Introduction to Economic Evaluation of Healthcare

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Evaluation of Medical Care (I)

TRADITIONAL ISSUES

Safety
Efficacy
Effectiveness

Side effects acceptable?
Can it work?
Does it work?

Evaluation of Medical Care (II)

ECONOMIC ISSUES

Efficiency

Are we getting the best outcome for the expenditure
Principles of Economic Assessment

- Rules exist for assessing costs and benefits
- Assumptions are made explicit
- As a result:
  - There is consistency of approach
  - It is clear what is included and excluded from calculations

Scarcity

- Resources are limited
- Choices must be made
- When a resource is used, opportunity to use it for something else is lost
- The value of a resource in its best alternative use is its "opportunity cost"

Economic Messages

- Primary economic message
  - The therapy is good (bad) value for cost.
- Other economic Messages
  - The disease poses a substantial burden on society in terms of morbidity, mortality, cost, and quality of life
  - Therapy reduces this burden
Who’s Listening?
Not the Congress:
“The Patient-Centered Outcomes Research Institute … shall not develop or employ a dollars per quality adjusted life year (or similar measure that discounts the value of a life because of an individual’s disability) as a threshold to establish what type of health care is cost effective or recommended. The Secretary shall not utilize such an adjusted life year (or such a similar measure) as a threshold to determine coverage, reimbursement, or incentive programs under title XVIII”

The Patient Protection and Affordable Care Act

Current US Users of CE and CB Analysis
• Common belief: CE/CB not used in US
  – NIH expert guideline panels and Environmental Protection Agency can and do use
  – Chambers et al.: By law, cannot be used by Medicare, but lack of estimate of cost-effectiveness associated with decreased likelihood of Medicare coverage decisions
  – Medicaid, Vaccines for children (But not formally)
  – Aspinall et al.: Veterans Health Administration “has emphasized use of cost-effectiveness data, especially for newer, costly drugs”
  – Neuman and Bliss: 12% of FDA DDMAC warning letters between 2002 and 2011 cite health economic violations

Current Users of CE and CB Analysis (2)
• U.S. cont.
  – Academy of Managed Care Pharmacy guidelines for pharmacoeconomic submissions to formularies
  – Delivery Systems: management or marketing?
  – Managed care plans -- but not that much (yet)
Economic Evaluation Methods Overview

- Types of analyses
- Study designs
- Types of outcomes
- Perspective
- Steps in economic evaluation

Types of Analyses

Types of Analysis

- Cost identification
- Cost-effectiveness / cost-utility
- Cost-benefit

Generally distinguished by:
- Outcomes included: e.g., costs alone vs costs and effects
- How outcomes are quantified: e.g., as money alone or as health and money
Cost Identification / Cost Minimization / Cost-Cost Analysis

Cost Identification, etc.
- Estimates difference in costs between therapies, but not difference in other outcomes
- Commonly conducted when no difference observed in effectiveness
  - “As no statistical significant difference among the mean QALYs gained with the different [hormonal therapies] was detected (p = 0.12), CUA was replaced by a cost minimization analysis.”


Appropriate Only When Therapies are Identical

Dish Network TV Spot, “Apples”, 2015
Cost-Identification Example

<table>
<thead>
<tr>
<th></th>
<th>Adenoidect</th>
<th>WW</th>
<th>Diff</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>URTI episodes</td>
<td>7.86</td>
<td>7.89</td>
<td>-0.03</td>
<td>-1.72 to 1.76</td>
</tr>
<tr>
<td>URTI days</td>
<td>66.25</td>
<td>67.2</td>
<td>-0.95</td>
<td>-10.5 to 4.5</td>
</tr>
<tr>
<td>Severe episodes</td>
<td>3.97</td>
<td>3.54</td>
<td>0.42</td>
<td>-0.63 to 1.52</td>
</tr>
<tr>
<td>Severe days</td>
<td>48.49</td>
<td>46.2</td>
<td>2.28</td>
<td>-15.6 to 20.2</td>
</tr>
<tr>
<td>School absence</td>
<td>1.75</td>
<td>1.9</td>
<td>-0.15</td>
<td>-0.78 to 0.48</td>
</tr>
<tr>
<td>Cost (Median)</td>
<td>$1995</td>
<td>$1215</td>
<td>$780</td>
<td>(NR)</td>
</tr>
</tbody>
</table>


