Introduction to Medical Decision Making and Decision Analysis

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Outline

• Decision analysis
  » Components of decision analysis
  » Building a tree: Example
  » Sensitivity analyses

• Markov models
  » Background
  » Constructing the model
  » Example
  » Monte Carlo simulations
Decision Analysis

- Decision analysis is a quantitative, probabilistic method for modeling problems under situations of uncertainty.
Making a Decision

• We make a decision when we irreversibly allocate resources.

• We typically use the following steps:
  » gather information
  » assess consequences of the alternatives
  » take an action

• Goal of decision analysis is to clarify the dynamics and trade-offs involved in selecting one strategy from a set of alternatives

• Usually, in everyday decision-making, we do not take the time to thoroughly analyze the decision
Decision Analysts

- Deliberately seek out new, creative alternatives
- Identify the possible outcomes
- Identify relevant uncertain factors
- Encode probabilities for the uncertain factors
- Specify the value placed on each outcome
- Formally analyze the decision.
Decisions Vary in Degree Of:

- **Complexity** -- large number of factors, multiple attributes, more than one decision-maker

- **Time factor** -- static (no change over time) vs. dynamic (time-dependent)

- **Uncertainty** -- *deterministic* vs. *probabilistic*. Deterministic means there is no uncertainty and the problem can be solved with a set of precise equations
Decision Analysis is Most Helpful

• For important, unique, complex, nonurgent, and high-stakes decisions that involve uncertainty

• “Decision Analysis = Decision Therapy.”
  » A great deal of work is done to decompose the decision problem, work out the relation between factors, specify probabilities for uncertain events, and identify what is at stake and how it might be affected by the decision
  » Constructing the tree, even before “solving” it mathematically, can provide important insights.
Cost-Effectiveness Analyses

• Cost-effectiveness analysis (CEA) is a methodology for evaluating the tradeoffs between health benefits and costs

• CEA is aid to decision making, not a complete resource allocation procedure
Cost-Effectiveness Ratio

Comparing a specific (new) intervention to a stated alternative (old) intervention

\[
\frac{\text{Cost}_{\text{new}} - \text{Cost}_{\text{old}}}{\text{Benefit}_{\text{new}} - \text{Benefit}_{\text{old}}}
\]

- Incremental resources required by the intervention
- Incremental health effects gained by using the intervention
Decision Model

- Schematic representation of all the clinical important outcomes of a decision.
- Used to combine knowledge about decision problem from many sources.
- Computes average outcomes (e.g., QALYs, costs, etc.) from decisions.
Elements of Decision Analysis

• Structure the problem
  » Identify decision alternatives
  » List possible clinical outcomes
  » Represent sequence of events

• Assign probabilities to all chance events

• Assign utility, or value, to all outcomes

• Evaluate the expected utility of each strategy

• Perform sensitivity analyses
Structuring the Problem

• Decision model (usually decision tree) is chosen to represent the clinical problem

• Model needs to be simple enough to be understood, but complex enough to capture the essentials of the problem

• Need to make a series of assumptions for modeling
Decision Node:

A point in a decision tree at which several choices are possible. The decision maker controls which is chosen.

Only 2 choices shown here. But can have more, as long as they are mutually exclusive.
Chance Node:

A point in a decision tree at which *chance* determines which outcome will occur.

Only 2 outcomes shown here. But can have more, as long as they are *mutually exclusive* and *collectively exhaustive*.
Some Definitions

• Mutually exclusive
  » The intersection of the events is empty
  » One (and only one) of the events must occur

• Collectively exhaustive
  » Events taken together make up the entire outcome space
  » At least one of the events must occur
Terminal Node:

Final outcome state associated with each possible pathway

20 LY

Patient cured

Some measure of value or worth needs to be applied to the terminal nodes (e.g., LYs, QALYs, costs)
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Example

• Symptomatic patient:
  » operate (risky)
  » medical management

• If disease present at surgery, must decide whether try for cure or palliate

• Want to evaluate surgery vs. medical management
surgery

disease present

survive

disease absent

operative death

cure

no cure

try
disease present

cure

operative death

survive

no cure

drug

survive

disease absent

cure

disease present

no cure

disease absent
Each path through the tree defines a unique potential result.

1. Decide to operate
2. Find disease at surgery
3. Try for surgical cure
4. Patient survives surgery
5. Surgery unsuccessful
Insert probabilities at each chance node. Sources include data from literature/studies, modeling, expert judgment...

