Overview of Decision Analysis and Its Application

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Outline
I. Decision Analysis
   - Background, Key Attributes, When to Use, Advantages, Limitations, Typical Steps
II. A Straightforward, Deterministic Example
   - Methodology, Results Presentation, Validation
IV. Conclusion and Summary

I. Decision Analyses

Decision Analysis

- Background
  - A systematic approach to decision making under conditions of uncertainty
  - Provides a formal, transparent, and orderly analytic approach to assist the decision maker in identifying the preferred course of action from competing alternatives

- Long history within public and private sectors
- Used in healthcare technology assessment to inform decision making at both individual and population levels
- At its essence, a 'simulated, mathematical, disease state model'
- May utilize expert opinion, literature-based results, data from prospective or retrospective analyses

- What is the effectiveness of a new treatment?
- What are the chances of an adverse event?
- What are the costs associated with treatment failure?
- How cost-effective are treatment alternatives?
- What statistical distributions surround costs, probabilities, or outcomes?
- What impact might random error have upon cost-effectiveness?
- Based on my threshold to pay for health care, is this a cost-effective option?

‘The aggregate of experts has been the traditional source of all the errors through medical history.’
- Forester
**Decision Analysis**

### Key Attributes

- All relevant aspects of the decision and relevant strategies are *explicitly* articulated:
  - Base Case
  - Perspective
  - Time Horizon
  - Treatment strategies
  - Probabilities
  - Costs
  - Outcomes
  - Uncertainty

### When to use?

- When randomized clinical trials (RCTs)...
  - Do not sufficiently capture data needed to support pharmacoeconomic decision making
  - Measure only surrogate outcomes
  - Compare treatments only to placebo (or less than gold standard)
- When analysts want...
  - To predict routine clinical care (effectiveness) from RCT data (efficacy)
  - To examine institution-specific results
  - To identify optimal strategies based on value

### Advantages

- Timely
- Inexpensive
- Ethical
  - May compare treatment options without additional RCTs
- Ability to synthesize current state of knowledge

### Limitations

- Potentially complicated structural and content validity aspects
- “Black-box” perception
- Potential for bias with discretionary nature of methods and data selection
- Method of combining data or synthesizing the current state of knowledge?
- Reliability of estimates
  - Results are only as robust as underlying model structure and data permit
  - Often requires assumptions to be made

### Typical Steps in Conducting a Decision Analysis

1. Establish the research question
2. Define the perspective (i.e., ‘Costs to whom’)
3. Define the base case(s) of analysis (e.g., patient and disease characteristics)
4. Specify treatment modalities and choose appropriate comparator(s) (e.g., least costly, standard of care, most-commonly used)
5. Model the disease state, define the time horizon, and choose surrogate and/or final outcomes
6. Populate the model with probabilities, costs, and outcome data
7. Verify the model, calculate and report results
8. Conduct additional sensitivity analyses

### ‘Straightforward’ Example
Scenario

You have been asked to compare two treatment options. Drug A is an agent that has been on the market for over 5 years and Drug B is a new product recently approved for prescribing. Using the data available below, employ decision analysis techniques to compare the cost-effectiveness of these two treatments.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Drug A</th>
<th>Drug B</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cure rate</td>
<td>70%</td>
<td>60%</td>
</tr>
<tr>
<td>Significant adverse event rate</td>
<td>20%</td>
<td>10%</td>
</tr>
<tr>
<td>Cost per course of treatment</td>
<td>$100</td>
<td>$150</td>
</tr>
<tr>
<td>Cost to treat adverse event</td>
<td>$25</td>
<td>$25</td>
</tr>
<tr>
<td>Cost of a treatment failure</td>
<td>$200</td>
<td>$200</td>
</tr>
</tbody>
</table>

Tasks

Steps in this ‘deterministic’ example

To obtain the:
1. Structure of the decision tree
2. Path probabilities
3. Path costs
4. Average costs of Drug A and Drug B
5. ‘Average’ effectiveness of Drug A and Drug B
6. Average cost-effectiveness of Drug A and Drug B
7. Incremental cost-effectiveness of the Drug B versus Drug A

Decision Tree Structure

Outcomes

Path Probabilities

Path Costs
### Average Costs

<table>
<thead>
<tr>
<th>Path</th>
<th>No ADR</th>
<th>ADR</th>
<th>Cure</th>
</tr>
</thead>
<tbody>
<tr>
<td>No ADR</td>
<td>0.8</td>
<td>0.2</td>
<td>0.7</td>
</tr>
<tr>
<td>ADR</td>
<td>0.8</td>
<td>0.1</td>
<td>0.3</td>
</tr>
<tr>
<td>Drug A</td>
<td>0.9</td>
<td>0.1</td>
<td>0.1</td>
</tr>
<tr>
<td>Drug B</td>
<td>0.9</td>
<td>0.1</td>
<td>0.1</td>
</tr>
</tbody>
</table>

#### Base Case

- **Tx Success** = 1 * (0.8 * 0.7) = 0.56
- **Tx Success** = 1 * (0.9 * 0.9) = 0.81

