Other Designs in Biomedical Research: An Introduction to Pharmacoeconomics and Economic Evaluation

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Objectives

• Introduce some of the basic concepts of economic evaluation.
• Illustrate how evidence is used in economic evaluation, and particularly the role of modeling.

Agenda

• Why are we doing more economic evaluation?
• Demystifying pharmacoeconomics
• Role of evidence and modeling: GUSTO Case Study


• % GDP to health spending: US—15% in 2003 vs. 8.5% OECD
• Per capita spending: US—$5,287 vs. $2,193 OECD median
• Hospital beds per 1000: US—2.9 vs. 3.7 OECD median
• Physicians per 1000: US—2.4 vs. 3.1 OECD median
• Nurses per 1000: US—7.9 vs. 8.9 OECD median
• MRI units per 1000: US—8.2 vs. 5.5 OECD median
• CT scanner per mill: US—12.8 vs. 13.3 OECD median

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• Demystifying pharmacoeconomics
• Role of evidence and modelling: GUSTO Case Study

COST AND OUTCOMES EVALUATION: BASIC ECONOMICS

• Scarcity of resources
• Need to make choices: “opportunity cost”
• Decisions need to be based on comparisons of costs and benefits
• Efficiency is not the same as cost cutting
• Importance of incentives
What is Pharmacoeconomic Research?
A branch of health economics primarily concerned with assessing the cost-effectiveness of drug therapies.
- Identifies and measures all costs and outcomes (clinical, health, quality-of-life, and survival).
- Goes beyond the safety and efficacy information that has historically been collected for clinical trials.
- Compares costs and outcomes of a new drug to those of a standard intervention (which ideally is the intervention most commonly used).
- Assesses the "value for money" of projected outcomes of therapy (e.g., Go/No go Decisions, Pricing, Strategic Marketing).

### Pharmacoeconomic Modelling of Drug Therapies: Key Outcomes

<table>
<thead>
<tr>
<th>Treatment Comparison</th>
<th>Clinical/Epidemiological Events</th>
<th>Pharmacoeconomic Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Drug Therapy A</td>
<td></td>
<td>Resource Cost</td>
</tr>
<tr>
<td>vs.</td>
<td></td>
<td>Quality of Life</td>
</tr>
<tr>
<td>Drug Therapy B</td>
<td></td>
<td>Survival Benefit</td>
</tr>
</tbody>
</table>

### Types of Pharmacoeconomic Analyses

<table>
<thead>
<tr>
<th>Method of Analysis</th>
<th>Cost Measurement</th>
<th>Outcome Measurement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cost-Consequences</td>
<td>$</td>
<td>Multidimensional listing of outcomes</td>
</tr>
<tr>
<td>Cost-Minimization (CMA)</td>
<td>$</td>
<td>Equivalence demonstrated in comparative groups</td>
</tr>
<tr>
<td>Cost-Effectiveness (CEA)</td>
<td>$</td>
<td>&quot;Natural&quot; cells (life-year gained, e.g., blood glucose, blood pressure); single outcome</td>
</tr>
<tr>
<td>Cost-Utility (CUA)</td>
<td>$</td>
<td>Life years adjusted for quality of life (QALY); multiple outcomes</td>
</tr>
<tr>
<td>Cost-Benefit (CBA)</td>
<td>$</td>
<td>$: multiple outcomes combined into one value.</td>
</tr>
</tbody>
</table>

### Types of Economics / Outcomes Analyses

- **Descriptive:** Cost or Burden of Illness
- **Economic Evaluations:**
  - Cost-consequences analysis—Descriptive
  - Cost-minimization analysis—Equal outcomes
  - Cost-effectiveness analysis—Clinical outcomes
  - Cost-utility analysis—QALY outcomes
  - Cost-benefit analysis—Monetary outcomes
  - Budget impact analysis—Aggregate net cost impact
- **Patient-Reported Outcomes Assessments**
  - Health Profile—domains of quality of life
  - Preferences, satisfaction, compliance, convenience
Cost-Benefit Analysis or Cost-Effectiveness Analysis?

- Problem is measuring the benefits
  » Ideally benefits measured in same units as costs
  » But very difficult to reveal consumer valuations in terms of “Willingness to Pay”
- Cost-Effectiveness Analysis is the practical solution
  » Benefits made comparable in physical units and/or utility metric
  » Financial streams incorporated in monetary units
  » Allows comparison between alternative technologies

Cost-Effectiveness Analysis (CEA) and the Incremental CE Ratio (ICER)

- CEA in health care is about comparing two alternatives (1 & 2):
  - The ICER = Cost 2 - Cost 1
  - Outcome 2 - Outcome 1
- Costs are measured in monetary units
- Outcomes can be measured in a variety of ways but must be in the same units.

