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Cost-Effectiveness Analysis: Applications to TB

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Protecting Health, Saving Lives—*Millions at a Time*

A Question to Consider

- Current standard for TB therapy:
  - 2 mos of isoniazid (H), rifampin (R), pyrazinamide (Z), ethambutol (E)
  - 4 mos of HR
- New regimen being developed:
  - 2 mos of HRZ + Moxifloxacin
  - 2 mos of HR + Mox
  - Probably equal in efficacy
- The new regimen is likely to be more expensive (Mox = $5, E = $0.03), but also more effective
  - Fewer defaults, more cures = fewer TB deaths
  - Will also save some health-system costs for TB treatment
- What regimen should be recommended?

How do We Answer this Question?

- Add up **costs** for each regimen
  - Drug costs
  - Health provider costs
  - Patient costs?
- Add up **effectiveness** for each regimen
  - How should we measure effectiveness?
    - Number of TB treatments completed
    - Number of lives saved
    - Something that could be compared to other health interventions (e.g., utility)
- Measure **cost-effectiveness**

Costs

- Economists measure costs as opportunity (economic) costs.
  - Lost benefit of a resource if used for best alternative use
    - Compared with financial cost = what is actually paid
  - Often not the actual price paid
    - Donated goods
    - Volunteer time
    - Distorted prices (price you pay isn't what something is worth)
- Must also consider the perspective of the costs.
  - For example, the time required for transport to the treatment facility might matter to the patient, but not the health system.
  - "Societal" perspective (including costs to everyone) theoretically preferred but often less practically useful.

Costing Exercise

- What is the cost, from a societal perspective, of 1 visit to TB clinic for medications?
  - Bus fare: $10 each way
  - Visit is free to the patient, but provider makes $40/hr
  - Patient's children stay with family member
  - Clinic visit takes 15 minutes
  - Round-trip bus transport takes 1 hour, 45 minutes
  - Walking round-trip takes all day (7 hrs, 45 minutes)
  - If the patient and family member were working, each could make $5/hr
  - Assume these are all the costs involved

Costing Exercise

- Walking to clinic: Patient pays nothing, but opportunity cost is:
  - $5/hr * 2 people * 8 hrs = $80 for lost wages
  - $40/hr * 15 mins = $10 for the provider (since provider could see someone else)
- Bus ride: Better alternative
  - $5/hr * 2 people * 2 hrs = $20 for lost wages
  - $20 for the bus
  - $10 for provider
- Opportunity cost: $50
  - *What is the cost from the clinic's perspective?*
  - *The patient's perspective?*

Costs: Other Considerations

- Inflation and discounting
  - Inflation: $20 bill will buy less next year than this year.
    - Important to specify the year of currency for any costs
  - Assume you know that $20 this year will be worth the same as $21 next year (5% inflation rate).
    - Which would you rather have: $20 in your hand, or the promise of $21 next year?
    - How much in next year's money is $21 today worth to you?
- Capital vs. recurrent costs
  - Must pay "up front" for some items (equipment, buildings)
  - These items will last a certain amount of time
  - Paying $100,000 for a machine today that will last 5 years is not the same as paying $20,000 every year
    - Because of inflation and discounting

Exercise: Inflation & Discounting

- Assume 5% inflation and 3% discount rate.
- What is the present value of a contract where you agree to pay $20,000/year for 5 years?
- First, inflation: how much is this in undiscounted 2012 US$?

Year	2012	2013	2014	2015	2016	Total
Inflated Equivalent	$20,000	$21,000	$22,050	$23,152	$24,310	
You Pay:	$20,000	$20,000	$20,000	$20,000	$20,000	$100,000
In 2012 US$:	$20,000	$19,048	$18,141	$17,013	$16,454	$90,656

Exercise: Inflation & Discounting

- Assume 5% inflation and 3% discount rate.
- What is the present value of a contract where you agree to pay $20,000/year for 5 years?
- Next, discounting: future US$ worth less than present.

Year	2012	2013	2014	2015	2016	Total
You Pay (in 2012 US$):	$20,000	$19,048	$18,141	$17,013	$16,454	$90,656
Discount Factor:	1	$1/(1.03)^1$	$1/(1.03)^2$	$1/(1.03)^3$	$1/(1.03)^4$	
After Discount:	$20,000	$18,493	$17,100	$15,569	$14,619	**$85,781**

Exercise: Inflation & Discounting

- After inflation and discounting, paying $85,781 “up front” is the same as paying $20,000 every year for 5 years.
  - All capital costs (machines, equipment, etc.) need to consider this type of calculation.

Costs: Other Considerations

- Fixed vs. variable costs
  - Cost per pill of moxifloxacin:
    - Machinery used to make the pills – costs the same amount no matter how many pills are made
    - Raw materials – cost depends entirely on how many pills are made
    - Staff used to run the machinery – cost depends partially on how many pills are made
  - In general, must calculate unit costs:

    (variable cost) + (fixed cost/number of units)

Costs: Other Considerations

- Currency conversion
  - 1 US$ might officially exchange for R$2
  - But 1 US$ will buy more in the US than R$2 in Brazil
    - Real is overvalued on currency markets
    - The “Big Mac index”:
      - Price of a Big Mac reflects inputs from agriculture, advertising, labor, etc.
      - How much does a Big Mac cost?

