Lecture 8: Decision Analysis

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Review Meta-Analysis Homework

- Perform a Peto analysis of the data
  - metan rt nt rc nc, or peto
- Perform a random effects (DerSimonian-Laird) analysis of the data
  - metan rt nt rc nc, or random
- Perform a Mantel-Haenzel analysis of risk ratios instead of odds ratios
  - metan rt nt rc nc, rr

<table>
<thead>
<tr>
<th>Analysis</th>
<th>Pooled</th>
<th>Lower</th>
<th>Upper</th>
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</thead>
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<tr>
<td>M-H OR</td>
<td>0.791</td>
<td>0.718</td>
<td>0.872</td>
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<tr>
<td>Peto OR</td>
<td>0.792</td>
<td>0.719</td>
<td>0.873</td>
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<tr>
<td>D+L OR</td>
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<tr>
<td>M-H RR</td>
<td>0.808</td>
<td>0.74</td>
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Decision Analysis

- Decision analysis is a set of tools for facilitating decision making
  - Implies that there is a decision to be made
  - Implies that there is a decision maker
  - Implies that there is an analyst
- Provides structure to the problems
- Helps clarify the utility of various options.

Decision Analysis

- Decision analysis tools formalize a clinical decision process
  - Cast them in mathematical terms
  - Alternative to a clinical trials
    - Clinical trials are costly—time, resources, opportunity costs
    - Clinical trials are usually limited to short term clinical benefits
    - Clinical trials do not address issues of effectiveness
  - May also augment clinical trials

Expected Value Paradigm

- The basic paradigm for decision analysis is expected value
- For a random variable $X$ with outcomes $x_1$ and $x_2$ which occur with probability $p$ and $(1-p)$:
  $$E(X) = px_1 + (1-p)x_2$$
- The action that is optimal is the one that yields the highest expected value
Expected Value Paradigm

• Treatment 1 gives you 10 years of life with 96% probability, but instant death with 4% probability
• Treatment 2 gives you 7 years of life with 99% probability, but instant death with 1% probability
• Which do you choose?

Expected value is:

- $E(Y_1) = .85 \times 10 + .15 \times 0 = 8.5$ Years
- $E(Y_2) = .99 \times 8.5 + .01 \times 0 = 8.4$ Years

Expected Value Paradigm

• Rationale is the over time, with repeated occurrences, this strategy yield the greatest gain or lowest losses
• Difficulties
  – May never actually achieve the expected reward
  – Humans may treat risk of loss and risk of gain asymmetrically
What is a Model?

- An abstraction of reality
- An representation of the events and relationships influencing a decision

Elements of a Decision Tree Model

Decision Nodes: Indicate that a choice is to be made. Usually there is only one of these per problem, and embodies the clinical question being raised.

Chance Nodes: Indicate a random process, and all possible outcomes that could be realized after a particular decision or outcome. These should be exhaustive.

Terminal Nodes: Depict the final outcome that results from going down a particular path within the tree. Most importantly, the terminal node places a value on the final outcomes.

Branches: Connect the Decision Nodes, Chance Nodes, and Terminal Nodes.
Building a Decision Tree

- Need to be as parsimonious as possible, BUT:
  - All relevant options must be considered
    - Surgery, medicine, observation
    - Time period of investigation
  - All relevant outcomes are included
    - Inconclusive test results
    - Operative mortality
    - Side effects of therapy

Steps in a Decision Tree Analysis

1. Frame the Question [most important, usually straightforward]
2. Structure the clinical problem [crucial, easy to get wrong]
3. Estimate the relevant probabilities [tedious]
4. Estimate the relevant values of the outcomes [tedious]
5. Analyze the tree [easy]
6. Test model assumptions [fun!]
7. Interpret the results [hard!]
Simple Example

- You admit a 60 year old woman with CREST syndrome (systemic inflammatory rheumatic disease), primary biliary cirrhosis, and longstanding hypertension for the evaluation of a mediastinal mass found on a routine chest x-ray. A chest x-ray 18 months earlier showed no mass. CT scan and angiography revealed a sacculan aneurysm of the ascending aorta, involving the innominate and left common carotid arteries. Cardiac cath revealed 80-90% stenosis of the RCA and LAD (left anterior descending) artery.

- Should the aneurysm be surgically repaired?
- On which parameters does the optimal decision depend?

Simple Example

- The internist says “She has a lot of other diseases, but they are all chronic. The aneurysm is expanding and may rupture.”
- The surgeon says “She has a lot of other diseases, therefore risk of operation is too high.”

