Tutorial: Optimization in Medicine

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Tutorial Summary

- History of Operations Research (OR) in Medicine

- Applications of Optimization in Medicine
  - Diet Problem
  - Radiation therapy
  - Kidney exchange

- Opportunities for future research and practice
History of OR in Medicine
Operations Research (OR)

OR is a multidisciplinary field that focuses on analytical methods for optimization of complex systems
OR History

OR emerged during World War II:

- Combination of British and U.S. Mathematicians and Scientists solving military problems:
  - Optimal size of navel convoys
  - U-boat detection strategies
  - Network interdiction

After WWII many new applications emerged:

- Factory scheduling
- Transportation logistics
- Product design
- Supply chain optimization
Health Care Delivery

There are many examples of OR in health care operations management (e.g. simulation, queuing, optimization):

- Outpatient appointment scheduling
- Surgery planning and scheduling
- Hospital bed management
- Emergency department patient flow
- Emergency vehicle location and routing
- Pharmacy inventory management
- Emergency preparedness
OR in Medicine

There is also a long history of applications of OR to medicine:

- Decision analysis
- Markov models
- Simulation
- Reliability models
- Statistical process control
Barriers to OR in Medicine

- Medicine is more complicated than a lot of industries
  - Some useful online dictionaries for medical terminology:

- The medical research literature is enormous

- There are privacy concerns and ethical considerations that limit the availability of data and performance of experiments
Decision Analysis

**Tutorial: How to Perform a Decision Analysis**

**Primer on Medical Decision Analysis:**

**Part 1—Getting Started**

ALLAN S. DETSKY, MD, PhD, GARY NAGLIE, MD, MURRAY D. KRAHN, MD, MSc, DAVID NAIMARK, MD, DONALD A. REDELMEIER, MD, MS(HSR)

This paper is Part 1 of a five-part series covering practical issues in the performance of decision analysis. The intended audience is individuals who are learning how to perform decision analyses, not just read them. The series assumes familiarity with the basic concepts of decision analysis. It imparts many of the recommendations the authors have learned in teaching a one-semester course in decision analysis to graduate students. Part 1 introduces the topic and covers questions such as choosing an appropriate question, determining the tradeoff between accuracy and simplicity, and deciding on a time frame. Key words: decision analysis; expected value; utility; sensitivity analysis; decision trees; probability. (Med Decis Making 1997;17:123-125)

Over the past ten years, our group at the University of Toronto has taught a one-semester course on decision analysis. Unlike educational initiatives that solely focus on readings about and discussions of decision analysis, our course has required that each student perform a decision analysis. This requires building a decision tree on paper, modeling that tree on a computer, obtaining probabilities and utilities by direct measurement or literature review, evaluating the tree, performing sensitivity analyses, presenting the study to peers, and writing up the analysis. Several of the students have gone on to publish their work. To pass the course, each student is required to develop a model that "works."

In this series and the accompanying note on presentation, we attempt to impart what we, as teachers, have learned about the practical issues of performing decision analysis. Much of what we have learned has come from teaching our students how to develop a working model.

The intended audience for this series is individuals who are learning how to perform decision analyses. The series assumes that the reader is already familiar with the concepts of decision analysis and has read and comprehended several decision analyses before trying his or her hand at one. Before embarking on this series, the reader should read a two-part users' guide aimed at consumers of decision analyses to achieve a grounding in basic concepts such as decision nodes, probability nodes, expected value, tree representation, sensitivity, and threshold analyses, and is also referred to two textbooks. The goal of the present series is to give practical suggestions for performing decision analysis.
DA Example 1: Treatment Decision

Treat?  
- Yes: $P(GO|T) \rightarrow$ Treat, Good Outcome  
  $P(BO|T) \rightarrow$ Treat, Bad Outcome  
- No: $P(GO|No\ T) \rightarrow$ No Treat, Good Outcome  
  $P(BO|No\ T) \rightarrow$ No Treat, Bad Outcome
DA Example 2: Cancer Screening

