Cost Effectiveness Analysis

Chapter 5

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Objectives

Upon completing this chapter, you will be able to:

- define and describe cost-effectiveness analysis (CEA)
- illustrate the use of a cost-effectiveness plane
- discuss the different methods of presenting CEA results
- discuss the appropriate application of CEA
    - compare mutually exclusive interventions
    - allocate resources between independent interventions
- address the advantages and disadvantages of CEA

- Suppose that our interest is the prolongation of life after renal failure and that we are comparing the costs and consequences of hospital dialysis with kidney transplantation

- In this case the outcome of interest—life-years gained—is common to both interventions; however, the interventions may have differential success in achieving this outcome, as well as differential costs

- Consequently we would not automatically lean towards the least-cost intervention unless it also resulted in a greater prolongation of life

- In comparing these alternatives we would normally calculate this prolongation and estimate incremental cost per unit of effect (that is, the extra cost per life-year gained of the more effective and more costly option)

- Such analyses, in which costs are related to a single, common effect that may differ in magnitude between the alternative interventions, are usually referred to as cost-effectiveness analyses (CEAs)

- the results of such comparisons may be stated either in terms of incremental cost per unit of effect, as in this example, or in terms of effects per unit of cost (life-years gained per dollar spent)

- CEA is a health economic evaluation which is used to compare competing treatment alternatives that have outcomes measured in natural units (clinical outcomes)

- if retrospective cost data are collected for more than 1 year or if the cost data are estimated for more than 1 year into the future, it is important to **adjust** or **discount** these costs to one point in time

- CEA is used to:
  - compare mutually exclusive interventions that are not therapeutically equivalent (**ICER**)
  - allocate resources between independent interventions (**ACER**)

When to use CEA?

- CEA is used when outcomes are measured in natural units ---clinical outcomes
- Examples of natural unit outcomes that can be used in CEA include:
  - number of lives saved/ increased life expectancy
  - number of cases cured/ decreased morbidity
  - number of cases prevented/decreased morbidity
  - number of deaths averted/ decreased mortality
  - laboratory values (such as reductions in hemoglobin A_{1c}, reduction in mm HG, reductions in low-density lipoprotein cholesterol levels etc.)

- CEA can provide valuable data
  - for resource allocation
  - to support drug policy
  - for formulary management and
  - for individual patient treatment decisions

- an intervention is considered cost effective if it is;
  - less costly and more effective
  - less costly and equally effective
  - more costly and more effective, with the added benefit (Δ E) worth the added cost (Δ C)
  - less costly and less effective, with the added benefit (Δ E) of the alternative not worth the added cost (Δ C)
- challenge:
  - decision as to whether the added benefit worth the added cost

- what value should be placed on the additional or incremental unit of health outcome (Δ E)?
  - what should policymakers and society be willing to pay for this additional or incremental unit of health gain?

