Cost-Effectiveness Analysis

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Outline

- Introduction to cost-effectiveness analysis (CEA)
- Choice criteria for CEA
- The cost-effectiveness frontier
- Net benefits (a transformation of CEA) and choice criteria
- Additional topics

Cost-Effectiveness Analysis (I)

- Estimates costs and outcomes of intervention
- Costs and outcomes are expressed in different units
  - If outcomes aggregated using measures of preference (e.g., quality-adjusted life years saved), referred to as cost utility analysis

Cost-Effectiveness Analysis (II)

- Results meaningful if:
  - Compared with other accepted and rejected interventions (e.g., against league tables), or
  - There exists a predefined standard (i.e., a threshold or maximum acceptable cost-effectiveness ratio or an acceptability criterion) against which they can be compared
    - e.g., $50,000 per year of life saved might be considered maximum acceptable ratio, or
  - Can define utility curves that trade off health and cost

Cost-Effectiveness "History"

- $/Life saved
- $/Year of life saved (YOL)
- $/Quality adjusted life year saved (QALY)
- ??? Outlawing QALYs ???

Why CEA Rather Than CBA?

- Not precisely clear
  - Potential difficulties in measurement
  - Discomfort with placing a dollar value directly on a particular person's life (rather than years of life in general)
  - QALYs / life years more equally distributed than wealth
  - Health more a "right" than a commodity
    - Implies 1 person 1 vote may be more appropriate than 1 dollar 1 vote
    - Cost-effectiveness analysis uses 1 QALY/year 1 vote

Cost-Effectiveness Ratios

- Cost-effectiveness ratio

$$\frac{Costs_1 - Costs_2}{Effects_1 - Effects_2}$$

- A ratio exists for every pair of options
  - 1 option (case series), no ratios calculated
  - 2 options, 1 ratio
  - 3 options, 3 ratios (option 1 versus option 2, option 1 versus option 3, and option 2 versus option 3)
- In "efficient" selection algorithm, don't necessarily calculate all possible ratios

Average Cost-Effectiveness Ratio

- Some dispute about definitions
  - e.g., Some use "average cost-effectiveness ratio" to refer to practice of dividing therapy's total cost by its total effect (including Treeage, a fairly ubiquitous piece of decision analysis software)
- Don't use this definition of average CER
- Recommend against dividing a therapy's total cost by its total effect
  - These ratios provide little to no information

Dividing a Therapy's Costs by Its Effects is "Generally Uninformative"

	Cost	Effect	Ratio
Example 1			
Rx1	500	.025	20,000
Rx2	780	.026	30,000
Example 2			
Rx1	500	.025	20,000
Rx2	1500	.05	30,000

Dividing a Therapy's Costs by Its Effects is "Generally Uninformative"

	Cost	Effect	Ratio
Example 1			
Rx1	500	.025	20,000
Rx2	780	.026	30,000
	(780-500) / (.026-.025) = 280,000		
Example 2			
Rx1	500	.025	20,000
Rx2	1500	.05	30,000
	(1500-500) / (.05-.025) = 40,000		

Average Cost-Effectivemess Ratio (2)

- Definition: Comparison of costs and effects of each intervention with a single option, often "do nothing" or usual care option

Example: Average Ratios and Sixth Stool Guaiac

# Guaiac Tests	Cost	Cases Detected	Avg Cost/ Case Detected *
1	7.75	.00659469	--
2	10.77	.00714424	5495
3	13.02	.00719004	8852
4	14.81	.00719385	11,783
5	16.31	.00719417	14,279
6	17.63	.00719420	16,480

* $(C_i - C_1) / (E_i - E_1)$

- Neuhauser and Lewicki, NEJM, 1975;293:226-8.

