Clinical Questions and Study Designs

We recommend you edit this document directly in a markdown editor, such as stackedit.

The purpose of this section is to give you practice in quickly identifying the research question and study design in clinical informatics studies. Combined with what you know about the biases inherent to different study designs, this skill will let you quickly identify if the study you are reading is well-suited to answer the question it raises.

For the abstracts listed below, identify the study type(s) and level(s) of analysis used in each and briefly explain your answer. For study designs, be explicit about cross sectional vs longitudinal, retrospective vs prospective, cohort vs case-control when applicable. Some study design names imply some of these information. For example, RCT implies prospective. For observational studies, name all properties to get full credit. For example, if a study is a longitudinal retrospective cohort study, and your answer is retrospective cohort, you will only get partial credit. If any component does not seem applicable and you omit it in the answer, provide an explanation.

Example:

Methods and Results: We analyzed the electronic medical records of 1.8 million subjects from the Stanford clinical data warehouse spanning 18 years using a novel text-mining and statistical analytics pipeline. We identified 232 PAD patients taking Cilostazol and created a control group of 1,160 PAD patients not taking this drug using 1:5 propensity-score matching, which computationally emulates randomization in a clinical trial. Over a mean follow up of 4.2 years, we observed no significant treatment effect of Cilostazol use on any major adverse cardiovascular event including stroke (OR = 1.13, CI [0.82, 1.55]), myocardial infarction (OR = 1.00, CI [0.71, 1.39]), or death (OR = 0.86, CI[0.63, 1.18]).

Study Design:

Retrospective cohort. The study is from medical records, so no experiment was run- that makes it observational. Data is taken over time, so it's longitudinal. The patients are included based on whether or not they are taking a drug (an exposure) and not based on whether or not they later experienced an event (an outcome)- that mean's it's a cohort study. The data was collected in the past, so it's a retrospective cohort study.

Level of Analysis:

Causal. The investigators are looking for a treatment effect and not just an association. They use a technique called propensity score matching to try and emulate randomization so that their inferences are causally interpretable.

Study 1

Inferring precise phenotypic patterns from population-scale clinical data is a core computational task in the development of precision, personalized medicine. The traditional approach uses supervised learning, in which an expert designates which patterns to look for (by specifying the learning task and the class labels), and where to look for them (by specifying the input variables). While appropriate for individual tasks, this approach scales poorly and misses the patterns that we don't think to look for. Unsupervised feature learning overcomes these limitations by identifying patterns (or features) that collectively form a compact and expressive representation of the source data, with no need for expert input or labeled examples. Its rising popularity is driven by new deep learning methods, which have produced high-profile successes on difficult standardized problems of object recognition in images. Here we introduce its use for phenotype discovery in clinical data. This use is challenging because the largest source of clinical data - Electronic Medical Records - typically contains noisy, sparse, and irregularly timed observations, rendering them poor substrates for deep learning methods. Our approach couples dirty clinical data to deep learning architecture via longitudinal probability densities inferred using Gaussian process regression. From episodic, longitudinal sequences of serum uric acid measurements in 4368 individuals we produced continuous phenotypic features that suggest multiple population subtypes, and that accurately distinguished (0.97 AUC) the uric-acid signatures of gout vs. acute leukemia despite not being optimized for the task. The unsupervised features were as accurate as gold-standard features engineered by an expert with complete knowledge of the domain, the classification task, and the class labels. Our findings demonstrate the potential for achieving computational phenotype discovery at population scale. We expect such data-driven phenotypes to expose unknown disease variants and subtypes and to provide rich targets for genetic association studies.

Study Design (10 points):

Observational Cross-sectional study. This study fits some of the characteristics of te cross-sectional study:

- First, the data were collected at one point of time (even though the data used are from episodic, longitudinal sequences of serum uric acid measurements in 4368 individuals)
- Also, the investigators did not interfere with the experiment
- This is not *Longitudinal* study because there is no clear indicator that the investigators monitored a same patient over the time

Level of Analysis (10 points):

Exploratory. This study aims to evaluate how unsupervised learning performing using Electronic Medical Records. Not doing any prediction or inference.

Study 2

We develop regression-based models for predicting severity of depression from EHR data, using structured diagnosis and medication codes as well as free-text clinical reports. We used two datasets: 35 000 patients (5000 depressed) from the Palo Alto Medical Foundation and 5651 patients treated for depression from the Group Health Research Institute.

Study Design (10 points):

Cross-sectional observation study. It is not clearly stated in the abstract that the investigator collected the data over the time. Therefore, it is hard to conclude it is a Longitudinal study. However, it there is a clear evidence showing the investigators collected the measurements over the time, then this should be **Longitudinal cohort study**.

Level of Analysis (10 points):

The abstract gave us a clear clue that the level of analysis for this study is **Predictive** because the model built will be used to predicting the severity of the depression using patient's EHR data.

