Assessment of Economic Evaluations

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Outline

- Pay attention. This is an important class
- The textbook has useful guidelines to evaluate EE studies
- We'll cover the information you need to judge if a study has the right methodology and what's the decision making context of the study
- We're also going to talk about the recommendations by the Panel on Cost-Effectiveness in Health and Medicine
- **Disclaimer**: We're doing things backwards. You still don't have all the information you need to assess an EE. However, it does seem to work

1. Does the study have a well-defined and answerable research question?

- Well-defined questions are clear about the **alternatives** being compared and the **perspective** of the analysis
- I would add that including the **time horizon** would be even better
- Recall that the main objective of an EE is to provide information so we can choose among alternatives
- Examples of research questions:

  Not-so-useful: Is it worth it to provide free LARCs to low-income women?
  Better: Does the state of Colorado saves money by providing free LARCs to low-income women?
  Much better: Does the state of Colorado saves money by providing free LARCs to low-income women 5 years after the program implementation compared to usual care?

1. Does the study have a well-defined and answerable research question?

- Example from the (first) panel on cost-effectiveness:
- "The PHS recommendation includes three possible strategies for increasing folic acid consumption in women of reproductive age: 1) improvement of dietary habits, 2) fortification of the US food supply, and 3) use of dietary supplements. This analysis was conducted to evaluate the cost-effectiveness of food fortification and supplementation... A decision to pursue a program to reduce neural tubes defects will be made by policy makers in the interest of society as a whole. Thus, the analysis is conducted from a societal perspective." (Gold et al. 1996, page 314.)

1. Does the study have a well-defined and answerable research question?

- "This study aimed to assess the impact of preoperative breast MRI staging on the costs of care. A prospective registry study was conducted to examine the clinical impact of preoperative breast MRI staging. A similar cohort of patients who did not receive a preoperative breast MRI was assimilated, and a micro-costing analysis was conducted for both groups to compare the total cost of care." (Bedrosian et al 2015)
- This information could be in the abstract or the intro, but it **should be somewhere** and it **should be clear**
- As a reader, you don't want to be wondering why they didn't discuss alternatives, perspective, or time horizon

2. Is there a complete description of all the alternatives?

- We can't tell if all the costs and consequences of an alternative were considered if we don't understand how the interventions were implemented
- As your textbook puts it: Can you tell **who** did **what** to **whom**, **where**, and **how often**? And then what happened (outcome)?
  1. Readers need to judge applicability to their own setting
  2. Readers should be able to assess if all the costs and consequences are included
  3. Readers may want to replicate the intervention
- The most common **sin** is that many papers do not explain what is "usual care" or "standard treatment"

Department of Definitions aka Jargon Alert

- Useful research jargon
- **Internal validity**: Internal validity is the extent to which a study establishes a true cause-and-effect relationship between a treatment and an outcome
- We often think that a randomized intervention has a strong internal validity. Cause and effect has been establish
- **External validity**: Are the results of a study applicable to other settings?
- A lot of clinical trials have strong internal validity but poor external validity
- Example: clinical trials of antidepressants

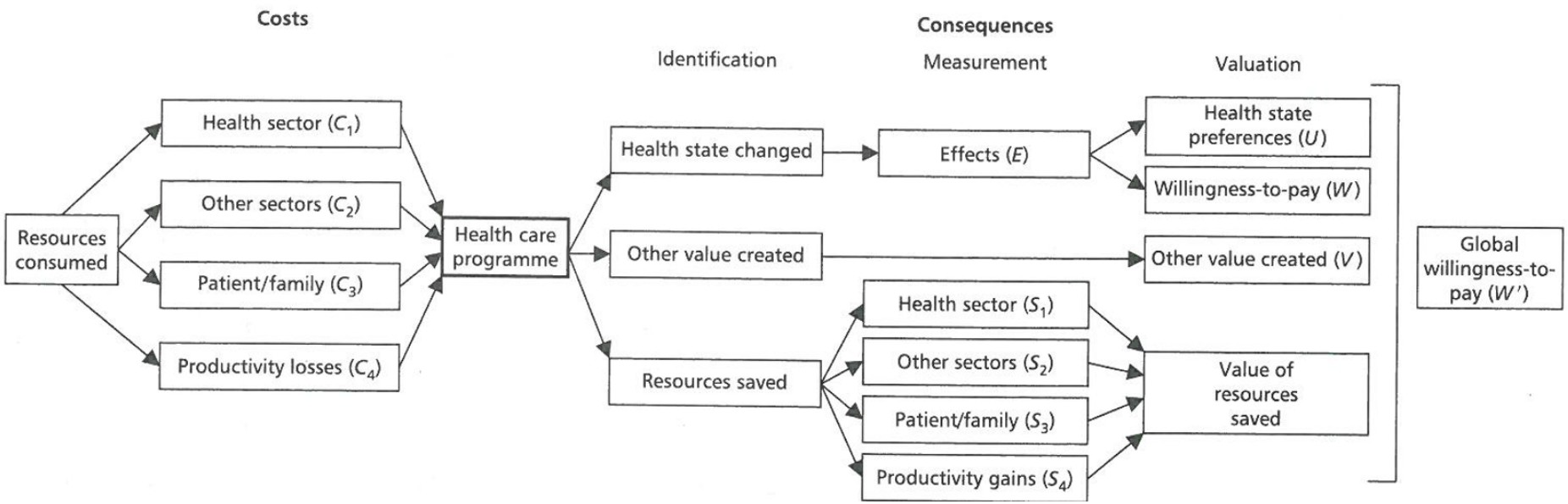
3. Was the effectiveness of the intervention established?

