Outcomes Research

- Evaluates outcomes of medical therapies (potentially including costs) and their impacts on people, organizations, and society
- Therapies can include drugs, devices, procedures, or broader programmatic or system interventions
- Outcomes can include mortality, morbidity, functional status, mental well-being, other aspects of health-related quality of life, cost, etc.

Pharmacoconomics
Pharmacoeconomics

- Outcomes research specifically focused on economic outcomes of pharmaceuticals
- Multidisciplinary methods
  - Medicine
  - Pharmacy
  - Economics
  - Decision sciences
  - Operations research
  - Statistics / biostatistics
  - Other social sciences

Pharmacoeconomic Messages

- Therapy is good/bad value
- Budget impact
- Burden of illness
  - Often flag waving: “This disease is important…”
- Specific messages addressed depend in part on:
  - Disease and therapy under evaluation
  - Other therapies available to treat condition
  - Interest of regulatory bodies, providers, payers, and patients

Pharmacoeconomic 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
Pharmacoeconomics Methods Overview

Economic Evaluation Methods Overview
• Types of analyses
• Types of outcomes
• Perspective
• Steps in economic evaluation

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

• 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 solely when two therapies of equal efficacy are compared

Death of Cost-Identification?

• Old version: If two therapies’ effects are identical, adopt cheaper of two therapies
  – Effect maximization corollary: If two therapies’ costs are identical, adopt more effective of two
• New version: Because we generally can’t conclude two therapies are identical (at most we fail to reject null hypothesis), cost-minimization analysis is unlikely to ever be appropriate
  – Substitute cost-effectiveness or cost-benefit analysis

Cost-Effectiveness Analysis

• Estimates differences in costs and differences in outcomes between interventions
  – Costs and outcomes measured in different units
• Incremental cost-effectiveness ratio
  \[
  \frac{\text{Costs}_1 - \text{Costs}_2}{\text{Effects}_1 - \text{Effects}_2}
  \]
• Results meaningful in comparison with:
  – Predetermined threshold/cut-off for willingness to pay
    • e.g., $50k-$100k / QALY or £20k-£30k / QALY
  – Other accepted and rejected interventions (league tables)
Cost-Utility Analysis

- Costs and outcomes measured in different units AND outcomes expressed in units of utility (e.g., QALYs)
- Referred to either as a fourth type of analysis or as a subset of cost-effectiveness analysis

Cost-Benefit Analysis

- Estimates differences in costs and differences in benefits in same (usually monetary) units
- As with cost-effectiveness, requires a set of alternatives
- Net benefit is preferred expression cost-benefit result
  \[- (Benefit_1 - Benefit_2) - (Cost_1 - Cost_2)\]

Types of Costs

- Direct: medical or nonmedical
- Time costs: Lost due to illness or to treatment
- Intangible costs
- Types of costs 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
What Effectiveness Measure?

- Can calculate a ratio for any outcome
  - Cost per toe nail fungus day averted
- For cost-effectiveness ratios to be an informative, must know willingness to pay for outcome
  - In many jurisdictions, quality-adjusted life year (QALY) is recommended outcome of cost-effectiveness analysis
- Some resistance to this outcome, particularly from U.S. Congress
  - [PCORI] “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”

Study Perspective

- Economic studies should adopt 1 or more “perspectives”
  - Societal
  - Payer (often insurer)
  - Provider
  - Patient
- Perspective helps identify services that should be included in analysis and how services should be cost out
  - e.g., patient out-of-pocket expenses may be excluded from insurer perspective
  - Not all payments may represent costs from societal perspective

Steps in Economic Evaluation

Step 1: Quantify costs of care
Step 2: Quantify outcomes
Step 3: Assess whether and by how much average costs and outcomes differ among treatment groups
Step 4: Compare magnitude of difference in costs and outcomes and evaluate “value for costs”
  - e.g. by reporting a cost-effectiveness ratio, net monetary benefit, or probability that ratio is acceptable
  - Potential hypothesis: Cost per quality-adjusted life year saved significantly less than $75,000
Step 5: Perform sensitivity analysis
What Data / When?

