Syllabus

Topics in Clinical Trials
Spring Semester 2016
Rice University course STAT 630
University of Texas GSBS course GS01 0813

Time: 9:25 – 10:40 a.m., Tuesday and Thursday
Locations: The locations of the lectures will change, but all locations are at M.D. Anderson.

Instructors:

Peter F. Thall, PhD  rex@mdanderson.org, 713-794-4162, Office FCT4.6014
Brian P. Hobbs, PhD bp@mdanderson.org, 713-794-4633 Office FCT 4.6050

Prerequisites:
STAT 410: INTRODUCTION TO REGRESSION AND STATISTICAL COMPUTING
STAT 431: OVERVIEW OF MATHEMATICAL STATISTICS

Lecture Schedule

<table>
<thead>
<tr>
<th>Thall</th>
<th>Hobbs</th>
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<tr>
<td>Tues 1/19 – FCT5.5049</td>
<td>Tues 3/08: FCT2.4144 (Room A)</td>
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<td>Thurs 1/21 – R2.2628 Main Building</td>
<td>Thurs 3/10: ACB4.1281ab</td>
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<td>Tues 1/26 – R2.2628 Main Building</td>
<td>Thurs 3/15: FCT2.4144 (Room A)</td>
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<td>Thurs 1/28 – R2.2628 Main Building</td>
<td>Thurs 3/17: FC1.2050</td>
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<td>Tues 2/2 – Y7.5302 Main Building</td>
<td>Tues 3/22: FCT2.4144 (Room A)</td>
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<td>Thurs 2/4 – FC1.2050</td>
<td>Thurs 3/24: FCT2.4144 (Room A)</td>
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<td>Tues 2/9 – FCT2.4144 (Room A)</td>
<td>Tues 3/29: FC3, Room 5</td>
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<td>Thurs 2/11 – Y7.5302 Main Building</td>
<td>Thurs 3/31: FC1.2050</td>
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<td>Tues 2/16 – FC3, Room 1</td>
<td>Tues 4/5: B6.4804</td>
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<td>Thurs 2/18 – FC1.2050</td>
<td>Thurs 4/7: FC1.2050</td>
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<td>Tues 2/23 – R2.2628 Main Building</td>
<td>Tues 4/12: FCT2.4144 (Room A)</td>
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<td>Thurs 2/25 – R2.2628 Main Building</td>
<td>Thurs 4/14: R2.2628 Main Building</td>
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<td>Tues 4/19: FCT2.4144 (Room A)</td>
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<td>Feb 29 – March 4</td>
<td>SPRING BREAK</td>
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<td>Wednesday May 4: TAKEHOME FINAL DUE</td>
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Software Download site  https://biostatistics.mdanderson.org/SoftwareDownload

Homeworks and Exam

Your course grade will be based on homework assignment and a takehome final exam. Homeworks will be a combination of problems to be solved, clinical trial designs to be constructed including computer simulations, and write-ups of published papers. In your homework write-ups:

1) Begin by stating the problem or giving reference(s) of the paper(s) to be explained.
2) Clearly define any notation before using it.
3) Use clear, complete, grammatically correct sentences.
4) Be complete, but as brief as possible.
5) You may use any references you like, but all of your work must be your own.
Reference Books


The lecture topics listed below will be covered as time permits. It is very unlikely that all topics listed below will be covered. Additionally, the topics may not be covered in the order given.

Lecture Topics for Dr. Thall

1. Why Conduct a Clinical Trial?
   a. Medicine and Statistics
   b. Randomness, Probability, and Bayesian Statistics
   c. Sequential Decision Making in Clinical Trials
   d. “Phase I → Phase II → Phase III” : A Dysfunctional Paradigm
2. Comparing Treatments
   a. Estimation and Comparison
   b. Simpson’s Paradox
   c. Bias and Bias Correction
   d. Randomization and Causality
   e. Adaptive Randomization
   f. Group Sequential Designs
3. Monitoring discrete single outcomes in phase II clinical trials
   a) Beta-binomial models and methods for binary outcomes [1]
   b) Dirichlet-multinomial design paradigm for multiple outcomes [2,3]
4. Exponential-gamma models and methods for event times in phase II [2]
5. Patient heterogeneity in phase II clinical trials
   a) Bayesian methods based on analysis of variance models [5]
   b) Methods based on Bayesian hierarchical models [6]
6. Phase I-II dose-finding based on Efficacy-Toxicity trade-offs
   a) The homogeneous case: Trinary and bivariate binary outcomes [7]
   b) Personalized dose-finding to incorporate covariates [8]
7. Dose-finding with two agents [9]
8. Dealing with multiple toxicities in phase I using total toxicity burden [10]
9. Utility-based dose-finding
   a) Single agent designs [11-13]
   b) Two agent designs [14-15]
   c) A two-cycle design [16]
10. Optimizing dose and schedule [17-20]
11. Phase II/III designs [21-23]
12. Prior effective sample size in Bayesian clinical trial design [30-32]
14. Data Mining: Post Hoc Evaluation of Dynamic Treatment Regimes [33,34]
15. Bayesian sensitivity analysis for treatment comparisons based on nonrandomized data [29]

References for Professor Thall’s Lectures

15. Thall PF, Nguyen HQ, Zinner RG. Parametric dose standardization for two-agent combinations in phase I-II trials with ordinal outcomes. Revised for *JRSS-C*.


**Lecture Topics for Dr. Hobbs**

1. Introduction to clinical trials, basic principles
2. Commonly used study designs
3. Randomization and blinding
4. Outcome adaptive randomization
5. Sample size and power calculation
6. Group sequential designs
7. Interim data monitoring, data safety and monitoring board
8. Meta-analysis and study reporting
9. Phase II – single arm designs, one-stage and multi-stage designs, designs based on predictive probability and Bayes factors
10. Phase II – randomized designs, Bayesian adaptive randomization designs
11. Commensurate priors and historical data in randomized comparative trials