Costs: Other Considerations

- Currency conversion
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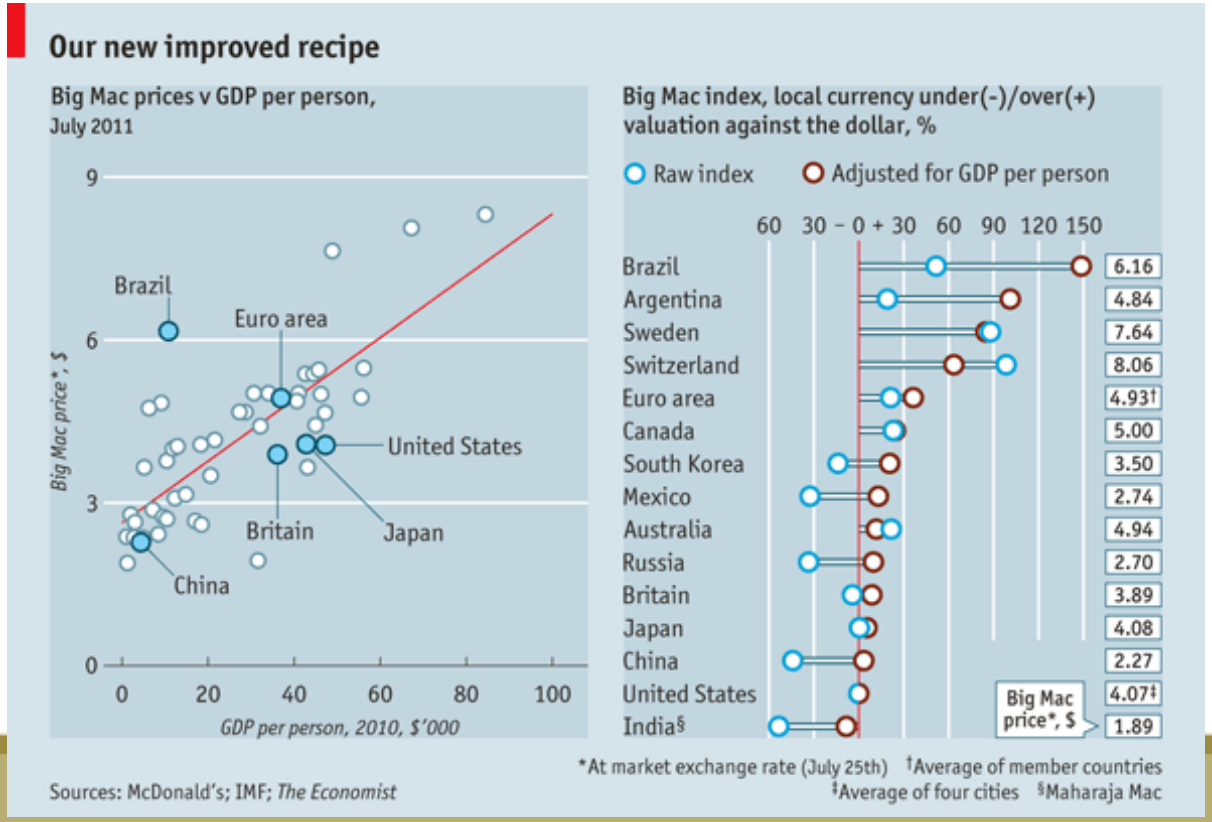

Costs: Other Considerations

- Currency conversion
  - 1 US$ might officially exchange for R$2
  - But 1 US$ will buy more in the US than R$2 in Brazil
  - Some costs depend on local “purchasing power”
    - Brazilian staff are paid in Reais, not US$
    - Minimum wage: US $7.25/hr, Brazil R$622/mo, Mozambique 2300 Mt/mo
    - If I have US$1,000, I get 140 hrs (<1mo) in USA, 3 mos in Brazil, 1 yr in Mozam.
    - But…if I have US$12, I get 3 Big Macs in USA, only 2 in Brazil
  - Other costs depend on exchange rate
    - Moxifloxacin is bought on the international market, in US$
    - If I take 1 US$ and exchange it for R$, I get the same amount of moxifloxacin (and have to pay the money changers)
  - Important to specify the currency used, and how it is converted
    - “International $” = based on purchasing power parity
    - “US$” = based on exchange rates

Costing in Practice…

	A	B	C	D	E	F	G	H	I	J	K	L	M	N
70		**RECURRENT COSTS**												
71	**1)**	**PERSONNEL COSTS**								Base Year GDP Deflator:	0			
72	Sr No.	Type of personnel	Contributors	FTE (full time equivalent)	% time allocation to the intervention	Gross salary		Benefits/allowances		Total salary		Year of cost	GDP Deflator	GDP adjustment
73						Financial	Economic	Financial	Economic	Financial	Economic			factor
74				(a)	(b)	(c)	(d)	(e)	(f)	(g)=a*b*[c+e]	(h)=a*b*[d+f]		(i)	(j)=BYF/(i)
75	1									0.00	0.00		0.00	1.00
76	Total personnel costs													
77	**2)**	**NON-MEDICAL MATERIALS & SUPPLIES**						Base Year GDP Deflator:		0				
78	No	Materials & supplies	Contributors	Quantity	% allocation to the intervention	Unit cost per item		Year of cost	GDP Deflator	GDP adjustment factor	Total cost		(%) allocation and estimated cost per s	
79						Financial	Economic				Financial	Economic		0
80				(a)	(b)	(c)	(d)	(e)	(f)	(g)=BYF/(f)	(h)=a*c*g*b	(h)=a*d*g*b	% allocation	Financial cost
81	1								0.00	1.00	0.00	0.00		0.00
82	**4)**	**MEDICAL SUPPLIES**												
83	No.	Medical supply	Contributors	Quantity	% allocation to the intervention	Unit cost per item		Year of cost	GDP Deflator	GDP adj. factor	Total cost		(%) allocation and estimated cost per s	
84						Financial	Economic				Financial	Economic		#REF!
85				(a)	(b)	(c)	(d)	(e)	(f)	(g)=BYF/(f)	(h)=a*b*c*g	(i)=a*b*d*g	% allocation	Financial cost
86	1								0.00	1.00	0.00	0.00		0.00
87	**5)**	**LABORATORY SUPPLIES**												
88	No.	Supplies	Contributors	Quantity	% allocation to the intervention	Unit cost		Year of cost	GDP Deflator	GDP adj. factor	Total cost		(%) allocation and estimated cost per s	
89						Financial	Economic				Financial	Economic		#REF!
90				(a)	(b)	(c)	(d)	(e)	(f)	(g)=BYF/(f)	(h)=a*b*c*g	(i)=a*b*d*g	% allocation	Financial cost
91	1								0.00	1.00	0.00	0.00		0.00
92	Total laboratory supplies cost:										**0.00**	**0.00**		**0.00**
93	**6)**	**TRANSPORT OPERATING COSTS**												
94	i)	Transport running cost												
95	Sr. No.	Vehicle	Contributors	Km. Covered **OR** Fuel used (lt)	% allocation to the intervention	Fuel cost per km **OR** per litre		Year of cost	GDP Deflator	GDP adj. factor	Total transport operating cost		(%) allocation and estimated cost per s	
96						Financial	Economic				Financial	Economic		#REF!
97				(a)	(b)	(c)	(d)	(e)	(f)	(g)=BYF/(f)	(h)=a*b*c*g	(i)=a*b*d*g	% allocation	Financial cost
98	1								0.00	1.00	0.00	0.00		0.00
99	Sub-total:										0.00	0.00		0.00
100	ii)	Other transport costs												
101	Sr. No.	Items e.g. vehicle rental or public transport costs (train, plane, taxi etc)	Contributors	Number	% allocation to the intervention	Rent **OR** charge per unit of duration (months)		Duration of use if rented	Transportation cost		Year of cost	GDP Deflator	GDP adj. factor	Total tran
102						Financial	Economic		Financial	Economic				Financial
103				(a)	(b)	(c)	(d)	(e)	(f)=a*b*d*e	(g)=a*b*d*e	(h)	(i)	(J)=BYF/(i)	(K)=(f)*(J)
104	1								0.00	0.00		0.00	1.00	0.00
105	Sub-total:													0.00

