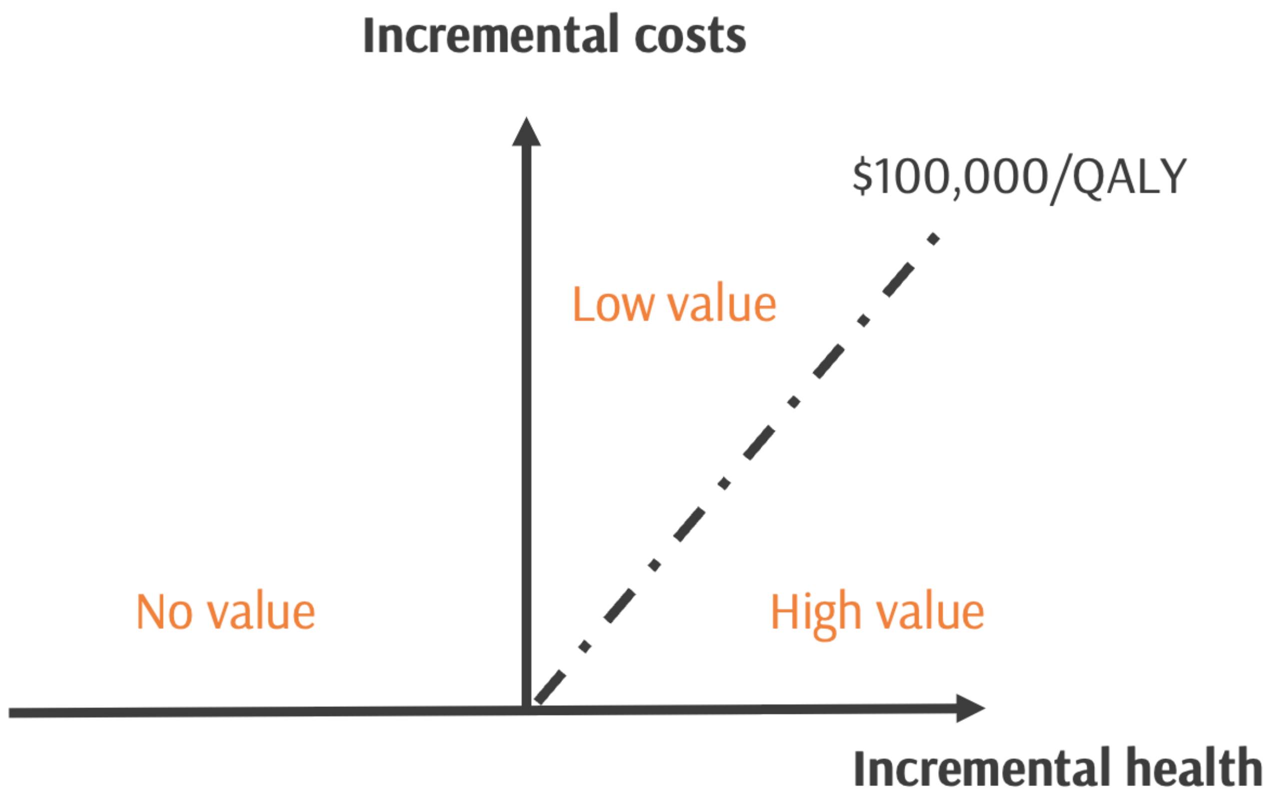
How do CEA Thresholds Guide Decisionmaking?