Incremental Cost-Effectiveness Ratios

- Average ratios not important when making selection from among all candidate therapies
- ICER = comparison of costs and effects among alternative options (i.e., excluding comparator used in calculation of average cost-effectiveness ratios)
- When there are only 2 options being evaluated, average and incremental cost-effectiveness ratios are identical

Guaiac Average and Incremental Ratios

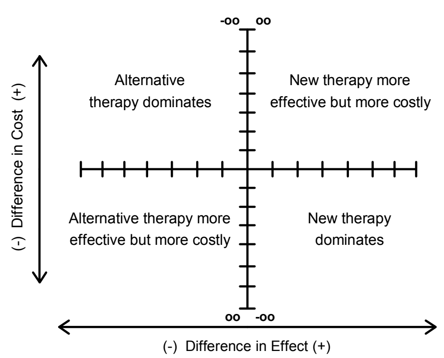
# Guaiac tests	Cost	Cases Detected	Average CER *	Increm CER **
1	7.75	.00659469	--	--
2	10.77	.00714424	5495	5495
3	13.02	.00719004	8852	49127
4	14.81	.00719385	11,783	469,816
5	16.31	.00719417	14,279	4,687,500
6	17.63	.00719420	16,480	44,000,000

* $(C_i - C_1) / (E_i - E_1)$

** $(C_i - C_{i-1}) / (E_i - E_{i-1})$

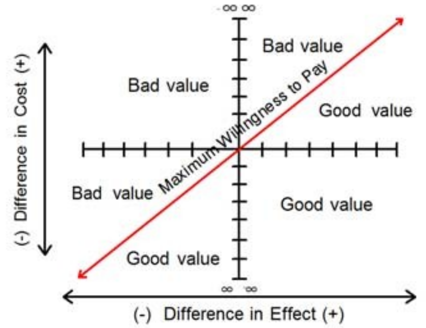
- Neuhauser and Lewicki, NEJM, 1975;293:226-8.

Cost-Effectiveness Plane



- Axes
- Origin
- Average ratios
- Incremental ratios

Good and Bad Value



Choice Criteria For Cost-Effectiveness Ratios

- Choose options with acceptable average and incremental cost-effectiveness ratios (i.e., whose ratios with all other options are acceptable)
- Subject to:
  - Budget Constraint?
  - Acceptable Ratio?
- Not accounting for uncertainty around ratios
- Consider 3 mutually exclusive options and a willingness to pay of 50k

Choice Criteria, Example 1

	Option 1	Option 2	Option 3
Expected Costs	10,000	135,000	270,000
Expected QALYs	20	25	30

Ratios	Option 2	Option 3	
Option 1	25,000	26,000	
Option 2	--	27,000	Adopt?

Choice Criteria, Example 2

	Option 1	Option 2	Option 3
Expected Costs	10,000	135,000	235,000
Expected QALYs	20	25	26

Ratios	Option 2	Option 3	
Option 1	25,000	37,500	
Option 2	--	100,0000	Adopt?

Choice Criteria, Example 3

	Option 1	Option 2	Option 3
Expected Costs	10,000	210,000	230,000
Expected QALYs	20	21	21.5

Ratios	Option 2	Option 3	
Option 1	200,000	146,667	
Option 2	--	40,000	Adopt?

Multitherapy Example

- Suppose 6 screening strategies have the following discounted costs and life expectancies:

Treatment	Cost	YOLS
No screening (S1)	1052	17.348
Sig Q10 (S2)	1288	17.378
Sig Q5 (S3)	1536	17.387
U+Sig, Q10 (S4)	1810	17.402
C Q(10) (S5)	2028	17.396
U+Sig, Q5 (S6)	2034	17.407

Frazier AL, et al. JAMA. 2000;284:1954-61.