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Ready

Cost: Summary/Return to Example

- To compare new vs. old TB regimens, need unit costs for:
  - Drugs
  - Health center visits
  - Other items (side effects?)
- For each cost, must consider:
  - Opportunity (not financial) costs
  - Perspective (patient vs. health system vs. society)
  - Inflation & discounting
  - Annualization of capital costs
  - Dividing fixed costs by number of units
  - Conversion to single currency (including currency year)
- Combine these costs to estimate the cost of each alternative.

Simplified Example: Cost of New TB Regimen

- Step 1: Select perspective
  - Health system
- Step 2: Select timeframe of analysis
  - Through completion of therapy
- Step 3: Measure (opportunity) costs
- Step 4: Convert to common currency
  - Inflate to common year, convert with PPP vs. exchange rate
  - Will use US$ in this example
- Step 5: Annualize capital costs
- Step 6: Calculate unit costs

Step 3: Measure Opportunity Costs

- Assume the following opportunity costs from the health system perspective:
  - $7/day for medications of the new regimen
  - $3/day for medications of the old regimen
  - Monthly doctor visit: R$20
  - Daily (5x/wk) DOT visit: R$2
  - Shelves cost R$200, last 1 year, no matter how many patients seen
    - 100 patients per year
  - Current TB program takes up 10% of the space of a health clinic, which costs R$200,000 to build and lasts 5 years.
  - R$2 = US$1 (currency conversion, though actually higher)
  - R$3 = Int$1 (purchasing power parity conversion)

Step 4: Convert to Common Currency (2012 US$)

- Assume the following opportunity costs from the health system perspective:
  - $7/day for medications of the new regimen
  - $3/day for medications of the old regimen
  - Monthly doctor visit: $10
  - Daily (5x/wk) DOT visit: $1
  - Shelves cost $100, last 1 year, no matter how many patients seen
    - 100 patients per year
  - Current TB program takes up 10% of the space of a health clinic, which costs US$100,000 to build and lasts 5 years.
- If these were measured in different years, would also need to inflate.

Step 5: Annualize Capital Costs

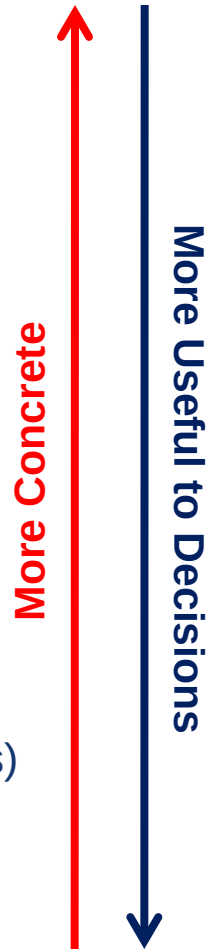
- Assume the following opportunity costs from the health system perspective:
  - $7/day for medications of the new regimen
  - $3/day for medications of the old regimen
  - Monthly doctor visit: $10
  - Daily (5x/wk) DOT visit: $1
  - Shelves cost $100, last 1 year, no matter how many patients seen
    - 100 patients per year
  - Current TB program takes up 10% of the space of a health clinic, which costs US$100,000 to build and lasts 5 years.
    - Annualized cost (5% discounting) = $2310/yr (*10% = $231)

Step 6: Calculate Unit Costs (Cost per Patient-Month)

	Old Regimen	New Regimen
Medications	$3/day * 30 days = $90	$7/day * 30 days = $210
Doctor visit	$10	$10
DOT visits	$1 * 22 weekdays = $22	$1 * 22 weekdays = $22
Shelves	$100/(600 patient-months per year) = $0.17	$100/(400 patient-months/year) = $0.25
Clinic space	$231/600 = $0.35	$231/400 * (2/3) = $0.35
Total	**US$122.52 (year 2012)**	**US$242.60 (year 2012)**

From Costs to Effectiveness

- Types of analysis:
  - Cost
    - Just add up the costs of each alternative
  - Cost-minimization
    - What is the alternative that minimizes costs?
  - Cost-consequence
    - Add up costs, but also add up consequences/effectiveness
  - Cost-effectiveness
    - Describe outcome as “cost per unit effectiveness”
  - Cost-utility
    - Effectiveness described explicitly in “utility” measures (e.g., QALYs/DALYs)
  - Cost-benefit
    - Effectiveness converted back into monetary terms



Back to the Example: TB Treatment Regimens

- 6 mos of standard therapy costs $122.52 * 6 = $735.12
  - Treating 100 people costs $73,512
- What does society get in return for this investment?
  - Estimated in Malawi:
    - 73% cured/complete treatment
    - 5% die (start treatment too late)
    - 11% default/fail (among the worst in the Western Hemisphere)
    - 11% not evaluated
- If we assume that those who don't complete treatment take half their therapy, then cost of treating 100 people is:
  - ($735.12 * 72) + ($735.12/2 * 28) ~ $63,000

Now the New Regimen

- 4 mos of standard therapy costs $242.60 * 4 = $970.40
  - Treating 100 people costs $97,040
- What does society get in return for this investment?
  - Assume that 1/3 of the defaulters no longer default:
    - 80% cured/complete treatment
    - 5% die (start treatment too late)
    - 15% default/fail/transfer
- If we assume that those who don't complete treatment take half their therapy, then cost of treating 100 people is:
  - ($970.40 * 80) + ($970.40/2 * 20) ~ $87,000

Cost and Cost-Minimization Analyses

- Cost analysis:
  - "Treating 100 people with the old regimen costs $63,000, and treating 100 people with the new regimen costs $87,000."
- Cost-minimization analysis:
  - "The old regimen minimizes costs, relative to the new regimen."
- These analyses provide very concrete data, but are not useful to decision-makers, unless the cheaper alternative is also equally or more effective.
  - Here, the new regimen is more expensive, but also more effective!