- There are multiple diagnostic tests for Cholangiocarcinoma
  - Magnetic resonance cholangiopancreatography
  - Endoscopic retrograde cholangiopancreatography

- MRCP is more expensive than ERCP but ERCP can have complications

- MRCP and ERCP have different sensitivity and specificity

Which one is “better”??
DA Example 2: Screening Procedure

- Decision tree from Talwalkar et al., *Hepatology*, 2004
DA Example 2: Model Parameters

<table>
<thead>
<tr>
<th>Variable</th>
<th>Estimate</th>
<th>Range</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>Probability of PSC</td>
<td>0.32</td>
<td>0.10-1.0</td>
<td>10</td>
</tr>
<tr>
<td>Probability of bile duct obstruction</td>
<td>0.70</td>
<td>0.35-1.0</td>
<td>10</td>
</tr>
<tr>
<td>Probability of choledocholithiasis</td>
<td>0.14</td>
<td>0.07-0.28</td>
<td>10</td>
</tr>
<tr>
<td>Probability of BD</td>
<td>0.14</td>
<td>0.07-0.28</td>
<td>10</td>
</tr>
<tr>
<td>Probability of ES</td>
<td>0.14</td>
<td>0.07-0.28</td>
<td>10</td>
</tr>
<tr>
<td>Probability of BD and ES</td>
<td>0.14</td>
<td>0.07-0.28</td>
<td>10</td>
</tr>
<tr>
<td>Probability of BD and biopsy</td>
<td>0.21</td>
<td>0.11-0.42</td>
<td>10</td>
</tr>
<tr>
<td>Probability of BD and stone extraction</td>
<td>0.21</td>
<td>0.11-0.42</td>
<td>10</td>
</tr>
<tr>
<td>Probability of any ERCP complication</td>
<td>0.08</td>
<td>0.04-0.16</td>
<td>10</td>
</tr>
<tr>
<td>Probability of post-ERCP abdominal pain</td>
<td>0.50</td>
<td>0.25-1.0</td>
<td>10</td>
</tr>
<tr>
<td>Probability of post-ERCP pancreatitis</td>
<td>0.33</td>
<td>0.16-0.66</td>
<td>10</td>
</tr>
<tr>
<td>Probability of post-ERCP perforation</td>
<td>0.17</td>
<td>0.09-0.34</td>
<td>10</td>
</tr>
<tr>
<td>Sensitivity of ERCP</td>
<td>0.96</td>
<td>0.50-1.0</td>
<td>10</td>
</tr>
<tr>
<td>Specificity of ERCP</td>
<td>1.00</td>
<td>0.50-1.0</td>
<td>10</td>
</tr>
<tr>
<td>Sensitivity of MRCP</td>
<td>0.82</td>
<td>0.50-1.0</td>
<td>10,11</td>
</tr>
<tr>
<td>Specificity of MRCP</td>
<td>0.98</td>
<td>0.50-1.0</td>
<td>10,11</td>
</tr>
<tr>
<td>Cost of diagnostic ERCP (US$)</td>
<td>408.25</td>
<td>204.12-816.50</td>
<td>Medicare</td>
</tr>
<tr>
<td>Medication cost of diagnostic ERCP</td>
<td>100.00</td>
<td>50.00-200.00</td>
<td>Institution, Medicare</td>
</tr>
<tr>
<td>Supply cost of diagnostic ERCP</td>
<td>115.00</td>
<td>57.50-230.00</td>
<td>Institution, Medicare</td>
</tr>
<tr>
<td>Cost of BD</td>
<td>102.28</td>
<td>51.14-204.56</td>
<td>Medicare</td>
</tr>
<tr>
<td>Cost of ES</td>
<td>113.52</td>
<td>56.76-227.04</td>
<td>Medicare</td>
</tr>
<tr>
<td>Cost of BD and ES</td>
<td>215.80</td>
<td>107.90-431.60</td>
<td>Medicare</td>
</tr>
<tr>
<td>Cost of BD and biopsy</td>
<td>116.89</td>
<td>58.44-233.78</td>
<td>Medicare</td>
</tr>
<tr>
<td>Cost of BD and stone extraction</td>
<td>303.85</td>
<td>151.92-607.70</td>
<td>Medicare</td>
</tr>
<tr>
<td>Cost of stone extraction alone</td>
<td>201.57</td>
<td>100.78-403.14</td>
<td>Medicare</td>
</tr>
<tr>
<td>Cost of MRCP</td>
<td>549.64</td>
<td>274.82-1099.28</td>
<td>Medicare</td>
</tr>
<tr>
<td>Cost of abdominal CT scan</td>
<td>346.10</td>
<td>173.05-692.20</td>
<td>Medicare</td>
</tr>
<tr>
<td>Hospitalization cost, post-ERCP abdominal pain</td>
<td>742.51</td>
<td>371.26-1485.02</td>
<td>Institution, Medicare</td>
</tr>
<tr>
<td>Hospitalization cost, post-ERCP pancreatitis</td>
<td>2127.53</td>
<td>1063.76-4255.06</td>
<td>Institution, Medicare</td>
</tr>
<tr>
<td>Hospitalization cost, post-ERCP perforation</td>
<td>3858.65</td>
<td>1929.32-7717.30</td>
<td>Institution, Medicare</td>
</tr>
</tbody>
</table>