Costs (in the Numerator)

- Direct medical
  » resources involved in providing medical services to treat a condition and its side effects
  » e.g. days in hospital, surgical procedures, clinic or office visits to physician, drugs, laboratory tests, nursing home days, home health care
- Direct non-medical
  » Non-medical resources used directly in conjunction with medical care consumption
  » e.g. transportation, lodging, modifications to home
- Indirect costs
  » resource costs associated with illness that indirectly affect societal output
  » e.g. lost productivity and earnings due to morbidity and mortality

Cost-Effectiveness Analysis

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  - Outcome 2 - Outcome 1
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Cost-Consequences Analysis: Example

<table>
<thead>
<tr>
<th></th>
<th>Azathioprine</th>
<th>CellCept</th>
</tr>
</thead>
<tbody>
<tr>
<td>Costs</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rejection Treatment</td>
<td>$6,000</td>
<td>$4,000</td>
</tr>
<tr>
<td>Graft Survival/Dialysis</td>
<td>21,000</td>
<td>19,000</td>
</tr>
<tr>
<td>Drug Cost</td>
<td>1,000</td>
<td>6,000</td>
</tr>
<tr>
<td>CMV Disease</td>
<td>2,000</td>
<td>2,000</td>
</tr>
<tr>
<td>Total First Year Cost.</td>
<td>$30,000</td>
<td>$31,000</td>
</tr>
<tr>
<td>Consequences</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rejection Rate</td>
<td>48.0%</td>
<td>32%</td>
</tr>
<tr>
<td>1 Year Graft Survival</td>
<td>89.0%</td>
<td>89.0%</td>
</tr>
<tr>
<td>SF-36—Physical Function</td>
<td>71.8</td>
<td>73.8</td>
</tr>
</tbody>
</table>

Cost-Minimization Analysis

- When the treatment outcomes of two alternatives are “identical”?
- Examples:
  » brand name drug vs. generic
  » two drugs in same class

Cost-Effectiveness Analysis

- CEA in health care is about comparing two alternatives (1 & 2):
  - The ICER = Cost 2 - Cost 1
  - Outcome 2 - Outcome 1
- Costs are measured in monetary units
- Outcomes can be measured in a variety of ways but must be in the same units.
### Examples of Effectiveness Measures Used in Cost-Effectiveness Analyses

<table>
<thead>
<tr>
<th>Study Reference</th>
<th>Clinical Field</th>
<th>Effectiveness Measure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Logan et al. (1981)</td>
<td>Treatment of hypertension</td>
<td>Mm/Hg blood pressure reduction</td>
</tr>
<tr>
<td>Schulman et al. (1990)</td>
<td>Treatment of hypercholesterolaemia</td>
<td>% serum cholesterol reduction</td>
</tr>
<tr>
<td>Hull et al. (1981)</td>
<td>Diagnosis of deep vein thrombosis</td>
<td>Cases of DVT detected</td>
</tr>
<tr>
<td>Sculpher and Buxton (1993)</td>
<td>Asthma</td>
<td>Episode-free days</td>
</tr>
<tr>
<td>Mark et al (1995)</td>
<td>Thrombosis</td>
<td>Years of life gained</td>
</tr>
</tbody>
</table>

### Cost-Utility Analysis

- Expresses the outcomes in a common metric that can be used for comparing different drugs or technologies.
- Benefits captured as "quality-adjusting" life years gained (QALYs).
- There are many theoretical controversies and measurement issues in this field, but QALYs are generally seen as a reasonable, practical measure of utility to the patient.

### Health Rating Scale for Measuring Utility

Two different health situations are described in the boxes below. They are hypothetical / imaginary situations - try to imagine how you would feel in those states. For each situation (A and B) draw a line to a single point on the scale that would reflect how you would rate the situation.

**Possible / Imaginary Situation A:** Your kidney transplant has been a success. You have plenty of energy and are able to do all you would like in terms of work and leisure activities. etc. etc. etc.

**Possible / Imaginary Situation B:** Your kidney has failed and you are on dialysis. You often feel tired and sluggish. etc. etc. etc. etc.

**Possible Outcome Measure:** QALY

**Quantity and Quality Of Life (Area Under The Curve (AUC))**

The QALY concept simultaneously captures gains from reduced morbidity (quality gains) and reduced mortality (quantity gains) - 1: full health - 0: death.