#### Average Costs (in $)

- **Drug A**: $165.00
- **Drug B**: $172.50

#### Multiply 'Path Probabilities' by 'Path Costs' and sum to yield 'Average Cost' for each pathway.

### Average Effectiveness

<table>
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<th>Cure</th>
</tr>
</thead>
<tbody>
<tr>
<td>No ADR</td>
<td>1.0</td>
<td>0.0</td>
<td>0.7</td>
</tr>
<tr>
<td>ADR</td>
<td>0.1</td>
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<tr>
<td>Drug B</td>
<td>0.9</td>
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### ‘Final’ Solution

**Average Cost-Effectiveness Ratio (Drug A)**

- Avg Cost Drug A / Avg Effect Drug A
- $210.56 per Treatment Success (i.e., cure without adverse drug event)

**Average Cost-Effectiveness Ratio (Drug B)**

- Avg Cost Drug B / Avg Effect Drug B
- $272.80 per Treatment Success (i.e., cure without adverse drug event)

**Incremental Cost-Effectiveness Ratio (ICE)**, Drug B versus Drug A

- ($272.80 - 165.00) / $(0.81 - 0.56)
- $70 per additional Treatment Success for Drug B versus Drug A

### III. ‘Actual’ Methodologies and Quality Assurance

#### Methodologies

- **Deterministic versus Stochastic**
  - **Deterministic**
    - Fixed parameters
    - Some results obtained each time
  - **Stochastic**
    - Includes randomness
    - Results may vary
- **Monte Carlo Simulations**
  - Assists in dealing with variability and uncertainty in models
  - Involves cycling cases through the model, seeking “random draws”
    - Often, n = 1,000, 5,000, or 10,000

#### Methodologies

- **Two ‘basic’ types of uncertainty**
  1) **Structural uncertainty**
     - Involves simplifying complex courses of treatment and disease states
  2) **Parameter uncertainty**
     - Defining, propagating, and presenting uncertainty throughout the model
     - **Probabilistic Sensitivity Analysis (PSA)**
       - Includes uncertainty of parameters with distributions in the model itself
         - Beta distribution : Bound by (0, 1)
         - Gamma distribution : Bound by (0, infinity)
         - Gaussian distribution : Standard normal curve
         - Multivariate distribution : When parameters are correlated
         - Others
Methodologies

Model over-simplification?

- Testing the impact of assumptions made
  - Straightforward Sensitivity Analysis
    - A “what if” analysis
      - Pecuniary change of various model components (i.e., key assumptions made, important/uncertain variables)
    - Model Averaging
      - Weighing factors placed upon various paths of the tree

Practical advice

- Seek the feedback and opinion of experts
- Determine and present which aspects of the tree impact results most
- Might different models or simulation techniques be required for various subgroups?

Markov Models

- Recursive, state-transition models wherein subjects may transition (move) from one state to another or remain in the current state
- May best capture:
  - Complex, time-varying courses of treatment
  - Disease natural histories that involve cycling between stages or recurrent/sequential events or patterns

Considerations

- Transition probabilities obtainable?
- Markov Chain
  - Constant transition probabilities
- Markov Process
  - Dynamic transition probabilities

Combining Evidence

- Meta Analysis
- Mixed Treatment Comparison
- Bayesian Statistics

Results Presentation

Incremental Cost-Effectiveness Ratio, ICER

- Statistical concerns of the ICER, Classic Arguments
  - Values do not indicate if treatment is cost-effective or not (yes/no)
  - Negative ICERs could be either “dominant” or “dominated” (“always choose versus “never choose”)
  - Appropriate calculation of confidence intervals
    - Fieller’s Theorem
      - Viewed as most accepted due to the manner through which covariance between cost and effects are controlled

\[
\text{Incremental Cost - Effectiveness Ratio} = \frac{\Delta \text{Total Costs}}{\Delta \text{Total (Natural) Units}}
\]
Quality Assurance (Validation)

ISPOR Task Force on Good Research Practices – Modeling Studies

- Emphasizes full transparency, reporting of structural assumptions and parameter estimates, use of sensitivity analysis

IV. Conclusion and Summary

Conclusion

When analyzing or conducting decision analyses, recognize:

- Results from models depend upon inputs
  - Clinical trial results most important
  - Assumptions can affect the results/credibility
- Robust models often require input from several areas of expertise
- Ensure robust inclusion of uncertainty, validation, transparency, and sensitivity analysis
- Decision models can be applied to a variety of decisions – not only pharmaceuticals

Summary

<table>
<thead>
<tr>
<th>Method</th>
<th>Description</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Decision Tree</td>
<td>Linear model</td>
<td>Begins at a decision node and moves in a unidirectional pattern to a terminal node</td>
</tr>
<tr>
<td>Monte Carlo Simulation</td>
<td>Static, Stochastic</td>
<td>Simultaneously varies multiple variables, where inputs/outputs do not vary with time but do include random variation</td>
</tr>
<tr>
<td>Markov Model</td>
<td>Recursive model</td>
<td>Involves time-dependent transitions between health states; cycles between nodes until an absorbing state is reached</td>
</tr>
<tr>
<td>Discrete Event Simulation</td>
<td>Dynamic, Stochastic (not discussed)</td>
<td>Simultaneously varies multiple variables, with inputs varying over time while random variation is included</td>
</tr>
</tbody>
</table>