Abbreviations: BD, balloon dilatation; ES, endoscopic sphincterotomy.
DA Example 2: Cancer Screening

Main Result: cost-effectiveness of MRCP vs. ERCP depends on prevalence of the disease.

Fig. 3. One-way sensitivity analysis demonstrating that prevalence rates above 45% for PSC would change the preferred test strategy from initial MRC to ERCP.
Markov Processes

Markov Models in Medical Decision Making:

A Practical Guide

FRANK A. SONNENBERG, MD, J. ROBERT BECK, MD

Markov models are useful when a decision problem involves risk that is continuous over time, when the timing of events is important, and when important events may happen more than once. Representing such clinical settings with conventional decision trees is difficult and may require unrealistic simplifying assumptions. Markov models assume that a patient is always in one of a finite number of discrete health states, called Markov states. All events are represented as transitions from one state to another. A Markov model may be evaluated by matrix algebra, as a cohort simulation, or as a Monte Carlo simulation. A newer representation of Markov models, the Markov-cycle tree, uses a tree representation of clinical events and may be evaluated either as a cohort simulation or as a Monte Carlo simulation. The ability of the Markov model to represent repetitive events and the time dependence of both probabilities and utilities allows for more accurate representation of clinical settings that involve these issues. Key words: Markov models; Markov-cycle decision tree; decision making. (Med Decis Making 1993;13:322–338)

A decision tree models the prognosis of a patient subsequent to the choice of a management strategy. For example, a strategy involving surgery may model the events of surgical death, surgical complications, and various outcomes of the surgical treatment itself. For practical reasons, the analysis must be restricted to a finite time frame, often referred to as the time horizon of the analysis. This means that, aside from death, the outcomes chosen to be represented by terminal nodes of the tree may not be final outcomes, but may simply represent convenient stopping points for the scope of the analysis. Thus, every tree contains terminal nodes that represent subsequent prognosis for a particular combination of patient characteristics and events.

There are various ways in which a decision analyst can assign values to these terminal nodes of the decision tree. In some cases the outcome measure is a crude life expectancy; in others it is a quality-adjusted life expectancy. One method for estimating life expectancy is the declining exponential approximation of life expectancy (DEALE)13 which calculates a patientspecific mortality rate for a given combination of patient characteristics and comorbid diseases. Life expectancies may also be obtained from Gompertz models of survival14 or from standard life tables.14 This paper explores another method for estimating life expectancy, the Markov model.

In 1963, Beck and Pauker described the use of Markov models for determining prognosis in medical applications.2 Since that introduction, Markov models have been applied with increasing frequency in published decision analyses.8–9 Microcomputer software has been developed to permit constructing and evaluating Markov models more easily. For these reasons, a revisit of the Markov model is timely. This paper serves both as a review of the theory behind the Markov model of prognosis and as a practical guide for the construction of Markov models using microcomputer decision-analytic software.