Step 1: Frame the Question

- What is the question?
- Whose Perspective should we take?
- What is the relevant outcome?
Step 1: Frame the Question

- What is the question?
  - Should we operate on this patient or observe?
- Whose Perspective should we take?
  - Perspective: Patient
- What is the relevant outcome?
  - Life expectancy

Step 2: Structure the Problem

- What does the decision tree look like?

Simple Example Tree

60 year old female with CREST, PBC, CAD, and AAA

- Operate
- Observe
Expand the Example

- How would you expand this example to accommodate:
  - Surgical Complications (e.g. stroke, MI)?
  - Aneurysm Rupture?

Surgical Complications

60 Year old female with CREST, PBC, CAD, and AAA

Aneurysm Rupture

60 Year old female with CREST, PBC, CAD, and AAA
Step 3: Analyze the Tree

• To analyze the tree we need model **parameters**:
  – Numerical values for probabilities and outcomes

Sources for Model Parameters

1. Primary Data from randomized trials
2. Observational data from existing data sets
3. Literature reviews
   a. Meta-analysis to combine results of multiple studies
4. Expert Opinion
   a. Panels
   b. Consensus development conferences
5. Your Best Guess
Model Parameters

- For our simple example assume:
  - Pr(Operative Death) = 0.15
  - Life expectancy with Surgery = 6.7 Years
  - Life expectancy without Surgery = 2.3 Years

Solving the Tree

- Goal is to find the optimal decision
- Called Rolling back or Folding back the tree
- Start from the right side of the tree
- Replace each chance node with the expected value of the branches that follow
- Do this until you arrive at a decision node

Solving the Tree

\[
Pr(\text{Die}) \times \text{LE(Die)} + (1-Pr(\text{Die})) \times \text{LE(Survive Surgery)} = 0.15 \times 0 + 0.85 \times 6.7 = 5.7 \text{ Years}
\]
Solving the Tree

- For small models rolling back may involve only a few computations of expected value
- For large models rolling back the tree may involve tens or hundreds of expected value calculations
- The optimal decision is the decision that carries the optimal expected value
  - May be the largest (as in life expectancy)
  - May be the smallest (as in infection rate)

Uncertainty

- So you compute the expected value of the strategies and conclude that surgery is the optimal strategy.
- Faced with the result, the surgeon responds,

“I don’t agree. Actually, her risk of surgery is higher than I estimated earlier. It’s more like 25%.”
Dealing with Uncertainty

• What uncertainty are we talking about?
  – Parameter uncertainty
  – Model uncertainty
  – Modeling process uncertainty

• Methods
  – Sensitivity analysis (1-way, 2-way, ... n-way)
  – Probabilistic sensitivity analysis
    • Probability intervals

Parameter Uncertainty

• Decision analysis models are complex functions of many input parameters
  – Probabilities, rates, quality of life weights, life expectancies, costs, etc.

• Each of these reflects underlying information of varying quality

• Uncertainty about the true numerical values of these parameters induces uncertainty in the final expected outcome

One-way Sensitivity Analysis

• Vary a model parameter across a reasonable range and recompute all expected values
  – Determine the optimal strategy for each new value
  – Determine at which point the optimal strategy changes

• Repeat for all (or a reasonable subset of) model parameters
One-way Sensitivity Analysis

- If there is a large number of model parameters, can summarize all 1-way sensitivity analyses with a tornado diagram.
- Present the variable with the widest swing across the range at the top.
- Smaller toward the bottom.

Tornado Diagram (Multiple 1-way)

Each parameter varied through its 95% confidence range, or min-max range. Diagram arranged from maximum to minimum effect on outcome.
Two-way Sensitivity Analysis

- Vary two model parameters at a time and re-compute all expected values
- Determine the optimal strategy for each new pair of values
  - Best to present graphically
- Graph region and boundary at which point the optimal strategy changes
- Repeat for sensible pairs of model parameters (e.g. sensitivity and specificity)

N-way Sensitivity Analysis

- 3-way: very hard to show
  - Some have made a “movie” so that flip through the 2-way graph to show how the boundaries move when a 3rd parameter is varied
- Impossible to show 4-way and higher in any way that makes sense
Probabilistic Sensitivity Analysis

- The purpose of using a probabilistic approach is to capture ALL the parameter uncertainty in the model
  - Take a draw from each model parameter distribution
  - Solve using backward induction assuming those values
  - Repeat N times
- Rather than having a single expected outcome, we get many realizations from the joint distribution of the parameters

Software

- Can do this in Excel
- Can do this in any matrix based programming language
  - R (www.r-project.org)
- There is also dedicated software
  - TreeAge Pro (www.treeage.com)
  - Excellent software, but pricey
Homework

- Read Thomas paper posted on the website