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 methods are broadly applicable to a range of clinical and epidemiological settings.

PREREQUISITES
The only prerequisite is that you have taken CLRES 2020, or an equivalent biostatistics course. However, if you have no familiarity with regression analysis, you may struggle with some of the concepts and methods. If you have taken CLRES 2021 and 2022 (linear and logistic regression), that will be more than sufficient as background knowledge on regression. Also, keep in mind, as with any CLRES course, I will assume that you have a basic knowledge of STATA software. I will give the specific commands as needed, but will assume that you know how to open Stata, conduct basic descriptive statistics, and create a log file to turn in for homework.

COURSE FORMAT
1. For each session, trainees will read/study 2-4 pertinent required papers before class, and sometimes have Stata assignments due in advance. Classroom activities, including lecture, analysis projects, and small group discussions will then expand upon those topics. To maximize the utility of classroom discussions and associated exercises, it is expected that all trainees complete all assignments ahead of class and be prepared to discuss their work; classroom activities will only briefly review the key concepts, and instead focus on expanding knowledge already gained from assignments. Please make sure that you have read the material and are prepared to discuss it further for the class. I will strive to minimize overlap between in-class activities and material that is already presented in the papers.
2. The majority of class time will be used for practical application of what has been learned by reading the assigned papers. This will be done through exercises using data, discussions of other research papers; small group discussions, debates, and other formats using active learning methods.

CLASS ACTIVITIES
Class activities will typically adhere to the following schedule, although more specific schedules are posted for each class.

- 1-1:05: Hand in homework (if applicable) and answer miscellaneous procedural questions
- 1:05-1:10: Pre-class assessment of required reading assignment
- 1:10-1:15: Discussion of any common themes from blackboard discussion (if needed)
- 1:15-1:50: Lecture presentation to describe key conceptual issues
- 1:50-2:20: Demonstration of STATA commands and results
- 2:20-2:40: Small group and class discussion to further explore key topics
- 2:40-2:45: Post-class assessment of class activities
- 2:45-3:00: Take-home points and transition to next lecture
Grading Components and Responsibilities

- Every class (starting with lecture 2) will start with a graded assessment using clickers and end with another graded assessment (including for lecture 1). Pre-class assessments will include questions on required reading, and the post-class assessment will be developed to assess topics covered from lecture and class activities. These questions are meant to stress basic concepts not details.
  - Points assigned: # correct responses (of 5 possible) from the beginning assessment and # correct (of 5 possible) for the ending assessment.

- Clickers will also be used during the class for the graded assessments and to assess participation. For in-class participation, full credit will be given as long as you respond to the questions – in fact, there may not be a correct answer for some questions.
  - Points assigned: 2.5 × (# responses / # questions asked) for each class

- Written homework is also due at the beginning of class on the assigned days, plus one additional assignment after the last class. Late homework assignments will be penalized 10% per day past the due date unless prior arrangements have been made with the instructor.
  - Points assigned: Each HW will include open format questions or calculations to be done in Stata, with subsequent interpretation of results. If complete, the total assignment will be graded from 11-20, where 11-12=major errors, 13-14=numerous moderately significant errors, 15-16=numerous minor errors or 1 moderately significant error, 17-18=a few minor errors, 19-20=essentially all correct. Up to 10 penalty points will be deducted for missing information, skipped questions, etc., to get a final score of 1-20.

- All homework assignments must be done individually; very similar papers will returned with a grade of 0% with no opportunity for a make-up.
- Class attendance is inherently required to take the assessments and for the participation points.
- I will also require that you post at least 5 questions or comments to blackboard, and respond to at least 5 other questions or comments (posted by other students) throughout the class. More than one reply can be posted for a given question or comment. These questions or comments can be as simple as “Hey I really didn’t understand the 5 phases of biomarker development – I don’t even know where to start in trying to understand them”, or they can be as complicated as providing an example from your research that you think relates to the given topic covered in the last lecture. As long as there is some reflection of course content in your question/response, you will receive full credit for that item. So for instance, a comment about how I like to drink coffee during class will not receive any credit since it does not reflect any course content (although coffee is pretty important to me…). I will give 5 days after each lecture for students to reply, after which time I will reply to those questions needing a response.
  - Points assigned: 3 × (# questions or comments posted + # replies posted, up to 5 each)

Final Exam
There will not be a final exam. Information covered in the last class will be assessed in the last homework assignment where you will have to develop a 1-page concept for a new project proposal in a topic of your choosing. Instead of using an exam format, knowledge gained from classes and reading assignments will be assessed through the homework and in-class assessments at the beginning and end of each lecture, as well as participation during the lecture.