Markov models are particularly useful when a decision problem involves a risk that is ongoing over time. Some clinical examples are the risk of hemorrhage while on anticoagulant therapy, the risk of rupture of an abdominal aortic aneurysm, and the risk of mortality in any person, whether sick or healthy. There are two important consequences of events that have ongoing risk. First, the times at which the events will occur are uncertain. This has important implications
Markov Processes

Markov processes have been used to define the probabilistic progression of many diseases...

"Markov models are useful when a decision problem involves risk that is continuous over time, when the timing of events is important, and when important events may happen more than once. Representing such clinical settings with conventional decision trees is difficult and may require unrealistic simplifying assumptions. Markov models assume that a patient is always in one of a finite number of discrete health states, called Markov states. All events are represented as transitions from one state to another."

Markov Models

Properties of Markov processes in medicine:
- May be stationary or non-stationary
- May be finite or infinite horizon
- Typically discrete decision epochs ranging from days to years

Useful outputs from Markov Models:
- Expected outcomes
- Mean first passage time
- Steady state probabilities
Example: Cardiovascular Disease

L: low cholesterol
M: medium cholesterol
H: high cholesterol
V: very high cholesterol
Pros and Cons

- What are some of the benefits of Markov models?

- What are some of the shortcomings of Markov models?
Discrete Event Simulation

Simulation of medical decisions: Applications of SLN*

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Indianapolis, Indiana 46202

Please see “The Simulation of Logical Networks (SLN)” in this issue for authors’ biographical sketches.

ABSTRACT
Simulation has been applied to several important medical decision problems using the SLN language. The applications to end-stage renal disease, chronic stable angina, renal artery stenosis, and treatment of hypertension and hypercholesterolemia are reviewed emphasizing the modeling considerations and results. These investigations support the utility of simulation in medical decisions and the applicability of SLN to these problems. The general applicability of simulation to medical decision problems must be evaluated in the context of available knowledge and data. The simulation of medical decisions does not produce dependence among observations so prevalent in discrete-event simulations, but to the extent that arbitrary criteria such as cost-effectiveness are estimated, statistical concerns remain. Simulation, particularly with SLN, can play an important role in medical protocol design.

INTRODUCTION
Fifty years ago the medical and financial impact of medical decisions was limited to individual patients. Minimal technology was available, so diagnosis and treatment were based on time-honored protocols offered by individual physicians. Today medical decisions are made in a far different environment. Expensive equipment and facilities have made economics a major consideration not only for individual patients but also for society, since costs are often shared by everyone through taxes, insurance, etc. The rapid growth in medical technology means that medical protocols must be revised often to include recent advances. Time-honored procedures cannot take advantage of the state-of-the-art developments in medicine. Complicating the problem further is that these new developments often offer a mixed set of benefits and costs. The practice of medicine itself reflects greater specialization so that individual physicians are increasingly unable to offer comprehensive care and cannot individually evaluate new developments.

Traditional approaches to evaluating methods for diagnosis and treatment are limited. Clinical trials, the major source of clinical experience, must be confined to experimentally verifiable hypotheses. These are both expensive and intricate, usually requiring considerable time and commitment. The proliferation of alternatives, the timeliness of evaluation, the use of human subjects, and the cost of experimental procedures mean that clinical trials must be reserved for issues where actual experiments are the only method of evaluation. Clinical judgment may supplement or replace experimental findings since the state of the art is changing so rapidly. Yet judgment is now more difficult because of the complexities of the technology and environment.