Choice Among Screening Strategies

- Which therapy should be adopted if the acceptability criterion is $40,000 / YOL Saved? $50,000 / YOL Saved?
- In what follows, demonstrate 2 (of 4) methods for selecting a single therapy from among these candidates
  - Methods all based on selecting therapy with an acceptable ratio
  - Methods transformations of one another -- use same information in slightly different ways -- and all yield identical choices

Method 1: Efficient Algorithm (MEA) for Choosing among Multiple Therapies (I)

- Suppose 6 therapies have the following discounted costs and life expectancies

Treatment	Cost	YOLS
No screening (S1)	1052	17.348
Sig Q10 (S2)	1288	17.378
Sig Q5 (S3)	1536	17.387
U+Sig, Q10 (S4)	1810	17.402
C Q(10) (S5)	2028	17.396
U+Sig, Q5 (S6)	2034	17.407

Efficient Algorithm: Step 1

- Rank order therapies in ascending order of either outcomes or costs (final ordering of nondominated therapies unaffected by variable chosen)

Treatment	Cost	YOLS
No screening (S1)	1052	17.348
Sig Q10 (S2)	1288	17.378
Sig Q5 (S3)	1536	17.387
C Q(10) (S5)	2028	17.396
U+Sig, Q10 (S4)	1810	17.402
U+Sig, Q5 (S6)	2034	17.407

Efficient Algorithm: Step 2

- Eliminate therapies that are strongly dominated (i.e., have increased costs and reduced effects compared with at least one other alternative)

Treatment	Cost	YOLS
No screening (S1)	1052	17.348
Sig Q10 (S2)	1288	17.378
Sig Q5 (S3)	1536	17.387
~~C Q(10) (S5)~~	~~2028~~	~~17.396~~
U+Sig, Q10 (S4)	1810	17.402
U+Sig, Q5 (S6)	2034	17.407

Efficient Algorithm: Step 3

- Compute incremental cost-effectiveness ratios for each adjacent pair of outcomes (e.g., between options 1 and 2; between options 2 and 3; etc.)

Treatment	Cost	YOLS	ICER
No screening (S1)	1052	17.348	--
Sig Q10 (S2)	1288	17.378	7867
Sig Q5 (S3)	1536	17.387	27,556
~~C Q(10) (S5)~~	~~2028~~	~~17.396~~	~~Dom~~
U+Sig, Q10 (S4)	1810	17.402	18,267
U+Sig, Q5 (S6)	2034	17.407	44,800

Efficient Algorithm: Step 4

- Eliminate therapies that are less effective (costly) but have a higher cost-effectiveness ratio (weakly dominated) than next highest ranked therapy
- Rationale: Rather buy more health for a lower cost per unit than less health for a higher cost per unit
  - e.g., eliminate S3 (sig,Q5), because:
    - S3 is less effective than next higher ordered S4 (U+sig,Q10) [17.387 YOLS vs. 17.402] AND
    - Incremental ratio for moving from S2 to S3 (27,556) is greater than incremental ratio from moving from S3 to S4 (18,267)
      - Implies that moving from S2 to S4 is more cost-effective than is moving from S2 to S3

Efficient Algorithm: Step 5

- Recalculate ICERs (e.g., between options 2 and 4)
  - Repeat steps 4 and 5 if necessary

Treatment	Cost	YOLS	ICER
No screening (S1)	1052	17.348	--
Sig Q10 (S2)	1288	17.378	7867
~~Sig Q5 (S3)~~	~~1536~~	~~17.387~~	~~27,556~~
~~C Q(10) (S5)~~	~~2028~~	~~17.396~~	~~Dom~~
U+Sig, Q10 (S4)	1810	17.402	21,750
U+Sig, Q5 (S6)	2034	17.407	44,800

Efficient Algorithm: Step 6

- Identify acceptable therapy

Maximum WTP	Therapy
<7867	S1
7867 to 21,749	S2
21750 to 44,799	S4
44,800+	S6

Full Cost-Effectiveness Table

Treatment	Cost	ΔC	YOLS	Δ Y	ICER
S1 No screening	1052	--	17.348	--	--
S2 Sig Q10	1288	236	17.378	0.030	7867
S3 Sig Q5	1536	--	17.387	--	WD
S5 C Q(10)	2028	--	17.396	--	SD
S4 U+Sig, Q10	1810	522	17.402	0.024	21,750
S6 U+Sig, Q5	2034	224	17.407	0.005	44,800