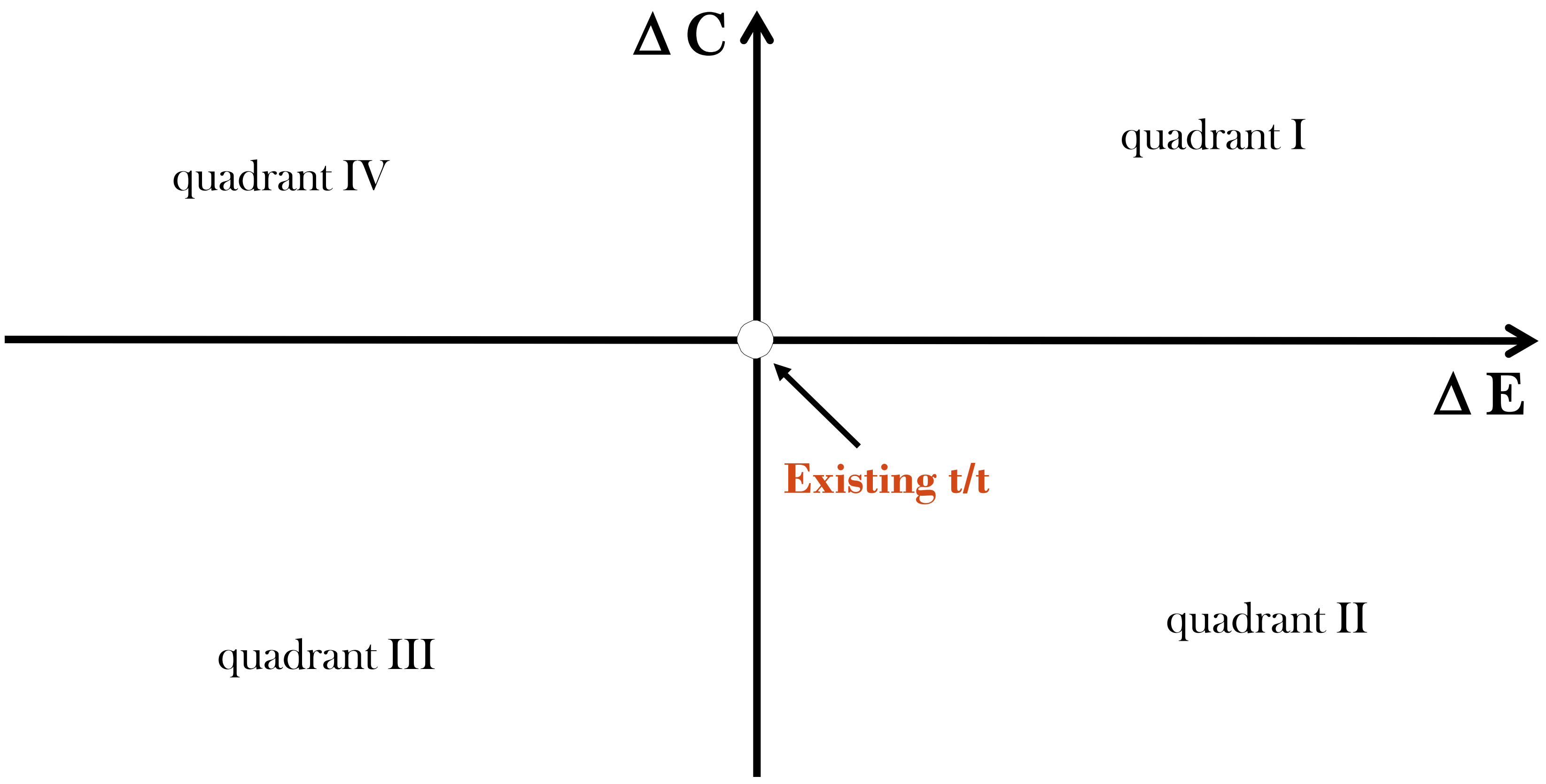
- WHO has set a threshold to decide whether the added benefit (Δ E) worth the added cost (Δ C) or not
- Alternatively, We can also use the INB technique