Increasingly, simulation modeling is being used in the analysis of health care decisions to synthesize available information. Models can combine existing knowledge with clinical judgment to gain insight into the problems of diagnosis and treatment. Decision analysis has played a particularly central role in the modeling activity. Stochastic modeling and optimization of decision trees are among other recently applied analytical techniques. Simulation also provides a suitable vehicle for the analysis of medical decisions and can promote insight into the design of diagnostic and therapeutic protocols. Simulation, unlike its more analytical alternatives, places fewer requirements on the decision system and can accommodate a greater variety of problems. The simulation language, SLN (Simulation of Logical Networks), was designed especially to facilitate modeling and analysis of decision systems and has been applied in particular to medical decisions. SLN has been described in a companion paper. In this paper, we will review a number of the medical decision applications of SLN and describe some of the general experiences from these simulation studies.

*This work was supported in part by grant 18-P-97515-03 from Health Care Financing Administration, Department of Health and Human Services.
DSE Example: Renal Disease

- Patients with end stage renal disease (ESRD) suffer from irreversible kidney failure
- Cost of treatment impact on quality of life is high
- There are 4 principal options for treatment:
  - Home hemodialysis
  - Center hemodialysis – performed at a dialysis clinic
  - Cadaveric donor transplant (CAD)
  - Live donor transplant (LRD)
DSE Example: Renal Disease

- **Inputs:** survival probabilities, costs, decision rules

- **Outputs:** expected lifespan, quality adjusted lifespan, expected discounted cost of treatment
DSE Example: Renal Disease

- Simulation is important because it is difficult to compare resource allocation policies:
  - Costs are frequently changing as new technology becomes available
  - Treatment effectiveness is changing over time
  - Randomization of patients to modes of treatment is viewed as unethical
Pros and Cons

- What are some of the major benefits of simulation models?
- What are some of the major shortcomings of simulation models?
Prescriptive vs. Descriptive Models

- The previous methods have in common that they are “descriptive”

- Optimization models are “prescriptive” in nature
Optimization in Medicine
Optimization in Medicine

Optimization\textsuperscript{1}:

- an act, process, or methodology of making something (as a design, system, or decision) as fully perfect, functional, or effective as possible;

Medicine\textsuperscript{1}:

- \textbf{1} \textit{a} : a substance or preparation used in treating disease \textit{b} : something that affects well-being
- \textbf{2} \textit{a} : the science and art dealing with the maintenance of health and the prevention, alleviation, or cure of disease \textit{b} : the branch of medicine concerned with the nonsurgical treatment of disease
- \textbf{3} : an object held in traditional American Indian belief to give control over natural or magical forces; \textit{also} : magical power or a magical rite

\textsuperscript{1}Merriam Webster Dictionary
Elements of an Optimization Model

Optimization models include the following basic elements

- Decision Variables
- Objective Function
- Constraints
Objective Functions

The objective in an optimization model could be:

- Maximize lifespan of a patient
- Maximize average lifespan of a population
- Minimize radiation exposure to healthy tissue
- Maximize radiation exposure to cancer tissue
- Minimize the probability of an adverse event
- Minimize costs
QALYs

HALYs and QALYs and DALYs, Oh My: Similarities and Differences in Summary Measures of Population Health

Marthe R. Gold¹, David Stevenson², and Dennis G. Fryback³

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Key Words burden of disease, cost-effectiveness analysis, health-related quality of life

Abstract Health-adjusted life years (HALYs) are population health measures permitting morbidity and mortality to be simultaneously described within a single number. They are useful for overall estimates of burden of disease, comparisons of the relative impact of specific illnesses and conditions on communities, and in economic analyses. Quality-adjusted life years (QALYs) and disability-adjusted life years (DALYs) are types of HALYs whose original purposes were at variance. Their growing importance and the varied uptake of the methodology by different U.S. and International entities makes it useful to understand their differences as well as their similarities. A brief history of both measures is presented and methods for calculating them are reviewed. Methodological and ethical issues that have been raised in association with HALYs more generally are presented. Finally, we raise concerns about the practice of using different types of HALYs within different decision-making contexts and urge action that builds and clarifies this useful measurement field.