SD = strong dominance; WD = weak dominance

Reduced Cost-Effectiveness Table

Treatment	Cost	ΔC	YOLS	Δ Y	ICER
S1 No screening	1052	--	17.348	--	--
S2 Sig Q10	1288	236	17.378	0.030	7867
S4 U+Sig, Q10	1810	522	17.402	0.024	21,750
S6 U+Sig, Q5	2034	224	17.407	0.005	44,800

Introduction to Method 2: Net Benefits

- A composite measure (part cost-effectiveness, part cost benefit analysis), usually expressed in dollar terms, that is derived by rearranging cost-effectiveness decision rule:

$$W > \Delta C / \Delta Q$$

where W = willingness to pay (e.g., 50 or 100K)

Net Benefits (II)

- Two forms of net benefit expression exist depending on rearrangement of expression
  - Perhaps most naturally for economists, net monetary benefits can be expressed on cost scale (NMB)

$$(W * \Delta Q) - \Delta C$$

  - OR net health benefits (NHB) can be expressed on health outcome scale:

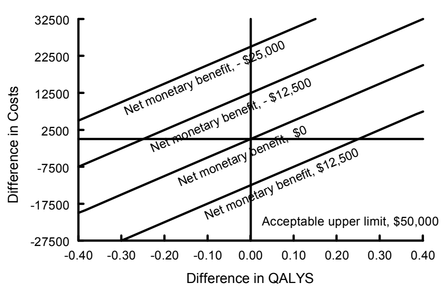
$$\Delta Q - (\Delta C / W)$$

    - Potential disadvantage: NHB undefined when WTP equals 0

NMB Rationale

- Overcomes problems associated with parametric tests of ratio
  - – Study result is a difference in means, not a ratio of means, and is always defined and continuous
- Substitutes a “poor-person’s” willingness to pay measure (the acceptability criterion) for more theoretically correct individually-measured willingness to pay
  - – Differs from cost-benefit analysis in that it does not aggregate individuals' willingnesses to pay
- All else equal, we should adopt programs with net monetary (health) benefits that are greater than 0 (i.e., programs with incremental cost-effectiveness ratios that are less than WTP

Net Benefits and CE Plane (I)



- On CE plane, NMB is represented by a family of lines all with slope equal to W

Net Benefits and CE Plane (II)

- Each line represents a single value of net benefits
  - – For NMB, -intercept (because at origin, W ∆Q = 0 and formula reduces to –∆C)
  - – For NHB, point where line intersects horizontal axis
- For line passing through origin, both NMB and NHB = 0
  - – Lines below and to right of net benefit=0 line have positive net benefits (i.e., acceptable cost-effectiveness ratios)
  - – Lines above and to left have negative net benefits

NMB and Multitherapy Example

- Returning to previous multitherapy example: suppose 6 therapies have following discounted costs and life expectancies

Treatment	Cost	YOLS
No screening (S1)	1052	17.348
Sig Q10 (S2)	1288	17.378
Sig Q5 (S3)	1536	17.387
C Q(10) (S5)	2028	17.396
U+Sig, Q10 (S4)	1810	17.402
U+Sig, Q5 (S6)	2034	17.407

- Which therapy should be adopted if acceptability criterion is $40,000 / YOL Saved? $50,000?