### The Technology Adoption Decision

Adapted from Black (1990)

- **Strategy A** more effective and more costly than strategy O
- **Strategy A** less effective and less costly than strategy O
- **Strategy A** less effective and more costly than strategy O (cost-effective - partial cost-offset)
- **Strategy A** more effective and less costly than strategy O (cost-saving - dominant strategy)

IV  +  Cost difference  I

0  A

Strategy A more effective and more costly than strategy O

Strategy A less effective and more costly than strategy O

Strategy A less effective and less costly than strategy O

Strategy A more effective and less costly than strategy O

Adapted from Black (1990)
Some Examples of ICER

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Costs (USD)</th>
<th>Survival</th>
<th>Quality of Life</th>
<th>QALY</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>$20,000</td>
<td>4.5 years</td>
<td>0.80</td>
<td>3.6</td>
</tr>
<tr>
<td>B</td>
<td>$10,000</td>
<td>3.5 years</td>
<td>0.90</td>
<td>3.15</td>
</tr>
</tbody>
</table>

Which treatment would you select? Which outcome do you value most?

Example: Cost per Quality-Adjusted Life Year--Hemodialysis (versus No Treatment)

Cost per Year for Dialysis: $50,000

Quality Adjustment Factor for Dialysis: 0.60

Quality Adjustment Factor for Death: 0.0

C-E Ratio = Incremental Cost / Incremental Benefit

= $50,000 - 0

= $83,000/QALY

FRAMING THE PROBLEM: PERSPECTIVE AND TIME HORIZON

- Perspective: Viewpoint of study determines which data to collect:
  - Hospital
  - Health Care System
  - Payer
  - Society

- Time horizon of study should be long enough to capture main costs and effects

League Tables, Cost Per QALY Threshold, and (Economic) Value

- **League Table**
  - Ranking or listing of possible spending options based on cost-utility ratio (i.e., Cost per QALY)

- **Cost Per QALY Threshold**
  - Cost-Utility Ratio (e.g., £30,000 per QALY; or US$50,000-173,000) below which most technologies are covered.

- **Economic Value**
  - Defined as willingness to pay: cost per QALY threshold has been interpreted as Societal WTP or Value

Agenda

- Why are we doing more economic evaluation?
- Demystifying pharmacoeconomics
- Role of evidence and modelling: GUSTO Case Study
GUSTO—Clinical Trial Features

- 4 different regimens: t-PA; streptokinase+IV heparin; streptokinase+subcut. heparin; t-PA+streptokinase.
- Total sample=41,021; US sample=23,105; economic study U.S. subsample=2,600.
- Found absolute decrease of 1% in 30-day mortality from all causes to t-PA treated patients.

Clinical Results

<table>
<thead>
<tr>
<th></th>
<th>SK</th>
<th>t-PA</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>mortality</td>
<td>7.3%</td>
<td>6.3%</td>
<td>0.001</td>
</tr>
<tr>
<td>hemorrhagic stroke</td>
<td>0.52%</td>
<td>0.72%</td>
<td>0.030</td>
</tr>
<tr>
<td>mortality/ nonfatal disabling stroke</td>
<td>7.8%</td>
<td>6.9%</td>
<td>0.006</td>
</tr>
</tbody>
</table>

GUSTO—Economic Substudy Features

- US sample=23,105 (initial hospitalization); telephone follow-up survey subsample=2,600.
- Telephone follow-up at 30 days, 6 months, and 12 months for medical use and quality of life.
- Took “societal” perspective (for costs).
- Performed cost-effectiveness and cost-utility analysis.
- Survival and costs discounted at 5%.
- Medical care costs based on Duke cost accounting system and Medicare payments.
- Long-term survival (to 15 years) projected using Duke cardiovascular registry database.

t-PA versus Streptokinase

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Cost</th>
<th>Survival at 1-year</th>
<th>Projected Life Expectancy</th>
<th>Quality of Life</th>
</tr>
</thead>
<tbody>
<tr>
<td>t-PA</td>
<td>$27,420</td>
<td>91.0</td>
<td>15.41</td>
<td>0.90</td>
</tr>
<tr>
<td>Streptokinase</td>
<td>$24,990</td>
<td>89.9</td>
<td>15.27</td>
<td>0.90</td>
</tr>
</tbody>
</table>

The NNT is 110 and the CNT is $243,000 to save one life.