- Quality adjusted life years (QALYS) are a commonly used objective
- A 0-1 scale is used to rate life years relative to a state of perfect health (1.0)
- There are standard surveys to elicit QALYs
Costs

- When costs are part of a model it is important to define the perspective of the decision maker
  - Patient
  - Third party payer
  - Caregiver
  - Society

- Some “costs” are difficult to measure
  - Time
  - Complexity
  - Adverse events
Constraints

The constraints in an optimization model could arise due to:

- Budget constraints
- Maximum allowable exposure to a treatment
- Minimum or maximum time between treatments
- Maximum allowable risk level
Examples of Optimization Models
Example 1: Diet Problem

- Assume your diet is based on the four “basic food groups”: pizza, coffee, red bull, and chocolate bars.
- Pizza costs $3/slice, coffee costs $1/cup, red bull costs $1.50/can, and chocolate bars cost $1 each.
- Each day, you must have at least 1500 calories, 10 oz of sugar, and 0.5 oz of caffeine.

<table>
<thead>
<tr>
<th></th>
<th>Pizza Slice</th>
<th>Coffee (1 cup)</th>
<th>Red Bull (1 can)</th>
<th>Choc. Bar</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calories</td>
<td>500</td>
<td>100</td>
<td>250</td>
<td>200</td>
</tr>
<tr>
<td>Sugar</td>
<td>0</td>
<td>0.5</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Caffeine</td>
<td>0</td>
<td>0.1</td>
<td>0.2</td>
<td>0.03</td>
</tr>
</tbody>
</table>
Example 1: Diet Problem

- **Decision variables:**
  - $X_1$: # of pizza slices
  - $X_2$: # cups of coffee
  - $X_3$: # cans of red bull
  - $X_4$: # chocolate bars

\[
\begin{align*}
\min & \quad 3X_1 + X_2 + 1.5X_3 + X_4 \\
\text{s.t.} & \quad 500X_1 + 100X_2 + 250X_3 + 200X_4 \geq 1500 \\
& \quad 0.5X_2 + 2X_3 + 3X_4 \geq 10 \\
& \quad 0.1X_2 + 0.2X_3 + 0.3X_4 \geq 0.5 \\
& \quad X_1, X_2, X_3, X_4 \geq 0
\end{align*}
\]
Stigler’s Diet Problem

The real diet problem...

<table>
<thead>
<tr>
<th>Nutrient</th>
<th>RDA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calories</td>
<td>3,000 kcal</td>
</tr>
<tr>
<td>Protein</td>
<td>70 grams</td>
</tr>
<tr>
<td>Calcium</td>
<td>0.8 grams</td>
</tr>
<tr>
<td>Iron</td>
<td>12 milligrams</td>
</tr>
<tr>
<td>Vitamin A</td>
<td>5,000 IU</td>
</tr>
<tr>
<td>Thiamine</td>
<td>1.8 milligrams</td>
</tr>
<tr>
<td>(Vitamin B₁)</td>
<td></td>
</tr>
<tr>
<td>Riboflavin</td>
<td>2.7 milligrams</td>
</tr>
<tr>
<td>(Vitamin B₂)</td>
<td></td>
</tr>
<tr>
<td>Niacin</td>
<td>18 milligrams</td>
</tr>
<tr>
<td>Ascorbic Acid</td>
<td>75 milligrams</td>
</tr>
<tr>
<td>(Vitamin C)</td>
<td></td>
</tr>
</tbody>
</table>


Stigler’s Diet Problem

Based on cost and nutrient content 77 candidate foods were reduced to 15 non-dominated foods.

Theoretically Optimal Diet:

<table>
<thead>
<tr>
<th>Food</th>
<th>August 1939</th>
<th>August 1945</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Annual Quantity</td>
<td>Annual Cost</td>
</tr>
<tr>
<td>Wheat Flour</td>
<td>370 lb.</td>
<td>$13.33</td>
</tr>
<tr>
<td>Evaporated Milk</td>
<td>57 cans</td>
<td>3.84</td>
</tr>
<tr>
<td>Cabbage</td>
<td>111 lb.</td>
<td>4.11</td>
</tr>
<tr>
<td>Spinach</td>
<td>23 lb.</td>
<td>1.85</td>
</tr>
<tr>
<td>Dried Navy Beans</td>
<td>285 lb.</td>
<td>16.80</td>
</tr>
<tr>
<td>Pancake Flour</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Beef Liver</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Total Annual Cost</td>
<td>$39.93</td>
<td>—</td>
</tr>
<tr>
<td>Total Daily Cost</td>
<td>$0.109</td>
<td>—</td>
</tr>
</tbody>
</table>