Conclusion: Adenoidectomy Vs Watchful Waiting

“...in children selected for adenoidectomy for recurrent URTIs, immediate adenoidectomy results in an increase in costs, whereas it confers no clinical benefit over an initial watchful waiting strategy.”
Is failure to detect a difference same as a demonstration of equivalence?

Problems With Cost Identification

• Old version
  – If two therapies’ effects are identical, adopt cheaper of two
    • Effect maximization corollary: If two therapies’ costs identical, adopt more effective of two
• New version
  – Generally can’t conclude two therapies are identical
    • At most fail to reject null hypothesis
  – Cost-minimization analysis unlikely to be appropriate

Confidence Levels Around Cost-Identification?
Cost-Effectiveness Analysis

• Estimates costs and outcomes of intervention
• Costs and outcomes measured in different units
• Costs usually measured in money terms; outcomes in some other units
• Incremental cost-effectiveness ratio:
  \[ \frac{\text{Costs}_1 - \text{Costs}_2}{\text{Effects}_1 - \text{Effects}_2} \]

Cost-Effectiveness A Relative Measure

• Cost-effectiveness is a relative measure; no program is “cost-effective” in abstract
  – Results meaningful in comparison with:
    • A predetermined standard
      – e.g., $50,000 per quality-adjusted year of life saved
    • Other accepted and rejected interventions (e.g., a league table)
Cost-effectiveness of extended buprenorphine–naloxone treatment for opioid-dependent youth: data from a randomized trial

Daniel Pohly, Henry A. Glick, Jianying Tang, Geetha A. Subramanian, Sabrina A. Poole & George E. Woodfill

Buprenorphine/Naloxone: Opioid Addicted Youth

• The data *

<table>
<thead>
<tr>
<th></th>
<th>Cost</th>
<th>Opioid Free Year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Usual Care</td>
<td>9210</td>
<td>0.319</td>
</tr>
<tr>
<td>Bup/Nal</td>
<td>9293</td>
<td>0.589</td>
</tr>
</tbody>
</table>

• Cost-effectiveness ratio

\[
\frac{9293 - 9210}{0.589 - 0.319} = \frac{83}{0.27} = 307
\]

95% CI, Dominates to 21,100/OFY

* 1-year results Pohly et al., Cost-effectiveness of extended buprenorphine-naloxone... Addiction. 2010;105:1616-24

What Value W?

• Can calculate a ratio for any outcome
  – e.g., Cost per opioid-free day
• To be informative, must know willingness to pay
• No general agreement on W*, maximum acceptable cost-effectiveness ratio
  – Differs by outcome
    • If 50k-100k per QALY, doesn’t mean it’s 50k-100k per opioid-free year
  – Can differ among decision makers
  – Single decision maker might consider use of different maximum acceptable cost-effectiveness ratios depending on other features of decision problem
Reported Values of WTP

- 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

Cost-Utility Analysis

- Specific type of cost-effectiveness analysis in which outcomes expressed in units of utility (e.g., quality-adjusted life years or QALYs)
  - In many jurisdictions, QALYs are recommended outcome of cost-effectiveness analysis

Choosing Among Alternative Interventions

<table>
<thead>
<tr>
<th>Costs</th>
<th>Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>A &lt; B</td>
<td></td>
</tr>
<tr>
<td>A &gt; B</td>
<td>B Dominant</td>
</tr>
<tr>
<td>A &gt; B</td>
<td>Incremental Cost-Effectiveness Analysis</td>
</tr>
<tr>
<td>A &lt; B</td>
<td>Incremental Cost-Effectiveness Analysis</td>
</tr>
<tr>
<td>A Dominant</td>
<td></td>
</tr>
</tbody>
</table>
Dominance and Choice