CEA - Data Collection

- CEA was conducted in a subset of US patients (n=2,600)
- Data collected via structured telephone interviews, followed up with source documentation
- Time points - 30 days, 6 months, 1 year
- Data collection focused on resource utilization and QoL variables

CEA - Modelling Survival

- Composite modelling approach
  - One year survival collected directly
  - Years 2-15 from Duke Cardiovascular Disease Database
  - Period beyond 15 years estimated using survival analysis
  - Age, sex, & infarct location used as covariates in survival analysis
- 5% discount rate used
CEA - Cost Analysis

- Initial hospitalization costs via Duke cost-accounting system
- Follow-up costs to one year via multiplication of average resource utilization and Medicare DRG reimbursement rates for each resource
- No cost differential after first year
- Drug acquisition costs from Red Book
- Expressed as 1993 US dollars

CEA - Quality of Life

- Dual approach used, with battery and utility measurement
- Battery included several questionnaires, focusing on different dimensions of QoL
- Utility measurement by time tradeoff method

CEA - Results

<table>
<thead>
<tr>
<th></th>
<th>SK</th>
<th>t-PA</th>
<th>Diff</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-Drug Costs</td>
<td>$24,575</td>
<td>$24,990</td>
<td>$415</td>
</tr>
<tr>
<td>Drug Costs</td>
<td>$320</td>
<td>$2,750</td>
<td>$2,430</td>
</tr>
<tr>
<td>Total Costs</td>
<td>$24,895</td>
<td>$27,740</td>
<td>$2,845</td>
</tr>
<tr>
<td>Life Yrs (undis)</td>
<td>15.27 yrs</td>
<td>15.41 yrs</td>
<td>0.14 yrs</td>
</tr>
<tr>
<td>Life Yrs (dis)</td>
<td>9.50 yrs</td>
<td>9.58 yrs</td>
<td>0.08 yrs</td>
</tr>
<tr>
<td>Cost/LYG (dis)</td>
<td>$32.678</td>
<td>$32.678</td>
<td>0.00</td>
</tr>
<tr>
<td>Utility</td>
<td>0.90</td>
<td>0.90</td>
<td>0.00</td>
</tr>
<tr>
<td>QALY (dis)</td>
<td>8.55 yrs</td>
<td>8.62 yrs</td>
<td>0.07 yrs</td>
</tr>
<tr>
<td>Cost/QALYG (dis)</td>
<td>$36,402</td>
<td>$36,402</td>
<td>0.00</td>
</tr>
</tbody>
</table>

NOTE: Numbers are rounded off, so CE ratios shown are not exact.

CEA - Sensitivity Analysis

- Parameters varied included
  - One year survival
  - Long-term survival
  - Discount rate
  - Cost differences in first year
  - Cost differences after first year
  - Utilities
  - Risk of stroke

CEA - Conclusion

- League table approach used in interpretation
- Concluded that treatment with accelerated t-PA rather than SK “... compares favorably with other therapies whose added medical benefit for dollars spent is judged by society to be worthwhile.”

  - Mark et al. (1995)

t-PA versus Streptokinase: Cost-effectiveness differs by age and location of the infarction

<table>
<thead>
<tr>
<th>Group of Patients</th>
<th>Increased Life Expectancy with t-PA</th>
<th>Cost-effectiveness Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary Analysis</td>
<td>0.14</td>
<td>$32,678</td>
</tr>
<tr>
<td>Inferior MI, age &lt; 40</td>
<td>0.03</td>
<td>$203,071</td>
</tr>
<tr>
<td>Anterior MI, age &lt; 40</td>
<td>0.04</td>
<td>$123,609</td>
</tr>
<tr>
<td>Inferior MI, age 40 - 60</td>
<td>0.07</td>
<td>$74,816</td>
</tr>
<tr>
<td>Anterior MI, age 40 - 60</td>
<td>0.10</td>
<td>$49,877</td>
</tr>
<tr>
<td>Inferior MI, age 61 - 75</td>
<td>0.16</td>
<td>$27,873</td>
</tr>
<tr>
<td>Anterior MI, age 61 - 75</td>
<td>0.20</td>
<td>$20,601</td>
</tr>
<tr>
<td>Inferior MI, age &gt; 75</td>
<td>0.26</td>
<td>$16,246</td>
</tr>
<tr>
<td>Anterior MI, age &gt; 75</td>
<td>0.29</td>
<td>$13,410</td>
</tr>
</tbody>
</table>
CONCLUSION:
Some Points to Remember

• Real-world decision-making requires a synthesis of different kinds of evidence.
• Different stakeholders pay different roles in the “system”, have different incentives, and have different needs for evidence and information.
• Increasing demand for economic evaluation
• Payers focus on value for money
• Economics helps but it does not make decisions
• Evidence from trials and the need for models
• Emerging role of pragmatic trials with CE
• Patient-centered outcomes; QOL, utility
• Need for transparency of studies
• Need to educate consumers of studies

Links to Important Information Sources

• International Society for Pharmacoeconomics and Outcomes Research (www.ispor.org)
• Center for Health System Change (www.hschange.org)
• Journal Health Affairs (www.healthaffairs.org)
• Academy of Managed Care Pharmacy (www.amcp.org)
• UK National Institute of Clinical Excellence (www.nice.org.uk)
• Harvard CEA Registry (www.hsph.harvard.edu/cearegistry/)

Thank you!

Questions?