Introduction to Cost-effectiveness Analysis

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Health Economic Evaluation

• The comparative analysis of alternative courses of action in terms of both their costs and consequences in order to assist policy decisions (Drummond et al)
1. Identify, measure and value costs and consequences
2. Comparison – Cost-effectiveness efficiency
3. Assist – not replace – decision making

Types of Economic Evaluation

<table>
<thead>
<tr>
<th>Types of Analysis</th>
<th>Costs</th>
<th>Consequences</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cost-Minimization</td>
<td>Monetary</td>
<td>Identical in all respects</td>
<td>Least cost alternative</td>
</tr>
<tr>
<td>Cost-Effectiveness</td>
<td>Monetary</td>
<td>Different magnitude of a common measure, e.g., LY gained, blood pressure reduction</td>
<td>Cost per unit of consequence; e.g., cost per LY gained</td>
</tr>
<tr>
<td>Cost-Utility</td>
<td>Monetary</td>
<td>Single or multiple effects (combined into a weighted index); valued as “utility” e.g., QALY</td>
<td>Cost per unit of consequence; e.g., cost per QALY gained</td>
</tr>
<tr>
<td>Cost-Benefit</td>
<td>Monetary</td>
<td>Same as CUA but valued in money (WTP)</td>
<td>Net $ cost: benefit ratio</td>
</tr>
</tbody>
</table>

Costs: Types of Costs

Types of Costs

- Total Cost
- Direct Cost
- Indirect Cost
- Intangible Cost
- Direct Medical Cost
- Direct Non-medical Cost
- Fixed Cost
- Semifixed Cost
- Variable Cost

- Capital and Overheads
- Staff
- Drugs
- Disposable equipment

Costs: Measurement

- Perfectly competitive market, price = opportunity cost
- Imperfections in health care market: price is not equal to opportunity cost
  - Examples: monopoly hospital charges, monopoly physician fees, negotiated drug prices, labour markets are imperfect, subsidy, inefficiencies in production, etc.
- Use of unadjusted prices introduce bias
- Need to use shadow prices/ social value of resources (perspective is important)
Costs: Perspectives

- Perspectives
  - Societal
  - Other Agencies
  - Health System
  - Hospital/Practice
  - Patient

Costs: Practical

- US: use cost-to-charge ratio
  - Cost-to-charge ratios are coefficients developed by expert panels to convert charges for medical services to their true economic costs
  - It produces average estimates of true costs
  - Per diem or average cost are used in numerous studies — less precise

Discounting

- Future streams of costs need to be discounted to reflect time preference and presented in terms of their present value
- Discounted present value of a stream of costs (year-begin):
  \[ \sum_{t=1}^{T} \frac{1}{(1+r)^t} \times \text{Cost}_t \]
- Similarly, discounted present value of a stream of effects:
  \[ \sum_{t=1}^{T} \frac{1}{(1+r)^t} \times \text{Effect}_t \]

Discounting

- Future costs should be discounted
  - Range 3-5% in the literature
  - Carry out sensitivity analysis
- Economists do not agree that health outcomes should be discounted
  - And those who agree, disagree about the rate
  - One recommendation: discount at the same rate and carry out sensitivity analysis

Annualising Capital Costs

- Capital costs represent an investment in asset which is used over time
- Two components
  - Opportunity cost of initial investment
  - Depreciation over time
- Annual economic cost = cost/annualising factor
  \[ E = \frac{K}{A(n,r)}; A(n,r) = \frac{1-(1+r)^{-n}}{r} \] if cost $1,200, expected length of life 9 years, discount rate 6%, annual cost = $176.43

Indirect Cost/ Productivity Cost

- Indirect costs are generally productivity costs for the patient and family
- How do we value productivity costs?
- Human Capital Approach (HC)
- Friction Cost Approach (FC)
- The US Panel Approach — synthesis of HC and FC approaches
Costs: Data Sources

- **Data Sources**
  - RCTs
  - Observational Studies
  - Administrative Databases
    - CIHI, Provincial Health Admin Data
  - Literature
  - Expert opinion
- **Depends on:**
  - Study question
  - Research Resources

