The Course

Course Title: Decision Analysis and Cost-Effectiveness Analysis
Course Number: 26-BE-7068C
Course Credits: 3.0
Semester: Spring, 2017
Course Homepage: http://canopy.uc.edu/
Pre-requisites: We assume that students have little prior experience with the "nuts and bolts" of decision modeling. Students should have fundamental knowledge of computer applications (such as Excel®) and concepts and experience using e-mail and the Internet through browsers like Firefox or Internet Explorer.

Course Description and Overview:
The course provides an introduction to methods and applications of decision analysis and cost-effectiveness in medical decision making. Both lectures and workshop/lab sessions will review basic principles of decision analysis and will be organized into a number of units including:
- Fundamentals of Building Decision Models
- Assessment of Patient Values and Quality of Life
- Bayes’ Rule and ROC Analysis
- Deterministic Sensitivity Analysis
- Fundamentals of Cost-Effectiveness Analysis
- Advanced Topics in Decision Analysis

The course format will consist of a series of didactic lectures, workshops, and detailed clinical examples. Computer-based exercises will be used during the workshops, using decision modeling software [Decision Maker for Windows - WinDM®], and Excel™ spreadsheets. The sessions will be highly interactive and you are encouraged to bring your own clinical problems for discussion.

The course will be very much "hands on." I will present lecture material concerning each topic and then in our next session move to a workshop format. You will be encouraged to work
together in small groups of 2 - 3 students to solve real problems. Many of the exercises will require you to perform certain calculations by hand, so please bring a calculator.

Finally, you will each develop a project over the course of the quarter and submit this by the last session. This can be a simple decision model or any other reasonable project. We will set aside time during the quarter to discuss project ideas. Your grade for the course will be based upon attendance and participation in class and the project. It is my hope that you will leverage your project into something you can present and publish in the peer-reviewed literature. I am looking forward to learning with you and hope we have a very interesting and productive quarter.

**Primary Learning Outcomes/Objectives:**
Through lectures, hands-on computer lab exercises, readings, discussions, and course projects participants will be able to:

- Demonstrate the ability to critically appraise and interpret decision and cost-effectiveness analyses published in the literature.
- Demonstrate knowledge of the symbolic notation used to develop decision simple decision tree models.
- Perform a “fold-back” of simple decision trees to calculate the expected utility of each strategy and explain which strategy is “best.”
- Use decision analytic software and spreadsheets to calculate the base case results of decision models, perform sensitivity analyses, and interpret the meaning of these results.
- Apply knowledge of decision analysis fundamentals to develop decision analytic models capturing diagnostic and/or treatment issues in clinical medicine or within other relevant area of professional practice (e.g., environmental sciences, public health and policy).
- Define the theoretical foundations of utility theory and demonstrate how this leads to specific preference-based utility assessment techniques.
- Use standard techniques to perform utility assessments on health states patients may experience.
- Apply the knowledge of probability theory and Bayes’ Rule to interpret the meaning of diagnostic test results (e.g., true positives, false negatives, true negatives, false positives).
- Describe the consequences of diagnostic test results using a decision analytical framework.
- Explain the value of diagnostic tests with regards to their ability to discriminate between patients with and without disease, and describe how the test characteristics of diagnostic tests are used to develop receiver operator characteristic (ROC) curves.
- Explain the importance of area under the ROC curve in comparing different diagnostic tests.
- Describe the relationship between the positivity criterion (or cutoff) used to interpret a diagnostic test result and the operating point on the ROC curve.
- Use decision analytic framework to describe the optimal operating point on an ROC curve, with reference to the consequences of false positive and false negative test results, and the prevalence of disease.
- Demonstrate ability to interpret one-way, two-way, and three-way deterministic sensitivity analyses.