Policy on Missed Class/Assessments
I will give an opportunity for a make-up assessment if you are required to miss class for a professional event (e.g. conferences) or have a family emergency. You will not be penalized for these instances as long as I know in advance. However, you must notify me ahead of time.
A brief presentation (of approximately 30 minutes) of the lecture components of class, and a summary of other class activities, will be videotaped for anyone who misses a lecture. Within approximately one week after each class, I will also post solutions to the pre- and post-class assessments. Any excused make up assessments must be made up within that time (before lecture notes are posted).
CALCULATION OF OVERALL GRADE
As described in the above section on grading components, the following totals represent possible points that can be accumulated. I will drop the 2 lowest pre-class and 1 lowest post-class assessment score.

- Clicker assessments at the beginning of class: 6 assessments × 5 = 30 possible points
- Clicker assessments at the end of class: 6 assessments × 5 = 30 possible points
- Participation during class: 8 lectures × 2.5 = 20 possible points
- Homework due at the beginning of 2 assigned classes and 1 due a week after the last class: 3 assignments × 20 = 60 possible points
- Blackboard questions and responses: 30 possible points
- Total Points Possible = 170

FINAL GRADING SCALE (BASED ON THE % OF 170 POINTS OBTAINED)

- 93 – 100 = A, 90-92 = A-
- 88 – 90 = B+, 80 – 87 = B, 78-79 = B-
- 75 – 79 = C+, 70 – 74 = C
- 60 – 69 = D and < 60 F
- I reserve the right to curve up the grades, but it’s highly unlikely I will need to (p<0.05).

Homework assignments, course information, and communication will be available at [http://courseweb.pitt.edu](http://courseweb.pitt.edu) as the course progresses.

SOFTWARE
We will use Stata version 11 for this class. There are different versions of STATA that you can use/purchase. The least expensive student version may be unable to handle the size of some of the data sets used for homework. In that case, you will need to use the lab computers in Parkvale 222.

TEXTBOOKS AND OPTIONAL ARTICLES
The articles needed for this class are listed as required or optional reading for their corresponding session. All of the articles can be freely downloaded from the university's library system.

The textbooks are optional, and I do not expect students to purchase them, nor will I expect that you have read them. I will use these 3 textbooks as references to help create class notes and expand on the required reading assignments. Although it is not necessary for this class, it may be useful for you to buy at least the Pepe textbook as a reference if you are planning on doing biomarker research, formulating prediction models, and/or assessing medical or other diagnostic tests as part of your career.

The role of the optional readings assignments is to provide articles which provide either 1) a more basic description that might be helpful to reinforce or better understand the key topics, or 2) expand in more detail on the key concepts for those with a specific interest in the given topic. As stated above, I will not expect you to have read the either the optional articles or the textbook.

DATASETS FOR HOMEWORK ASSIGNMENTS
In addition to referring to Pepe’s textbook for lecture notes, I will also use the datasets on her website for Homework assignments. The website is [http://labs.fhcrc.org/pepe/book/#datasets](http://labs.fhcrc.org/pepe/book/#datasets). Data sets are available in Stata format.
REFERENCE (OPTIONAL) TEXTBOOKS
- This text covers a wide range of biomarker-related study design and analysis issues, although the level of mathematics is probably higher than what most of ICRE trainees would prefer. Therefore, it serves as a reasonable reference text, but needs to be supplemented substantially for purposes of this class. I do not recommend that you try to read it cover to cover for this class, but rather refer to the class-specific readings I note for each lecture.

- This text book provides a more indepth references for some of the topics. I will not expect you to buy this book; I will provide the needed information via class notes. It's an excellent reference for PhD students in statistics or biostatistics (which we've had in this class in the past).

