Innovations in Medical Cost-Effectiveness Analysis

David Meltzer MD, PhD
The University of Chicago
Objectives

• To introduce important theoretical innovations in cost-effectiveness analysis
  – Perspective
  – Future costs
  – Self-selection in cost-effectiveness analysis
  – Empirical cost-effectiveness
  – The value of research
Background on Medical Cost-Effectiveness Analysis

• Origins in academic medicine in 1970s
• Seeks to maximize welfare/health (quality-adjusted life years (QALYs)) given constrained resources
  – Incremental cost-effective ratio (ICER): cost/QALY
• Applications
  – Government, especially outside the U.S.
    • e.g., UK National Institute for Health and Clinical Excellence
    • US: Office of Technology Assessment, recent CMS, FDA interests, not Patient Centered Outcomes Research Institute (PCORI)
  – Private payers
  – Clinicians
  – Pharmaceutical companies
    • “Pharmacoeconomics”
Perspective

• Private
  – HMO, consumer

• Public
  – Medicare, Medicaid, state mental health system

• Societal
  – Include all costs and benefits no matter to whom they accrue
  – Policy analysts (i.e., US Panel on Cost-Effectiveness in Health and Medicine Reference Case)
Recommendations for Conduct, Methodological Practices, and Reporting of Cost-effectiveness Analyses
Second Panel on Cost-Effectiveness in Health and Medicine

September 13, 2016
Experiences since the Original Panel

• Many CEAs, most not using the societal perspective
• Even when stating using societal perspective – important elements often omitted
• Decision makers using CEA – often have taken more focused perspective
Perspective: Second Panel’s Considerations

- Appeal of societal perspective
- Potential to disregard revealed preferences of decision makers
- Is there a single “societal perspective”?
- Need to promote quality and comparability
Recommendation – Reference Cases:

• All studies represent a reference case analysis based on a **health sector perspective** and a reference case based on a **societal perspective**

• Measure health effects in QALYs

• Intended to enhance consistency and comparability
Recommendation: Health Sector Perspective

• Results should be summarized in ICER
• NMB and NHB may also be reported
• Range of CE thresholds should be considered
Recommendation: Impact Inventory

• Include impact inventory table which lists the health and non health impacts of an intervention

• Main purpose is to ensure that all consequences, including those outside the formal healthcare sector, are considered regularly and comprehensively

• Provides a framework for organizing, thinking about, and presenting various types of consequences
## The Impact Inventory

<table>
<thead>
<tr>
<th>Sector</th>
<th>Type of Impact (list category within each sector with unit of measure if relevant)*</th>
<th>Included in This Reference Case Analysis From... Perspective?</th>
<th>Notes on Sources of Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Health Care Sector</td>
<td>Societal</td>
</tr>
<tr>
<td><strong>Formal Health Care Sector</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Health</strong></td>
<td>Health outcomes (effects)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Longevity effects</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Health-related quality-of-life effects</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Other health effects (eg, adverse events and secondary transmissions of infections)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Medical costs</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Paid for by third-party payers</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Paid for by patients out-of-pocket</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Future related medical costs (payers and patients)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Future unrelated medical costs (payers and patients)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Informal Health Care Sector</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Health</strong></td>
<td>Patient-time costs</td>
<td>NA</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Unpaid caregiver-time costs</td>
<td>NA</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Transportation costs</td>
<td>NA</td>
<td></td>
</tr>
<tr>
<td><strong>Non-Health Care Sectors (with examples of possible items)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Productivity</strong></td>
<td>Labor market earnings lost</td>
<td>NA</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Cost of unpaid lost productivity due to illness</td>
<td>NA</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Cost of uncompensated household productiona</td>
<td>NA</td>
<td></td>
</tr>
<tr>
<td><strong>Consumption</strong></td>
<td>Future consumption unrelated to health</td>
<td>NA</td>
<td></td>
</tr>
<tr>
<td><strong>Social Services</strong></td>
<td>Cost of social services as part of intervention</td>
<td>NA</td>
<td></td>
</tr>
<tr>
<td><strong>Legal or Criminal Justice</strong></td>
<td>Number of crimes related to intervention</td>
<td>NA</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Cost of crimes related to intervention</td>
<td>NA</td>
<td></td>
</tr>
<tr>
<td><strong>Education</strong></td>
<td>Impact of intervention on educational achievement of population</td>
<td>NA</td>
<td></td>
</tr>
<tr>
<td><strong>Housing</strong></td>
<td>Cost of intervention on home improvements (eg, removing lead paint)</td>
<td>NA</td>
<td></td>
</tr>
<tr>
<td><strong>Environment</strong></td>
<td>Production of toxic waste pollution by intervention</td>
<td>NA</td>
<td></td>
</tr>
<tr>
<td><strong>Other (specify)</strong></td>
<td>Other impacts</td>
<td>NA</td>
<td></td>
</tr>
</tbody>
</table>
Accounting for Future Costs in Medical Cost-Effectiveness Analysis
Background: Accounting for Future Costs