Cost-Consequence Analysis

	Old Regimen	New Regimen
Cost (per 100 people)	$63,000	$87,000
Consequences (per 100)		
Deaths	5	5
Successful Treatments	73	80
Failures	22	15

- Report costs and (measurable) consequences, nothing more.
- Let decision-makers draw their own conclusions.
  - “Is it worth it for me to spend the extra money to achieve the better outcomes?”
- Advantage: Fewer assumptions
- Disadvantage: Less useful for decision-making

Cost-Effectiveness Analysis

- Convert (measurable) **consequences** into (modeled) **effectiveness** measures.
  - What are decision-makers interested in?
- For example:
  - Deaths averted:
    - Assume that 25% of failures/defaults eventually die.
  - Years of life lost:
    - Assume that each person who dies would have a life expectancy of 30 years (approximately the average L.E. in Brazil at the average age of TB cases)
  - Secondary TB cases averted:
    - Assume that each failure/default goes on to generate 1 secondary case.
    - Each secondary case has perhaps a 1 in 20 chance of death

The ICER:
Incremental Cost-Effectiveness Ratio

$$\frac{C_{new} - C_{old}}{E_{new} - E_{old}}$$

How much does it COST to switch from the old to the new regimen?

How much MORE EFFECTIVE is it to switch from the old to the new regimen?

ICER Example

- Old regimen:
  - Costs $63,000
  - 5 deaths + 22 failures = 10.5 expected deaths
  - 22 secondary TB cases = 1.1 expected deaths
- New regimen:
  - Costs $87,000
  - 5 deaths + 15 failures = 8.75 expected deaths
  - 15 secondary TB cases = 0.75 expected deaths

$$\frac{\$87{,}000 - \$63{,}000}{9.5 - 11.5} = \frac{\$24{,}000}{-2}$$

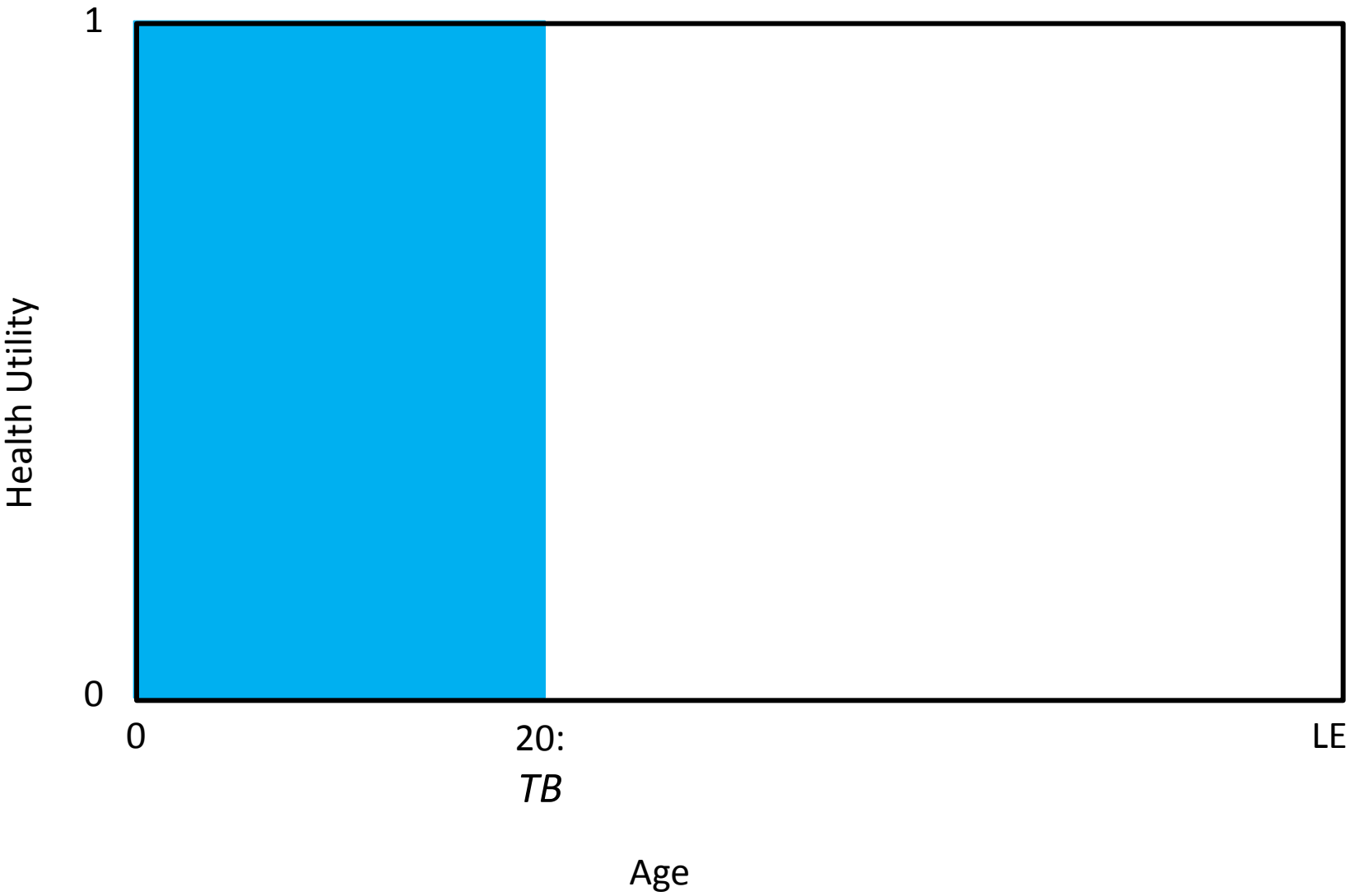
- $12,000 per death averted

Health Utility

- Specific type of effectiveness measure
- "Adjusted" years of life, where:
  - 1 = Life lived in perfect health
  - 0 = Death
- Ways to measure health utility:
  - Standard Gamble
    - "I will offer you a bet. If you win the bet, you live the rest of your life in perfect health, instead of your current health state. If you lose, you die instantly. Would you take this bet if your risk of dying was 1 in 100? 1 in 20? 1 in 10?"
  - Time-Tradeoff
    - "If you have 100 years left to live in your current health state and could trade those years for a smaller number of years in perfect health, would you trade them for 99 years? 95 years? 90 years?"
  - Visual Analogue Scale
    - "Using this 'thermometer,' rate your current quality of life from 0 to 100."