COST-EFFECTIVENESS PLANE

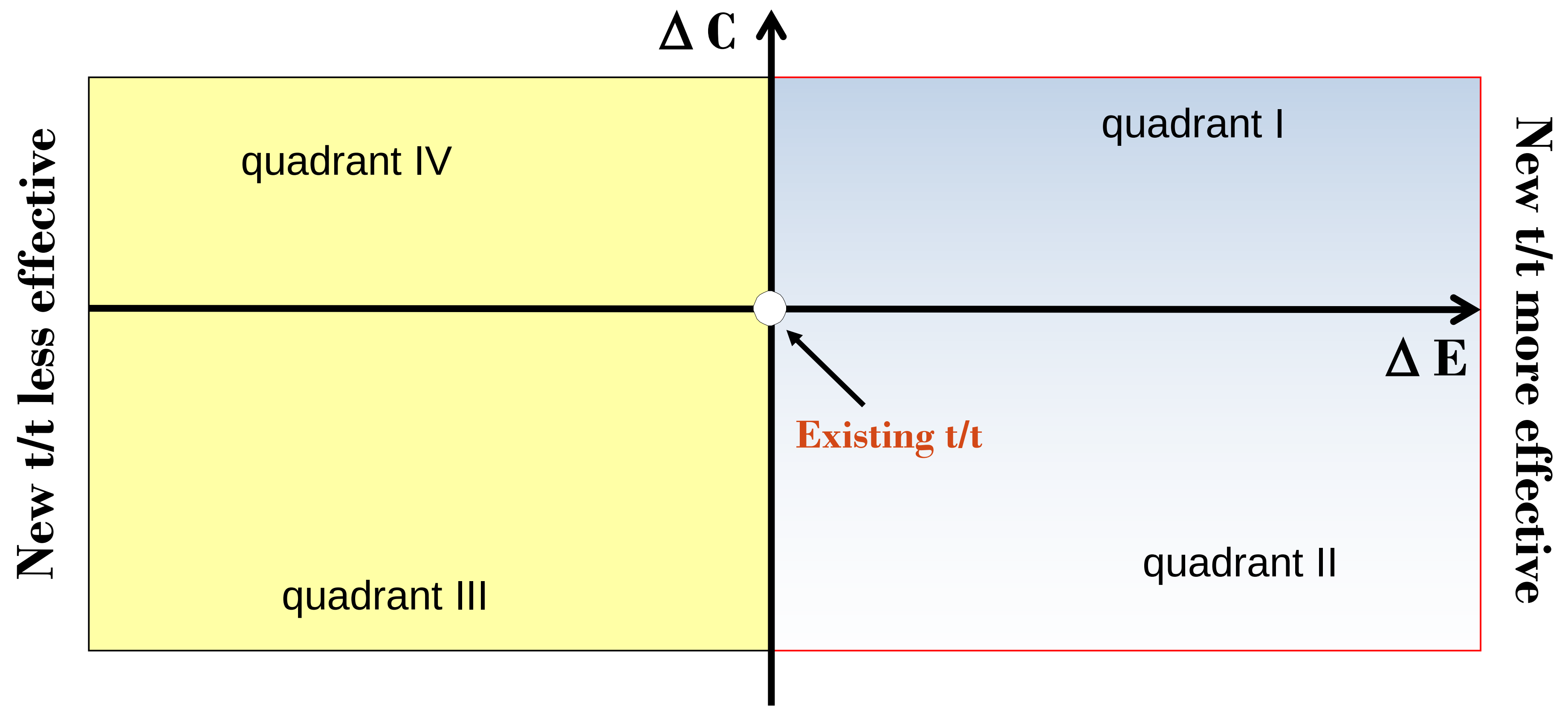
- cost-effectiveness plane is a graphical depiction of cost effectiveness comparisons