• Save patient with medical care today who requires care in the future. Should we count that as a cost?
  – Related illness?
    • Angioplasty today, count bypass in future?
  – Unrelated illness?
    • Influenza vaccine today, count dialysis in future?
  – Non-medical costs and benefits?
    • Suicide prevention today, earnings in future?
      Consumption in future?
Traditional Treatment of Future Costs and Benefits in CEA

- Analyses generally **include**:
  - Future benefits
    - Length of life/Quality of life = QALYs
  - Future medical costs for related illnesses

- Analyses generally **exclude**:
  - Future medical costs for unrelated illnesses
    - Few exceptions: Weinstein, OTA
  - Future non-medical costs

- Controversies reflect weak theoretical foundation of CEA
Theoretical Background: Phelps & Garber (1997)

• Use lifetime utility maximization model
• Conclude: Obtain same relative rankings of interventions if you include or exclude future medical costs for unrelated illness as long as they are:
  • treated consistently
  • truly unrelated = “conditional independence”
Theoretical Background: Meltzer (1997)

• Use lifetime utility maximization model
• Conclude:
  – Must include all future net resource use
    • Medical costs - both related and unrelated - and future non-medical costs net of earnings
    • “Net resource use” = consumption + medical expenditures - earnings
    • From -$10,000/year @ age 25 to +$20,000/year @ age 85
  – Relative rankings of interventions not independent of future costs
    • Analyses that omit future costs favor interventions that extend life over those that improve quality of life
  – Phelps/Garber inadvertently assume net annual resource use is zero
Lifetime Utility Maximization Model: Utility Function and Budget Constraint

\[ \sum_{t=0}^{T} \beta^t S_t(\tilde{m}_t)u(c_t, h_t(\tilde{m}_t)) \]  \hspace{1cm} (1) 

\[ \sum_{t=0}^{T} \frac{1}{(1+r)^t} S_t(\tilde{m}_t)(c_t + m_t) = \sum_{t=0}^{T} \frac{1}{(1+r)^t} S_t(\tilde{m}_t)(i_t) \]  \hspace{1cm} (2)
Lifetime Utility Maximization Model: First Order Conditions

\[
\frac{1}{(1+r)^t} S_t(m_t) + \sum_{\tau=t}^{T} \frac{1}{(1+r)^\tau} \frac{\partial S_\tau(m_\tau)}{\partial m_\tau} (c_\tau + m_\tau - i_\tau) \\
\sum_{t=\tau}^{T} \left[ \beta^t \frac{\partial s_\tau(m_\tau)}{\partial m_\tau} u(c_\tau, h_\tau(m_\tau)) + s_\tau(m_\tau) \frac{\partial u(c_\tau, h_\tau(m_\tau))}{\partial m_\tau} \right] (3)
\]
Theoretical Background: Meltzer (1997)

- Use lifetime utility maximization model
- Conclude:
  - Must include all future net resource use
    - Medical costs - both related and unrelated - and future non-medical costs net of earnings
    - “Net resource use”= consumption + medical expenditures - earnings
    - From -$10,000/ year @ age 25 to +$20,000/year @ age 85
  - Relative rankings of interventions not independent of future costs
    - Analyses that omit future costs favor interventions that extend life over those that improve quality of life
  - Phelps/Garber inadvertently assume net annual resource use is zero
Intuition

