Overview and Objectives:

This course focuses on basic concepts and analysis methods of time-to-event data and their application to problems in the health and biomedical sciences. The course is designed for medical researchers with non-biostatistics majors. Scholars will work with clinical datasets, and learn to analyze the data and explain their findings. This rigorous first course in biostatistics will serve as a prerequisite for other biostatistics courses.

At the completion of the course, the trainees should:

- recognize when it is necessary to account for time in the analysis of yes/no outcomes, and learn to appropriately summarize time-to-event data;
- understand different types of censoring, and learn to estimate and interpret survival characteristics;
- compare survival rates in different groups;
- assess the relationship of risk factors and survival times using the Cox regression model, and assess the appropriateness and adequacy of the model;
- understand issues in the design, analysis, and interpretation of studies involving time-dependent covariates;
- develop analytic skills through the analysis of data sets taken from the fields of medicine and public health; and
- develop oral and written communication skills through the description of analytic strategies and the summarization and interpretation of results.

Competencies:

This course focuses on the Data Analysis competency domain of the clinical research competencies that the ICRE uses. Every session covers elements of the Applied Analytic Techniques competency, with the learning objective of: “Determine and apply a range of appropriate statistical techniques to answer research questions and explain the implications of missing data on conclusions drawn from statistical results.”

Responsibilities:

- Students will be assigned 3 homework and 1 final project that will be graded. You are encouraged to work together on homework assignments, but you should write up your results individually and independently. Final project should be done independently without consultation except the instructors. All homework assignments (hard copy) are to be submitted by the due date.
- Evaluation criteria for this class will be based on completion of the homework, the in-class final quiz score, and the final project score.
Prerequisites:
CLRES 2021: Regression and ANOVA and CLRES 2022: Logistic Regression (or equivalent).

Course Requirements and Grading Scale:

30% Homework (no late homework submission accepted.)
10% In-class final quiz
60% Final project

For the computation of the final letter grades, the grading scale will be based on the items listed above. We will also take into account the average performance of students.

NOTE: No late submission would be considered or graded.

NOTE: Homework assignments, syllabus, course contents and materials, and communication will be available on CourseWeb at http://courseweb.pitt.edu.

Attendance Policy:

- **Lecture**: It is required for students to attend the lectures.
- **Recitation**: Recitation is optional.
- **Final quiz**: Students must physically show up in class to take the quiz.

**Note**: Students are expected to sign-in to lecture and recitation (computer provided in suite lobby). If a problem is encountered with the sign-in system, please contact the course instructor(s) as well as Ms. Juliana Tambellini at tambellinijm2@upmc.edu immediately.

Required Textbook:


Supplemental Textbook(s):

Computer package:

Stata 15, Stata Press, College Station, Texas (www.stata.com)

We recommend that students purchase or have ready access to this program. A yearly license can be purchased through University of Pittsburgh CSSD for $5. CSSD is located in Bellefield Hall. Stata is also available at the course computer labs, at the Posvar Hall, and at the Falk library in Scaife Hall.

Highly recommended books for Stat component of the course


Academic Integrity:

Students in this course will be expected to comply with the University of Pittsburgh's Policy on Academic Integrity (http://www.provost.pitt.edu/info/ai1.html). Any student suspected of violating this obligation for any reason during the semester will be required to participate in the procedural process, initiated at the instructor level, as outlined in the University Guidelines on Academic Integrity. This may include, but is not limited to, the confiscation of the examination of any individual suspected of violating University Policy. Furthermore, no student may bring any unauthorized materials to an exam, including dictionaries and programmable calculators.

Disabilities:

If you have a disability that requires special testing accommodations or other classroom modifications, you need to notify both the instructors and the Disability Resources and Services no later than the 2nd week of the term. You may be asked to provide documentation of your disability to determine the appropriateness of accommodations. To notify Disability Resources and Services, call 412-648-7890 (Voice or TTD) to schedule an appointment. The Office is located in 216 William Pitt Union.