- Disease present:
  - Surgery: 10% cure, 90% no cure
  - Disease absent:
    - Survive: 99% cure, 1% death
    - Operative: 10% cure, 90% death

- Disease present:
  - Drug: 10% cure, 90% no cure
  - Disease absent:
    - Survive: 99% cure, 1% death
    - Operative: 10% cure, 90% death

- Cure:
  - Try: 90% cure, 10% no cure
  - Palliate: 98% survive, 2% death
  - Operative: 10% cure, 90% no cure

Drug: 10% cure, 90% no cure
Assign a value to the outcome at each endpoint

AVERAGE OUTCOMES

Operative death: 0 life years

Death from progression of the disease: 2 life years

Cure: 20 life years
Compute average results, working right to left...

Average LYs here:

\[ \text{Average LYs} = 10\% \times 20 + 90\% \times 2 \]

\[ = 0.1 \times 20 + 0.9 \times 2 \]

\[ = 2.0 + 1.8 \]

\[ = 3.8 \text{ LY} \]
Replace these chance nodes with the average...

Average LYs here:
\[ = 10\% \times 20 + 90\% \times 2 \]
\[ = .1 \times 20 + .9 \times 2 \]
\[ = 2.0 + 1.8 \]
\[ = 3.8 \text{ LY} \]
Replace these chance nodes with the average...

Average LYS here:

= \(10\% \times 20 + 90\% \times 2\)
= \(.1 \times 20 + .9 \times 2\)
= \(2.0 + 1.8\)
= \(3.8\) LYS
Replace next chance node with the average...

Average LY here:

\[
\text{Average LY here:} = 10\% \times 3.8 + 90\% \times 20
\]

\[
= .1 \times 3.8 + .9 \times 20
\]

\[
= .38 + 18
\]

\[
= 18.38 \text{ LY}
\]
Replace next chance node with the average...

Average LY here:

\[
\text{Average LY here:} = 10\% \times 3.8 + 90\% \times 20
\]

\[
= .1 \times 3.8 + .9 \times 20
\]

\[
= .38 + 18
\]

\[
= 18.38 \text{ LY}
\]
Continue this process...

Average LY here:
\[ = 98\% \times 3.8 + 2\% \times 0 \]
\[ = .98 \times 3.8 + .02 \times 0 \]
\[ = 3.72 + 0 \]
\[ = 3.72 \text{ LY} \]

\[ = 3.72 \text{ LY} \]
Continue this process...

Average LY here:

\[
\text{Average LY} = 0.98 \times 3.8 + 0.02 \times 0
\]

\[
= 3.72 + 0
\]

\[
= 3.72 \text{ LY}
\]
Continue this process...

Average LY here:
\[= 90\% \times 20 + 10\% \times 2\]
\[= .90 \times 20 + .1 \times 2\]
\[= 18 + .2\]
\[= 18.2 \text{ LY}\]
Continue this process...

- **Surgery**
  - Disease present: 10%
  - Disease absent: 90%

- **Drug**
  - Average LY here:
    
    $\text{Average LY} = \text{90\%} \times 20 + \text{10\%} \times 2$
    
    $= .90 \times 20 + .1 \times 2$
    
    $= 18 + .2$
    
    $= 18.2 \text{ LY}$
Continue this process…

Average LY here:
\[ = 90\% \times 18.2 + 10\% \times 0 \]
\[ = 0.9 \times 18.2 + 0.1 \times 0 \]
\[ = 16.38 + 0 \]
\[ = 16.38 \text{ LY} \]
Continue this process...

- **Disease Present**
  - 10% surgery
  - 90% drug

- **Disease Absent**
  - 99% survive
  - 1% operative death

**Average LY here:**

\[
= 90\% \times 18.2 + 10\% \times 0 \\
= 0.9 \times 18.2 + 0.1 \times 0 \\
= 16.38 + 0 \\
= \text{16.38 LY}
\]
At a **Decision Node** you choose which path you wish to take -- no averaging!

Here, we would choose to try for cure -- obviously!
disease present

10% try cure 16.38 LY

90% surgery

90% disease absent

10% drug

1% operative death

99% survive

20 LY

0 LY

18.38 LY
Continue working from right to left, averaging out at Chance Nodes, and choosing best branch at Decision Nodes...

Average LY here:
= 99% x 20 + 1% x 0
= .99 x 20 + .01 x 0
= 19.8 + 0
= **19.8 LY**
**disease present**

- **10%**
  - try **16.38 LY**

**disease absent**

- **90%**
  - surgery **18.38 LY**

- **19.8 LY**

Average LY here:

\[
= 99\% \times 20 + 1\% \times 0 \\
= 0.99 \times 20 + 0.01 \times 0 \\
= 19.8 + 0 \\
= **19.8 LY**
\]
Average LY here:

\[= 0.1 \times 16.38 + 0.9 \times 19.8\]
\[= 1.638 + 17.82\]
\[= 19.46 \text{ LY}\]
surgery

Average LY here:

\[ = 0.1 \times 16.38 + 0.9 \times 19.8 \]

\[ = 1.638 + 17.82 \]

\[ = 19.46 \text{ LY} \]
The outcome for each decision is more apparent now:

Surgery (intending cure) produces an average of 19.46 LY.