- This text is very different from the other two, and is very conceptual and high-level, with insufficient details on the formulas and math to serve as a single reference text. It is however an excellent supplement to the other text with discussions that help clarify some of the more conceptual or big-picture aspects of more advanced topics.

DISABILITY RESOURCES AND SERVICES
The ICRE supports and follows the diversity policies of the Office of Diversity, Health Sciences. Students needing support and/or accommodation may request it through the University's Office of Disability Resources and Services. If you have a disability that requires special testing accommodations or other classroom modifications, you need to notify both the instructor and Disability Resources and Services no later than the second 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.

POLICY ON 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.

Examples of violating this policy include, but are not limited to, copying material from the internet (or elsewhere) without proper citations, sharing homework solutions with other students, and looking at another student’s response during pre- or post-class assessments. These examples, however, are only a few illustrations, and not meant to represent an exhaustive list.
Course Schedule:

Session 1: Introduction to Biomarkers, Medical Tests, and Classification Accuracy

Learning Objectives:
At the conclusion of this class, trainees will be able to describe the concept and importance of biomarkers and calculate and interpret basic measures of classification accuracy.

Learning Topics:
- Describe the concept of a biomarker and its utility in clinical research.
- Describe the relationship between biomarkers, diagnostic tests and other medical tests.
- Calculate measures of classification accuracy, by hand and in STATA, and describe their strengths and limitations of each.

Required Reading:
  - [http://www.nature.com/clpt/journal/v69/n3/full/clpt200113a.html](http://www.nature.com/clpt/journal/v69/n3/full/clpt200113a.html)
  - Goal: define key concepts and definitions in biomarker research
  - [http://cancerres.aacrjournals.org/content/66/6/2953.full](http://cancerres.aacrjournals.org/content/66/6/2953.full)
  - Goal: Illustrate common application of biomarkers in cancer research.
  - Goal: Describe the broad challenges associated with conducting biomarker research in cancer.

Optional Reading:
- Chapter 1, and part of Section 2.7 of Azuaje
- Chapters 1-2 of Pepe
- Chapter 1 and 2.1-2.2 of Zhou, et al.

Class Activities:
- 1:00-1:15: Provide an overview of the syllabus and class procedure
- 1:15-1:20: Pre-class assessment of required reading (which will not count for a grade)
- 1:20-1:25: Pre-course assessment of topics to be covered (also does not count for a grade)
- 1:25-2:00: Lecture presentation on calculating measures to assess classification accuracy
- 2:00-2:20: Small group and class discussion to further explore key topics
- 2:20-2:40: Demonstration of STATA commands and results
- 2:40-2:45: Graded post-class assessment of class activities
- 2:45-3:00: Summary of take-home points and transition to next lecture
Session 2: Phases of, and Designs for Biomarkerer Studies

LEARNING OBJECTIVES:
At the conclusion of this class, trainees will be able to describe the five phases of biomarker development and conduct some of the associated statistical procedures in STATA.

LEARNING TOPICS:
- Describe the five phases of biomarker development.
- Describe the primary objectives, associated study designs and statistical methods for each phase.
- Describe how the terms differential expression, discrimination, prediction, screening, validation, and effectiveness associated with each phase.
- Write, run and save a simple do file in STATA.
- Describe the role of program documentation in reproducible research.

REQUIRED READING:
  - http://jnci.oxfordjournals.org/content/93/14/1054.short
  - Goal: Define the 5 stages of biomarker development.
  - http://www.cceb.upenn.edu/biostat/conferences/ClinTrials12/
  - Goal: Provide specific illustrations for design of biomarker studies and describe other related key concepts.
- Pepe, et al. Pivotal evaluation of the accuracy of a biomarker used for classification or prediction: standards for study design. JNCI. 2008;100:1432-1438.
  - http://jnci.oxfordjournals.org/content/100/20/1432.short
  - Goal: Further expand on key concepts in designing biomarker trials.