ICER = ΔC / ΔE = $90,000 / QALY

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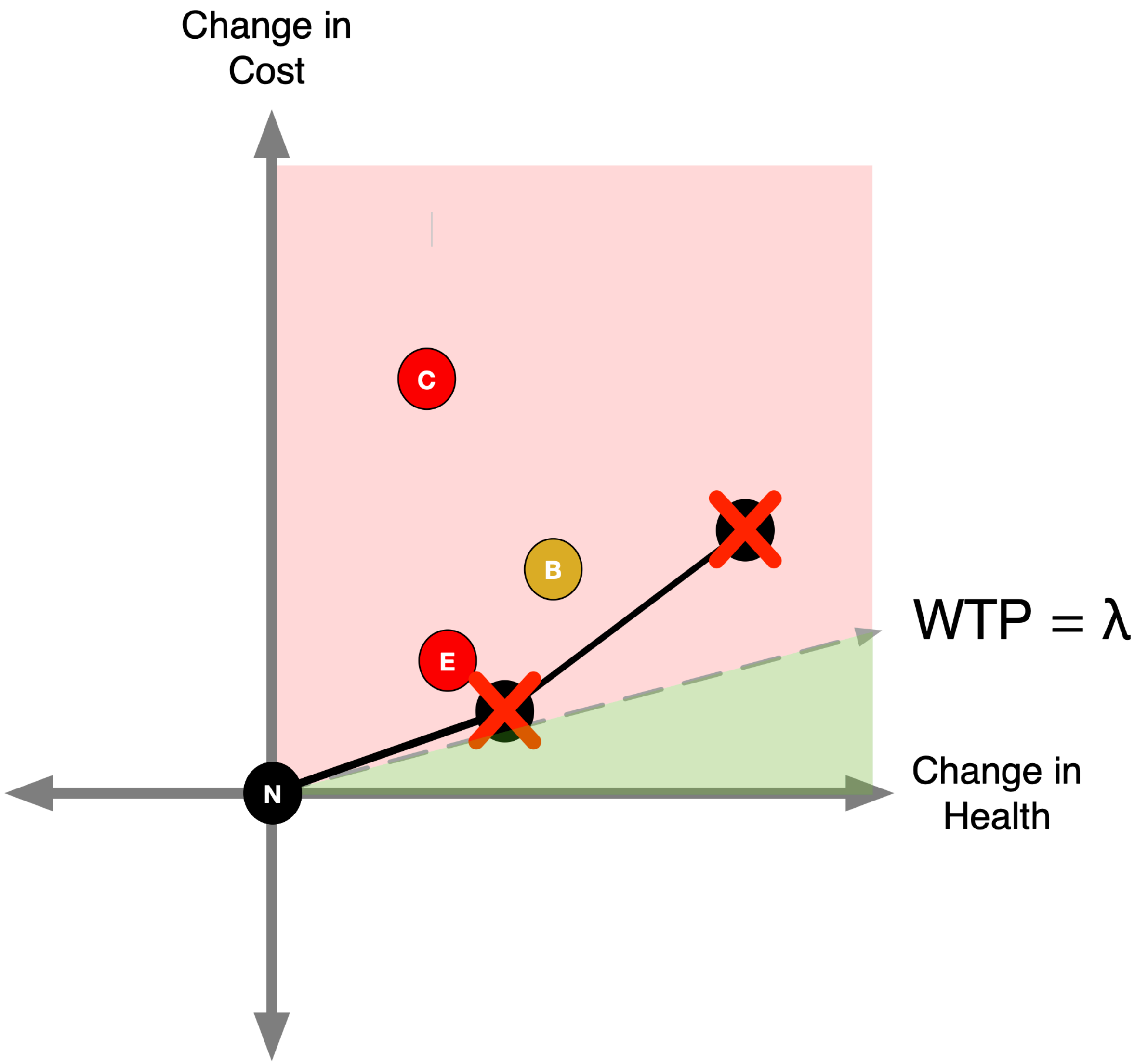
CEA Thresholds