- the point on the plane where the *x* and *y* axis cross indicates the starting point of costs and effectiveness for the standard comparator **(existing t/t)**

COST-EFFECTIVENESS PLANE

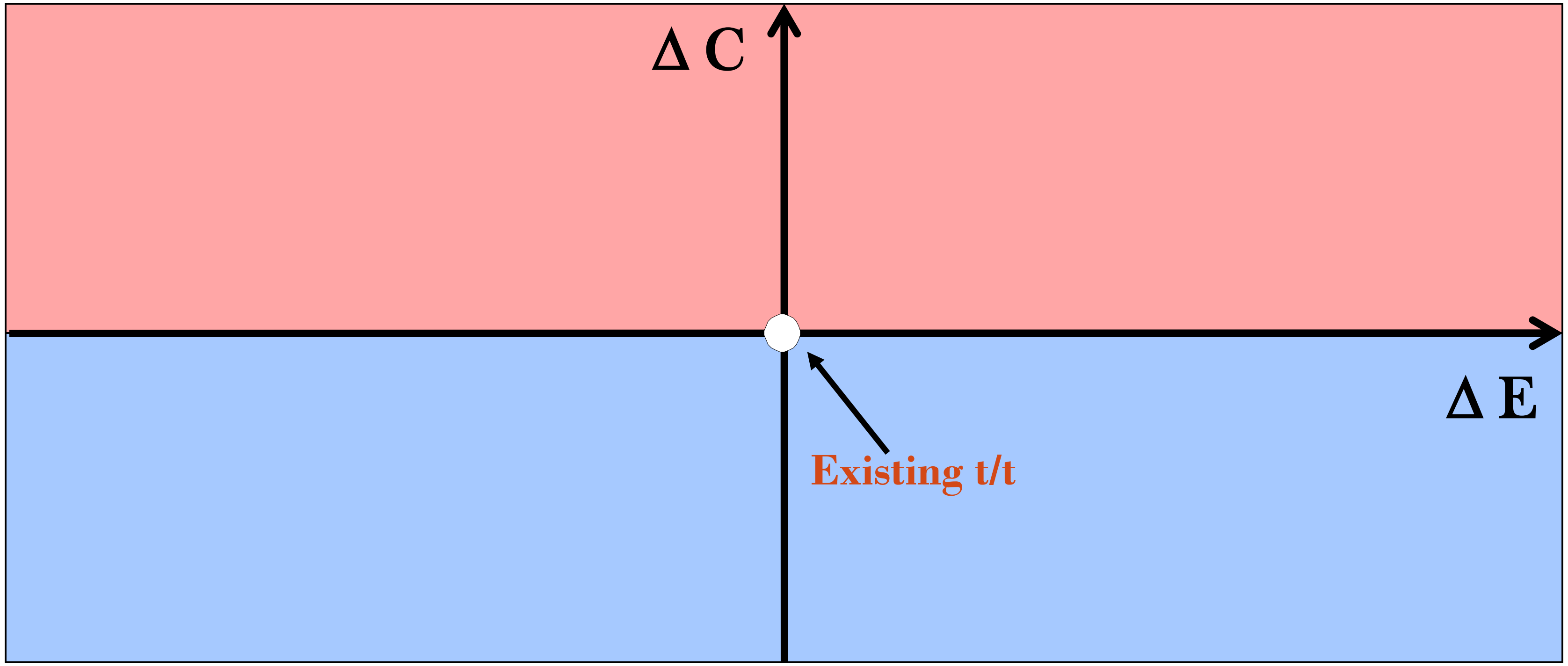


Looking at Effectiveness on the Cost-Effectiveness Plane



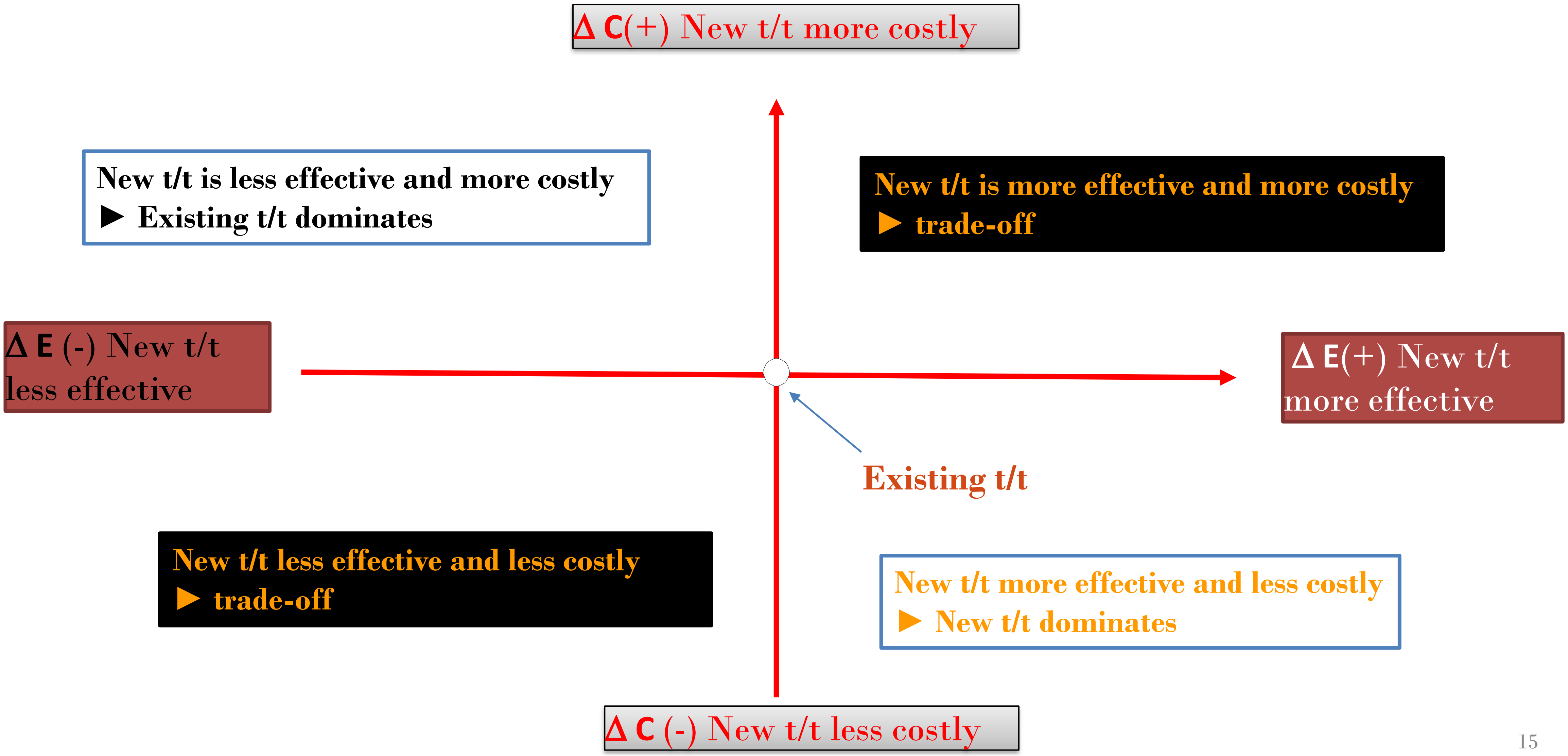
Looking at Cost on the Cost-Effectiveness Plane