Copyright notice:

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Other links:

- The Institute for Clinical Research Education
- University of Pittsburgh
Course Schedule

Module 1: Person-time Data (I)

At the conclusion of this module, students will be able to:

1. Define, estimate, and interpret cumulative incidence
2. Define, estimate, and interpret person-time incidence rate
3. Define and interpret incidence rate ratio
4. Perform one-sample and two-sample cumulative incidence rate(s)
5. Perform one-sample person-time incidence rate(s)
6. Perform two-sample person-time incidence rates via incidence rate ratio
7. Give mathematical relationship between cumulative incidence and person-time incidence rate

Required Reading:

- Rosner’s Book Chapter 14.1-14.4

Module 2: Person-time Data (II) and Time-to-event Data

At the conclusion of this module, students will be able to:

1. Define and interpret stratified incidence rate ratio
2. Understand and perform crude and adjusted person-time incidence rate ratio
3. Perform homogeneous test among incidence rate ratio across strata
4. Recognize time-to-event data
5. Recognize and describe the type of research question addressed by a survival analysis
6. Define censored data
7. Define and interpret a survival function
8. Define and interpret a hazard function. Understand the relationship between hazard function and person-time incidence rate.
9. Give examples and interpretations of different shapes of hazard functions
10. Identify the basic data layout for survival analysis

Required Reading:

- Rosner’s Book Chapter 14.5-14.7
- Kleinbaum and Klein, Chapter 1

Homework assignment 1:

- Due: TBD
Module 3: Nonparametric Analysis (I)  Chang

At the conclusion of this module, students will be able to:

1. Understand, estimate, and interpret survival rate of the Kaplan-Meier method
2. Understand, estimate, and interpret cumulative hazards of the Nelson-Aalen method

Required Reading:

- Kleinbaum and Klein, Chapter 2

Date: January 18, 2017
Module 4: Nonparametric Analysis (II)  Yabes

At the conclusion of this module, students will be able to:

1. Compute a log-rank test
2. Compare two (or more) survival functions using the log-rank or weighted log-rank tests
3. Decide when a log-rank test or a weighted log-rank test (generalized Wilcoxon, Terone-Ware, or Peto-Peto) is more appropriate to test the equality of two (or more) survival functions
4. Interpret and draw conclusions on the equality of two (or more) survival functions

Required Reading:

- Kleinbaum and Klein, Chapter 2

Homework assignment 2:

- Due: TBD

Module 5: Cox Proportional Hazards Model (I)  Yabes

At the conclusion of this module, students will be able to:

1. State and recognize the general form of the Cox proportional hazards (PH) model
2. Describe the properties of the Cox PH model
3. State and recognize the meaning of the PH assumption
4. Describe the properties of the baseline hazards function from a Cox PH model
5. Interpret effect of a covariate and hazard ratio from a Cox PH model
6. State and recognize what an adjusted survival curve is and how to estimate adjusted survival function using a Cox PH model
7. Determine and explain whether the PH assumption is satisfied when graphs of the hazards functions or survival functions for two groups are given
8. Perform different methods to evaluate the PH assumption and explain the differences among these methods
9. Perform overall goodness-of-fit of a Cox PH model using the Cox-Snell residual plot and interpret the results

**Required Reading:**

- Kleinbaum and Klein, Chapters 3, 4, and 6

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**Module 6: Cox Proportional Hazards Model (II) Yabes**

**At the conclusion of this module, students will be able to:**

1. Recognize when and how to perform a stratified Cox procedure
2. Evaluate the effect of a predictor from a stratified Cox model
3. State the no-interaction assumption; describe and carry out a test of the no-interaction assumption; and describe and carry out an analysis when no-interaction assumption is not satisfied.

**Required Reading:**

- Kleinbaum and Klein, Chapter 5

**Homework assignment 3:**

- Due: TBD

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**Module 7: Time-dependent Cox models Yabes**

**Parametric Survival Models**

**At the conclusion of this module, students will be able to:**

1. State and recognize the general form of the Cox model extended for time-dependent covariates
2. Differentiate between time-dependent covariate and a time-dependent covariate-effects models
3. Perform a Cox model with time-dependent covariates and interpret the results
4. Determine when to use, how to perform and interpret common parametric survival regression models
5. Distinguish between proportional hazards and accelerated failure time models

**Required Reading:**

- Kleinbaum and Klein, Chapters 6 and 7
Students are expected to physically show up in class to take the final quiz.

At the conclusion of this session, students will be able to:

1. Recognize various scenarios in which multivariate failure time data may arise
2. Identify analysis approaches for multivariate failure time data.
3. Determine when to use, how to analyze and interpret time-to-event data with competing risks

Required Reading:

- Kleinbaum and Klein, Chapters 8 and 9