*Developed by Mark H. Eckman, MD, MS*
*Division of General Internal Medicine and Center for Clinical Effectiveness*
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University of Cincinnati
College of Medicine

- Explain the concept of the “threshold” in sensitivity analyses.
- Demonstrate knowledge of fundamental principles of health economic analysis, and explain the differences between cost analysis, cost-benefit analysis, cost-effectiveness analysis, and cost-utility analysis.
- Explain how the marginal (or incremental) cost-effectiveness ratio is calculated.
- Describe the significance and interpretation of the marginal cost-effectiveness ratio for any given cost-effectiveness analysis.
- Explain the concepts of dominance and extended dominance in cost-effectiveness analyses.
- Explain the fundamental “Markovian Assumption.”
- Describe the differences between types of Markov models, including Markov Chains, Markov Cohort Simulations, and First Order Monte Carlo Markov models.
- Explain the purpose of probabilistic sensitivity analysis.
- Describe the fundamental process of Second Order Monte Carlo simulation.
- Interpret and explain the results of a cost-effectiveness acceptability curve.
- Apply the theoretical knowledge of decision analysis and the hands-on experience gained through the lab and homework exercises to construct and analyze decision models.

Textbook and Supplies:
All materials are available through Canopy, and will be downloaded to your computers in our electronic classroom in the MSB.

In addition to the material described above, we will use Decision Making in Health and Medicine: Integrating Evidence and Values by Hunink et. al. (Cambridge University Press, 2014). There are also interesting case studies in the journal Medical Decision Making (http://mdm.sagepub.com/), published over the past twenty plus years. You should read the relevant sections of the syllabus and the textbook before each session so that you get the most out of the course.

Lab Sessions:
Computer-based exercises will be used during the workshops, using decision modeling software [Decision Maker for Windows - WinDM®], and Excel® spreadsheets. The sessions will be highly interactive and you are encouraged to bring your own clinical problems for discussion. Through lab sessions, each participant will develop a final project and a specific guideline will be provided.

Methods of Instruction:
This course is organized around 6 fundamental topics or units. The general format entails didactic sessions followed by hands-on laboratory sessions during which students are given the opportunity to gain a more concrete appreciation of the underlying concepts and the available software tools. Collaboration in small groups during the workshop sessions is highly encouraged. Readings and other course materials available in both the spiral bound course booklet and Blackboard should be read as each unit is covered. Familiarizing yourself with the materials before lectures and workshops is highly encouraged. Students are also encouraged to continue.
working on laboratory/workshop exercises at home. A video recording (made in 2009) of every session is also available on blackboard should you miss a session.

**Discussion & Class Participation**
Participation in classroom discussion is an important and integral part of your learning experience. It also gives me a sense of how well you understand the material.

**Group Work**
"Two heads are better than one" is a common expression that captures the value of group work. In this course, group activities will help you work with different classmates in order to produce a more diverse learning experience (e.g., building an effective learning community/social interaction). I encourage you to work in small groups during our laboratory/workshop sessions. In addition, you should team up with a partner for your class project. Given the diversity of backgrounds our students have, this can also enrich your experience. For instance, those with clinical backgrounds can team up with those who are more methodologically oriented. This type of multidisciplinary collaboration can lead to very rewarding outcomes.

**Specific Activities and Projects Related to the Course:**
Students are expected to complete readings and exercises in each unit. Your weekly assignments will be on the Discussion Board. The following are the major activities and projects in this course:

- Participants will be assigned readings from our textbook and the spiral bound course materials.
- Participants are encouraged to continue work at home on problems and examples from the workshop sessions.
- Participation is the “heart” of this highly interactive course. It is essential that all students participate actively in classroom discussions.
- All participants are expected to be self-motivated risk takers prepared for new experiences. As professionals it is important that each participant recognize their responsibility to seek out the support and the help that they may need to complete all assignments. Support is available in the form of on-line tools, computer- and text-based materials, peer support, and instructor support.
- Each participant will complete and present to the class one final project. This is the capstone experience of the course and will demonstrate your ability to translate the concepts you have learned into action and deliverables. All projects will be presented during our last 2 or 3 sessions and submitted to me via email.

