BIOM 611: **Statistical Methods for the Design and Analysis of Experiments Spring 2018**

Description: This introductory course provides a foundation for the fundamental concepts in biostatistics as they relate to experimental design and analysis. We focus on defining research questions, carefully choosing appropriate analytic tools and interpreting the results of the analyses, including limitations of the analysis. The course has three units:

- Unit 1 introduces statistical concepts and their application to simple study designs. We begin with the broad topic of 'reproducibility' and the role statistics plays in methods, results and inferential reproducibility. We focus in detail on two key inferential methods: hypothesis testing and estimation. We consider how to evaluate the strength of evidence supporting a particular research hypothesis, consider the generalizability of our conclusions. and estimate the magnitude of an effect, and the precision of our estimate. Estimation of statistical power and sample size are discussed along with the impact of poor statistical power on results reproducibility. This first unit illustrates concepts using relatively simple methods, focusing on individual samples and considering single sample tests/estimates of proportion, and tests/estimates of means or medians.
- Unit 2 generalizes the methods from Unit 1 to study designs with two samples.
- Unit 3 concludes by considering differences in means and proportions between multiple groups and associations between quantitative variables. Analysis of variance (ANOVA) including two-way ANOVA is considered in detail. The issue of inferential reproducibility in the context of multiple comparisons is used to motivate approaches to adjust for multiple comparisons. Correlation and regression models are introduced.

Both parametric and non-parametric (rank-based) approaches to inference will be discussed.

Statistical methods will be implemented using the freely available software package Rcmdr. Rcmdr is based on R; it allows students to import and analyze data using menu-driven options. The final output from an Rcmdr analysis is a code file and the output of the code (either an html, pdf or word file) integrates analyses from R with documentation. Rcmdr can thus be used for methods reproducibility. Initially we will use the menu-driven options; as the course progresses students will learn how to download and use various R packages, and to create simple R codes. **At this point, we do not anticipate parallel instruction using R or RStudio.**

The primary goal of BIOM 611 is not instruction in R coding.

This course is **not recommended** for students with a moderate to strong quantitative/computational background.

Attendance: Lecture attendance is graded through polling software.

Participation in Lecture: Participation in lectures through polling software is a required part of this course. I will poll in the lectures, to encourage participation and to help me assess understanding. We use Turning Technologies polling software (Turning Point Mobile) to poll students in the classroom. A web-enabled device is needed with the Turningpoint mobile app. This device is recommended for the first class and required after the first class. Beginning with week 2, polling and attendance will be graded.
A subscription for BIOM 611 is required and can be purchased from the bookstore. Once registered Turning Technologies will link your account with Canvas. The fee per semester is around $18.

Please visit www.turningtechnologies.com/student-info for specific registration instructions.

Labs: The lab will require a laptop with access to the internet. R is currently not available through mobile devices. This year we will work exclusively with Rcmdr. Each week you will work with a group of other students, and the group will be required to hand in a lab report. Typically these lab reports will document the work that you did in class exploring different analytical tools in Rcmdr.

Course Notes: Course notes and/or supplemental reading will be included on the Canvas website each week. The course notes are new this year. The notes follow the lecture very closely.

R Materials: We provide detailed commands in lab materials. The Fox text book described below is useful but not necessary. The Karp website also provides a nice introduction to Rcmdr.

Fox, J 2016. Using the R Commander: A point and click interface for R. Chapman & Hall. (CRC Press) (Optional Resource: we will provide detailed commands for implementing methods)

https://cran.r-project.org/doc/contrib/Karp-Rcommander-intro.pdf

Website: CANVAS through https://upenn.instructure.com/

All of the materials for student use are linked through modules. The file folders are for use by the instructors. The file folders are not organized in a fashion intended for use by students.