Medical management yields an average of 18.38 LY.

The incremental benefit of Surgery versus Medical Management is:

\[ 19.46 - 18.38 = 1.08 \text{ LY} \]
Repeat this Decision Analysis Using Other Outcome Measures

• Instead of just using average life years, can use QALYs at each endpoint.

• If you use both costs and QALYs at each endpoint:
  » Then can calculate the incremental cost effectiveness of surgery versus medical management
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Sensitivity Analysis

- Systematically asking “what if” questions to see how the decision result changes.
- Determines how “robust” the decision is.
- Threshold analysis: one parameter varied
- Multi-way analysis: multiple parameters systematically varied
Sensitivity Analysis: Probability of Operative Death

![Graph showing sensitivity analysis with life expectancy and probability of operative death. The graph includes a threshold and base case for surgery and drug treatments.]
Two-Way Sensitivity Analysis: $p_{\text{Disease}}$ vs. $p_{\text{OperativeDeath}}$
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What is a Markov Model?

Mathematical modeling technique, derived from matrix algebra, that describes the transitions a cohort of patients make among a number of mutually exclusive and exhaustive health states during a series of short intervals or cycles.
When to use a Markov Model?

- Problem involves risk that is continuous over time
- Timing of events is important
- Important events may happen more than once
Properties of a Markov Model

- Patient is always in one of a finite number of health states
- Events are modeled as transitions from one state to another
- Contribution of utility to overall prognosis depends on length of time spent in health states
- During each cycle, the patient may make a transition from one state to another
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Constructing a Markov Model

• Choose set of mutually exclusive health states

• Determine possible transitions between these health states
  » State transitions
  » Transition probabilities

• Determine clinical valid cycle length
Cycle Length

• Clinically meaningful time interval
• Entire life of patient, relatively rare events → yearly
• Shorter time frame, frequent events, rate changing rapidly over time → monthly or weekly
• Availability of probability data?
Markovian Assumption

- Behavior of the process subsequent to any cycle depends only on its description in that cycle
  - No memory of earlier cycles
- How do we get around this?
  - New health states
  - Tunnel states
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State Transition Diagram

- WELL
- SICK
- DEAD

The diagram illustrates the transitions between the states of being well, sick, and dead.
Evaluation

• Compute number of cycles spent in each health state
  – Expected utility = \sum_{s=1}^{n} t_s

• Define incremental utility for spending a cycle in given health state
  – Expected utility = \sum_{s=1}^{n} t_s \cdot u_s
Quality-adjusted life expectancy

$$= (t_w \times u_w) + (t_s \times u_s)$$

$$= (2.5 \times 1) + (1.25 \times 0.7)$$

$$= 3.9 \text{ QALYs}$$
Calculation of Outcomes with a Markov Model

- Assume absorbing health state (death)
- Methods:
  - Matrix algebraic solution
  - Markov cohort simulation
  - Monte Carlo simulation
Fundamental Matrix Solution

- Requires constant transition probabilities
- Does not require simulation
- Requires matrix algebra
Transition Probability Matrix

<table>
<thead>
<tr>
<th></th>
<th>Well</th>
<th>Sick</th>
<th>Dead</th>
</tr>
</thead>
<tbody>
<tr>
<td>Well</td>
<td>0.75</td>
<td>0.20</td>
<td>0.05</td>
</tr>
<tr>
<td>Sick</td>
<td>0</td>
<td>0.70</td>
<td>0.30</td>
</tr>
<tr>
<td>Dead</td>
<td>0</td>
<td>0</td>
<td>1</td>
</tr>
</tbody>
</table>

Starting Probability Vector: $\begin{bmatrix} 1 & 0 & 0 \end{bmatrix}$
Markov Cohort Simulation

• Large number of patients are followed as a cohort
• Time dependent probabilities and utilities may be easily incorporated into the analysis
• Does not provide information on the distribution or variance of expected values
Markov Cohort Simulation

Time

\( t \)