Yuk!
Model Assumptions

- What assumptions are being made in this model?
- Are the assumptions realistic?
Example 2: Radiation Treatment

- Patient with a tumor in the spine area is to receive radiation therapy
- An external beam is passed through the body harming both cancerous and healthy tissue
- Goal is to minimize damage to healthy tissue while delivering required dose to cancer tissue

Example 2: Radiation Treatment

- In practice many beams are used simultaneously. They are delivered via a rotating gantry with a multi-leaf collimator.

- Attenuation and scatter cause radiation to be absorbed outside the direct path.
Example 2: Radiation Treatment

Rotating Gantry

Multileaf Collimator
Example 2: Radiation Treatment

Brain Cancer: 2-Beam Example

1. Tumor
2. Spine
3. Brain
Example 2: Radiation Treatment

Decision Variables:
- Exposure times for beams 1 and 2: \((x_1, x_2)\)

Treatment Requirements:
- Dose delivered must be sufficient to kill the malignant cells
- The aggregate dose must not exceed established tolerance levels (measured in Kilorads)
- The goal is to select beam durations to generate the “best” dose distribution
Example 2: Radiation Treatment

Data for the Design of Radiation Therapy

<table>
<thead>
<tr>
<th>Area</th>
<th>Fraction of Dose Absorbed per unit time (ms)</th>
<th>Restriction on Total Average Dosage, Kilorads</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Beam 1 Dose</td>
<td>Beam 2 Dose</td>
</tr>
<tr>
<td>Brain</td>
<td>0.4</td>
<td>0.5</td>
</tr>
<tr>
<td>Spine</td>
<td>0.3</td>
<td>0.1</td>
</tr>
<tr>
<td>Tumor</td>
<td>0.5</td>
<td>0.5</td>
</tr>
<tr>
<td>Center of tumor</td>
<td>0.6</td>
<td>0.4</td>
</tr>
</tbody>
</table>
Example 2: Radiation Treatment

2-Beam LP Formulation:

Minimize \( Z = 0.4x_1 + 0.5x_2 \)

s.t. \( 0.3x_1 + 0.1x_2 \leq 2.7 \)
\( 0.5x_1 + 0.5x_2 = 6 \)
\( 0.6x_1 + 0.4x_2 \geq 6 \)
\( x_1 \geq 0, x_2 \geq 0 \)

Find a feasible solution to this problem
Feasible Region

\[ 0.6x_1 + 0.4x_2 \geq 6 \]

\[ 0.3x_1 + 0.1x_2 \leq 2.7 \]

\[ 0.5x_1 + 0.5x_2 = 6 \]
Alternative Models

- What other criteria could be used to define the objective function?

- What are the shortcomings of this model? How might it be improved?
Kidney disease affects 26 million people in the U.S.

The only treatment options are:
- Dialysis
- Transplant (live or deceased donor)

Currently more than 350,000 people are on dialysis and more than 80,000 candidates waiting
Example 3: Cross-matching

Compatibility is determined by two primary factors:

- Blood type
- Tissue antibodies

Blood type compatibility

Donor:
- O
- A
- B
- AB

Recipient:
- O
- A
- B
- AB
Example 3: Kidney Exchange

Donors

Recipients

Examples Adapted From:
Example 3: Kidney Exchange

Some interesting videos on kidney exchanges:

CNN Article on 10 transplant chain:


Videos on Kidney Exchange:

http://www.youtube.com/watch?v=L4vTZT9Up5M

http://www.youtube.com/watch?v=cGHEmfvX6_E

http://www.youtube.com/watch?v=qkzCE6Ccdm0

http://www.youtube.com/watch?v=cGHEmfvX6_E
Example 3: Criteria for Donation

- Number of matches
- Number of priority matches
- Immunologic concordance
- Travel requirements
Example 3: Model Formulation