New t/t more costly



New t/t less costly

MAKING DECISIONS WITH THE COST-EFFECTIVENESS PLANE



- if an intervention is more expensive and more effective than the standard comparator, this point will fall in quadrant **I**, and the tradeoff of the increase in costs for the increase in benefits would need to be considered

- if an intervention is less expensive and more effective than the standard comparator, the point would fall in quadrant **II**, and the new t/t would **dominate** the standard comparator

- if an intervention is less costly and less effective than the standard comparator, the point would fall in quadrant III, and again a tradeoff would have to be considered. (Do the cost savings of the new t/t outweigh its decrease in effectiveness?)

- if an intervention is more expensive and less effective than the standard comparator, the point would fall in quadrant IV, and the new t/t would be dominated by the standard comparator

- interventions which fall in either quadrant II or IV are considered " dominant" and do not need ICERs to be calculated as they are either
  - more effective and less costly (II), or
  - more expensive and less effective (IV)

- interventions falling in quadrant II are typically always accepted, while those falling in quadrant IV are typically rejected

- Since interventions in quadrant I are more effective but more costly, and those in quadrant III are less effective but less costly, ICERs need to be calculated and compared

- Once the ICER between two interventions is calculated, the decision to accept the most cost-effective intervention (which falls in either quadrants I and III) often depends on maximum ICER for which policy makers will accept

- The willingness to pay threshold for policy makers will vary depending on health care objectives and budgets

In general if:

- $\Delta E > 0; \Delta C < 0$ → dominant (more effective and less costly)
- $\Delta E < 0; \Delta C > 0$ → dominated (less effective and more costly)
- $\Delta E < 0; \Delta C < 0$ → trade-off
- $\Delta E > 0; \Delta C > 0$ → trade-off

Example 1: In a cost effectiveness analysis of lowering blood pressure with a fixed combination of perindopril and indapamide in type 2 diabetes mellitus, the change in cost was $ -50 and the change in outcome was 0.5 life years in remaining life times. Show whether perindopril-indapamide combination is cost effective or not when compared with other blood pressure lowering medication using cost effectiveness plane.

Methods of presenting CEA results

- Three methods of presenting cost effectiveness results:
  - Average Cost Effectiveness ratio (ACER)
  - Marginal Cost Effectiveness ratio (MCER)
  - Incremental Cost Effectiveness ratio (ICER)

Average Cost Effectiveness Ratio/ACER

- is ratio of costs to outcomes for a single intervention

$$\textbf{ACER of intervention A} = \frac{\text{Cost of intervention A}}{\text{Outcome of intervention A}}$$

- used to choose the alternative with the least cost per outcome

- Average cost effectiveness ratio can be used to compare efficiencies of various interventions
  - higher average cost indicates that the resource utilization is less efficient
  - E.g. average cost per condom distributed for an STD clinic Vs. average cost per condom distributed for outreach program

- ACER reflects the cost per outcome of an intervention independent of other alternatives

- it is used to allocate resources between independent interventions when available budget is limited
  - Example: Hepatitis B vaccination Vs. HIV testing

- not used to compare mutually exclusive interventions

Example 2: The following table shows t/t costs and number of strokes that can be prevented using preventive strategies A & B. Determine the average cost effectiveness ratios of the two strategies.

Preventive strategies	Total cost for 100 patients	Strokes prevented	Average cost effectiveness ratio/ACER
A	$10,000	10	$1000/stroke prevented
B	$60,000	50	$1200/stroke prevented

Marginal Cost Effectiveness Ratio/MCER

- marginal cost effectiveness ratio is ratio of additional costs to a single additional outcome

$$\text{MCER} = \frac{\text{Cost of intervention A}' - \text{Cost of intervention A}}{\text{Outcome of intervention A}' - \text{Outcome of intervention A}}$$

- it examines effects of scale within a single program
  - does cost per health outcome increase or decrease as program changes in size?

Example 3: The following table shows costs and number of cases that can be prevented using program A and expanded program A (A'). Determine the marginal cost effectiveness ratio.