OPTIONAL READING:
- Hellquist, et al. Effectiveness of population-based service screening with mammography for women ages 40 to 49 years. Cancer. DOI: 10.1002/cncr.25650
  - Goal: Provide an illustration of a stage 5 effectiveness biomarker study.
- Section 8.1 of Pepe; Chapter 3 of Zhou; Sections 2.1-2.2, 2.4 and 2.6 of Azuaje

CLASS ACTIVITIES
- 1-1:05: Answer any miscellaneous procedural questions
- 1:05-1:10: Graded pre-class assessment of required reading assignment
- 1:10-1:15: Discussion of any common themes from blackboard discussion (if needed)
- 1:15-1:50: Lecture presentation on biomarker study designs
- 1:50-2:20: Demonstration of STATA commands and results
- 2:20-2:40: Small group and class discussion to further explore key topics
- 2:40-2:45: Graded post-class assessment of class activities
- 2:45-3:00: Take-home points and transition to next lecture
Session 3: The ROC curve and other Classification Statistics

**Learning Objectives:**
At the conclusion of this class, trainees will be able to describe the concepts of ROC curves, area under the ROC curve and alternative measures for classification, and interpret associated results.

**Learning Topics:**
- Describe the concept of an ROC curve, and when it is appropriate and useful.
- Interpret the area under the ROC curve.
- Describe the NRI and IDI approaches to assessing classification.
- Calculate classification measures in STATA.

**Required Reading:**
  - [http://www.ajronline.org/content/184/2/364.full](http://www.ajronline.org/content/184/2/364.full)
  - Goal: Describe the basic concept and utility of the ROC curve
  - [http://www.clinchem.org/content/54/1/17.full.pdf](http://www.clinchem.org/content/54/1/17.full.pdf)
  - Goal: Describe alternative measures to the ROC curve
  - [http://www.aje.oxfordjournals.org/content/early/2011/106/14/aje.kwr086](http://www.aje.oxfordjournals.org/content/early/2011/106/14/aje.kwr086)
  - Goal: Describe another alternative measure to the ROC curve

**Optional Reading:**
  - [http://www.cceb.upenn.edu/biostat/conferences/ClinTrials12/](http://www.cceb.upenn.edu/biostat/conferences/ClinTrials12/)
  - Goal: Provide further reinforcement of the applicable methods.
  - [http://www.epibiostat.ucsf.edu/courses/RoadmapK12/SIGS/Pencina.pdf](http://www.epibiostat.ucsf.edu/courses/RoadmapK12/SIGS/Pencina.pdf)
  - Goal: Provide the original reference and more detail on the applicable methods.
- Section 2.7 of Azuaje
- Chapters 4-5 of Pepe
- Sections 2.3-2.12 of Zhou, et al.

**Class Activities**
- 1-1:05: Answer any miscellaneous procedural questions
- 1:05-1:10: Graded pre-class assessment of required reading assignment
- 1:10-1:15: Discussion of any common themes from blackboard discussion (if needed)
- 1:15-1:50: Lecture presentation on ROC curves, the NRI, and the IDI
- 1:50-2:20: Demonstration of STATA commands and results
- 2:20-2:40: Small group and class discussion to further explore key topics
- 2:40-2:45: Graded post-class assessment of class activities
- 2:45-3:00: Take-home points and transition to next lecture
Session 4: Data Reduction and Multiple Testing

Learning Objectives:
At the conclusion of this class, trainees will be able to describe the concepts of data reduction and multiple testing, and identify applicable scenarios. Trainees will also be able to calculate principle components in STATA and apply that approach to other regression methods.

Learning Topics:
- Describe the motivations for multiple testing and data reduction.
- Identify the main approaches to adjusting for multiple testing.
- Calculate Bonferroni and false discovery rate adjustments in STATA.
- Identify the main approaches to data reductions.
- Calculate principle components as use them as predictor variables in STATA.

Required Reading:
  - Goal: Describe the general challenges leading to the need for multiple comparisons
  - Goal: Define a specific approach to controlling false significant results.
  - http://www.springerlink.com/content/87m464129v48q233/
  - Goal: describe the general concept of principal components for data reduction

Optional Reading:
- Section 2.3 of Azuaje
  - Goal: Provide a more detailed description of multiple testing methods.
- Rothman. No adjustments are needed for multiple comparisons. Epidemiology. 1:43-46
  - Goal: Describe an alternative perspective on the need for multiple testing.