Objective: To maximize the number and quality of donor-to-recipient matches

Only certain matches are allowable. The “cost” defines a measure of risk associated with performing the transplant

<table>
<thead>
<tr>
<th>Donor 1</th>
<th>Recipient 1</th>
<th>Recipient 2</th>
<th>Recipient 3</th>
<th>Recipient 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.2</td>
<td>M</td>
<td>M</td>
<td>0.01</td>
<td></td>
</tr>
<tr>
<td>Donor 2</td>
<td>M</td>
<td>0.5</td>
<td>0.01</td>
<td>0.2</td>
</tr>
<tr>
<td>Donor 3</td>
<td>0.3</td>
<td>0.1</td>
<td>0.4</td>
<td>M</td>
</tr>
<tr>
<td>Donor 4</td>
<td>M</td>
<td>0.01</td>
<td>0.3</td>
<td>0.2</td>
</tr>
</tbody>
</table>
Example 3: Model Formulation

- **Greedy Solution:**
  - Loop through donors and allocate the best kidney one at a time
  - What is the objective function value?

- Write an optimization model for this problem including:
  - Decision variables
  - Objective function
  - Constraints
Example 3: Model Formulation

Min $Z = 0.2x_{11} + Mx_{12} + Mx_{13} + 0.01x_{14} + Mx_{21} + 0.5x_{22} + 0.01x_{23} + 0.2x_{24}$

$+ 0.3x_{31} + 0.1x_{32} + 0.4x_{33} + Mx_{34} + Mx_{41} + 0.01x_{42} + 0.3x_{43} + 0.2x_{44}$

S.T.: $x_{11} + x_{12} + x_{13} + x_{14} = 1$  
      $x_{21} + x_{22} + x_{23} + x_{24} = 1$
      $x_{31} + x_{32} + x_{33} + x_{34} = 1$
      $x_{41} + x_{42} + x_{43} + x_{44} = 1$

$x_{11} + x_{21} + x_{31} + x_{41} = 1$  
      $x_{12} + x_{22} + x_{32} + x_{42} = 1$
      $x_{13} + x_{23} + x_{33} + x_{43} = 1$
      $x_{14} + x_{24} + x_{34} + x_{44} = 1$

$x_{ij} \geq 0 \ (i = 1, 2, 3; \ j = 1, 2, 3, 4)$
Vendor Packages for Optimization

- Lindo
- COIN
- Excel Solver
- EXPRESS
- ILOG OPL
- Matlab
- SAS
Key Takeaway Messages

- Optimization models are “prescriptive”, searching through many possible decisions to find the choice that maximizes or minimizes a defined criteria.

- Optimization models explicitly define decision making criteria (objective) and constraints.

- There are examples of optimization models in many branches of medicine and many opportunities for future research.
Useful Reference
Questions?
Example of Medical Terminology

*Magnetic Resonance Cholangiography Technique.* All ERCP procedures were completed within 24 hours of the preceding MRC. The examinations were performed using a General Electric Signa 1.5 Tesla MR scanner (Milwaukee, WI). Image acquisition was performed using a phase array torso multicoil. Two acquisitions each were performed in the axial and coronal planes using a single-shot fast-spin echo pulse sequence with a repetition time of infinity, average echo time equal to 90 milliseconds, matrix size equal to 256/256, and slice thickness of 5 mm with 0-mm skip. Each image slice required 2 seconds. Total breath-hold time averaged 20 seconds per patient. Multiple breath-hold scans were also performed to image the entire hepatic parenchyma if required. Three additional acquisitions were performed in the coronal plane and in planes approximately 45° oblique to the porta hepatis. A slice thickness of 5 cm, requiring a single 2-second breath hold, was used for the additional acquisitions.

Translation: MRC uses a tiny camera to take a picture of your bile duct.