- Old version: Calculate cost-effectiveness ratios only when one therapy cost more and is more effective
  - Other outcomes indicate either dominance (e.g., cost less and does more) or a toss-up (e.g., equal cost and effect)
- New version: Omit calculation of cost-effectiveness ratios only when one therapy costs significantly less and is significantly more effective (i.e., significantly dominates the alternative)
  - e.g., when one therapy is significantly more effective but its cost-savings are not significant, the resulting CI for the CER may indicate we can’t be confident that the value of the two therapies differs

League Table Cost per QALY

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Ratio (US $*)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CABG for Left Main CAD</td>
<td>4,200</td>
</tr>
<tr>
<td>Neonatal Intensive Care (Birthweight 1-1.499 kg)</td>
<td>4,500</td>
</tr>
<tr>
<td>Neonatal Intensive Care (Birthweight .500-.999 kg)</td>
<td>31,800</td>
</tr>
<tr>
<td>CABG for Single Vessel Disease</td>
<td>36,300</td>
</tr>
<tr>
<td>School TB Testing Program</td>
<td>43,700</td>
</tr>
</tbody>
</table>

* 1983 value 

Source: Torrance, 1986

Alternatives to QALYS

- Years of life gained
- Lives saved
- Successful treatments
- Cases of illness avoided
- Intermediate outcomes gained

BUT TO BE INFORMATIVE, NEED TO UNDERSTAND WILLINGNESS TO PAY FOR SUCH OUTCOMES
Cost-Benefit Analysis

Cost-Benefit Analysis (I)
- Estimates differences in costs and benefits in same units
  - Usually money, but any common unit possible
- As with cost-effectiveness, requires a set of alternatives
- Net benefit is preferred: benefit/cost ratio
  - Net benefit: \((Benefit_1 - Benefit_2) - (Cost_1 - Cost_2)\)
- Alternative: Benefit-cost ratio (potentially problematic)
  - BC Ratio: \((Benefit_1 - Benefit_2) / (Cost_1 - Cost_2)\)

Long-term cost-minimization analysis comparing laparoscopic with open (Lichtenstein) inguinal hernia repair

A. Edlund\(^1\), P. Carlson\(^2\), A. Rosenblad\(^3\), A. Montgomery\(^4\), L. Bengtson\(^5\) and C. Backstrom\(^6\) for the Swedish Multicenter Trial of Inguinal Hernia Repair by Laparoscopy (SMIL) study group.

\(^1\)Department of Surgery, Gothenburg University, Sweden; \(^2\)Gothenburg University, Surgical Sciences, Sweden; \(^3\)Lund University, Clinical Sciences, Sweden; \(^4\)Lund University, Medical Sciences, Sweden; \(^5\)Malmö University Hospital, Malmö, Sweden; \(^6\)Department of Surgery, Gothenburg University, Sweden.
Cost-Benefit Analysis, Inguinal Hernia Repair

Net benefit: (2662.7+107.9+1767.0)-(1952.1+23.4+2270.1) = -292 (p=.02)

Net Monetary Benefit (NMB)
- Composite measure (part cost-effectiveness, part cost benefit analysis), usually expressed in dollar terms, derived by rearranging cost-effectiveness decision rule:
  \( W^* > \frac{\Delta C}{\Delta Q} \)
  where \( W^* \) = maximum acceptable cost-effectiveness ratio (e.g., 50,000 per QALY)
- NMB routinely (but not necessarily) expressed on cost scale, known as net monetary benefit (NMB)
  \( (W \times \Delta Q) - \Delta C \)
- Particularly important for statistical evaluation of cost-effectiveness analysis (e.g., sample size; direct statistical testing by use of patient-level data; etc.)

