Clinical Questions and Study Designs

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):

This study design is a `retrospective cohort study`. To start, the reseracher does not interfere with world, they use data that has historically existed, making this an observational. Next, the longitudinal nature of the serum uric acid measurements makes this a longitudinal study. Moreover, the groups are split based on phenotypical features, making this a cohort study. Finally, we reach our leaf classification of retospective cohort study as this data was collected for other purposes and re-used for the study.

Level of Analysis (10 points):

This level of analysis is `inferential`. The study summarizes all data included and interprets by discussing what the findings of the study show about the world. They also mention that they've demonstrated potential discovery at a 'population scale' quanitifying if this study will hold in a new cohort. However, they do not look to see how averages affect each other, and their is not prediction involved, making this an inferential study

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):

This study is a `case-control` study. The researcher does not interfere with the world and the measurements are taken over time bringing us to a longitudinal study. Next, the groups in in the study are defined concerning what ended up happening to them - if they had depression or not and if they were

treated for depression. We then look back historically for some sort of exposure or signal that would allow us to predict this outcome, making this a case-control study.

Level of Analysis (10 points):

This level of analysis is `predictive.` Based off of certain exposures, we are trying to predict depression using these labeled datasets. The fact that this is a regression task makes this a predictive analysis.

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):

This is an `experiemental` study. The researchers directly interfere in order to bring systolic blood presure down to a target goal of less than 120 mm Hg. When there is interference by the researchers, we automatically have a experimental study.

Level of Analysis (10 points):

This level of analysis is `Causal.` Randomized Control Trial always implies causal analysis. We can see this by traversing the analysis tree. The data is summarized, and interpretted. The randomized trial participants ensures that these findings will be consistent throughout any chosen cohort. The researchers are directly investigating if systolic blood pressure affect fatal / nonfatal cardiovascular events on average, making this a causal 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):

This is a `prospective study.` The researchers do not effect the world and the exams are multiple years apart, meaning we have a longitudinal study. Next, the cohorts are broken up into 4 groups at the beginning of the study due to their varying sode intake. Finally, the baseline and secondary test were captured specifically for this study, making it a prospective study.

Level of Analysis (10 points):

This level of analysis is `inferential.` The data is summarized and interpretted. Moreover, the study looks at how SSB intake affects VAT volume — the cohort agnostic nature makes these results likely to hold in a new study. However, there is no discussion concerning how changing one metric affects the other, and there is no prediction involved. Altogether, that makes this an inferential study.

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):

This study is a `retrospective` cohort study. The researchers do not interfere with the world and the data is collect over a longitudinal seven year period. Next, the groups are defined at the begninning of the study based off of thier drug exposure making this a cohort study. Finally, this data already existed in the world for other purposes, and was re-purposed for this research, making this a retrospective study.

Level of Analysis (10 points):

This level of anlysis is `descriptive.` The data is summarized however there is no interpretation of the data, simply just presenting of findings, making this a descriptive study.

Feedback (0 points)

How much time did you spend on this assignment?

4 hours

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

A | B | C | D | E |

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

B

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

None