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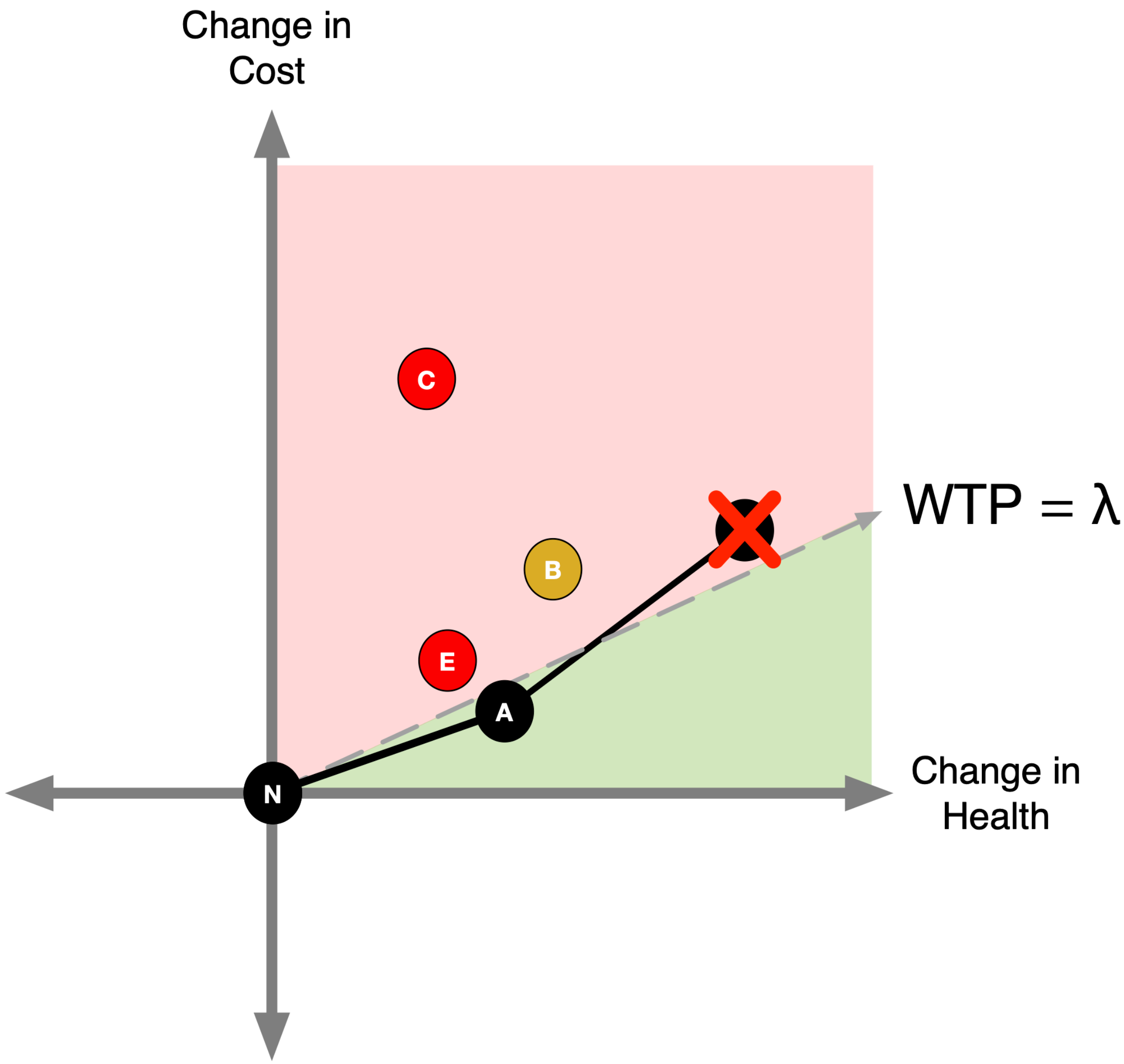
CEA Thresholds



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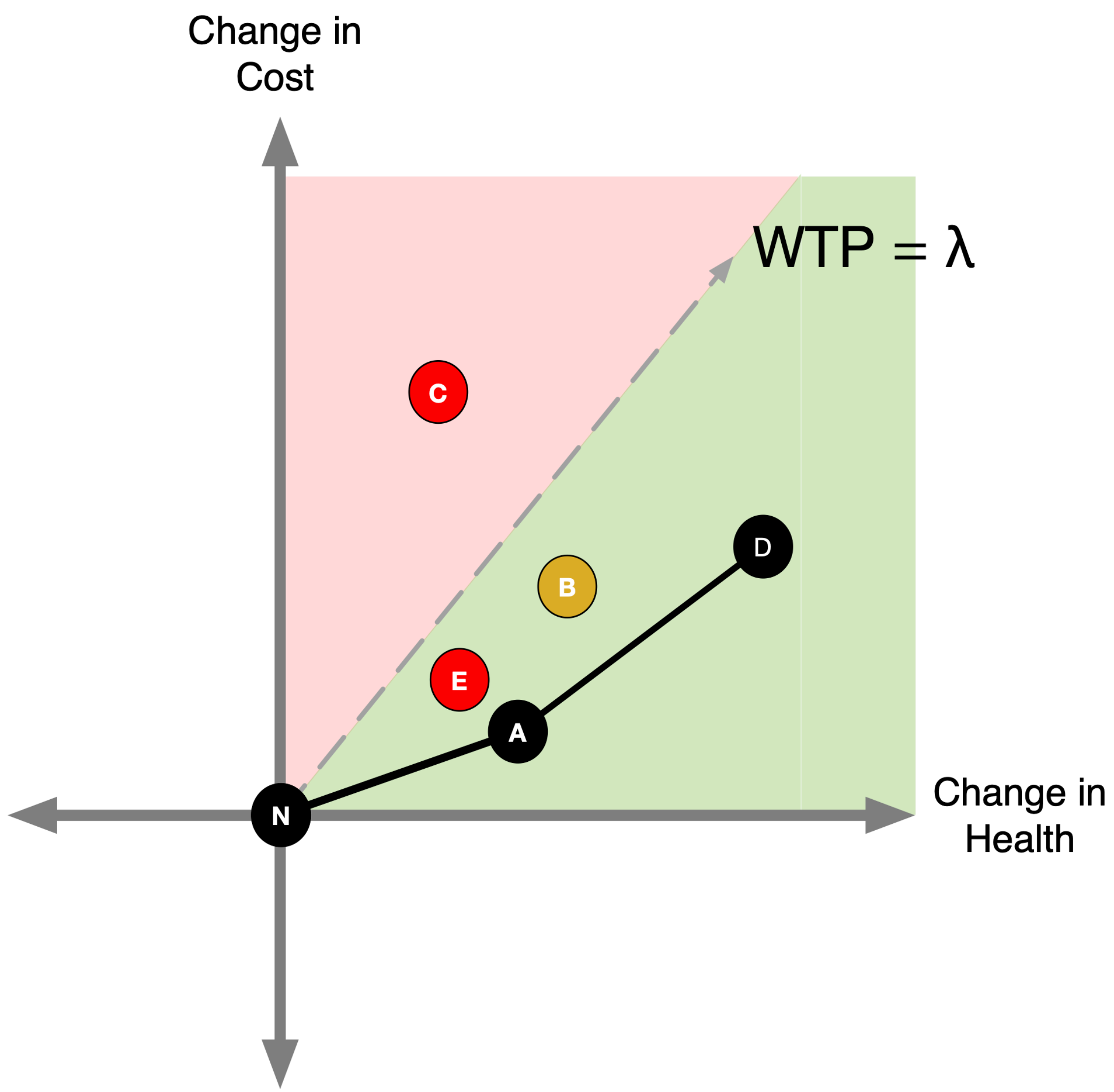
CEA Thresholds