CBA VS NMB
- Principal difference between CBA and NMB is in how willingness to pay is estimated
  - When estimated at the individual level, and ideally, when principles of welfare economics are employed, use of WTP yields CBA
  - When calculated as a decision maker’s rule of thumb (e.g., 50,000 or 100,000), use of W yields NMB, a simple transformation of CEA
Review

• Investigators compared 2 treatments, “LessCost” and “MoreCure”
• Found that “LessCost” was less expensive and recommended its adoption by physicians
  – 1000 vs 1200

• What type of economic analysis are investigators carrying out?
• Do you agree with their conclusion?

Example 2

• Investigators compared 2 treatments, “LessCost” and “MoreCure.” Observed the following:

<table>
<thead>
<tr>
<th></th>
<th>MoreCure</th>
<th>LessCost</th>
<th>Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cost</td>
<td>1200</td>
<td>1000</td>
<td>200</td>
</tr>
<tr>
<td>Benefit</td>
<td>3000</td>
<td>1500</td>
<td>1500</td>
</tr>
</tbody>
</table>

• Authors concluded that MoreCure is net beneficial.

• What type of economic analysis are investigators carrying out?
• Do you agree with their conclusion?

Example 3

• Investigators compared 2 treatments, “LessCost” and “MoreCure.” Observed that MoreCure cost 200 more than LessCost and provided 0.03 additional QALYs
• Authors recommended that MoreCure was good value for cost

• What type of economic analysis are the investigators carrying out?
• Do you agree with their conclusion?
Study Designs

- Clinical trials
  - Economic evaluation in clinical trials widespread
  - Little to no selection bias, but potential issues of generalizability
- Observational studies
  - Often more generalizable, but problems with selection bias
- Decision models
  - Often used to address pressing questions for which direct data are not available
  - Shares strengths and weaknesses of source data
  - Added uncertainties related to combining data from multiple sources and projection beyond the data

Decision Analysis Approaches

- Most frequently used healthcare decision analytic approaches
  - Decision trees
  - Markov models
- Less frequently used approaches
  - Discrete event simulation
  - Dynamic transmission models
  - Partitioned survival models
  - Compartment models
Decision Trees

• "Models" that use a tree-like structure to organize thoughts and data about problems (e.g., treatment decisions) and their consequences
• Characterized by decisions, chances, and outcomes
• Results based on probabilities and "rewards" for outcomes
• Time usually not directly modeled in decision trees

Markov Models

• Repetitive decision trees used for modeling conditions that have events that may occur repeatedly over time or for modeling predictable events that occur over time (e.g., screening for disease at fixed intervals)
  – e.g., Cycling among heart failure classes or screening for colorectal cancer
• Use of Markov models simplifies presentation of tree structure
• Markov models explicitly account for timing of events

Types of Costs and Effects
Types of Costs and Effects

- Direct: medical or nonmedical
- Time costs: Lost due to illness or to treatment
- Intangible costs
- Quality-adjusted life years
- Types of costs and effects included in an analysis depend on:
  - What is affected by illness and its treatment
  - What is of interest to decision makers
    - e.g., a number of countries’ decision makers have indicated they are not interested in time costs

Direct Cost

![Diagram of Direct Cost]

- Units
- Costs
- Variable Costs
- Fixed Costs

Marginal Cost (I)

- Costs incurred in providing an extra unit of service, or savings realized by providing one less unit
- Calculation unaffected by fixed costs
Marginal Versus Average Cost

- Suppose that:
  - Total drug costs = $50
  - Total doses = 10
  - Average cost / dose = 5

- Suppose, however that:
  - 9 doses = $49
  - 10 doses = $50
  - Marginal cost of 10th dose = $1