**Final Project**
The final project will integrate many of the concepts you have acquired in this course. Most students will develop a decision model and analysis as their project. The topic of the final project is entirely up to you. The scope and complexity of the project should be appropriate for the amount of time you have in a single quarter. We will dedicate one session early in the quarter to review your project ideas, to make sure you are on the right track with a feasible plan. Furthermore, I encourage you to continue work on your project after the course has ended. We
have arranged a research elective that you can take after the course is completed, to continue working on your project and taking it to the “next level.” Many students have used their projects as a nidus for developing a more complete model and analysis of sufficient quality and importance to present at relevant meetings of regional and national organizations. Many have also gone on to publish their work in peer-reviewed clinical journals. As mentioned above, I encourage you to work in pairs on your projects. This will both distribute the workload, and also lead to a more enriching experience. The last 2 sessions of our class during exam week, will be used to present your projects. Presentation format should be a powerpoint slide show, no more than 10 minutes in length, allowing about 5 minutes for questions and discussion from you classmates. On the last day of class (hopefully 4/30/2015), each group must submit a copy of their powerpoint slides along with a 5 to 10 page report, including figures and diagrams. These can be sent to me electronically via email.

**Evaluation of Student Progress & Grading:**
Disciplined preparation is essential if the participant wants to derive from this course all of the value of collaborative study and hands on activities. Students/final grade will be determined by their performance on the following:

- Course attendance (30%)
- Participation during class discussions and workshops (10%)
- Final project, including presentation and submission (60%)

**Grading Scale**
The standard UC grading scale and quality points and definitions are follows:

<table>
<thead>
<tr>
<th>Grade</th>
<th>Numerical Score</th>
<th>Description</th>
<th>Quality Points</th>
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</thead>
<tbody>
<tr>
<td>A</td>
<td>96-100%</td>
<td>Excellent</td>
<td>4.0</td>
</tr>
<tr>
<td>A-</td>
<td>91-95%</td>
<td></td>
<td>3.67</td>
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<tr>
<td>B+</td>
<td>87-90%</td>
<td></td>
<td>3.33</td>
</tr>
<tr>
<td>B</td>
<td>82-86%</td>
<td>Good</td>
<td>3.00</td>
</tr>
<tr>
<td>B-</td>
<td>78-81%</td>
<td></td>
<td>2.67</td>
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<tr>
<td>C+</td>
<td>74-77%</td>
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<td>2.33</td>
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<tr>
<td>C</td>
<td>70-73%</td>
<td>Satisfactory</td>
<td>2.00</td>
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<tr>
<td>F</td>
<td>69 &amp; below</td>
<td>Fail</td>
<td>0.00</td>
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<tr>
<td>I</td>
<td>Incomplete</td>
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<td>W</td>
<td>Withdraw</td>
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Contact your instructor: Please feel comfortable to e-mail me any time during the quarter about problems encountered with the courseware, assignments, or any condition which might preclude your completing all of the assignments. I will make every effort to respond to your needs by phone, email, or in person. I will frequently stay after class for a short while to facilitate questions and discussion.

Technical Questions: Contact UC Blackboard at 513-556-1602 or email to canopy@uc.edu.

Students with Disabilities
If you have any disability that may impair your ability to complete this course successfully, please let me know during the first week of the quarter.

<table>
<thead>
<tr>
<th>Date</th>
<th>Unit</th>
<th>Topics Covered</th>
<th>Reading/Assignments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Week 1</td>
<td>Fundamentals of Building Decision Models</td>
<td>Introduction/Logistics &amp; Organization</td>
<td>Textbook Chapters 1 -3</td>
</tr>
<tr>
<td>1/10 – 1/12</td>
<td></td>
<td>Pre-Test</td>
<td>Unit 1(^1) – Lecture 1:</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Lecture: Introduction &amp; Overview; Designing and Evaluating Decision Trees</td>
<td>Pauker &amp; Kassirer. Medical Progress. Decision</td>
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<tr>
<td></td>
<td></td>
<td>• Principles of Medical Decision Making -</td>
<td>Analysis.</td>
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<tr>
<td></td>
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<td>○ Structuring the Problem</td>
<td>Kassirer, et al. Decision Analysis: a progress</td>
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<td></td>
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<td>○ Probabilities</td>
<td>report.</td>
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<td>○ Utilities</td>
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<td>○ A Medical Example</td>
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<td>○ Patient-Specific Decision Making</td>
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<tr>
<td></td>
<td>Workshop: Tree Construction &amp; Fertilization</td>
<td>Lecture: Decision Modeling – A Detailed Clinical Example</td>
<td>Unit 1 – Workshop 1:</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Jehovah’s Witness Clinical Example -</td>
<td>Eckman et al. Principles of Therapeutic</td>
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<td>○ Spreadsheet Exercises</td>
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<tr>
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<td>Decision Maker Model</td>
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<tr>
<td>Week 2</td>
<td></td>
<td>Lecture: Decision Modeling – A Detailed Clinical Example</td>
<td>Unit 1 – Lecture 2:</td>
</tr>
<tr>
<td>1/17– 1/19</td>
<td></td>
<td>• Review steps in performing a decision analysis</td>
<td>Eckman et al. Can patients be</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Can patients be anticoagulated following intracerebral hemorrhage? A decision analysis</td>
<td>anticoagulated after intracerebral hemorrhage?</td>
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<tr>
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<td></td>
<td>A decision analysis.</td>
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<tr>
<td>Week 3</td>
<td>Workshop: More Trees to Plant and Ponder</td>
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| 1/24 – 1/26 | Several clinical scenarios are presented with the task to build simple decision trees to model these situations -  
| | o Paper and pencil exercise  
| | o Structure models in DecisionMaker™ |