• Phases I and II
  – Incidence and prevalence-based burden of illness
    • Incidence-based - lifetime costs of the disease for a cohort with incident disease
    • Prevalence-based - costs of disease during a given time period for prevalent cases
  – Natural history modeling
  – Preplanning for phase III economic studies

Phase III

• Cost / Efficacy studies in clinical trials
  – Provides economic data for registration, pricing, and early use
• Decision modeling of impacts of intervention
• Budget impact studies
Phase IV

- Cost / Effectiveness studies in usual care
  - Comparisons made in more realistic settings with more realistic protocols against comparators of interest to individual decision makers
  - Allow decision makers to assess whether economic results from phase III trials are generalizable to usual care
- Decision modeling of impacts of intervention
- Post marketing surveillance studies
  - Observational data to evaluate costs, effectiveness, and adverse experiences related to the drug

Who is Listening?

- PE Recommendations/Guidelines (Partial list)
  - Australia
  - Austria
  - Brazil
  - Baltic countries
  - Belgium
  - Brazil
  - China
  - Denmark
  - Egypt
  - Finland
  - France
  - Hungary
  - Italy
  - Mexico
  - Netherlands
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Use in US

- Common Belief: “Pharmacoeconomic data not used in US”
  - NIH expert guideline panels and Environmental Protection Agency can and do use
  - Chambers et al.: Lack of an estimate of cost-effectiveness associated with a decreased likelihood of Medicare coverage
  - 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
  - Academy of Managed Care Pharmacy guidelines for pharmacoeconomic submissions to formularies

Alsultan: Role of Pharmacoeconomics in Saudi Arabian Formulary Decision Making *

- Decision Criteria
  - Efficacy: 98% very/extremely important
  - Safety: 98% very/extremely important
  - Acquisition cost: 86% important/very important
  - Other: 33% very/extremely important
- Ever used PE data: 75% yes
- Data usefulness: 39% very/extremely helpful
- Influence of data: 25% very/extremely influential
- Knowledge: 8% very/extremely knowledgeable

*Lafii et al.: Jordan Rational Drug List *

- No formal requirement for use of pharmacoeconomic data
- Pharmacoeconomic evidence “not influential” in formulary decisions
- Recommendations:
  - Enhance capacity for generating, accessing, and/or applying health economic analysis to priority setting decisions
  - Remove organizational and structural impediments


Sources of Pharmacoeconomic Data

- Self generation by local experts
  - ISPOR chapters
- Multinational trials
- International collaborations between local scientists and scientists in other countries
  - Sunday’s rotavirus example
  - Nice International
- Data borrowed from elsewhere
  - Transferability

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Pichon-Riviere: Latin America Transferability Survey

<table>
<thead>
<tr>
<th>Transferability of</th>
<th>Researchers</th>
<th>Decision Makers</th>
</tr>
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<tbody>
<tr>
<td>Economic Evaluation</td>
<td>6.8</td>
<td>6.5</td>
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<tr>
<td>Budget Impact</td>
<td>5.9</td>
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<tr>
<th>Barriers to Use</th>
<th>Researchers</th>
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</tr>
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<tr>
<td>Healthcare cost differences</td>
<td>6.6</td>
<td>7.9</td>
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<td>Epidemiology differences</td>
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</tr>
<tr>
<td>Health care system diff</td>
<td>6.5</td>
<td>7.8</td>
</tr>
</tbody>
</table>

1 = not useful/less transferable; 10 = very useful/more transferable

Summary

• International use of pharmacoeconomic data growing
  – Improve value of healthcare
  – Manage healthcare budgets
• Multidisciplinary science: medicine, pharmacy, economics, decision sciences
• General methods well developed, but some areas – such as how best to transfer data across settings – still undergoing development
• Opportunities for data collection available throughout the drug development process
• International need for education of researchers, decision makers, and the general public