Programs	Prevented cases	Total costs
Program A	30	$450
Expanded program A (A')	36	$600

Incremental Cost Effectiveness Ratio /ICER

- incremental cost effectiveness ratio is ratio of additional costs to additional outcomes obtained when one intervention is compared to the next most effective intervention

$$\text{ICER} = \frac{\text{Cost of intervention - Cost of alternative intervention}}{\text{Outcome of intervention - Outcome of alternative intervention}}$$

- ICER is the difference in total costs of two therapies divided by difference in effectiveness of the two interventions

- ICER shows the cost per unit outcome of switching from the less effective and less costly t/t option to the more effective and more costly t/t option

- it is used to determine the magnitude of the added cost for each unit health improvement

- ICER is used to used to compare mutually exclusive interventions

- **Mutually exclusive**
  - only one alternative can be chosen

Incremental cost Vs average cost

- incremental cost- the increased cost of an intervention relative to an alternative

Incremental cost Vs marginal cost

- incremental cost relates to alternative interventions

- marginal cost relates to the same intervention

Example 3: The following table shows t/t costs and number of life years that can be saved using two drugs A & B.

a. determine the incremental cost effectiveness ratio (**ICER**).

b. how do you interpret the result?

Mutually Exclusive Interventions	Outcomes (Life Years saved)	Costs
Treatment A	9	$90,000
Treatment B	11	$110,000

Ans.

Mutually Exclusive Interventions	**Outcomes (Life Years saved)**	**Costs**	**△ Outcome**	**△ Cost**	**ICER**
Treatment A	9	$90,000	---	---	---
Treatment B	11	$110,000	2	$20,000	$10,000

a. ICER = $10,000 per additional Life Year saved
b. Interpretation: on average, it costs $1,000 to save one additional life year using drug B

WHO cost effectiveness Threshold

- If ICER < the country's GDP per capita --- very cost effective
- If ICER 1-3 times the country's GDP per capita --- cost effective
- If ICER > 3 times the country's GDP per capita --- not cost effective
- In other words,
  - If ICER ≤ 3x GDP per capita, choose the more costly and the more effective t/t option
  - If ICER > 3x GDP per capita, choose the less costly and the less effective t/t option

Comparison of Mutually Exclusive Interventions - ICER

- Steps in comparing mutually exclusive interventions
  1. rank the interventions in increasing order of effectiveness
  2. eliminate strongly dominated interventions
     - if an intervention is less effective and more costly than its alternative, it is **strongly dominated**
  3. estimate ICER of least effective intervention compared to next most effective intervention

Steps…cont'd

4. eliminate weakly dominated interventions
   – if the ICER of an intervention is higher than that of the next most effective intervention, it is **weakly dominated**
5. make decisions

Example 4: Among the following mutually exclusive programs, choose the most cost effective program for implementation in Ethiopia? (GDP per capita of Ethiopia is $863)

Mutually Exclusive programs	Outcomes (Averted Cases)	Costs
Program A	100	$ 50,000
Program B	150	$ 130,000
Program C	110	$ 170,000

Step 1: Order by Increasing Effectiveness

Mutually Exclusive programs	Outcomes (Averted Cases)	Costs
Program A	100	$ 50,000
Program C	110	$ 170,000
Program B	150	$ 130,000

Step 2: Check for Dominance

Mutually Exclusive programs	Outcomes (Averted Cases)	Costs
Program A	100	$ 50,000
Program C	110	$ 170,000
Program B	150	$ 130,000

Step 3: Eliminate Dominated Programs

Mutually Exclusive programs	Outcomes (Averted Cases)	Costs
Program A	100	$ 50,000
Program B	150	$ 130,000

Step 4: Re-Calculate ICER without dominated programs

Mutually Exclusive programs	Outcomes (Averted Cases)	Costs	△ Outcome	△ Cost	ICER
Program A	100	$ 50,000	_	_	_
Program B	150	$ 130,000	50	$80,000	$1,600

Since the ICER is less than 3x the GDP per capita of Ethiopia ($ 1,600 vs $2,589), program B is the most cost effective for implementation in Ethiopia.

- **Example 5:** Among the following t/t options, which one is the most cost effective for a country which has a GDP per capita of $900? What about for a country which has a GDP per capita of $200?