Accuracy of Costing

- **Micro-costing**
  - Each component of resource use is estimated
  - Corresponding unit costs are derived
- **Case-mix group**
  - Cost for each category of case
- **Disease-specific per diem**
  - Average daily treatment cost in each disease
- **Average per diem**
  - Averages the per diem over all patients
  - Choice is dependent on availability of data & resources

Cost-effectiveness Analysis (CEA)

- In CEA, Health outcomes are measured in natural physical units
  - Compare different programs aimed at the same health problem -- e.g., number of cancer cases detected through screening programs; lost days averted due to endoscopic versus open carpal tunnel release.
  - Compare different programs, aimed at different problems, but with outcomes of the same type -- e.g., kidney dialysis versus coronary care units versus smoking programs for saving lives.

CEA Examples

- **General Outcome Measures**
  - Life-years Gained
  - Disability Days Avoided
    - Influenza immunization program versus community safety education program
  - Intermediate outcomes: Cases Averted; # of Asthma attacks avoided; change in infection rate; percentage reduction in blood pressure
  - Intermediate effects could be problematic – establish a link between intermediate effects and final outcomes
  - QALY is preferable

Incremental Cost-effectiveness Ratio (ICER)

- **ICER**
  \[
  ICER = \frac{Cost_{new} - Cost_{old}}{Effect_{new} - Effect_{old}} = \frac{\Delta C}{\Delta E}
  \]
  - \(\Delta C\) = Incremental resources required by the intervention
  - \(\Delta E\) = Incremental health effects gained by the health intervention
  - ICER: how much does it cost to get a unit of effect?
- **Ratio of difference in expected cost to difference in expected effectiveness**

Example

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Tx A</th>
<th>Tx B</th>
</tr>
</thead>
<tbody>
<tr>
<td>Live 1</td>
<td>350k</td>
<td>180k</td>
</tr>
<tr>
<td>Live 2</td>
<td>200k</td>
<td>80k</td>
</tr>
<tr>
<td>Die 1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Die 2</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

- **Tx A**
  - Expected cost = \((0.9 \times 350k) + (0.1 \times 200k) = 335k\)
  - Expected eff. = \((0.9 \times 10) + (0.1 \times 0) = 9.0\) yrs
- **Tx B**
  - Expected cost = \((0.8 \times 180k) + (0.2 \times 80k) = 160k\)
  - Expected eff. = \(0.8 \times 6 + 0.2 \times 0 = 4.8\) yrs

IC = 175k; IE = 4.2; IC/IE = 41,667

It costs $41,667 per additional life year to move from TxB to TxA.
Dominance

- Dominance \( \Delta E \)

<table>
<thead>
<tr>
<th>More ( \Delta C )</th>
<th>More</th>
<th>Same</th>
<th>Less</th>
</tr>
</thead>
<tbody>
<tr>
<td>Added effect</td>
<td>7</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td>worth added cost?</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- \( \Delta C \)

<table>
<thead>
<tr>
<th>More ( \Delta C )</th>
<th>Same</th>
<th>Less</th>
</tr>
</thead>
<tbody>
<tr>
<td>3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Accept Treatment</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(weak dominance)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- Other reasons to adopt treatment?

<table>
<thead>
<tr>
<th>More ( \Delta C )</th>
<th>Same</th>
<th>Less</th>
</tr>
</thead>
<tbody>
<tr>
<td>9</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Accept Treatment</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(weak dominance)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- \( \Delta C \)

<table>
<thead>
<tr>
<th>More ( \Delta C )</th>
<th>Same</th>
<th>Less</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Accept Treatment</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(strong dominance)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- Is reduced effect acceptable given reduced cost?