- This evidence usually comes from clinical trials, meta-analysis, or observational studies
- The usual caveats about meta-analysis are applicable here. **External validity** is a concern
  1. Publication bias
  2. Appropriate methodology to combine results
  3. Lack of **internal validity** of studies included
  4. Rare events/statistical problems
- A CEA study should be crystal clear about the source of effectiveness measures
- CEA studies often piggyback clinical trials. Sometimes, they don't and the the measure of effectiveness is very murky and problematic

4. Were all the important and relevant costs and consequences identified?

- This is a very important component of an EE
- BUT... it's hard to judge this guideline without knowledge of the subject
- The **perspective** and the **time horizon** guide these decisions

Costs and consequences



4. Were all the important and relevant costs and consequences identified?

- Examples
  - In the free-LARCs program, we should take into account that there is infrastructure needed to carry out the program
  - Same with the example of large-scale screening for celiac and diabetes
  - Cost of testing in the celiac and diabetes example
  - In the tobacco cessation study, we need to consider the training of providers, the cost of updating the electronic medical records systems for referrals... But, how do we attribute the share of costs to the tobacco cessation program and not to ther programs?
- In EEs, **we need to think about all these details and decide** which costs and consequences to include

4. Were all the important and relevant costs and consequences **identified**?

- This can get complicated fast and you can go a bit crazy thinking about all the cost and consequences
- Life becomes a lot easier when you remember some principles:
  1. EE involves the comparison of alternatives. If cost and consequences are the **same between alternatives**, you don't have to worry about them
  2. Some costs are **so small that they won't make a difference** either way
  3. The **perspective** and **time horizon** will rule things out
- In a good paper, the authors do a good job justifying these decisions
- Go back to previous slide and see what could be ignored

4. Were all the important and relevant costs and consequences **identified**?

- There has been so much confusion in practice that the new recommendations from the Panel on CEA is to include an **Impact Inventory Template**:

Figure 1. Impact Inventory Template

Sector	Type of Impact (list category within each sector with unit of measure if relevant)[a]	Included in This Reference Case Analysis From...Perspective?		Notes on Sources of Evidence
		Health Care Sector	Societal	
Formal Health Care Sector				
Health	Health outcomes (effects)			
	Longevity effects	☐	☐	
	Health-related quality-of-life effects	☐	☐	
	Other health effects (eg, adverse events and secondary transmissions of infections)	☐	☐	
	Medical costs			
	Paid for by third-party payers	☐	☐	
	Paid for by patients out-of-pocket	☐	☐	
	Future related medical costs (payers and patients)	☐	☐	
	Future unrelated medical costs (payers and patients)	☐	☐	
Informal Health Care Sector				
Health	Patient-time costs	NA	☐	

5. Were costs and consequences **measured** accurately?

- The previous guideline was about the **identification** of relevant costs and consequences
- This guideline is about correctly **measuring** or **counting** cost and consequences
- For example, we figured out that we need to take into account the cost of training in the CFPI and the cost of tests for celiac and diabetes. This guidelines is about assessing if the study correctly calculated the hours or material for training and the number of tests needed
- Some things appear trivial, but in reality are not: a study assumed 1 test per screening, but maybe that's wrong. Maybe it should 2 tests per one screening because some test need to be repeated
- How do you know? Well, you need to know the details of the intervention