<table>
<thead>
<tr>
<th>Week 4</th>
<th>Utilities</th>
<th>Lecture: Patient Values and Preferences</th>
<th>Workshop: Hands-On Utility Assessments</th>
</tr>
</thead>
</table>
| 1/31 – 2/2 | | Motivating clinical examples –  
| | o Woman with BRCA1 mutation considering prophylactic mastectomy/oopherectomy  
| | Expected utility theory  
| | Using utilities to quality-adjust survival  
| | Risk attitude  
| | Techniques for valuing outcomes  
| | o Rating scale  
| | o Standard reference gamble  
| | o Time tradeoff  
| | Time Preference  
| | Transforming rating scale values into utilities  
| | Health indices  
| | Utility assessment for mild and severe angina -  
| | o Using computerized utility assessment program: The Gambler™  
| | o Place utilities in already prepared decision model “Jehovah single vessel.tre” |

| | Unit 1 – Workshop 2  
| | Textbook Chapter 4  
| | Unit 5 – Lecture 1  
| | Unit 5 – Workshop 1 |
### Week 5
2/7 – 2/9

<table>
<thead>
<tr>
<th>Utilities</th>
<th>Students Present and Discuss Project Plans</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bayes’ Rule &amp; ROC Analysis</td>
<td>Lecture: Bayes’ Rule &amp; the Interpretation of Diagnostic Tests</td>
</tr>
<tr>
<td></td>
<td>• Basic Terminology</td>
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<td></td>
<td>o Gold standard</td>
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<td></td>
<td>o Sensitivity (True Positive Rate)</td>
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<td>o Specificity (True Negative Rate)</td>
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<td>o False Positive Rate</td>
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<td>o False Negative Rate</td>
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<td></td>
<td>o Pre-test probability</td>
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<td>o Post-test probability</td>
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<td></td>
<td>o Predictive value positive</td>
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<td>o Predictive value negative</td>
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<tr>
<td></td>
<td>• Bayes’ Rule (Theorem)</td>
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<tr>
<td></td>
<td>o Algebraic Formulation</td>
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<td>o Bayes’ Flow Diagram</td>
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<td>o Odds Likelihood Formulation</td>
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<td>o LR +</td>
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<td>o LR-</td>
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<tr>
<td></td>
<td>o Pre-test odds</td>
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<td>o Post-test odds</td>
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<td></td>
<td>o Converting from probabilities to odds and from odds to probabilities</td>
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<tr>
<td></td>
<td>o Sequential application of Bayes’ Rule</td>
</tr>
<tr>
<td></td>
<td>• Sources of bias in the evaluation of tests</td>
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<td></td>
<td>o Verification bias</td>
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<td>o Spectrum bias</td>
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<td></td>
<td>o Publication bias</td>
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### Week 6
2/14 – 2/16

| Workshop: Test Characteristics & Bayes’ Rule |
| Lecture: Introduction to ROC Curve Analysis |
| | • Odds-likelihood solution for woman with suspected giant cell arteritis |
| | • Tabular Bayes’ approach to 45-year old man undergoing exercise stress testing |
| | • The use of tests for screening |

