UMDNJ- School of Public Health
Piscataway/New Brunswick Campus

Department of Biostatistics

Course Title: Advanced topics in Biostatistics” (BIST 0690)
Coordinator: Weichung Joe Shih

Spring 2007: Special advanced topic: Group Sequential and Adaptive designs
Instructor(s):
  W.J. Shih e-mail: Shihwjl@umdnj.edu
  K. K. Gordon Lan e-mail: GLan@prdus.jnj.com
Course Schedule: Thursdays, 6:15 pm to 9:00 pm
Location: SPH Building Rm 234

Credits: 3

Prerequisites: Students should have at least completed Advanced Biostatistics Theory I (BIST 0700) and should be either in preparation of or have passed the doctoral qualifying exams when taking this course.

Brief description: This is an advanced level course to provide students who are in research for doctoral thesis topics with in-depth survey and synthesis of recent developments in biostatistics. In particular, in the Spring 2007, the advanced topic is in the area of group sequential and adaptive designs.

Learning objectives: At the conclusion of the course the student will
  1) Have a knowledge of the development in theory and application of Group Sequential methods and the new area of adaptive designs.
  2) Advance their skills in developing biostatistical methodology for solving problem in biopharmaceutical science, especially in data monitoring aspects for clinical trials.
  3) Identify their interest in certain problems for future dissertation research topics.

Textbooks:
  (1) Group Sequential Methods with Applications to Clinical Trials (by Jennison & Turnbull, Chapman & Hall/CRC)
  (2) Statistical Monitoring of Clinical Trials – A Unified Approach (by Proschan, Lan and Wittes, Springer)

Course schedule:

Week 1. Introduction to the general framework of sequential versus fixed size designs in the context of monitoring clinical trials. Starting with Wald’s SPRT (Sequential probability ratio test) to introduce essential statistical characteristics for studying sequential methods such as expected sample size, overall type-I error rate and power, and issues in blinding and study integrity preservation, DSMB setting and functional structure in practice.
Week 2. Power: Conditional, Unconditional, Predictive. Stochastic curtailment; Continuous, binary, and survival outcomes for comparing two independent populations, and a unified formulation. Information time and independent increment property; Connection between estimation, Sums, Z-scores, and Brownian Motion.

Week 3. Example of Equal-space/increment procedures (Pocock, OBrien-Fleming, Haybittle, etc.) Two-sided and one-sided tests boundaries; unequal increments and flexible alpha-spending approach; more general family of alpha-spending families (power family, gamma family); both alpha & beta spending functions. Example of mega trial. Computer software.

Week 4. Bayesian monitoring procedures and a comparison with frequentist boundaries.

Week 5. Intro/Review of GLM. The normal linear and mixed models. Group sequential design for longitudinal data. Covariate adjustment.

Week 6. Literature reading assignment to students (for presentation and report as final exam in Weeks 12-14.) Review and catch up.

Week 7. Inference/Analysis following a sequential test. Distribution theory (likelihood, sufficiency, lack of completeness), conditional inference. Point estimate and confidence intervals; repeated p-values and confidence intervals.

Week 8. Survival sequential data analysis. When is Brownian motion not appropriate? Options when Brownian motion does not hold

Week 9. Multiple endpoints; secondary endpoint after primary endpoint.

Week 10. Monitoring for safety. Looking for a single adverse event; looking for multiple adverse events.

Week 11. Internal pilot study, sample size re-estimation, two stage designs; adaptive group sequential designs. Other topics in adaptive designs.

Week 12. Student presentations (3-5 students) and discussion

Week 13. Student presentations (3-5 students) and discussion

Week 14. Student presentations (3-5 students) and discussion

Week 15. Review