Class Activities
- 1:05-1:10: Collect Homework #1 on assessing classification accuracy.
- 1:05-1:10: Answer any miscellaneous procedural questions
- 1:10-1:15: Graded pre-class assessment of required reading assignment
- 1:15-1:20: Discussion of any common themes from blackboard discussion (if needed)
- 1:20-1:50: Lecture presentation on multiple testing and data reduction
- 1:50-2:20: Demonstration of STATA commands and results
- 2:20-2:40: Small group and class discussion to further explore key topics
- 2:40-2:45: Graded post-class assessment of class activities
- 2:45-3:00: Take-home points and transition to next lecture
Session 5: Modern Regression, Machine Learning and Other Ways to (Over-) Fit Data

LEARNING OBJECTIVES:
At the conclusion of this class, trainees will be able to identify the main types of modern regression methods, including parametric and non-parametric models. Trainees will also be able to described the key concepts of selected methods, including classification trees, neural networks, support vector machines and basic clustering algorithm, and will be able to run selected analyses in STATA.

LEARNING TOPICS:
- Describe the strengths and limitations of standard regression models for prediction and prognosis.
- Identify the main classes of modern regression methods, and describe their differences from standard methods.
- Describe the key features of classification trees, neural networks, support vector machines and basic clustering algorithm, including their primary strengths and limitations.
- Implement selected methods in STATA.

REQUIRED READING:
  - [http://www.springerlink.com/content/2664](http://www.springerlink.com/content/2664)
  - [http://cebp.aacrjournals.org/cgi/repreintframed/14/4/981](http://cebp.aacrjournals.org/cgi/repreintframed/14/4/981)
  - Goal: Provide an illustration of using classification trees for biomarker panels.
  - [http://www.pnas.org/content/102/21/7677.short](http://www.pnas.org/content/102/21/7677.short)
  - Goal: Provide an illustration of using other alternative methods for biomarker panels.

OPTIONAL READING:
- Section 3.3 and 3.4 of Azuaje

CLASS ACTIVITIES
- 1-1:05: Answer any miscellaneous procedural questions
- 1:05-1:10: Graded pre-class assessment of required reading assignment
- 1:10-1:15: Discussion of any common themes from blackboard discussion (if needed)
- 1:15-1:50: Lecture presentation on modern regression models
- 1:50-2:20: Demonstration of STATA commands and results
- 2:20-2:40: Small group and class discussion to further explore key topics
- 2:40-2:45: Graded post-class assessment of class activities
- 2:45-3:00: Take-home points and transition to next lecture
Session 6: Methods for Reducing Classification Bias in Prediction Modeling

Learning Objectives:
At the conclusion of this class, trainees will be able to describe the concept of classification bias and identify relevant scenarios. Trainees will also be able to describe resampling approaches to minimizing bias and conduct these methods in STATA.

Learning Topics:
- Describe the concept of bias and how it differs from random variability.
- Describe the main types of classification bias that arise in biomarker research.
- Describe the concept of resampling and related approaches for bias reduction.
- Describe strengths and limitations of different resampling methods and contrast them with independent validation.
- Calculate validated and cross-validated classification estimates and ROC curves in STATA.

Required Reading:
  - Goal: Describe the need for, and an example of validating prediction models.
  - http://bioinformatics.oxfordjournals.org/content/21/15/3301.full
  - Goal: Describe resampling procedures for reducing classification bias.

Optional Reading:
  - Goal: Describe a more detailed justification for needing to validate prediction results.

Class Activities:
- 1-1:05: Answer any miscellaneous procedural questions
- 1:05-1:10: Graded pre-class assessment of required reading assignment
- 1:10-1:15: Discussion of any common themes from blackboard discussion (if needed)
- 1:15-1:50: Lecture presentation on methods for reducing classification bias
- 1:50-2:20: Demonstration of STATA commands and results
- 2:20-2:40: Small group and class discussion to further explore key topics
- 2:40-2:45: Graded post-class assessment of class activities
- 2:45-3:00: Take-home points and transition to next lecture
Session 7: Implementation and Validation of Clinical Prediction Rules

**LEARNING OBJECTIVES:**
At the conclusion of this class, trainees will be able to describe the stages of building and interpreting a clinical prediction rule, including evaluating bias, and fitting associated models in STATA.