Numeric NMB Selection Method

- Can follow a modified version of method 1 to calculate incremental NMB
- Weak dominance can either be identified (a negative INMB followed by a positive INMB) OR it will not affect choice of optimal therapy
  - But may affect calculated values of INMB for "reduced table"

Comparing 6 Strategies' Monetary Benefits

- Because of issues related to identification of weak dominance, maby be easier to select optimal therapy based on monetary benefit (MB) for each therapy based on its own costs and effects rather than incremental costs and effects

Step 1: Calculate Monetary Benefit

- Step 1. Calculate each therapy's MB (also referred to as NB) by multiplying therapy's average (NOT incremental) effect times WTP and subtracting therapy's average cost

$$MB_i = W\bar{Q}_i - \bar{C}_i$$

- Select therapy with greatest MB
- Yields same conclusions as other methods for selecting a therapy

Method 2

	Cost	YOLS	NMB, $40K	NMB, $50K
No Scr (S1)	1052	17.348	692,868 *	866,348
Sig, Q10 (S2)	1288	17.378	693,832	867,612
Sig, Q5 (S3)	1536	17.387	693,944	867,814
U+Sig, Q10 (S4)	1810	17.402	**694,270**	868,290
C,Q10 (S5)	2028	17.396	693,812	867,772
U+Sig,Q5 (S6)	2034	17.407	694,246	**868,316**

* (40,000 * 17.348) = 693,920; subtracting 1052 = 692,868

Simultaneous Comparison

- Description of selection algorithm may suggest a path through different options, with adoption of lower cost/ effect pairs before adoption of higher cost/effect pairs
- Not true
  - All 4 algorithms are simply step-by-step procedures that simultaneously compare all options as done by:
    - Identifying tangency between NMB lines and " health production" frontier, or
    - Comparing MBs

Goal of Selection Process

- Choose options with acceptable average and incremental cost-effectiveness ratios
  - Choose options whose ratios with all other options are acceptable
- Implication: cannot ignore economic value of U and Sig2 every 10 years and U and Sig2 every 5 years when evaluating Sig2 every 5 years or colonoscopy every 10 years

What Is Maximum Acceptable Ratio?

- Traditionally, cost-effectiveness ratios less than $40,000 to $50,000 per QALY saved (or NMB cost lines defined using these ratios) have been considered acceptable
- Little analytic attention has been given to identifying an appropriate acceptability criterion
- Continuing debate about whether threshold in U.S. has increased (e.g., at a minimum to $100,000 per QALY)
- Not clear that thresholds derived for point estimate of cost-effectiveness ratio should be used to determine theshold for upper limit of confidence interval for CE ratio

What Is Maximum Acceptable Ratio?

- US Gov't
  - EPA: 9.1 M / life (~222K / undiscounted YOLS)
  - FDA: 7.9 M / life (~176K / undiscounted YOLS)
  - DOT: 6 M / life (~133K / undiscounted YOLS)
- Australia: $AU 42K - 76K /YOLS
- Italy: €60,000/QALY
- Netherlands: €80 000/QALY
- Sweden: SEK 500,000 (€54,000) / QALY
- UK: £20 - 30K / QALY
- WHO report: 3 times GDP per DALY

Are All Ratios of Equal Value?

- Mortal, relatively incurable diseases vs. diseases that principally affect quality of life
  - Are acceptable ratios for former higher than for latter?
    - NICE, appraisal committees can consider 'giving greater weight to QALYs achieved in later stages of terminal diseases'" (Nature, 09/2009)
  - As more treatments become available and disease appears less incurable, does acceptable incremental ratio for new therapies begin to approach "standard" acceptable ratio?
- Small budgetary impact

Are All Ratios of Equal Value? (II)

- Identifiable individuals
- Do individuals have a set of "social preferences" that differ from their "individual preferences"
  - $1,000,000 to cure 100 blind invalids
  - $1,000,000 to cure 100 blind healthy individuals
- Compensation for risks imposed by society

Acceptability and Lower Left Quadrant?