• Consider two interventions with equal current cost that both produce one QALY
  • $A$ increases life expectancy by one year at QOL=1
  • $B$ increases life expectancy by two years at QOL=0.5

• Which is preferred?
  – From utility side: Indifferent
  – From cost side: $A$ preferred since it saves the costs of supporting an extra year of life
  – Hence, $A$ preferred overall

• Omitting future costs favors interventions that extend life ($B$) versus those that increase QOL ($A$)
Accounting for Future Costs

\[
\frac{\Delta \text{cost}}{\Delta \text{QALY}} = \frac{\Delta \text{present cost}}{\Delta \text{QALY}} + \frac{\Delta \text{future cost}}{\Delta \text{QALY}}
\]

\[
= \frac{\Delta \text{present cost}}{\Delta \text{QALY}} + \frac{C \cdot \Delta \text{LY}}{\Delta \text{QALY}}
\]

\[
= \frac{\Delta \text{present cost}}{\Delta \text{QALY}} + C \cdot \frac{\Delta \text{LY}}{\Delta \text{QALY}}
\]
Consumption, Medical Expenditure, Earnings and Net Resource Use by Age
Present Value of Future Net Resource Use Per Year of Life Saved by Averting Death (by Age)
## Approximate Effects of Future Costs

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Cost/QALY without future costs</th>
<th>C</th>
<th>ΔLE/ΔQALY</th>
<th>C*(ΔLE/ΔQALY)</th>
<th>Cost/QALY with future costs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment Severe Hypertension</td>
<td>$18,000</td>
<td>-$5,000</td>
<td>1.03</td>
<td>-$5,200</td>
<td>$12,800</td>
</tr>
<tr>
<td>Men Age 40</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Treatment Severe Hypertension</td>
<td>$60,000</td>
<td>$8,000</td>
<td>1.07</td>
<td>$8,500</td>
<td>$68,500</td>
</tr>
<tr>
<td>Men Age 60</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adjuvant Chemo</td>
<td>$67,000</td>
<td>$8,000</td>
<td>18</td>
<td>$144,000</td>
<td>$211,000</td>
</tr>
<tr>
<td>Duke’s C Colon</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CA Men Age 60</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hemodialysis for ESRD</td>
<td>$117,000</td>
<td>$8,000</td>
<td>1.5</td>
<td>$12,000</td>
<td>$129,000</td>
</tr>
<tr>
<td>Men Age 60</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
All healthcare costs, related or unrelated, should be considered either when survivals under alternative interventions are not the same or when cost components cannot be readily identified as related to the target condition.
Effects of Self-Selection on Cost-Effectiveness
Background

- Traditional CEA uses preferences (utilities) that average across individuals.
- However, utilities may vary across individuals or populations and influence expected benefits of treatment.
  - Implies cost-effectiveness can vary for individuals or populations that differ in preferences.
- Preferences can also affect treatment choice.
  - Specifically, patients whose preferences favor an option may be more likely to choose it.
- How might “self-selection” affect cost-effectiveness?
Standard CEA with Heterogeneous Individuals

Blue Dots = Treated Patients
Perfect Self-Selection

Blue Dots=Pts gain from Tx; Orange Dots=Pts lose from Tx
Effect of Perfect Self-Selection on CEA

Blue Dots=Pts gain from Tx; Orange Dots=Pts lose from Tx (reject)
Empirical Self-Selection

Blue Dots=Pts choose Tx; Orange Dots=Pts reject Tx
Background: Diabetes in the Elderly

- Diabetes care guidelines call for intensive lowering of glucose among younger patients
- However, unclear if this should apply to older patients
  - Gains in life expectancy smaller
  - Side effects of treatment may dominate
  - CE models of intensive therapy in older patients:
    - Minimal or even negative effects on QALYs
    - Not cost-effective
      - Know many patients refuse intensive therapy
- Suggests self-selection may have important effects on CEA in diabetes
Methods