Cost Estimation

- Standard economic assumption
  - Purchase price = cost
- Health care (particularly U.S.)
  - Purchase price ≠ cost or there is no price to observe
- Difference relates to:
  - Health care consumers not having adequate information
  - High levels of insurance
  - Regulation
  - Hospital internal costing policies; free care
  - Economies of scale / fixed costs
Cost Estimation Paradox
- Evaluation most difficult when it is most needed
  - Markets don’t exist and costs are hard to determine
- Easiest when it is needed least
  - Markets exist and costs are observable

Indirect Cost (I)
- Human capital approach
  - Advantages
    • Easy to measure
    • Assess actual gains / losses in productivity
  - Disadvantages
    • Not theoretically correct measure
    • Poor proxy for “Willingness to Pay” (although in some common situations may be a lower bound)
    • "Undervalues" anyone not earning a wage

Indirect Cost (II)
- Willingness to pay approach
  - Advantages
    • Theoretically correct measure
  - Disadvantages
    • Function of ability to pay
    • May be difficult to measure in practice
QALYs

- Economic outcome that combines preferences for both length of survival and quality into a single measure
- Help us decide how much to pay for therapies that:
  - Save fully functional lives/life years
  - Save less than fully functional lives/life years
    - e.g., heart failure drug that extends survival, but extra time spent in NYHA class III
  - Don't save lives/life years but improve functioning
    - e.g., heart failure patients spend most of their remaining years in class I instead of class III

QALY Scores

- QALY or preference scores generally range between 0 (death) and 1 (perfect health)
  - E.g., health state with a preference score of 0.8 indicates that year in that state is worth 0.8 of year with perfect health
  - There can be states worse than death with preference scores less than 0

Prescored Health State Classification Instruments

- Dominant approach for QALY measurement uses prescored health state classification instruments (indirect utility assessment)
- Participants report their functional status across a variety of domains
- Preference scores derived from scoring rules that usually have been developed from samples from general public
Point of View / Perspective

• Society
• Patient
• Payor (e.g., insurance company, employer)
• Provider (e.g., hospital)

Study Perspective

• Economic analyses should adopt 1 or more “perspectives”
• Perspective helps identify services that should be included in the analysis and how services should be costed out
  – e.g., patient out-of-pocket expenses may be excluded from insurer perspective
  – Not all payments may represent costs from the societal perspective
Sensitivity Analysis
• Demonstrates dependence/independence of a result on a particular assumption
• Identifies critical values of variables
• Identifies uncertainties requiring further research

Discounting
• Costs and benefits incurred now are greater than those with a similar nominal value incurred later
• Future costs and benefits must be expressed in terms of present value

\[ PDV = \sum_{t=0}^{\infty} \frac{C_t}{(1+r)^t} \]
Discounting: an Example

- Assume that a program costs $1,000 this year and for next 2 years

\[
PDV = \frac{1000}{1.03^1} + \frac{1000}{1.03^2} + \frac{1000}{1.03^3}
\]

i.e., \(PDV = 970.87 + 942.60\)

Hence, \(PDV = 2,913.47\)

Issues in Discounting

- What is appropriate discount rate for costs?
- Should monetary costs and non-monetary outcomes be discounted at same rate?

Distributional Issues

<table>
<thead>
<tr>
<th></th>
<th>Program 1</th>
<th>Program 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Net Cost</td>
<td>250,000</td>
<td>250,000</td>
</tr>
<tr>
<td>Net Effect</td>
<td>10 Years</td>
<td>10 Years</td>
</tr>
<tr>
<td>C/E Ratios</td>
<td>25,000</td>
<td>25,000</td>
</tr>
<tr>
<td># of Patients who Benefit</td>
<td>1</td>
<td>5</td>
</tr>
</tbody>
</table>
Features in Health Economic Analysis

- Consistent application of rules
- Marginal costs
- QALYS (and other measures of preference)
- Perspective
- Discounting

Objectives of Health Economic Assessments

- Economic assessments of health care aim at demonstrating most efficient use of available resources, not cuts in expenditures