<table>
<thead>
<tr>
<th>More ( \Delta C )</th>
<th>Same</th>
<th>Less</th>
</tr>
</thead>
<tbody>
<tr>
<td>6</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Accept Treatment</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(weak dominance)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- \( \Delta C \)

<table>
<thead>
<tr>
<th>More ( \Delta C )</th>
<th>Same</th>
<th>Less</th>
</tr>
</thead>
<tbody>
<tr>
<td>8</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Accept Treatment</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(strong dominance)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The Cost-effectiveness Plane

New treatment more costly (+)

- New treatment more effective (+)
- Existing treatment more effective (+)
- Maximum WTP per unit of effect

New treatment less costly (-)

- New treatment less effective (-)
- Existing treatment more effective (+)
- Maximum WTP per unit of effect

Cost-effective Treatment

Maximum WTP per unit of effect

Valuation

- Valuation is determined by benefits sacrificed elsewhere (opportunity cost)
- Valuation requires a trade-off between benefits
- Valuation either in terms of
  - Utility (e.g., QALY)
  - Money (e.g., WTP)
QALY Gained from an Intervention

QALY
- Adjust quantity of life years saved to reflect a valuation of the quality of life
- If healthy, QALY = 1; unhealthy, QALY < 1
- Identify possible health states – consider all relevant dimensions of QoL
- Derive utility weights for each state
- Multiply life years (spent in each state) by weight for that state

Combining Quality of Life with Length of Life

How Are Utility Values Determined?
- Judgment
- Values from the literature
- Direct measurement of preferences
- Use a multi-attribute utility instrument to assign quality of life scores (utilities) to health states
  - Health Utilities Index (HUI)
  - EQ-5D (Euroqol)
  - SF-6D (based on SF-36)
  - QWB (Quality of Well-Being)
  - AQoL (Assessment of Quality of Life)
- Undertake new measurement of utilities
  - Can tailor to your study outcomes, but it may be complex and costly

Measuring Preferences
- Stated preference methods
  - Favoured by Psychologists
  - Direct scaling of alternative health states
  - Rating Scale (RS) or Visual Analogue Scale (VAS)
- Revealed preference methods
  - Favoured by Economists; philosophy is that choices reveal preferences (and hence utility)
  - The Time Trade-off (TTO)
    - Certainty, time-based choices
  - The Standard Gamble (SG)
    - Uncertainty, risk-based choices

Monetary Values
- Three Techniques for Shadow Pricing
  - The Human Capital Approach
    - Based on the present value of future earnings
    - Easy to calculate, but ethically indefensible and theoretically inconsistent
  - The Revealed Preference Method (WTA & WTP)
    - Based on observed wealth-risk trade-offs
    - Accounts for “real” preferences/values, but difficult control for confounders
  - The Contingent Valuation Method (WTA & WTP)
    - Based on direct survey
    - Direct valuation is possible, but based on hypothetical survey
    - Discrete Choice Experiments
Uncertainty

- Uncertainty surrounding everything
  - Health Outcomes
  - Probabilities of various health outcomes
  - Resource utilization
  - Costs
  - Discount rate
- Need to analyze if this uncertainty really matters
  - One-way (univariate), two-way (bivariate); or multi-way (multivariate) sensitivity analysis
  - Deterministic Sensitivity Analysis
    - How variation in parameter values affect the results
  - Probabilistic Sensitivity Analysis
    - How parameter distributions affect the results

Decision Analytic Modelling

- We have to make decisions about alternative courses of actions that have uncertain health outcomes and costs
- Decision analytic modelling is about making these decisions explicit while considering the consequences of these decisions
- Three Types of Models:
  - The Decision Tree
  - The Markov Model
  - Markov Model & Time
  - The Microsimulation Model

Decision Tree Example 1

- Example: Breast Cancer Screening Outcomes

<table>
<thead>
<tr>
<th></th>
<th>Cancer</th>
<th>No Cancer</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive</td>
<td>True Positive (A)</td>
<td>False Positive (B)</td>
<td>A+B</td>
</tr>
<tr>
<td>Negative</td>
<td>False Negative (C)</td>
<td>True Negative (D)</td>
<td>C+D</td>
</tr>
<tr>
<td>Total</td>
<td>A+C</td>
<td>B+D</td>
<td>A+B+C+D</td>
</tr>
</tbody>
</table>

Sensitivity = A/(A+C)
Specificity = D/(B+D)

Breast Cancer Screening: Decision Tree

- P(D+) = prob of having cancer = 0.004; 1– P(D+) = (1-0.004)
- Sensitivity = 0.829; specificity = 0.855