• Interviewed 500 older diabetes patients to obtain data on preferences
  – Conventional and intensive glucose lowering (using insulin or oral medications)
  – Blindness, end-stage renal disease, lower extremity amputation
• Collected data on treatment choices and patient characteristics by medical records review
• Used CDC simulation model of intensive therapy for type 2 diabetes and patient-specific demographic, health, and preference data to get person-specific estimates of lifetime costs and benefits
• Analyses of cost-effectiveness of intensive vs. conventional therapy contrasting all patients vs. perfect self-selection vs. empirical self-selection
### Results: Intensive vs. Conventional Therapy

<table>
<thead>
<tr>
<th>CE Approach</th>
<th>Group</th>
<th>N</th>
<th>Change in Costs ($)</th>
<th>Change in QALYs</th>
<th>CE Ratio ($/QALY)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Standard</strong></td>
<td>Full Population</td>
<td>543</td>
<td>8076</td>
<td>-0.49</td>
<td>--</td>
</tr>
<tr>
<td><strong>Perfect Self-Selection</strong></td>
<td>(\Delta QALY &gt; 0)</td>
<td>403</td>
<td>8165</td>
<td>0.40</td>
<td>20K</td>
</tr>
<tr>
<td></td>
<td>(\Delta QALY &lt; 0)</td>
<td>131</td>
<td>7906</td>
<td>-3.25</td>
<td>--</td>
</tr>
<tr>
<td><strong>Empirical Self-Selection</strong></td>
<td>Self-identified intensive insulin therapy</td>
<td>154</td>
<td>7948</td>
<td>0.17</td>
<td>47K</td>
</tr>
<tr>
<td></td>
<td>All others</td>
<td>364</td>
<td>8164</td>
<td>-0.80</td>
<td>--</td>
</tr>
</tbody>
</table>
Implications

• Results of standard CEA may be misleading
  – CEAs should consider the importance of self-selection
• Provides framework to value guidelines, decision-aids, or improved patient-doctor communication to make care more consistent with patient preferences
• Suggests framework to design co-payment systems to enhance cost-effectiveness of therapies
• Provides insight into policy making for voluntary vs. involuntary interventions
Empirical Cost-Effectiveness Analysis
Non-selective Use and Empirical Cost-effectiveness

• Cost-effectiveness analyses of interventions often stratify cost-effectiveness by indication

• Yet technologies are often used non-selectively

• The actual (empirical) costs and effectiveness of an intervention may be strongly influenced by patterns of use
Example: Cox-2 Inhibitors vs. NSAIDs

<table>
<thead>
<tr>
<th></th>
<th>ΔQALY</th>
<th>ΔCOST</th>
<th>$/QALY</th>
<th>Fraction Users</th>
</tr>
</thead>
<tbody>
<tr>
<td>High Risk</td>
<td>0.085</td>
<td>4721</td>
<td>56K</td>
<td>39%</td>
</tr>
<tr>
<td>Low Risk</td>
<td>0.026</td>
<td>14123</td>
<td>537K</td>
<td>61%</td>
</tr>
<tr>
<td>Overall</td>
<td>0.042</td>
<td>11584</td>
<td>276K</td>
<td></td>
</tr>
</tbody>
</table>
## Cost-Effectiveness of Pap Smears

<table>
<thead>
<tr>
<th>Frequency</th>
<th>Increase in LE vs. no screening</th>
<th>Increase in Cost vs. no screening</th>
<th>Average Cost per Life-Yr Saved</th>
<th>Marginal Increase in LE</th>
<th>Marginal Increase in Cost</th>
<th>Marginal Cost per Life-Yr Saved</th>
<th>Percent US Women who get Pap smears who get them at this Frequency</th>
<th>Percent of Pap Smears in US given at this Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>3 years</td>
<td>70 days</td>
<td>$500</td>
<td>$2,600/LY</td>
<td>70 days</td>
<td>$500</td>
<td>$2,600/LY</td>
<td>0.18</td>
<td>0.07</td>
</tr>
<tr>
<td>2 years</td>
<td>71 days</td>
<td>$750</td>
<td>$3,900/LY</td>
<td>1 day</td>
<td>$250</td>
<td>$91,000/LY</td>
<td>0.19</td>
<td>0.16</td>
</tr>
<tr>
<td>1 year</td>
<td>71 days 8 hours</td>
<td>$1,500</td>
<td>$7,300/LY</td>
<td>8 hours</td>
<td>$750</td>
<td>$830,000/LY</td>
<td>0.63</td>
<td>0.77</td>
</tr>
<tr>
<td>Average in the US</td>
<td></td>
<td>$6,400/LY</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>
Implications of Empirical CEA for Choice of Interventions