Utility Measures: DALYs & QALYs

- DALY = “Disability-Adjusted Life Year”
  - “Disability weights” (1 – utility) assigned using standard scenarios
  - Do not change from one setting to another
  - Age & sex can be incorporated, also discounting, but nothing else
  - Standardized formula available
  - Calculate as years of life lost (YLL) + years of life with disability (YLD)
  - DALYs are bad = want to avert them
- QALY = “Quality-Adjusted Life Year”
  - More of a “pure” utility measure
  - Ask people in your cohort (or people like them) to answer traditional utility questions for each health state
  - Each year in that health state is weighted by this value
  - Takes into account all external factors that weigh into decisions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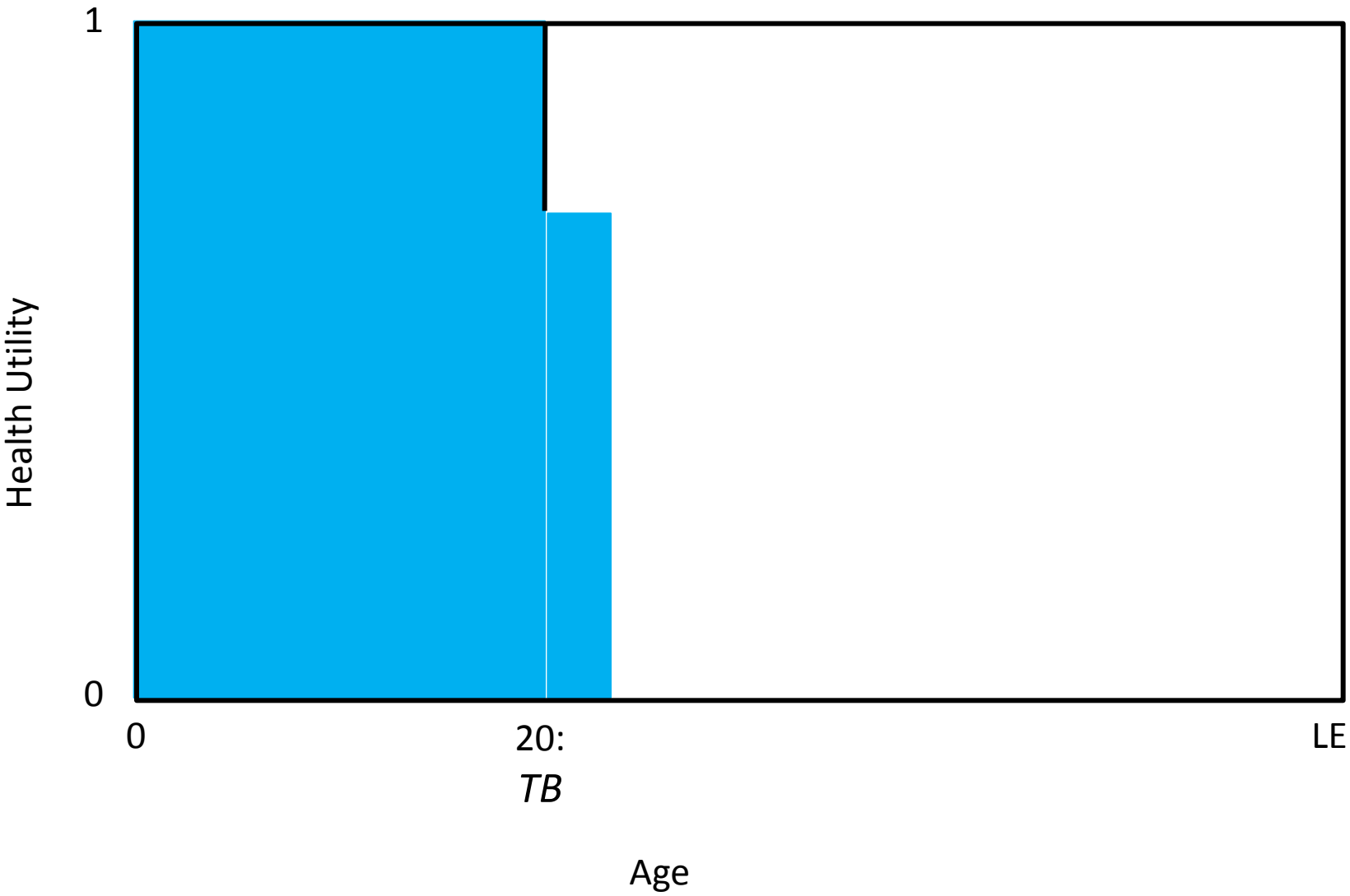