Study 3

We showed that among adults with hypertension but without diabetes, lowering systolic blood pressure to a target goal of less than 120 mm Hg, as compared with the standard goal of less than 140 mm Hg, resulted in significantly lower rates of fatal and nonfatal cardiovascular events and death from any cause. Trial participants randomized to the lower systolic blood-pressure target (intensive-treatment group), as compared with those assigned to the higher target (standard-treatment group), had a 25% lower relative risk of the primary outcome; in addition, the intensive-treatment group had lower rates of several other important outcomes, including heart failure (38% lower relative risk), death from cardiovascular causes (43% lower relative risk), and death from any cause (27% lower relative risk).

Study Design (10 points):

Experimental Study. The keyword for the determination is *randomized*. The participants are randomly assigned to the treatment (or control) group, which is a key feature for an experimental design

Level of Analysis (10 points):

Casual. One key point is the investigators are looking for the treatment effect. we also learned that the casual effect relationship almost always required RCT which is the study design used in this study.

Study 4

The quantity (volume, cm(3)) and quality (attenuation, Hounsfield Unit) of abdominal adipose tissue were measured using computed tomography in 1003 participants (mean age 45.3 years, 45.0% women) at examination 1 and 2 in the Framingham's Third Generation cohort. The 2 exams were ≈ 6 years apart. At baseline, SSB and diet soda intake were assessed using a valid food frequency questionnaire. Participants were categorized into 4 groups: none to <1 serving/mo (nonconsumers), 1 serving/mo to <1 serving/week, 1 serving/week to 1 serving/d, and ≥ 1 serving/d (daily consumers) of either SSB or diet soda. After adjustment for multiple confounders including change in body weight, higher SSB intake was associated with greater change in VAT volume (P trend<0.001). VAT volume increased by 658 cm(3) (95%

confidence interval [CI], 602 to 713), 649 cm(3) (95% CI, 582 to 716), 707 cm(3) (95% CI, 657 to 757), and 852 cm(3) (95% CI, 760 to 943) from nonconsumers to daily consumers. Higher SSB intake was also associated with greater decline of VAT attenuation (P trend=0.007); however, the association became nonsignificant after additional adjustment for VAT volume change. In contrast, diet soda consumption was not associated with change in abdominal adipose tissue.

Study Design (10 points):

Longitudinal prospective cohort study

- Researchers observed the participants over time without any active intervention indicates this study is an observational study
- This is Longitudinal study because it tracks the same group of participants over the period of time (approximately 6 years) by taking 2 data points: base line and after 6 years.
- The participants are included based on their SSB or diet soda consumption and not based on their later experience (or outcome) - Cohort study
- This study is prospective because it starts with assessing participant's beverage intake at baseline and then follow over time to measure the changes in abdominal adipose tissue. The outcomes are measured after the data on beverages intake has already been collected. This indicate the study looks forward in time.

Level of Analysis (10 points):

Inferential. Based on the abstract, the question which investigator trying to answer is to find out whether SSB intake or diet soda was associated with adverse change in both VAT quality and quantity. Which is typical Inferential analysis.

Study 5

Polypharmacy is increasingly common in the United States, and contributes to the substantial burden of drug-related morbidity. Yet real-world polypharmacy patterns remain poorly characterized. We have counted the incidence of multi-drug combinations observed in four billion patient-months of outpatient prescription drug claims from 2007-2014 in the Truven Health MarketScan® Databases. Prescriptions are grouped into discrete windows of concomitant drug exposure, which are used to count exposure incidences for combinations of up to five drug ingredients or ATC drug classes. Among patients taking any prescription drug, half are exposed to two or more drugs, and 5% are exposed to 8 or more. The most common multi-drug combinations treat manifestations of metabolic syndrome. Patients are exposed to unique drug combinations in 10% of all exposure windows. Our analysis of multi-drug exposure incidences provides a detailed summary of polypharmacy in a large US cohort, which can prioritize common drug combinations for future safety and efficacy studies.

Study Design (10 points):

Longitudinal cohort study. At the begining, the study sounds like a cross-sectional because the investogators get the data (2007 - 2014) at one point of time. But when we look closer, even though the data were collected at a single point of time, the investigators still aggregating the data from 2007 to 2014 and this makes this qualify as *Longitudinal* study. Also, the data being compared are defined based on what happened to the samples at the beginning of the study. This is one key characteristics of a *Cohort study*. However, the investigators are not doing any prediction nor explaining why polypharmacy happened and this is the reason why it is not qualify as either prospective nor retrospective.

Level of Analysis (10 points):

Exploratory. Key point here is the investigators are trying to explain the incidence and not trying to find the relation or explaining why the incidence happened. and there is no evidence showed the investigators doing further experiments with the new samples.

Feedback (0 points)

How much time did you spend on this assignment?

- **8 hours including the TA session and discussion with peers**

How much did you learn? Choose one (type your answer after the table):

A **B** **C** **D** **E**

a great deal a lot a moderate amount a little none at all

- A

Did you do any of the following: go to office hours, post on canvas, e-mail TAs? If so, which?

- I attended the TA office hours and join the discussion with others