Breast Cancer Screening: ICER

<table>
<thead>
<tr>
<th>Strategy</th>
<th>Mean Cost (QALY)</th>
<th>Incremental Cost (QALY)</th>
<th>Mean Effect (QALY)</th>
<th>Incremental Effect (QALY)</th>
<th>ICER</th>
</tr>
</thead>
<tbody>
<tr>
<td>No Screening</td>
<td>$36.38</td>
<td></td>
<td>0.882</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Biennial Screening</td>
<td>$46.81</td>
<td>$10.43</td>
<td>0.9165</td>
<td>0.0283</td>
<td>$369</td>
</tr>
</tbody>
</table>

Breast Cancer Screening: Uncertainty

- Sensitivity of the test: 0.740 – 0.890
- As the sensitivity of the screening procedure increases, the ICER of biennial vs. no screening falls from $421 to $333, implying an improved cost-effectiveness
Breast Cancer Screening: Uncertainty

- Specificity of the test: 0.839 – 0.901
  - As the specificity of the screening procedure increases, the ICER of biennial vs. no screening falls from $455 to $187, implying an improved cost-effectiveness.

Decision Tree Example 2: Carpal Tunnel Syndrome

- Prevalence of CTS: 1-8%
- Open surgery
  - Relatively less expensive
  - Entails significant morbidity
  - Complications are expensive
- Endoscopic technique
  - Relatively more expensive
  - Reduced morbidity if successful
  - Complications are expensive


**Vasen et al (1999): Base Case Scenario**


**Vasen et al (1999): Sensitivity analysis on probability of career ending due to complications (i.e., Nerve Laceration)**
Vasen et al (1999): Sensitivity analysis on days lost due to complications

Base Case: 365 days

Strengths and Weaknesses of Decision Trees

- **Strengths of Decision Trees**
  - Intuitive and visual form of the model
  - Quick and easy to generate results
  - Appropriate when there are limited number of health states and relatively short model duration

- **Weaknesses of Decision Trees**
  - Elapse of time not explicit in decision trees
  - Tree can become unwieldy if:
    - events repeat
    - many possible outcomes or health states
    - the sequence of events is too long and complicated, likely to occur when modelling treatment of chronic diseases
    - the study perspective is long-term in nature

Markov Model: Example 1

- Bubble diagram; State A: 200<CD4<500; State B: Cd4 <200; State C: AIDS; State D: Dead
- Arrows represent transitions

Transition Probabilities

<table>
<thead>
<tr>
<th></th>
<th>State A</th>
<th>State B</th>
<th>State C</th>
<th>State D</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Monotherapy</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>State A</td>
<td>0.721</td>
<td>0.202</td>
<td>0.067</td>
<td>0.01</td>
</tr>
<tr>
<td>State B</td>
<td>0</td>
<td>0.581</td>
<td>0.407</td>
<td>0.012</td>
</tr>
<tr>
<td>State C</td>
<td>0</td>
<td>0</td>
<td>0.75</td>
<td>0.25</td>
</tr>
<tr>
<td>State D</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1.0</td>
</tr>
<tr>
<td><strong>Combination Therapy</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>State A</td>
<td>0.858</td>
<td>0.103</td>
<td>0.034</td>
<td>0.005</td>
</tr>
<tr>
<td>State B</td>
<td>0</td>
<td>0.787</td>
<td>0.207</td>
<td>0.006</td>
</tr>
<tr>
<td>State C</td>
<td>0</td>
<td>0</td>
<td>0.873</td>
<td>0.127</td>
</tr>
<tr>
<td>State D</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1.0</td>
</tr>
</tbody>
</table>

Annual Costs

Monotherapy/ Combination Therapy

<table>
<thead>
<tr>
<th></th>
<th>State A</th>
<th>State B</th>
<th>State C</th>
<th>State D</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Monotherapy</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Direct</td>
<td>£1701</td>
<td>£1774</td>
<td>£6948</td>
<td>-</td>
</tr>
<tr>
<td>Community</td>
<td>£1055</td>
<td>£1278</td>
<td>£2039</td>
<td>-</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>£2756</strong></td>
<td><strong>£3052</strong></td>
<td><strong>£9007</strong></td>
<td>-</td>
</tr>
</tbody>
</table>