5. Were costs and consequences **measured** accurately?

- An common problem is usually **overhead costs**. How do you separate resources from the initiative from those of other operations?
- We will cover some shortcuts
- In the next two classes we will start going over the details of measuring costs
- Example: In CEA grants you add a statement that costs from the initiative will be separated from costs of performing the research

6. Were costs and consequences **valued** correctly?

- Guideline 4 is about identification; guideline 5 about measuring. This guideline is about **valuation**
- In other words, we have quantity (q). Does the study assign value or prices (p) correctly? Remember, cost $= p * q$
- Example:

  In the CFPI we identified the cost of delivery as something that we need to take into account (guideline 4)
  We are going to multiply births averted by an estimate of pregnancies that end in delivery (guideline 5)
  - Now we need to figure out how we transform those items into monetary units (this guideline; guideline 6)
- One possibility: use Medicaid payments. What about UC charges for deliveries? Would that be valid?

7. Were costs and consequences discounted?

- Comparison of costs and benefits should be made at the same time but in many interventions cost and benefits have different timing
- In prevention programs costs are incurred in the present but benefits in the future (HPV vaccine; screening for diabetes)
- Some costs are **saved** in the future. The idea of screening for diabetes early is to prevent serious complications in the future
- Regardless of when costs and outcomes happen, we need to **compare them at the same time**; that's the role of discounting
- We'll cover discounting in more detail
- **Caveat**: Short-term (say, less than five years) studies usually do not discount

8. Was an incremental analysis of costs and consequences of alternatives performed?

- Last week we talked about the incremental cost-effectiveness ratio or ICER
- The idea is to compare **incremental** costs and benefits. $\frac{C2-C1}{E2-E1}$ But why?
- **Because we are always interested in making a decision between alternatives**
- **Pay attention**: We do not care if the cost per unit of effectiveness of one alternative is less than the other
- It doesn't matter if this year's ski boots are more expensive per unit of quality than last year's model. What matters is if the incremental (extra/additional) cost justifies the incremental benefit
- **Before you start wondering**: Yes, this is NOT intuitive

Example

	Cost ($)	Effect (years)	Average (cost/effect)
Intervention 1	7,000	0.400	17,500
Intervention 2	10,000	0.420	23,810

- Intervention 2 is $23,810 per year of life gained
- Intervention 2 is both more expensive and more effective
- Difference in averages is $23,810 - 17,500 = \$6,310$

Example

	Cost ($)	Effect (years)	Average (cost/effect)
Intervention 1	7,000	0.400	17,500
Intervention 2	10,000	0.420	23,810

- Difference in averages is $23,810 - 17,500 = \$6,310$. But I just told you that we should consider instead incremental costs versus incremental benefits:

$$ICER_1 = \frac{C_2 - C_1}{E_2 - E_1} = \frac{10,000 - 7000}{0.42 - 0.4} = \frac{3,000}{0.02} = \$150,000$$

Example

- $150,000 is a lot more than $6,300. What is the problem?
- The relevant decision is whether we carry out Intervention 2 versus Intervention 1
- So we want to assess if the extra cost justifies the extra benefit
- The average cost per unit of benefit is not informative and it is not the relevant comparison
- Alternative 2 is $3,000 more expensive but it provides only 0.02 extra years of life
- Not too hard to come up with examples of same average costs but very different ICERs

ICER example II

	Cost ($)	Effect (years)	Average (cost/effect)
Intervention 1	7,000	0.400	17,500
Intervention 2	10,000	0.420	23,810

Changing some numbers:

	Cost ($)	Effect (years)	Average (cost/effect)
Intervention 1	7,000	0.400	17,500
Intervention 2	15,000	0.630	23,810

Now Intervention 2 is also $6,310$ per unit of effect ($\frac{15000}{0.63} = 6,310$). Therefore, if we use **average effectiveness** as criterion we should be **indifferent** between the two alternatives

ICER example II

- What about ICER?:

$$ICER_2 = \frac{15,000 - 7,000}{0.630 - 0.4} = \frac{8,000}{0.22999} = \$34,785$$

- \$34,785 seems better than before. For sure, **NOT indifferent between the two alternatives**
- In the second case, Intervention 2 is more expensive ($\Delta\$8,000$) but a lot more effective ($\Delta 0.23$)
- Using ICER matches the decision we want to make. **Do we do Alternative 1 or 2?**
- A silly example: Beer A is \$3 and gives you 0.6 of satisfaction; Beer B is \$4.5 and gives you 0.8 of satisfaction. So A (3/0.6=5) is cheaper per unit of satisfaction than B (4.5/8=5.625). You should buy A
- But... we are trying to figure out if we should buy B instead of A: $\frac{4.5-3}{0.8-0.6} = 7.5$. That's the extra cost per unit of satisfaction. Is \$7.5 per unit of satisfaction worth it?