Mutually Exclusive Interventions	Outcomes (Life years saved)	Costs
treatment A	30	$ 20,000
treatment B	10	$ 5,000
treatment C	15	$ 13,000
treatment D	11	$17,000

Step 1; Arrange in increasing order of effectiveness

Mutually Exclusive Interventions	Outcomes (Life years saved)	Costs
treatment B	10	$ 5,000
treatment D	11	$17,000
treatment C	15	$ 13,000
treatment A	30	$ 20,000

Step 2; Check for dominance

Mutually Exclusive Interventions	Outcomes (Life years)	Costs
Treatment B	10	$ 5,000
Treatment D	11	$17,000
Treatment C	15	$ 13,000
Treatment A	30	$ 20,000

Step 3; Remove dominated treatment option

Mutually Exclusive Interventions	Outcomes (Life years saved)	Costs
Treatment B	10	$ 5,000
Treatment C	15	$ 13,000
Treatment A	30	$ 20,000

Step 4; Re-calculate ICER without dominated t/t option

Mutually Exclusive Interventions	Outcomes (Life years saved)	Costs	△Outcome	△Cost	ICER
Treatment B	10	$ 5,000		---	---
Treatment C	15	$ 13,000	5	$8,000	$1,600
Treatment A	30	$ 20,000	15	$ 7,000	$ 467

Step 5 ; Remove t/t option C since it is weakly dominated by t/t A

Mutually Exclusive Interventions	Outcomes (Life years)	Costs	△ Outcome	△ Cost	ICER
Treatment B	10	$ 5,000			
Program C	15	$ 13,000	5	$ 8,000	1,600
Treatment A	30	$ 20,000	15	$ 7,000	467

Step 6; Recalculate the ICER without the weakly dominated t/t option

Mutually Exclusive Interventions	Outcomes (Life years)	Costs	△ Outcome	△ Cost	ICER
Program B	10	$ 5,000	---	---	---
Program A	30	$ 20,000	20	$ 15,000	**$ 750**

Since the ICER is less the GDP per capita ($ 750 vs $ 900), program A (the more effective and more costly option) is the most cost effective.

- To overcome some of the disadvantages with using the ICER, an increasingly popular method of presenting results in CEA studies is converting the results to a Incremental Net Benefit (INB)

- The INB calculation requires defining the willingness to pay threshold for effectiveness, and studies should use the country-specific value

- The willingness to pay threshold reflects how much policy makers will spend to gain one extra unit of health outcome (i.e. effectiveness)

- The INB is calculated using the following formula:

  [Maximum WTP × Incremental Effectiveness]—Incremental Cost

- the maximum acceptable **willingness to pay,** is represented by lambda (λ)

$$INB = (\lambda \times \Delta \text{ Effectiveness}) - \Delta \text{ Costs}$$

  - λ represents society's willingness to pay for a unit of health

- if INB > 0, the more effective and more costly option is cost-effective
- if INB < 0, the less effective and less costly option it cost-effective

- Example 6: Costs and outcomes for BreatheAgain were compared with inhaled corticosteroids. BreatheAgain had total costs of $537 and provided 90 symptom free days (SFDs) compared with $320 and 45 SFDs for ICS. The incremental cost effectiveness ratio (ICER) was $4.82 per extra SFD. It has been suggested that a day without asthma symptoms is worth at least $5 (Rutten-van Molken *et al.*). Which one is cost effective at λ = $5.00?

Ans.

$$INB = (\lambda \times \Delta \text{ SFDs}) - \Delta \text{ Costs}$$

$$INB = (\$5 \times 45 \text{ SFDs}) - \$217$$

$$INB = \$\ 8$$

- Because the INB is greater than zero, BreatheAgain is more cost-effective than inhaled corticosteroids when $\lambda = \$5.00$.

Resource Allocation between Independent Interventions-ACER

- Steps

1. calculate average cost effectiveness ration/ACER
2. rank the programmes in increasing order of ACER
3. calculate cumulative outcomes and cumulative costs
4. decide the maximum benefit you can gain from your budget (make resource allocation decisions)

- Example 7: Imagine you have $4,700,000 available and 10 independent programmes you could invest in.
- The costs and outcomes of each programme, compared to a relevant alternative are given in the table shown in the next slide. In which programmes should you invest to maximize total QALYs i.e., to be technically efficient?