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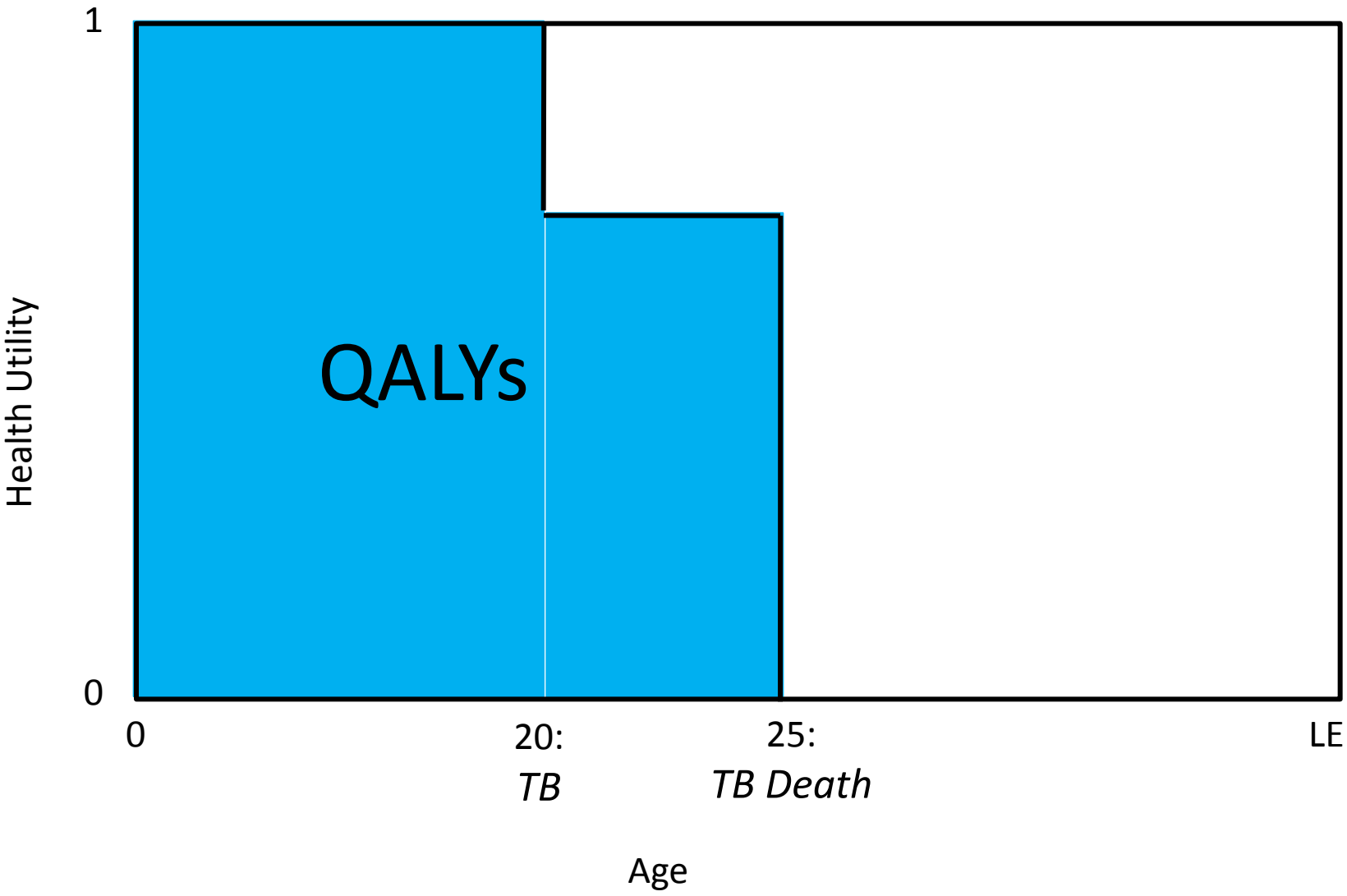
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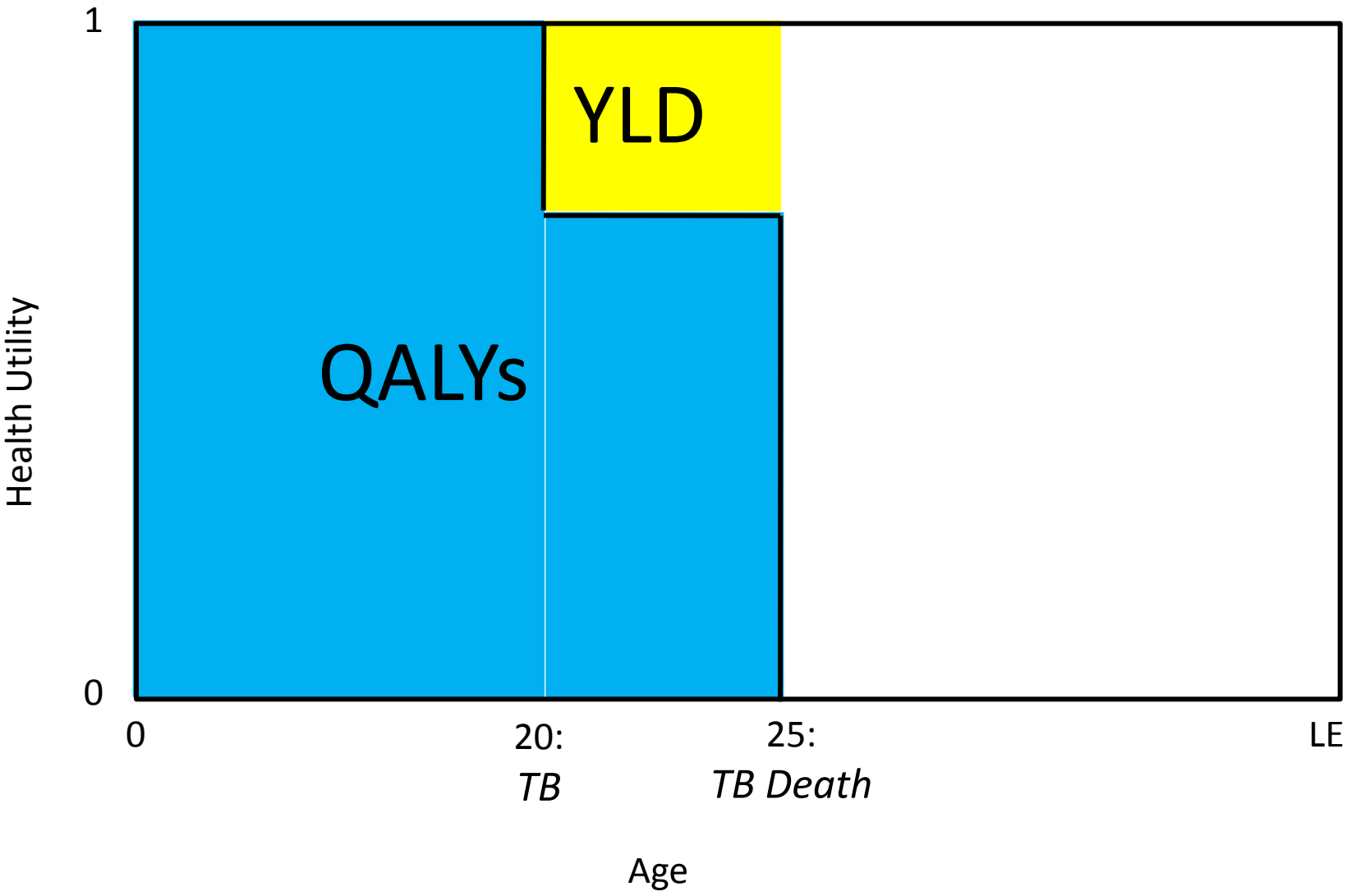
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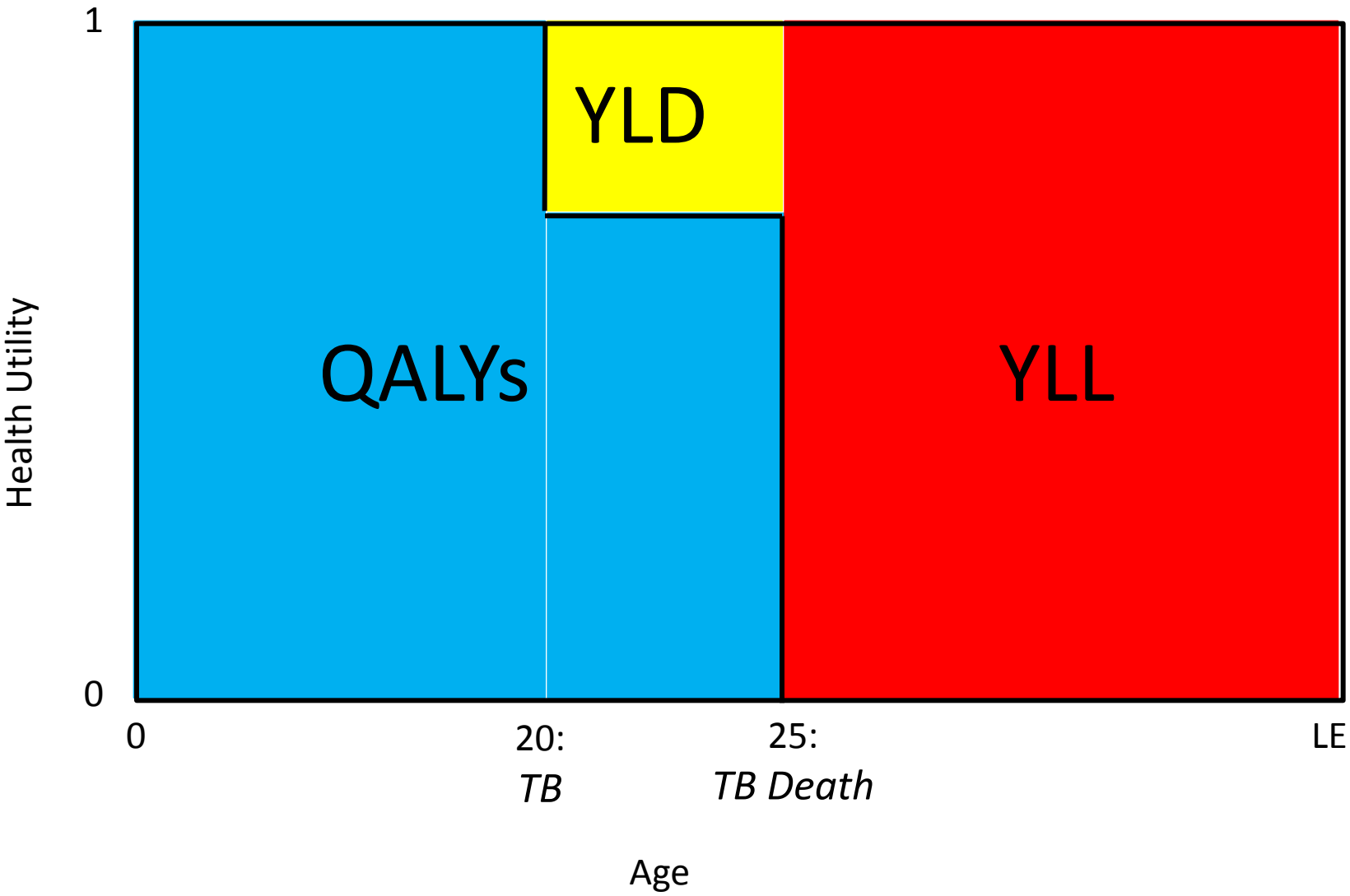
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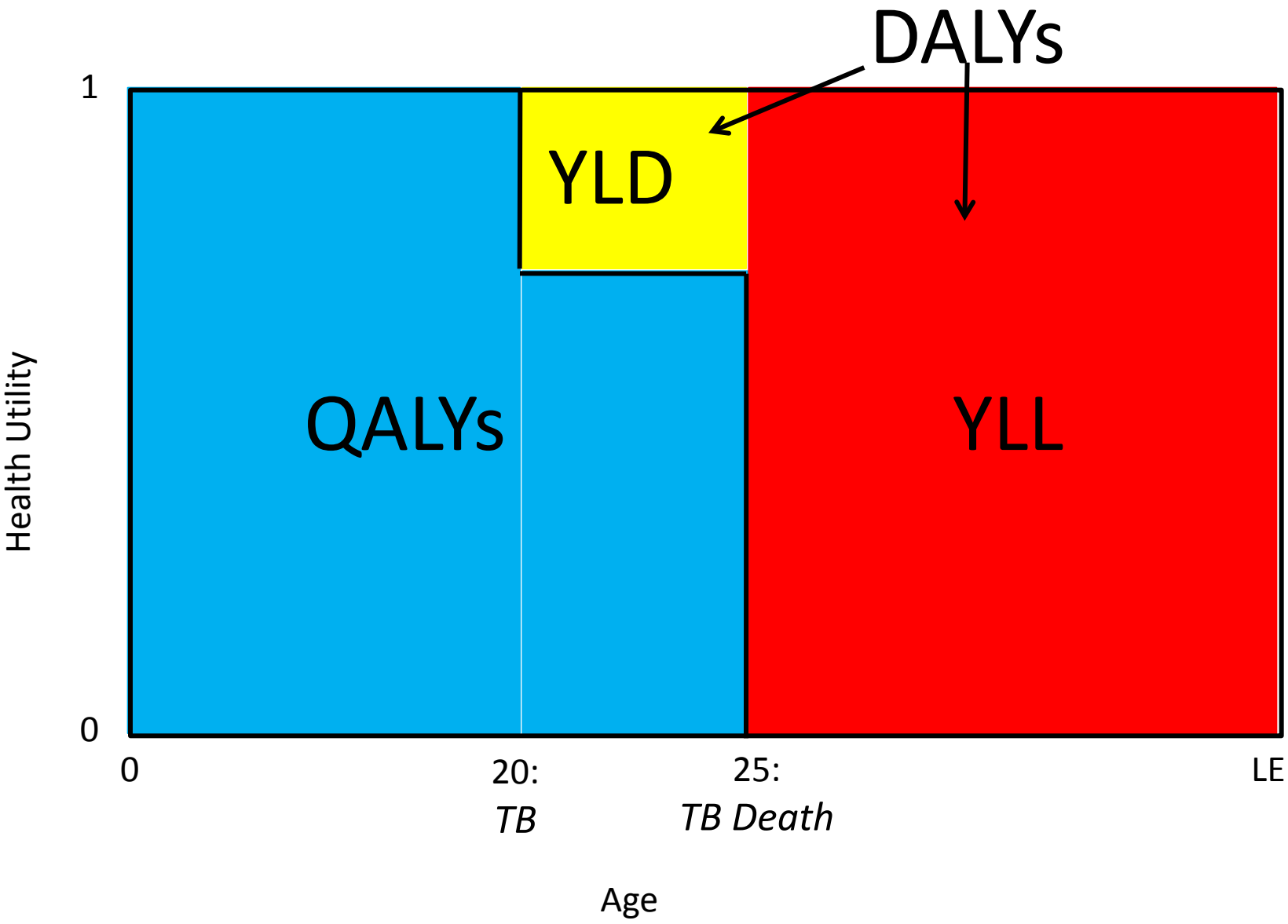
DALYs
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TB Death
LE
Age