### Textbook Chapters
5 & 7

- Unit 2 – Lecture 1
- Steinberg. Assessment of Diagnostic Technology.
- McNeil et al. Primer on certain elements of medical decision making.
- Ost et al. The negative predictive value of spiral computed tomography...
- Wells et al. Use of a clinical model for safe management of patients with suspected pulmonary embolism.
- Relationship between distribution of test results in patients with and without disease and the ROC curve
- Positivity criterion (test cutoff) and operating point on ROC curve
- Area under the ROC curve
  - Methods of calculation
    - Parametric (e.g., Dorfman & Alf technique)
    - Non-parametric (trapezoidal technique)
  - To describe test’s ability to discriminate between patients with and without disease
  - Use in comparing tests to one another
- Choice of optimal operating point
- Motivating clinical example

| Week 7  
<table>
<thead>
<tr>
<th>2/21 – 2/23</th>
<th>Bayes’ Rule &amp; ROC Analysis</th>
<th>Students Present and Discuss Project Plans</th>
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</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Workshop &amp; Lecture: A Decision Analytic Approach to Determining the Optimal Operating Point on the ROC Curve</td>
</tr>
<tr>
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<td>Clinical scenario – woman with suspected herpes simplex encephalitis</td>
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<td>Decision Fan approach</td>
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<td>Alternate Decision Tree approach using sensitivity analysis</td>
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<td>Using the likelihood quotient to determine optimal operating point</td>
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<td>Algebraic solution of decision tree foldback</td>
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<td>Spreadsheet template</td>
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<td>Examine factors that influence the optimal operating point</td>
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<td>Another clinical scenario – testing the blood supply for HIV</td>
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<td>Using the likelihood quotient</td>
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<td>Interval likelihood ratio</td>
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<td>Assigning utilities to the outcomes</td>
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<tr>
<td></td>
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<td>Decision tree approach</td>
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</tbody>
</table>

Unit 2 – Workshop & Lecture 2

### Week 8
2/28 – 3/2

<table>
<thead>
<tr>
<th>Bayes’ Rule &amp; ROC Analysis</th>
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</table>

**Workshop & Lecture: A Decision Analytic Approach to Determining the Optimal Operating Point on the ROC Curve (Continued)**

**Lecture: Sensitivity Analysis and Interpretation of Results**

- Deterministic Sensitivity Analyses
  - One-way
  - Two-way
  - Multi-way
  - Clinical Example – Patient-specific decision making for warfarin therapy in atrial fibrillation: How will genetics and imaging help?
  - More Clinical Examples

- Using sensitivity analyses to capture patient-to-patient variability
  - Clinical examples

**Threshold Approach to Decision Making**

### Week 9
3/7 – 3/9

<table>
<thead>
<tr>
<th>Deterministic Sensitivity Analysis</th>
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</table>

**Students Present and Discuss Project Plans**

**Workshop: Sensitivity Analysis**

- Calculation of Testing Threshold and Test-Treatment Threshold
  - Decision tree approach
  - Algebraic solution
  - Incorporation of Bayes’ Rule into decision model
  - Review of factors that influence these thresholds

- Two-Way Sensitivity Analyses
- Three-Way Sensitivity Analyses
- The Threshold Approach to Clinical Decision Making
  - Clinical Scenarios – Brain biopsy in patient with suspected herpes simplex encephalitis

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Textbook Chapter 6
Eckman et al. *Patient-specific decision making for warfarin therapy in non-valvular atrial fibrillation*...