**LEARNING TOPICS:**
- Describe primary objectives for, and stages of building, testing and validating a prediction rule.
- Describe sources of bias and how a statistical model is utilized for clinical decision making.
- Conduct multiple steps of modeling for clinical prediction rules in STATA.

**REQUIRED READING:**
  - Goal: Illustrate the use of prediction rules in cancer research.
  - Goal: Illustrate the use of a prediction rule for pneumonia risk.
  - Goal: Further describe principles for development and utility of prediction rules.
  - [http://www.annals.org/content/125/5/406.full](http://www.annals.org/content/125/5/406.full)
  - Goal: Further describe principles for development and utility of prediction rules.

**OPTIONAL READING:**
- Vickers and Cronin. Everything you always wanted to know about evaluating prediction models (but were afraid to ask). *Urology.* 2010;76(6):1298-1301.
  - Goal: Provide an overview of key issues in developing and evaluating prediction rules.
  - Goal: Provide a more detailed discussion of statistical concerns for prediction rules.

**CLASS ACTIVITIES**
- **1-1:05:** Collect Homework #2 on modeling approaches for biomarker panels.
- **1:05-1:10:** Answer any miscellaneous procedural questions
- **1:10-1:15:** Graded pre-class assessment of required reading assignment
- **1:15-1:20:** Discussion of any common themes from blackboard discussion (if needed)
- **1:20-1:50:** Lecture presentation on clinical prediction rules
- **1:50-2:20:** Demonstration of STATA commands and results
- **2:20-2:40:** Small group and class discussion to further explore key topics
- **2:40-2:45:** Graded post-class assessment of class activities
- **2:45-3:00:** Take-home points and transition to next lecture
Session 8: Grant Writing with Applications to CER and Personalized Medicine

**LEARNING OBJECTIVES:**
At the conclusion of this class, trainees will be able to describe the role of biomarkers in comparative effectiveness research (CER) and their relevance to personalized medicine. Trainees will also be able to calculate sample sizes for selected designs, describe connections between phases of biomarker research, previously discussed concepts, and corresponding research designs for a grant application.

**LEARNING TOPICS:**
- Describe the main priority areas for CER and the corresponding relevance of biomarker studies.
- Describe the concepts of heterogeneity of treatment effects, personalized medicine, biomarker signatures, and their relevance to CER, and identify some of the relevant statistical approaches.
- Identify how regression analysis does or does not identify individualized treatment effects.
- Connect goals and stages of biomarker research to specific aims and analysis plans.
- Identify how the previously-studied methods do or do not apply to a given conceptual goal.
- Calculate selected sample size estimates applicable to grant writing.

**REQUIRED READING:**
  - Goal: Provide an introduction to the concept of CER.
  - [http://content.healthaffairs.org/content/30/12/2259](http://content.healthaffairs.org/content/30/12/2259)
  - Goal: Describe challenges/approaches for biomarkers, CER and personalized medicine.
  - Goal: Summarize some main concepts in the course for consideration in grant writing.

**OPTIONAL READING:**
- Sections 8.2-8.7 of Pepe, Sections 2.8-2.9 of Azuaje, and Chapter 6 of Zhou

**CLASS ACTIVITIES**
- 1:00-1:05: Answer any miscellaneous procedural questions
- 1:05-1:10: Graded pre-class assessment of required reading assignment
- 1:10-1:15: Discussion of any common themes from blackboard discussion (if needed)
- 1:15-1:50: Lecture presentation on grant writing, CER and personalized medicine
- 1:50-2:20: Demonstration of STATA commands and results
- 2:20-2:40: Small group and class discussion to further explore key topics
- 2:40-2:45: Graded post-class assessment of class activities
- 2:45-3:00: Take-home points and transition to next lecture

Date TBD after final session: Collect Homework #3 on design of, and analysis plans for biomarker studies.