Example: TB & HIV

- Standard disability weights:
  - TB: 0.264 (~0.25)
  - HIV with ART access: 0.236 (TB/HIV not reported)
- Assume the following:
  - Successfully Treated TB: 0.125 DALYs (YLD: 6 months * 0.25)
  - Default but Eventually Cure: 0.5 DALYs (YLD: 2 years * 0.25)
  - Die: 25.5 DALYs (YLD: 2 years * 0.25, YLL: 25)

Cost-Utility Analysis

	Old Regimen	New Regimen
Cost (per 100 people)	$63,000	$87,000
Utility (per 100)		
Deaths	5 * 25.5 = 127.5 DALYs	5 * 25.5 = 127.5 DALYs
Successful Treatments	73 * 0.125 = 9 DALYs	80 * 0.125 = 10 DALYs
Failures: Survive	22 * 0.75 * 0.5 = 8.25 DALYs	15 * 0.75 * 0.5 = 5.6 DALYs
Failures: Die	22 * 0.25 * 25.5 = 140.25 DALYs	15 * 0.25 * 25.5 = 95.6 DALYs
Total	**285 DALYs**	**238.7 DALYs**

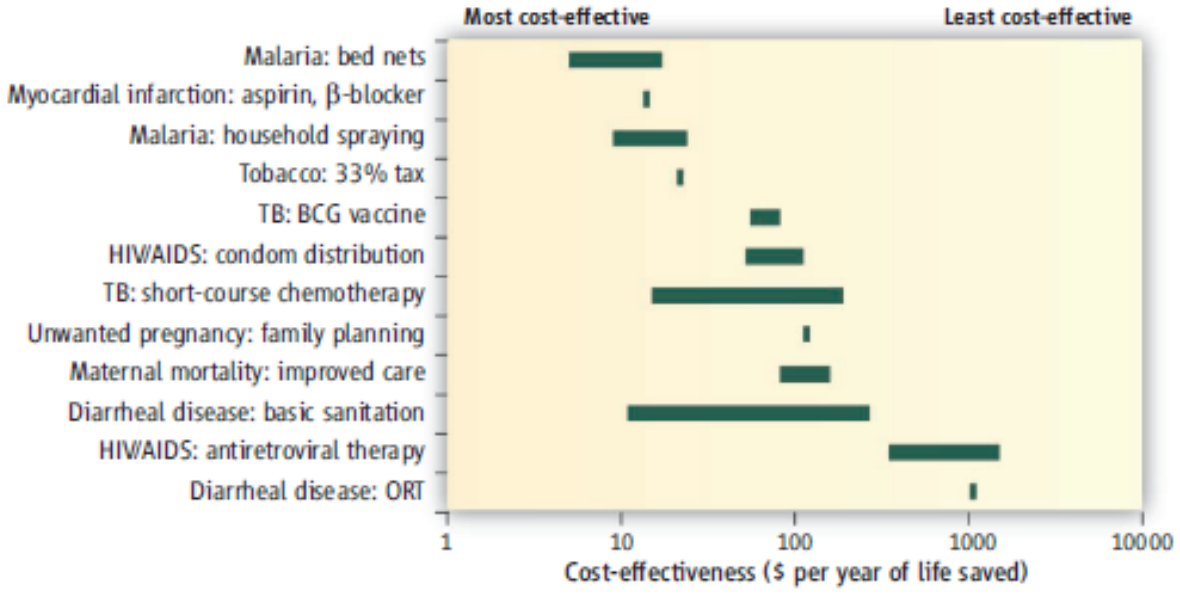
Cost-Utility Analysis: ICER

$$\frac{\$87{,}000 - \$63{,}000}{238.7 - 285} = \frac{\$24{,}000}{-46.3}$$

$518 per DALY averted

Why is utility more meaningful than deaths averted (or other effectiveness measures)?

- Cost-utility analyses have been done for many interventions.
  - Enables comparison against many other interventions
- Standard cost-effectiveness thresholds exist.
  - WHO: Cost per DALY/QALY < GDP per capita = “highly cost-effective”
  - Caveat: These thresholds are rarely applied.
    - We are generally willing to spend more to avert an AIDS DALY than a TB DALY.



Bongaarts & Over, Science 2010; 358:1359

So, Back to the Example

- New TB regimen: $518 per DALY averted
- Brazil's GDP: ~$11,000 per capita
  - Mozambique ~$1,000 (USA ~$48,000)
  - New regimen is better than the standard "highly cost-effective" threshold, in this simplified analysis.
  - However, may be more expensive than other TB interventions
    - "Cost-effective by standard thresholds" doesn't mean "should be done"

One Step Further: Cost-Benefit Analysis

- Convert effectiveness measures into monetary terms.
  - We often don't like to place a monetary value on health.
- For example, "1 DALY averted in Brazil = $11,000"
- Calculate the *incremental net monetary benefit (NMB)*:
  - (value of DALY averted)*($E_{new} - E_{old}$) – ($C_{new} - C_{old}$)
  - ($11,000)*(46.3) – ($24,000)
  - $509,000 – $24,000
  - $485,000
  - "At a valuation of $11,000 per DALY averted, using the new regimen in 100 patients will result in a gain of $485,000."
- Clearly states which intervention is preferred.
  - But hides that the "money" being saved is actually DALYs averted

Summary

- Costs
  - Opportunity (not financial) costs
  - Perspective (patient vs. health system vs. society)
  - Inflation & discounting
  - Annualization of capital costs
  - Dividing fixed costs by number of units
  - Conversion to single currency (including currency year)
- Effectiveness
  - Consequences -> Effectiveness -> Utility -> Benefit
  - Utility measures: QALYs/DALYs, preference elicitation methods
  - Conduct *incremental* analyses
  - Compare against global threshold or “next alternative”