- Economists usually treat ratios in upper right and lower left quadrants symmetrically
  - If won't spend more than $50,000 per QALY saved for a more costly and more effective new therapy in upper right quadrant, then won't spend more than $50,000 per death averted for more costly, more effective alternative therapy in lower left quadrant
  - i.e., adopt a less costly and less effective new therapy if its ratios of savings per QALY lost were greater than $50,000 compared with alternative

Acceptability and Lower Left Quadrant? (II)

- Some have suggested that preferences for gains and losses of health are asymmetric
  - Common assumption: people need to be paid more to give up health than they are willing to pay to gain health (possibly an income effect)
- Such asymmetries can be incorporated into decision making for individual therapies, but complicates NMB calculation, construction of acceptability curves, and league-table decision making

Negative Cost-Effectiveness Ratios

- If point estimates for differences in costs and effects are of opposite signs (either increased costs and decreased effectiveness or decreased costs and increased effectiveness), resulting cost-effectiveness ratio will be negative
- Magnitude of negative point estimates for ratios in same quadrant does not provide information about relative preferability of these different therapies

Negative Ratios (II)

- When comparing two options and resulting cost-effectiveness ratio (or CI of ratio) is negative, do not report negative value (because magnitude conveys little if any information)
  - Instead simply report that ratio represents that therapy is dominant/dominated
- If lower and upper limits of confidence interval (CI) for CE ratio are both negative, relative magnitude of two limits provides information about whether or not CI includes Y axis of CE plane (return to this idea when we discuss sampling uncertainty for CERs)

Take Home Messages (I)

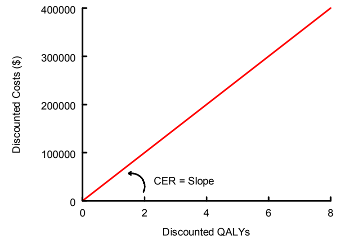
- Decision making using cost-effectiveness ratios requires attention to average and incremental cost-effectiveness ratios
- To make decisions using these ratios, they must be compared to:
  - Other accepted and rejected interventions (e.g., against league tables), or
  - A predefined standard (i.e., an acceptability criterion) against which they can be compared (e.g., $50,000 per year of life saved might be considered largest acceptable ratio), or
  - (Rarely or never:) Utility curves trading off health and cost

Take Home Messages (II)

- Use of a predefined standard (e.g., $50,000 per year of life saved) equates decision making using cost-effectiveness ratios and decision making using net monetary benefits
- Do not report magnitude of negative point estimates of cost-effectiveness ratios

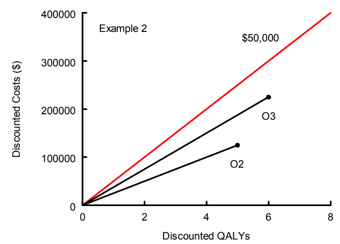
APPENDIX
Alternative Method

Introduction to Method 3: Frontier Analysis (Geometry of Choice)



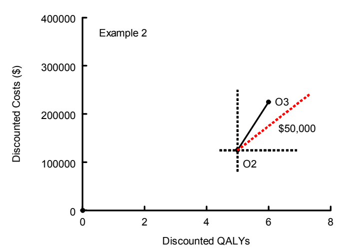
- Can also identify optimal strategy using cost-effectiveness plane
- Often focus on upper right quadrant, where new therapies increase both costs and outcomes

Choosing Among Frontier Options (1)



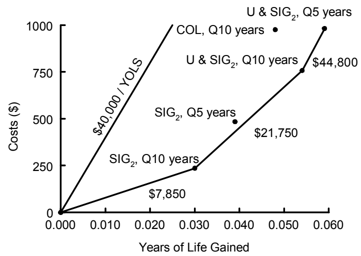
- Options 2 and 3 both have acceptable average cost-effectiveness ratios (e.g., below $50,000/YOLS)

Choosing Among Frontier Options (2)