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CEA Thresholds

Cost-Effectiveness Thresholds: the Past, the Present and the Future

Praveen Thokala[1] · Jessica Ochalek[2] · Ashley A. Leech[3] · Thaison Tong[1]

Different ways thresholds have been estimated: - “supply-side” (UK & Europe) - “demand-side” (US) - per capita consumption (US/LMICs)

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Opportunity cost ("supply-side")

- Decision should be informed by the value of what will be given up as a consequence of those cost.
  - Known as the "opportunity cost."
- If resources are committed to the funding of one intervention, then they are not available to fund and deliver others **(shopping spree concept)**
- The opportunity cost of a commitment of resources is the health forgone because these "other" interventions that are available to the health system cannot be delivered.
- Source: See K Claxton on the estimation of the NICE threshold in the UK / Woods et al, & others

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Opportunity cost ("supply-side")

Annals of Internal Medicine

ORIGINAL RESEARCH

A Health Opportunity Cost Threshold for Cost-Effectiveness Analysis in the United States

David J. Vanness, PhD; James Lomas, PhD; and Hannah Ahn, MS

Opportunity cost ("supply-side")

> If you don't consider the budget under which you are operating, then some medications could take up half the budget and displace interventions that produce significant health gain OR in the US, could increase premiums or take away $$ from other sectors

> Academics have argued that the threshold should be lower/on the more conservative end for higher priced therapies (NICE uses a budget impact threshold of 20,000 GBP/QALY for these higher priced therapies as opposed to 30,000 GBP/QALY for others)

Willingness to pay (“demand-side”)

Updating Cost-Effectiveness — The Curious Resilience of the $50,000-per-QALY Threshold

Peter J. Neumann, Sc.D., Joshua T. Cohen, Ph.D., and Milton C. Weinstein, Ph.D.

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CEA Thresholds in LMICs

Use and Misuse of Cost-Effectiveness Analysis Thresholds in Low- and Middle-Income Countries: Trends in Cost-per-DALY Studies

Ashley A. Leech, PhD, MS, David D. Kim, PhD, MS, Joshua T. Cohen, PhD, Peter J. Neumann, ScD*

Center for the Evaluation of Value and Risk in Health, Institute for Clinical Research and Health Policy Studies, Tufts Medical Center, Boston, MA, USA

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CEA Thresholds in LMICs

- Past WHO guidelines recommended countries use following guidelines: An intervention is cost-effective if cost/DALY averted is less than 1-3X per capita GDP of country
- Some have argued the WHO's guidelines may be too high and result in adoption of interventions that displace existing services that provide greater health benefit.
- Suggest 0.5 GDPpc is a more appropriate benchmark for low-income countries and 0.71 GDPpc for middle-income countries (see Woods et al 2016)