The famous sixth stool Guaiac

- **Research question**: What is the right protocol for asymptomatic colon cancer screening? How many stool tests (occult blood)? 1, 2? 6?
- Neuhauser and Lewicki (1975)
- Made some assumptions about the cost of the test ($4 for first and $1 for the rest) and about prevalence of colon cancer (72/10,000) and sensitivity of test
- **Digression**: The paper was published in 1975, but still. $4 and $1 for a medical test????

The famous sixth stool Guaiac

Number of tests	Costs	Cases Detected	Costs/Cases	x10,000
1	$ 77,511	659,469	0.118	$ 1,175
2	$ 107,690	714,424	0.151	$ 1,507
3	$ 130,199	719,003	0.181	$ 1,811
4	$ 148,116	719,385	0.206	$ 2,059
5	$ 163,141	719,417	0.227	$ 2,268
6	$ 176,331	719,420	0.245	$ 2,451

- Not much difference in costs/effect from, say, 4 to 5 or 5 to 6

The famous sixth stool Guaiac

- Now calculate ICER sequentially:

Number of tests	Costs	Cases Detected	Costs/Cases	ICER
1	$ 77,511	659,469	0.118	
2	$ 107,690	714,424	0.151	0.5
3	$ 130,199	719,003	0.181	4.9
4	$ 148,116	719,385	0.206	46.9
5	$ 163,141	719,417	0.227	469.5
6	$ 176,331	719,420	0.245	4396.7

- Example 6 versus 5: (176,331 - 163,141)/(719,420-719,417) = \$13,190/3 = 4396.7

The famous sixth stool Guaiac

- "... the marginal cost of the sixth test may be 20,000 times the average cost"
- For 10,000: $43,966,667!!!
- Why? The extra cost of testing is large but the benefits start shrinking fast

The famous sixth stool Guaiac

	Incr cost	Incr cases
2 vs 1	$ 30,179	54,955
3 vs 2	$ 22,509	4,579
4 vs 3	$ 17,917	382
5 vs 4	$ 15,025	32
6 vs 5	$ 13,190	3

- Two lessons: 1) It pays off to think analytically, and 2) Thinking at the margin is the right approach for making decisions

9. Was uncertainty of estimates taken into account?

- One (a bit cynical) way to think about EE is that it is **(systematic) guessing**: every number comes with uncertainty
- With individual-level data, we can use confidence intervals and other statistical tools (like bootstrapping) to measure some of the uncertainty
- We will talk more about **types of uncertainty** when we cover different ways of doing sensitivity analysis
- A good study **explores the effect of changing a number** on the overall conclusions
  - Which variables are uncertain?
  - What is the plausible range?
- A growing area of research/concern in CEA: **heterogeneity** of effects. (Even the stool test paper talks about high/low risks patients)

9. Was uncertainty of estimates taken into account?

- How did they come up with numbers for the sensitivity analysis?
  - Is it done in an ad hoc way?
  - From the literature?
  - Expert opinion?
- Different types of sensitivity analysis
  - One way
  - Multiway
  - Scenario analysis
  - Threshold analysis
  - Probabilistic sensitivity analysis (PSA)
- **My view**: A paper without a sensitivity analysis is a **bad paper**

9. Was uncertainty of estimates taken into account?

- The new panel recommendations state:

  "The items included in a cost-effectiveness analysis and the manner in which they are valued involve numerous **choices**. Analysts should be **transparent** about how they have conducted the analyses, and convey how the results **change with alternative assumptions**. **Sensitivity analysis** should describe the assumptions to which the results for different perspectives are sensitive."