Instructors & Activities:

Course Director: Mary Putt, PhD, ScD (621 Blockley), Ph (215) 573-7020
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Administrative Assistant: *Joyce Jones woodwarj@pennmedicine.med.upenn.edu*

Teaching Assistants: *Victoria Arthur*, BA
Carrie Caswell, MS
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Lingziao Zhang, MS

Office Hours: After lab & TBD: See CANVAS Announcements

Activity	Instructor	Time	Location
Lectures	*Putt*	*Tu 11.00-12.30*	*Austrian Auditorium*
In-class Exam		*27 Feb 11.00-12.30*	*Smilow Auditorium*
Labs		*Tu-Fr: 15.30-17.00*	*252 BRB II/III*
Coursework Review		*Mn: 15.30-17.00*	*Austrian Auditorium (OPTIONAL)*

Week	Unit	Date	Topic
1		16 January	*Lecture:* Course Organization. Goals and expectations. Self-assessment and discussion of student goals. Reproducibility: methods, results and inferential. Basic definitions: Probability & Sampling *Lab:* The binomial distribution & Sampling. Installing R, and Rcmdr.
2	1	23 January	*Lecture*: Probability Distributions for categorical random variables. The Binomial Distribution. Conceptual hypothesis

			testing: 3-step method. What is a p-value? Single sample test of proportion (Exact binomial test) Probability distributions for continuous random variables:The normal distribution. The central limit theorem and the sampling distribution of the mean. The normal distribution. The central limit theorem and the sampling distribution of the mean. *Lab:* Importing data, making a graph and summary statistics. Methods reproducibility: Creating an R markdown file with integrated comments and results. Saving code and output Data management in R. Subset data, save dataset, creating and modifying variables. Probability distributions in Rcmdr, exact binomial test.
3	1	30 January	*Lecture:* Review of hypothesis testing and exact binomial test. Distribution of the sample mean Concept of a standardized statistic and approximate (large-sample) tests. Single-sample inference for proportions using a Z-test. Continuity correction. *Lab:* Data manipulations. More graphical procedures. Single sample hypothesis testing. Choosing between tests; assessing validity assumptions.
4	1	6 February	*Lecture* Single-sample inference for continuous random variables. Non-parametric methods. Quantile plots. Tests of normality (with caveats) *Lab:* One-sample T-test, Wilcoxon Signed Rank Test, Sign-test, Assessing normality; graphical approaches and hypothesis tests. Choosing between tests; assessing validity assumptions
5	1	13 February	*Lecture* Type I and Type II errors in hypothesis testing, Sample size determination, Impact of sample size on reproducibility. Are small p-values less likely than large p-values when the null hypothesis is true? What happens if your experiment has low statistical power and you reject the null hypothesis; impact on reproducibility. *Lab:* Sample size determination. Type I and Type II error exercises. Understanding how low statistical power impacts reproducibility
6	1	20 February	*Lecture:* Estimation & Confidence Intervals (Single Sample Categorical and Continuous Variables). Exact, approximate (large-sample) and bootstrap methods. Lab: Estimation, Single sample proportions (large sample and exact), T-intervals, Assessing validity assumptions. Binomial confidence intervals: exact and Wilson Score. T-intervals. Bootstrap confidence intervals.
		26 February	*Optional Review session: Student questions*
7		27 February	**Midterm Exam** Format TBD
			Midterm Break
8	2	13 March	*Lecture:* Two-sample proportions. Metrics (risk difference, risk ratio, odds ratio). Z-test. Pearson's Chi-square test. Fisher's exact test. Paired data: McNemar's test. Two-sample T-tests. Lab: Two-sample tests (Proportions and T-tests)
9	2	20 March	*Lecture:* Two-sample continuous data continued. Wilcoxon Rank Sum test. Paired data; Paired t-test. Power and Sample size. Results Reproducibility. Introduction to contingency tables. Lab: Wilcoxon Tests, Two-sample Bootstrap Confidence Intervals. Choosing between tests. Sample size calculations.
10	2	27 March	*Lecture*: Contingency tables continued. Issues with multiple comparison: Inferential reproducibility. Family-wise error rate.

