
CLRES 2025

Design and Analysis of Biomarker Studies

Course Instructor:
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Class Dates: November 1 - 29, 2010

- (with no class 11/24/2010)

Meeting time: MW 1:00 – 3:00 pm

Course Summary and Objectives: The objective of this course is to identify, describe and apply the statistical and epidemiological knowledge, tools and perspectives necessary for effectively designing, analyzing and interpreting biomarker studies. Only a brief introduction is provided on clinical and laboratory aspects of biomarker development; instead, the course will focus on the study design and associated analysis issues given a particular biomarker, or panel of biomarkers, and a corresponding set of clinical outcomes. Although applications and perspectives will focus on cancer research, the described methods are broadly applicable to a range of clinical and epidemiological settings.

Prerequisites: CLRES 2020 or other comparable biostatistics course, and ideally CLRES 2021 and 2022 (linear and logistic regression), **or permission of instructor** (which I will give as long as you have some comfort level with regression analysis).

Also, keep in mind, like almost all CLRES courses, I will assume that you have a basic knowledge of STATA software. I will give the commands you need, but will assume that you know how to open Stata, conduct basic descriptive statistics, and create a log file to turn in for homework.

Grading and Responsibilities:

- There will be reading assignments from selected articles; completion of the assigned readings may be much easier after they are covered in class, so you don't have to read them ahead of time.
- Trainees will be assigned written homework exercises that will be graded. All homework will be assigned with a due date. Late homework assignments will be penalized 10% per day over the due date unless prior arrangements have been made with the instructors.
- There will be a presentation required based on an article of your choice. The presentation must be given on the designated day for any credit, or make arrangements with me to present it ahead of time. I encourage you select an article that is of specific professional interest to you. I must have your presentation ahead of time so all presentations are loaded before we start.
- All homework assignments must be done individually; very similar papers will not be accepted.
- Class attendance is required and considered in the grading; if you must miss a given class, I will consider using participation in other class to make up that portion of your grade.
- The final exam will be a combination of multiple choice and short answers to assess your understanding of the main concepts (not use of STATA or involved calculations; that will be assessed through homework).

Grading Requirements: Class attendance = 5%, Class presentation = 15%, Final exam = 20%, and Homework = 60% (15% per assignment; 4 homeworks total).

Final Grading Scale: 90 – 100 = A, 85 – 89 = B+, 80 – 84 = B, 76 – 79 = C+, 70 – 75 = C, 60 – 69 = D and < 60 F.

Homework assignments, course information, and communication will be available at <http://courseweb.pitt.edu> as the course progresses.

Software: We will use Stata version 11 for this class (although it's ok if you have version 10). There are different versions of STATA that you can use/purchase. Any one of them is acceptable for this class.

Xinxin Dong will be the teaching assistant for this class. She will help me with some grading and Stata components of the class. There is, however, no lab or recitation component to the class.

Final Presentation Format:

The presentation must be done in Power Point, and you must hand in hard copies of your slides (3/page).

1. Title slide and main objectives (2 slide) – 30 seconds
2. Background and significance of the general problem (about 2 slides) – 1 minute
3. Background on the biomarker or panel of biomarkers, including a very brief summary of the scientific measurement issues (about 2 slides) – 1 minute
4. Study design and related approaches (about 2 slides) – 1 minute
5. Statistical methods (about 2 slides) – 1 minute
6. Results and conclusions (about 2 slides) – 1 minute
7. Summary of how the article related to, or went beyond this class; including strengths and limitations (about 2 slides) – 1 minute

*NOTE: the selected article must be a study of biomarkers which includes analysis of real data (e.g. not be a review article). The total length of time you have for your presentation will depend on the number of students enrolled

Textbook:

There is no required text for this class. I will pull some lecture material from the following textbook:

The Statistical Evaluation of Medical Tests for Classification and Prediction. By Pepe. Oxford University Press. 2004.

Primary Reference: (to be read before class starts or asap after) Phases of Biomarker Development for Early Detection of Cancer. By Pepe, et al. *Journal of the National Cancer Institute.* 2001;93(14):1054-1061.

Course Syllabus:

Date: Monday, November 1, 2010

Session 1 An introduction to biomarker studies

At the conclusion of this lecture, the student will be able to :

1. Describe the utility and applications of biomarkers
2. Describe the five phases, and associated goals, of biomarker development
3. Understand the differences between differential expression, discrimination studies, and outcome prediction and classification models

Date: Wednesday, November 3, 2010

Session 2 Phase I and Phase II Studies: Preclinical/exploratory studies and clinical assay development

At the conclusion of this lecture, the student will be able to :

1. Understand the basic issues associated with phase I preclinical and phase II clinical assay studies
2. Be able to conduct appropriate statistical analysis to assess differential expression and discriminatory ability associated with a given biomarker
3. Be able to calculate and interpret classification rates, sensitivity, specificity, and ROC curves
4. Determine sample size and power estimates for phase I and phase II studies
5. Improve grant and manuscript writing skills specific to biomarker research

Date: Monday, November 8, 2010

Session 3 The concept of classification bias and associated statistical methods

At the conclusion of this lecture, the student will be able to :

1. Understand the main types of classification bias that arise in biomarker research
2. Select appropriate re-sampling based methods to minimize classification bias
3. Understand the strengths and practical limitations of using separate data for training, testing and validation

Date: Wednesday, November 10, 2010

Session 4 Phase III and IV Studies: Retrospective banked serum and prospective screening studies

At the conclusion of this lecture, the student will be able to :

1. Describe the goals, limitations, and design of phase III and IV biomarker studies
2. Understand how to select, conduct and interpret the associated statistical methods, including logistic regression and survival analysis
3. Understand issues of temporal association and other related to pre- versus post-disease biomarker measurements
4. Understand issues related to true operating characteristics of the screening test
5. Determine the appropriate sample size or statistical power for phase III and IV studies
6. Improve grant and manuscript writing skills specific to biomarker research

Date: Monday, November 15, 2010

Session 5 More Advanced Statistical Methods for Classification

At the conclusion of this lecture, the student will be able to:

1. Understand the need for, and strengths and limitations of multiple testing methods
2. Apply the false discovery rate to controlling false significant results
3. Understand the basic differences between standard and modern regression methods
4. Describe the differences between the main types of modern regression methods
5. Understand the strengths and limitations of using modern regression methods
6. Incorporate modern regression methods into grant writing applications

Date: Wednesday, November 17, 2010

Session 6 Population effectiveness and applications to comparative effectiveness research

At the conclusion of this lecture, the student will be able to :

1. Describe the goals, limitations, and design of a phase V biomarker studies
2. Describe the role of biomarker studies in comparative effectiveness research and personalized medicine
3. Understand how to select, conduct and interpret the associated statistical methods
4. Improve grant and manuscript writing skills specific to biomarker research

Date: Monday, November 22, 2010

Session 7 Review for the final and class presentations

Review for the Final Exam: First 0.5 hour of class

Presentations: Last 1.5 hour of class

Date: Monday, November 29, 2010

Session 8 Population effectiveness, Finish article presentations and Take Final Exam

Presentations: first hour of the class.

Take Final Exam: second hour of the class.