PHARMACOECONOMICS

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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.

Pharmacoeconomics

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."

    Lazarro et al. Archivio Italiano di Urologia, Andrologia. 2007:79:104-7
- 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?

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?

Who is Listening

- PE Recommendations/Guidelines (Partial list)
  - Australia
  - Austria
  - Brazil
  - Baltic countries
  - Belgium
  - Brazil
  - China
  - Denmark
  - Egypt
  - Finland
  - France
  - Hungary
  - Italy
  - Mexico
  - Netherlands
  - Norway
  - Poland
  - Russia
  - South Korea
  - Spain
  - Sweden
  - Taiwan
  - Thailand
  - U.K.

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 knowledgable

* Alsultan MS. The role of pharmacoeconomics in formulary decision making in different hospitals in Riyahd, Saudi Arabia. Saudi Pharmaceutical Journal. 2011;19:51-56.

Lafi 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

* Lafi R, Robinson Sm Williams I. Economic evaluation and the Jordan Rational Drug list: an exploratory study in national-level priority setting. Value Health. 2012;15:771-6.

Sources of Pharmacoeconomic Data

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

Pichon-Riviere: Latin America Transferability Survey

	Researchers	Decision Makers
Transferability of		
Economic Evaluation	6.8	6.5
Budget Impact	5.9	5.9
Barriers to Use		
Healthcare cost differences	6.6	7.9
Epidemiology differences	6.1	7.5
Health care system diff	6.5	7.8

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

Pichon-Riviere A, Augustovski F. Transferability of health technology assessment reports in Latin America. Int J Tech Assess in Health Care. 2012;28; 180-6.

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