			Bonferroni method. Introduction to one-way ANOVA. Lab: Contingency tables. Ordered predictor variable: Cochran Armitage test for trend. Pairwise hypothesis testing and confidence intervals. Maintaining family-wise error rate.
11	2 & 3	3 April	*Lecture* One-way ANOVA (continuous outcome, single categorical predictor), Approaches to maintaining family-wise error rates (Tukey HSD, Holm-Bonferonni), Kruskal Wallis. Two-way ANOVA (Additive model) Lab: One-way ANOVA, Kruskal Wallis. Pairwise tests and corrections for multiple comparisons
12	3	10 April	*Lecture*: Two-way ANOVA (Deciding between and Additive and Interaction Model). Issues with balanced and unbalanced designs. Introduction to linear regression models. Lab: Two-way ANOVA and Kruskal-Wallis, P-value adjustment methods, Tukey HSD confidence intervals, Two-way ANOVA for balanced and unbalanced designs. Simple linear regression.
13	3	17 April	*Lecture* Linear Regression & Correlation continued. Lab: Correlation (Pearson and Spearman) Linear Regression continued. Assessment of fit. Multiple linear regression.
	All	23 April	*Optional Review Session: Student Questions*
14	3	24 April	*Lecture* Instructor discretion: Loose ends and/or review. Lab: No lab
			Provide solution to assignment: Reading days and office hours
EXAMINATION PERIOD		3 May	**Take-home Final** Due 9 May

Assessment:

Component	Contribution to Grade (%)
Weekly Homework (Canvas Quiz)	
Class Attendance (Turning Point, 2 free absences)	*10*
Class Participation (Turning Point, drop lowest 2 grades)	*10*
Weekly assignments (drop lowest 2 grades)	*15*
Lab Reports (Group work)	*10*
Examinations	
Midterm Exam	*20*
Final	*35*

An absolute grade of at least 90 guarantees an A- or better; a grade of at least 80 guarantees a B- or better.

Weekly Homework: Intended to reinforce lecture and lab material and provide experience applying statistical methods and interpreting results of the analysis. *Homework is set up in the CANVAS quiz format and must be submitted through CANVAS.* Late submissions are penalized 10% for the first 8 hours after the due time; it does show up as late on our grade books. Late homework beyond 8 hours will be assigned a grade of 0, unless you have a health-related issue or unexpected circumstances (see below).

Due times for coursework show on CANVAS and will generally be 11:59 PM on Tuesdays.

Check the announcements before starting your coursework; any comments, hints, or corrections will be posted there. Announcements are organized by date.

Assignments are learning experiences not mini-tests. Don't get bogged down and overly frustrated. I encourage students to seek help through either: (1) in-person office hours (gold standard—typically we can solve problems in person). (2) discussion boards through CANVAS. If you send me or your TA an email we will post to CANVAS discussion boards—it's helpful if you just post directly to CANVAS. We answer questions posted to the discussion board on CANVAS.

A 'typical' student should expect to devote around **6-12 hours per week for coursework outside of lab and lecture**.

Discussion Board Schedule: I will check discussion boards and respond once per day during normal business hours (8AM to 5PM weekdays & generally not on weekends). I typically do not respond to homework questions on Tuesdays after 2 PM. Students are encouraged to respond to each others' questions.

Midterm Exam: The midterm will focus on statistical concepts with less emphasis on applications.

Final Examination: The final examination is take-home. It is cumulative and will involve both concepts and data analysis.

Grade Changes: Any grade changes to a TA or myself must be requested in person (not email).

Academic Integrity: Unless specifically indicated in writing, students may work together but must submit individually constructed responses to questions. **Doing otherwise constitutes a violation of the code of academic integrity**. Students must work independently on all exams. All students enrolled at Penn are responsible for understanding and following the Penn code of academic integrity. Please see *provost.upenn.edu/policies/pennbook/2013/02/13/code-of-academic-integrity*

Students with Disabilities: The University of Pennsylvania is committed to providing equal educational opportunities to all students, including students with disabilities. Penn does not discriminate against students with disabilities and provides reasonable accommodation to a student's known disability in order to afford that student an equal opportunity to participate in University-sponsored programs.

Excused Work; Unexpected Circumstances

Please contact me if you experience health problems, or any other unexpected circumstances, that impact your progress in the course.