*Pauker & Kassirer. The threshold approach to clinical decision making.*
<table>
<thead>
<tr>
<th>Week 10</th>
<th>3/14 – 3/16</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>• Spring Break</td>
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<table>
<thead>
<tr>
<th>Week 11</th>
<th>3/21 – 3/23</th>
</tr>
</thead>
<tbody>
<tr>
<td>Workshop: Sensitivity Analysis – (continued)</td>
<td></td>
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<tr>
<td>Lecture: Fundamentals of Cost-Effectiveness Analysis</td>
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<tr>
<td>• Motivating Context: Why Worry about the Cost of Medical Care?</td>
<td></td>
</tr>
</tbody>
</table>
| • Three Dimensions of Clinical Economics  
  o Type of analysis  
  o Perspective of analysis  
  o Types of costs & benefits considered |
| • Discounting  
  • Clinical Examples  
  • Issues & Pitfalls  
  • Critical Appraisal of Health Economic Analyses |

| Textbook Chapter 9 |
| Drummond et al. Users’ Guide to the Medical Literature: XIII. How to use an article on economic analysis of clinical practice. |

<table>
<thead>
<tr>
<th>Week 12</th>
<th>3/28 – 3/30</th>
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<tbody>
<tr>
<td>Workshop: Cost-Effectiveness Analysis</td>
<td></td>
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</tbody>
</table>
| • Calculation of the marginal cost-effectiveness ratio  
  • Dominance  
  • Extended Dominance  
  • Cost-effectiveness frontier  
  • Clinical Example – cost-effectiveness of warfarin for patients with atrial fibrillation  
    o Working with Decision Maker™ model  
    o Basecase foldback  
    o Working with bindings  
    o Sensitivity analyses  
    o The impact of adding a third strategy (aspirin)  
    o The impact of discounting |

| Eckman et al. Making decisions about antithrombotic therapy in heart disease: Decision analytic and cost-effectiveness issues. |
### Lecture: Cost-Effectiveness Analysis – A Detailed Clinical Example
- Testing for Factor V Leiden Mutation in Patients with Venous Thromboembolism

### Lecture: Markov Modeling
- The “Markovian Assumption”
- Rates vs. transition probabilities
- Markov processes and chains
- Markov cohort simulation
  - Spreadsheet solution
  - Decision Tree solution
- Fundamental matrix solution – Markov Chain
- Markov cycle tree
- Individual (first order) Monte Carlo simulation
- Fine tuning life expectancy calculations
  - Half cycle correction
  - Age correction
  - Age offset

### Students Present and Discuss Project Plans

### Week 13
4/4 – 4/6

#### Advanced Topics in Decision Analysis

### Lecture: Markov Modeling
- The “Markovian Assumption”
- Rates vs. transition probabilities
- Markov processes and chains
- Markov cohort simulation
  - Spreadsheet solution
  - Decision Tree solution
- Fundamental matrix solution – Markov Chain
- Markov cycle tree
- Individual (first order) Monte Carlo simulation
- Fine tuning life expectancy calculations
  - Half cycle correction
  - Age correction
  - Age offset

### Textbook
Textbook Chapters 10 – 11

### Week 14
4/11 – 4/13

#### Advanced Topics in Decision Analysis

### Lecture: Probabilistic Sensitivity Analysis using Second Order Monte Carlo Simulation
- Motivation
- Differences between 1<sup>st</sup> and 2<sup>nd</sup> order Monte Carlo simulations
- Probabilistic sensitivity analysis
- Cost-Effectiveness plane
- Cost-Effectiveness acceptability curve
- Choice of distributions for model parameters
  - Beta
  - Logit
  - Log normal
- Generating distributions in a spreadsheet
  Clinical example – drotrecogin alpha in the treatment of patients with severe sepsis

### Lecture: Tolls & Tunnels

### Week 15  
4/18 – 4/20  
**Project Work**  
Finish Work on Projects – NO CLASS

### Week 16  
4/25 – 4/27  
**Exam Week: Project Presentations**  
Projects Due – Project Presentations  
**Written Project Summaries andPowerpoint files due on 4/27/17!**

- Motivating clinical scenario (Need for Tunnel States)  
  - Timing of aneurysm repair in patient with a recent myocardial infarction  
- Temporary states  
- Rates vs. probabilities  
- Calculations  
  - Rates from cumulative probabilities  
  - Transition probabilities from rates  
- Tolls  
  - Motivation  
  - Clinical example – Cost-effectiveness of oral vs. intravenous therapy for patients with early Lyme disease

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1 Refers to units available on-line in Blackboard.

*In order to meet the course objectives this syllabus may be modified at the discretion of the instructor(s).*