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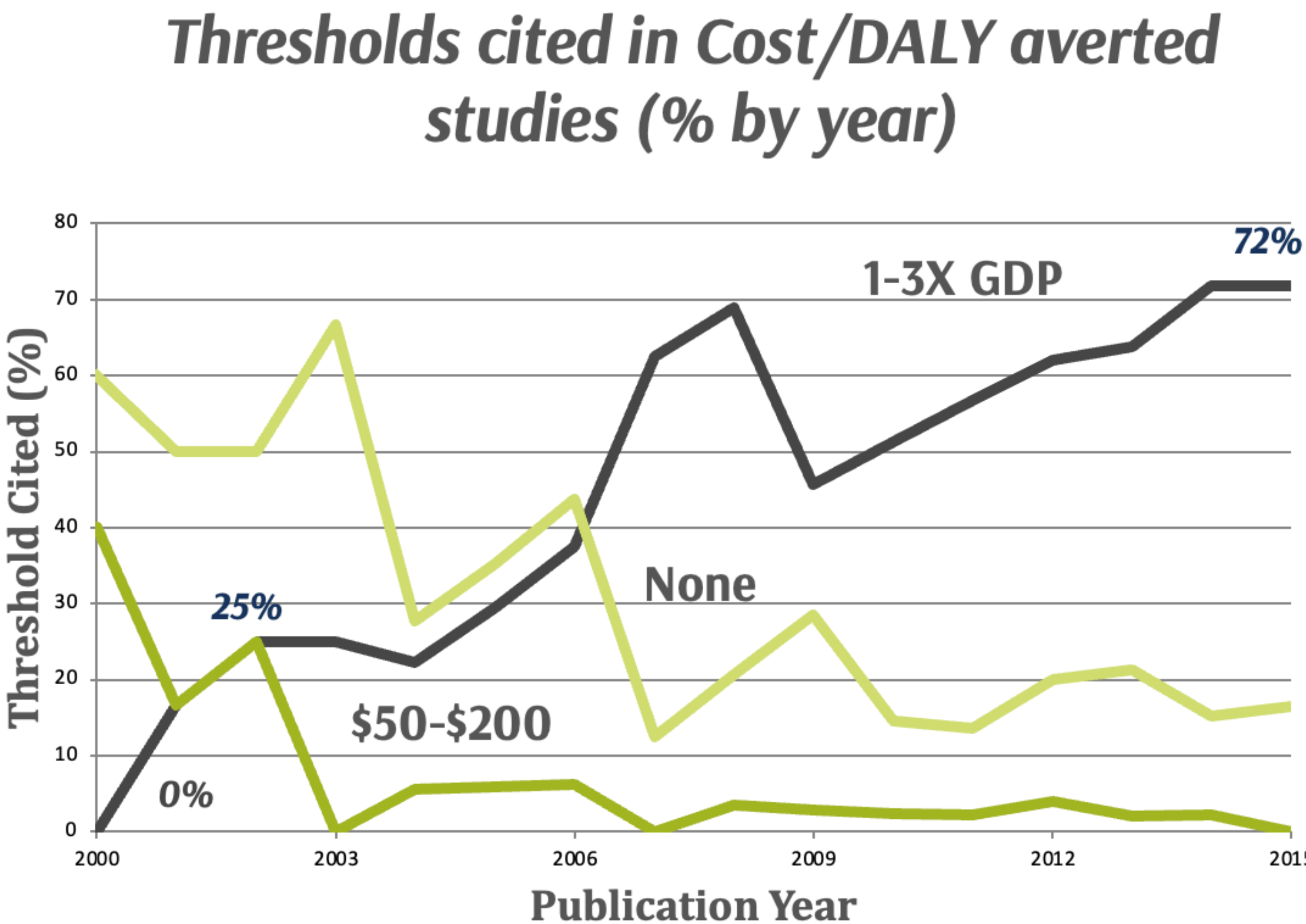
CEA Thresholds in LMICs



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HIV Example From Earlier

Strategy	Incremental Cost	DALYs Averted	Incremental Cost per DALY Averted	Status
No prophylaxis	0	0.00		
TMP-SMX	4,498	2.56	1,757	
TMP-SMX, azithromycin	1,158	0.48	2,413	
TMP-SMX, azithromycin, fluconazole	2,652	0.56	4,736	
TMP-SMX, azithromycin, fluconazole, ganciclovir	12,523	1.02	12,277	
TMP-SMX, fluconazole	**1,102**	**-0.03**		**Dominated (Strong)**
TMP-SMX, ganciclovir	**6,032**	**-0.40**		**Dominated (Strong)**
TMP-SMX, fluconazole, ganciclovir	**1,270**	**-0.03**		**Dominated (Strong)**
TMP-SMX, azithromycin, ganciclovir	**8,216**	**0.23**		**Dominated (Extended)**

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HIV Example from Earlier

- If our CE threshold was 2x GDP (GDP = $2,500), which option would we choose as decision makers?
- If our CE threshold was 1x GDP (GDP = $2,500), which option would we choose as decision makers?

Next: ICER Case Study

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