10. Did the study address all the issues that are relevant to the decision makers and other users?

- Compare own results to previous results?
- Generalize own results to other settings? (Sensitivity analysis helps here)
- Discuss how the findings (like ICERs) can be interpreted?
- Do they suggest a conclusion on cost-effectiveness? This is often missing from some studies. It shouldn't. Should be part of the discussion section
- The ICER should always be put in context

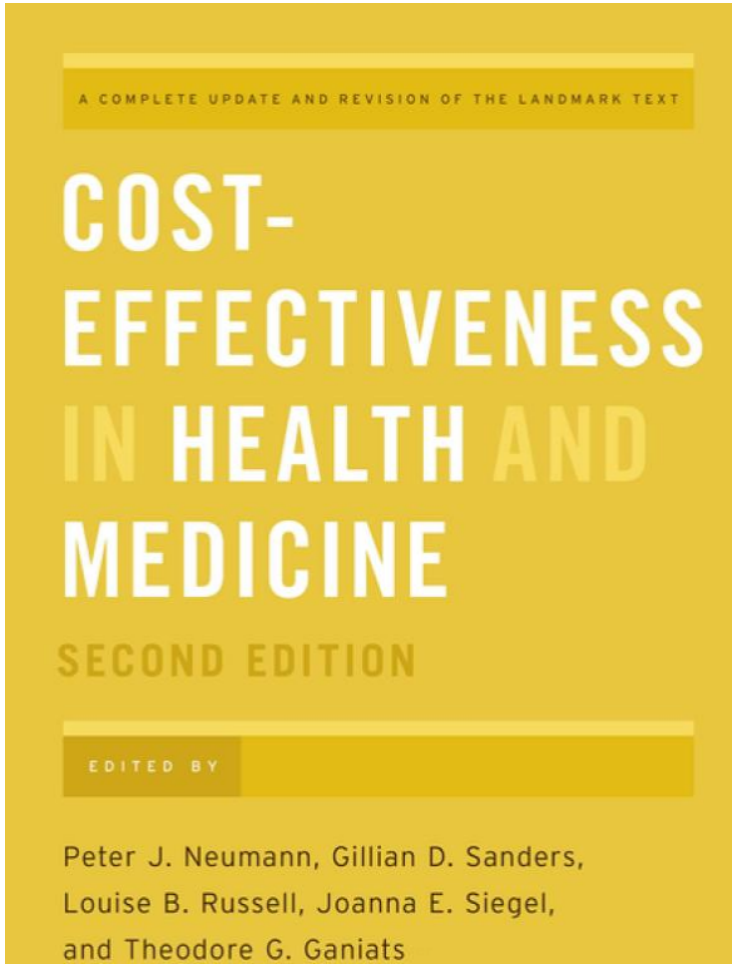
Summary

- These guidelines are very useful
- The nuances of each of them will become clear by the end of the class
- If you ever write a CEA paper, come back to these guidelines
- Not the only set of guidelines

The Panel on Cost-Effectiveness in Health and Medicine

- A group of academics got together to write recommendation on how to conduct cost-effectiveness studies
- "The divergence of methods used to conduct CEA interferes with the ability of decision makers charged with resource allocation to make appropriate comparisons of cost-effectiveness ratios across programs." (Weinstein et al 1996).
- The result was the "Gold" book
- After 20 years, the Gold book was revised (still gold by the way)

The Panel on Cost-Effectiveness in Health and Medicine



- If you care about CEA, I recommend you buy the book (about $40)
- Read the summary recommendations Sanders et al (2016)

The Panel on Cost-Effectiveness in Health and Medicine

Recommendations themes

1. Measuring terms in the numerator of ICER (costs)
2. Valuing the health consequences in the denominator of ICER (benefits)
3. Estimating effectiveness of interventions (i.e. making sense of results)
4. Time preference and discounting
5. Handling uncertainty in CEA
6. Reporting guidelines

The Panel on Cost-Effectiveness in Health and Medicine

1. I'll mention the new recommendations from time to time
2. Perhaps the most important (and difficult to do) are:
   - The **societal perspective** should always be included
   - The relevant decision-making perspective should be included
   - Costs are **opportunity costs** (very difficult in practice)
   - Always include an Impact Inventory
   - Creating of a reporting checklist

Big picture and homework

- First two classes provided an overview of EEs and the key themes/elements
- The rest of the class will provide details (but we will always circle back to big picture)
- Homework: you will apply the 10 guidelines to the two articles you read for Homework 1
- The textbook has an example but I want you **write less and be more concise**
- Don't worry if you don't understand the methods. We will get there, I promise