• Need to consider how an intervention will be used in deciding if it will be welfare improving

• Highlights importance of efforts to promote selective use

• Suggests that “inferior” technologies may sometimes be preferred if their use can be better controlled
Value of Research
Value of Diagnostic Testing

Test

Don’t Test

\[ \text{Max}\{pU(T|S)+(1-p)U(N|H), \ pU(N|S)+(1-p)U(N|H)\} \]
Testing as Value of Information

Max\{pU(T|S)+(1-p)U(N|H), pU(N|S)+(1-p)U(N|H)\}
Research as Value of Information

Test

S

U(T|S)

pU(T|S)+(1-p)U(N|H)

H

U(N|H)

Don’t Test

S

Max\{pU(T|S)+(1-p)U(T|H),

pU(N|S)+(1-p)U(N|H}\}
Value of Information Approach to Value of Research

• Without information
  – Make best compromise choice not knowing true state of the world (e.g. good, bad)
    • With probability p: get $V(\text{Compromise}|G)$
    • With probability $1-p$: get $V(\text{Compromise}|B)$

• With information
  – Make best decision knowing true state
    • With probability p: get $V(\text{Best choice}|G)$
    • With probability $1-p$: get $V(\text{Best choice}|B)$

• Value of information
  $= E(\text{outcome}) \text{ with information} - E(\text{outcome}) \text{ w/o information}$
  $= \{p*V(\text{Best choice}|G) + (1-p)*V(\text{Best choice}|B)\} - \{p*V(\text{Compromise}|G) + (1-p)*V(\text{Compromise}|B)\}$
  $= \text{Value of Research}$
Practical Applications of Value of Information

- VOI requires modeling population value of information

\[ VOI = \sum_{t} \beta^t \times D(t) \times I(t) \times N_t \times IVOI \]

where

- \( \beta^t \) is time preference discount factor
- \( D(t) \) is depreciation of knowledge over time
- \( I(t) \) is extent of implementation
- \( N_t \) is number of eligible individuals in each cohort
- \( IVOI \) is individual VOI

- VOI based on decision models
  - IVOI modeled with decision model
  - UK (NICE): Alzheimer’s Disease Tx, wisdom teeth removal

- Minimal modeling approaches to VOI
  - IVOI comes (nearly) directly from clinical trial
  - US (NIH): CATIE Trial of atypical antipsychotics

- Bound with more limited data (conceptual VOI, burden of illness)
# Quantitative VOI Estimates

<table>
<thead>
<tr>
<th>Topic Area</th>
<th>VOI Estimate ($ Million)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MR in Knee Trauma</td>
<td>8</td>
</tr>
<tr>
<td>LVAD as Destination Therapy</td>
<td>8</td>
</tr>
<tr>
<td>Azithromycin vs. Augmentin in Sinusitis (ignoring costs)</td>
<td>40</td>
</tr>
<tr>
<td>Pegylated Liposomal Doxycycline in Ovarian CA</td>
<td>206</td>
</tr>
<tr>
<td>Azithromycin vs. Augmentin in Sinusitis (including costs)</td>
<td>250</td>
</tr>
<tr>
<td>Treatment of Intermittent Claudication</td>
<td>573</td>
</tr>
<tr>
<td>Cognitive Behavioral Therapy for Post-partum Depression</td>
<td>603</td>
</tr>
<tr>
<td>Typical/Atypical Antipsychotics in Schizophrenia</td>
<td>124,658</td>
</tr>
</tbody>
</table>
Thank you!