Independent Programmes	Outcomes (QALYs)	Costs ($)
P1	100	1,200,000
P2	222	2,000,000
P3	100	2,200,000
P4	500	500,000
P5	100	5,000,000
P6	150	4,500,000
P7	500	8,000,000
P8	500	1,000,000
P9	200	1,200,000
P10	100	1,800,000

Step 1; Calculate average cost effectiveness ration/ACER

Independent Programmes	QALYs	Costs ($)	ACER ($)
P1	100	1,200,000	12,000
P2	222	2,000,000	9,000
P3	100	2,200,000	22,000
P4	500	500,000	1,000
P5	100	5,000,000	50,000
P6	150	4,500,000	30,000
P7	500	8,000,000	16,000
P8	500	1,000,000	2,000
P9	200	1,200,000	6,000
P10	100	1,800,000	18,000

Step 2; Rank the programmes by increasing ACER

Independent Programmes	QALYs	Costs ($)	ACER ($)
P4	500	500,000	1,000
P8	500	1,000,000	2,000
P9	200	1,200,000	6,000
P2	222	2,000,000	9,000
P1	100	1,200,000	12,000
P7	500	8,000,000	16,000
P10	100	1,800,000	18,000
P3	100	2,200,000	22,000
P6	150	4,500,000	30,000
P5	100	5,000,000	50,000

Step 3; Calculate cumulative outcomes and cumulative costs

	QALYs	Costs ($)	ACER ($)	Cumulative benefits/QALYs	Cumulative costs
P4	500	500,000	1,000	500	500,000
P8	500	1,000,000	2,000	1,000	1,500,000
P9	200	1,200,000	6,000	1,200	2,700,000
P2	222	2,000,000	9,000	1,422	4,700,000
P1	100	1,200,000	12,000	1,522	5,900,000
P7	500	8,000,000	16,000	2,022	13,900,000
P10	100	1,800,000	18,000	2,122	15,700,000
P3	100	2,200,000	22,000	2,222	17,900,000
P6	150	4,500,000	30,000	2,372	22,400,000
P5	100	5,000,000	50,000	2,472	27,400,000

Step 4; Decide the maximum benefit you can gain from your budget

	QALYs	Costs ($)	ACER ($)	Cumulative benefits/QALYs	Cumulative cost
P4	500	500,000	1,000	500	500,000
P8	500	1,000,000	2,000	1,000	1,500,000
P9	200	1,200,000	6,000	1,200	2,700,000
P2	222	2,000,000	9,000	1,422	4,700,000
P1	100	1,200,000	12,000	1,522	5,900,000
P7	500	8,000,000	16,000	2,022	13,900,000
P10	100	1,800,000	18,000	2,122	15,700,000
P3	100	2,200,000	22,000	2,222	17,900,000
P6	150	4,500,000	30,000	2,372	22,400,000
P5	100	5,000,000	50,000	2,472	27,400,000

- Example 8: Results of a cost effectiveness analysis of testing and antiviral treatment strategies for adult influenza are summarized in the following table. Using the WHO cost effectiveness threshold, which management strategy is most cost effective for a nation with GDP per capita of $200?

Management Strategies	**Outcomes (Illness Days Avoided)**	**Total costs**
No testing or treatment	0	0
Amantadine	0.54	$97.50
Rimantadine	0.59	$119.10
Zanamivir	0.74	$137.10
Testing then amantadine	0.44	$115.00
Testing then rimantadine	0.48	$125.50
Treating then zanamivir	0.60	$134.30

- Example 9: Imagine you have 18,000,000 EthB available and 10 independent interventions you could invest in. The costs and benefits of each intervention are shown in the following table. In which interventions should you invest to be technically efficient?

Interventions	Cost (EthB)	Outcome (QALYs)
Cholesterol testing and diet therapy only (all adults)	1,200,000	100
Neurosurgical intervention for head injury	2,000,000	222
Neruosurgical intervention for subarachnoid haemorrhage	2,200,000	100
Pacemaker implementation	500,000	500
Valve replacement for aortic stenosis	5,000,000	100
Kidney transplant	4,500,000	150
Breast cancer screening	8,000,000	500
Hospital haemodialysis	1,000,000	500
Neurosurgical intervention for malignant intracranial tumors	1,200,000	200
Erythropoietin treatment for anaemia in dialysis patients	1,800,000	100

- **Advantages of CEA**
  - relatively simple to carry out
- **Disadvantages of CEA**
  - this method is not used to directly compare interventions that have different objectives/ goals
  - the inability to provide interdisease comparisons
    - E.g. cost per unit reduction in blood pressure cannot meaningfully be compared with costs per unit reduction in blood glucose
  - in CEA method outcomes are measured in natural units (single dimension)
  - therefore, it cannot incorporate other aspects of outcome into the cost-effectiveness ratio
  - E.g. quantity and quality of life and life years saved cannot be collapsed in to one unit (QALY)