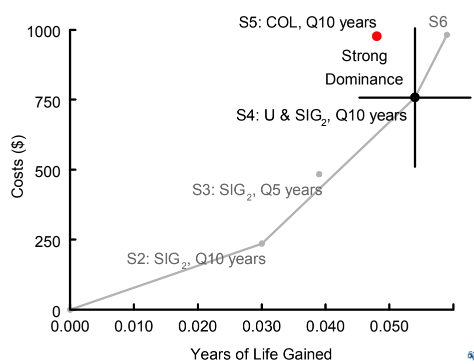
- To evaluate incremental ratio, shift origin to option with lowest acceptable average cost- effectiveness ratio, and reimpose $50,000 acceptability criterion

Colorectal Cancer Screening Example

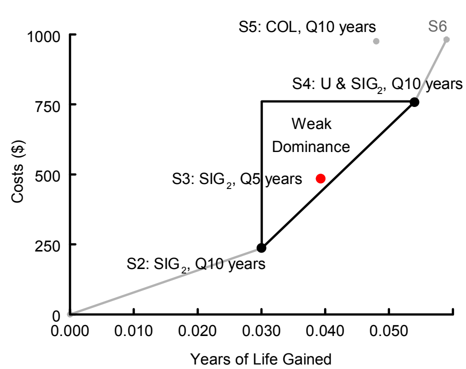


- The convex hull represents therapies that for a given level of effect have lowest cost (or for a given level of cost have highest effect)

Strong Dominance



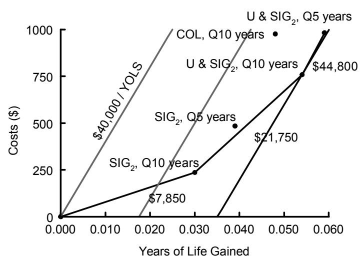
Weak Dominance



Sig_2,q5 and Frontier

- Weakly dominated, but
  - Uncertainty (i.e., confidence region) might be such that we may not be able to exclude it from frontier
  - Weakly dominated therapies that lie close to frontier, "might be considered [a] reasonable alternative...if there were noneconomic reasons to prefer them, such as patient or physician acceptability, availability, or other factors." Mark D. JAMA. 287;202:2428-9.

Method 3. Choice Using a Predefined Maximum Acceptable C-E Ratio



- As with ROC curve, choose therapy with tangency between frontier and lowest line with slope defined by maximum willingness to pay for health outcome

Method 2 Recommendations

Maximum WTP	Therapy
<7867	S1
7867 to 21,749	S2
21750 to 44,799	S4
44,800+	S6

NMB and Multitherapy Example

- Returning to previous multitherapy example: suppose 6 therapies have following discounted costs and life expectancies

Treatment	Cost	YOLS
No screening (S1)	1052	17.348
Sig Q10 (S2)	1288	17.378
Sig Q5 (S3)	1536	17.387
C Q(10) (S5)	2028	17.396
U+Sig, Q10 (S4)	1810	17.402
U+Sig, Q5 (S6)	2034	17.407

- Which therapy should be adopted if acceptability criterion is $40,000 / YOL Saved? $50,000?

Numeric INMB Selection Method

- Can follow a modified version of method 1 to calculate incremental NMB (INMB)
- Modifications include:
  - In step 3, calculate INMB rather than cost-effectiveness ratios
  - Proceed to selection algorithm (after next slide) if:
    - All INMB are positive, OR
    - All INMB are negative, OR
    - First N_i therapies have positive INMB and remaining N_j therapies have negative INMB

Numeric INMB Selection Method (2)

- For some values of WTP it is impossible to identify weak dominance from pattern of resulting INMB estimates
  - e.g., all can be positive or all can be negative
- When identification is possible, we observe a therapy with a negative INMB followed by a therapy with a positive INMB
- As with the CE algorithm, in that case:
  - Step 4: Remove first therapy with a negative INMB (weakly dominated) and recalculate INMB
  - Repeat until there are no therapies with negative INMB interspersed among positives
  - Proceed to selection algorithm