Well \( \rightarrow \) Sick \( \rightarrow \) Dead

Well \( \rightarrow \) Sick \( \rightarrow \) Dead

\( t+1 \)
Markov Cohort Simulation

Time

<table>
<thead>
<tr>
<th></th>
<th>Well</th>
<th>Sick</th>
<th>Dead</th>
</tr>
</thead>
<tbody>
<tr>
<td>t</td>
<td>Well</td>
<td>0.75</td>
<td>0.05</td>
</tr>
<tr>
<td></td>
<td>0.20</td>
<td>0.05</td>
<td>1.0</td>
</tr>
<tr>
<td>t+1</td>
<td>Well</td>
<td>Sick</td>
<td>Dead</td>
</tr>
<tr>
<td></td>
<td>0.70</td>
<td>0.70</td>
<td>0.30</td>
</tr>
</tbody>
</table>
Markov Cohort Simulation

Time

\( t \) => Well (0.75) \rightarrow Sick (0.20) \rightarrow Dead (1.0) \rightarrow Well (0.05)

\( t+1 \) => Well (0.70) \rightarrow Sick (0.30) \rightarrow Dead (1.0) \rightarrow Well (1.0)

Cycle (allows time dependence)
Quality-of-Life Adjustments

1.0 \rightarrow \text{Well}

0.5 \rightarrow \text{Sick}

0.0 \rightarrow \text{Dead}
Expressed as a Markov Tree:
Structure
Expressed as a Markov Tree: Transition Probabilities
Expressed as a Markov Tree: Utilities

Markov

Well

Sick

Dead
# Running the Model

<table>
<thead>
<tr>
<th>Cycle</th>
<th>Well</th>
<th>Sick</th>
<th>Dead</th>
<th>Cycle Reward</th>
<th>Total Reward</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0.5</td>
<td>0.5</td>
</tr>
<tr>
<td>1</td>
<td>0.75</td>
<td>0.20</td>
<td>0.05</td>
<td>0.85</td>
<td>1.35</td>
</tr>
<tr>
<td>2</td>
<td>0.56</td>
<td>0.29</td>
<td>0.15</td>
<td>0.71</td>
<td>2.06</td>
</tr>
<tr>
<td>3</td>
<td>0.42</td>
<td>0.32</td>
<td>0.26</td>
<td>0.58</td>
<td>2.64</td>
</tr>
<tr>
<td>4</td>
<td>0.32</td>
<td>0.31</td>
<td>0.38</td>
<td>0.47</td>
<td>3.11</td>
</tr>
</tbody>
</table>
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Monte Carlo Simulation

• Determines the prognoses of a large number of individual patients
• Each patient runs through model until death – repeat large number of times ($\sim 10^4$)
• Provides a distribution of survival
  » Standard deviation
  » Variance
Monte Carlo Simulation

WWSD

Well → Well
Well → Sick
Well → Dead

Sick → Sick
Sick → Dead

Dead → Dead

1
2
3
4
Probabilistic Sensitivity Analysis
(2nd order Monte Carlo)

- Decision tree estimates of probabilities and utilities are replaced with probability distributions (e.g. logistic-normal)
- The tree is evaluated *many* times with random values selected from each distribution
- Results include means and standard deviations of the expected values of each strategy
## Characteristics of Markov Approaches

<table>
<thead>
<tr>
<th>Feature</th>
<th>Markov Cohort</th>
<th>Monte Carlo</th>
<th>Matrix</th>
</tr>
</thead>
<tbody>
<tr>
<td>Transition Probabilities</td>
<td>Time-dependent</td>
<td>Time-dependent</td>
<td>Constant</td>
</tr>
<tr>
<td>Incremental Utilities</td>
<td>Time-dependent</td>
<td>Time-dependent</td>
<td>Constant</td>
</tr>
<tr>
<td>Accuracy</td>
<td>Dependent on cycle length</td>
<td>Dependent on number of trials</td>
<td>Cycle-independent</td>
</tr>
<tr>
<td>Computation</td>
<td>Moderate</td>
<td>Most</td>
<td>Least</td>
</tr>
<tr>
<td>Variability Measures</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
</tr>
</tbody>
</table>
Some Things to Remember

• Use of Markov models are appropriate in a number of situations

• Tradeoff between simplicity of conventional decision tree versus fidelity of Markov process

• When using decision trees OR Markov trees:
  » Assumptions and input variables should be as transparent as possible
  » Adequate sensitivity analysis should be performed
  » Modeling as well as clinical expertise should be consulted
Summary: Medical Decision Analysis

- Clearly defines alternatives, events, and outcomes
- Formal method to combine evidence
- Can prioritize information acquisition
- Can help healthcare providers to make medical decisions under uncertainty
Decision Analysis Software

• Decision Maker
  » http://infolab.umdnj.edu/windm/

• DATA by TreeAge
  » http://www.treeage.com

• Excel spreadsheet models

• Other software packages
Where To Go For More

- Society for Medical Decision Making (http://www.smdm.org)