Monotherapy Drug Costs = £2278
Combination Therapy Drug Costs = £2087

Outcomes were assessed in terms of changes in mean survival duration, so no HRQoL Costs are discounted at 6%

HIV Example Results

- **Monotherapy**
  - Expected LYs = 7.99
  - Expected Cost = £44,663

- **Combination Therapy**
  - Expected LYs = 8.94
  - Expected Cost = £50,602

- **Gained LYs = 8.94-7.99 = 0.95**
- **Increased Cost = £50,602 - £44,663 = £5,938**
  - Estimated ICER = £6,276
Markov Model: Example 2

- Bubble diagram; Arrows represent transitions (Briggs and Sculpher, 1998)

Using PSA to Assess Uncertainty

- cAsymp: mean = 500; SD = 127.6 (Gamma Dist.)
- cProg: mean = 3000; SD = 510.2 (Gamma Dist.)
- cDrug: mean = 1000; SD = 102.0 (Gamma Dist.)
- uAsymp: mean = 0.95; SD = 0.026 (Beta Dist.)
- uProg: mean = 0.75; SD = 0.077 (Beta Dist.)
- tpProg: mean = 0.01; SD = 0.003; CI [0.005 - 0.015] (Log-normal)
- tpDcm: mean = 0.15; SD = 0.026 (Beta Dist.)
- Effect: mean = 0.5; SD = 0.051; CI [0.4 - 0.6] (Log-normal)

PSA Results (10,000 simulations)

- No Drug Arm
  - Mean Cost = £12,130 (Std Dev = £1,927)
  - Mean Effect = 9.24 QALYs (Std Dev = 0.52 QALYs)
- Drug Arm
  - Mean Cost = £20,899 (Std Dev = £2,006)
  - Mean Effect = 10.50 QALYs (Std Dev = 0.49 QALYs)

Distributions of ICERs

- At WTP = 6k, 80% of our simulation points recommend No Drug Therapy
- At WTP = 9k, 90% of our simulation points recommend Drug Therapy
Markov Model: Example 3

- E. Ewara, G. Zaric, S. Welch and S. Sarma (under review)
  - Colorectal Cancer: second most common cause of cancer death in Canada; 22,000 new cases in 2011
  - 15-25% of patients metastatic
  - 40-50% will develop metastases
  - First-line treatment for metastatic Colorectal Cancer in Ontario: Bevacizumab plus FOLFIRI
  - Two Alternative Options:
    - Cetuximab plus FOLFIRI
    - Panitumumab plus FOLFIRI

The Data

- Cohort of interest 1,216 patients
  - Diagnosed with MCRC in 2008 or 2009.
  - Received first-line Bevacizumab + FOLFIRI
  - ICES CD-link data
- Randomized Clinical Trial data
  - First-line Cetuximab + FOLFIRI
  - First-line Panitumumab + FOLFIRI
  - Second-line FOLFOX and FOLFOX + Bevacizumab
  - Third-line Panitumumab
  - Best-Supportive Care

Transition Probabilities and Costs

- Survival Analysis
  - Two year follow-up from date of diagnosis
    - 1st line Bevacizumab + FOLFIRI PFS
  - Weibull Distributions fit to Kaplan-Meier curves
  - Determine monthly state-dependent transition probabilities
  - Average monthly state-dependent direct medical costs: Hospitalizations, Cancer Clinic Visits, physician Costs, Home Care Visits, ODB Drug costs, Cancer Drug Costs
- Utilities were determined from literature
- Costs and utilities were discounted at 5%
### The Results

<table>
<thead>
<tr>
<th>Treatment Strategy</th>
<th>Cost</th>
<th>QALY</th>
<th>ICER</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bevacizumab + FOLFIRI</td>
<td>$150,573</td>
<td>1.749</td>
<td></td>
</tr>
<tr>
<td>Cetuximab + FOLFIRI</td>
<td>$153,731</td>
<td>1.741</td>
<td>Dominated</td>
</tr>
<tr>
<td>Panitumumab + FOLFIRI</td>
<td>$173,931</td>
<td>1.716</td>
<td>Dominated</td>
</tr>
</tbody>
</table>

**Thank You**