INMB Selection Algorithm

- If all INMB are negative, select reference therapy
- If first N_i therapies have positive INMB and remaining N_j therapies have negative INMB choose therapy with greatest effectiveness among those therapies with positive INMB
- If all INMB are positive, select therapy with largest effectiveness

Efficient Algorithm: Step 3

- Calculate $INMB_{20000}$

Treatment	Cost	YOLS	INMB
No screening (S1)	1052	17.348	--
Sig Q10 (S2)	1288	17.378	364
Sig Q5 (S3)	1536	17.387	-68
~~C Q(10) (S5)~~	~~2028~~	~~17.396~~	~~SD~~
U+Sig, Q10 (S4)	1810	17.402	28
U+Sig, Q5 (S6)	2034	17.407	-124

Efficient Algorithm: Steps 4 and 5

- Recalculate $INMB_{20000}$ (e.g., between options 2 and 4)
  - Repeat steps 4 and 5 if necessary)

Treatment	Cost	YOLS	INMB
No screening (S1)	1052	17.348	--
Sig Q10 (S2)	1288	17.378	***364***
~~Sig Q5 (S3)~~	~~1536~~	~~17.387~~	~~WD~~
~~C Q(10) (S5)~~	~~2028~~	~~17.396~~	~~SD~~
U+Sig, Q10 (S4)	1810	17.402	-42
U+Sig, Q5 (S6)	2034	17.407	-124

- Based on selection algorithm, select S2

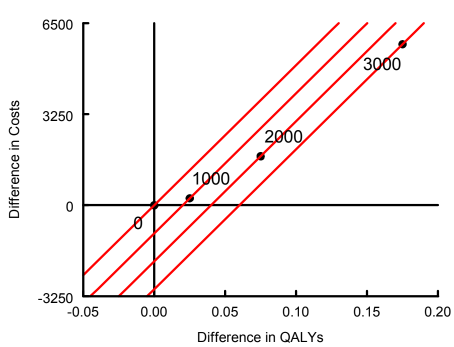
Calculate $INMB_{40,000}$

Treatment	Cost	YOLS	INMB	INMB
No screening (S1)	1052	17.348	--	--
Sig Q10 (S2)	1288	17.378	964	964
Sig Q5 (S3)	1536	17.387	112	~~WD~~
~~C Q(10) (S5)~~	~~2028~~	~~17.396~~	~~SD~~	~~SD~~
U+Sig, Q10 (S4)	1810	17.402	***326***	***438***
U+Sig, Q5 (S6)	2034	17.407	-24	-24

Calculate $INMB_{50,000}$

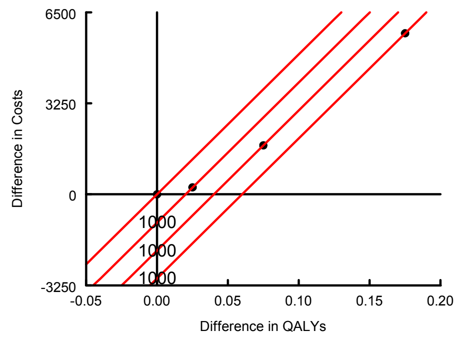
Treatment	Cost	YOLS	INMB	INMB
No screening (S1)	1052	17.348	--	--
Sig Q10 (S2)	1288	17.378	1264	1264
Sig Q5 (S3)	1536	17.387	202	~~WD~~
~~C Q(10) (S5)~~	~~2028~~	~~17.396~~	~~SD~~	~~SD~~
U+Sig, Q10 (S4)	1810	17.402	426	678
U+Sig, Q5 (S6)	2034	17.407	***26***	***26***

Averge NMB



ICERs = 10,000, 30000, and 40,000

Incremental NMB



Unlike ICERs, Monotonicity Not Required for INMB