MATH-449 - Biostatistics
EPFL, Spring 2022
Problem Set 1

1. Determine whether each of these questions are phrased as causal questions or not (yes or no).

   a) Does the Moderna vaccine reduce the risk of severe COVID-19 infection? ***Yes - this is a question about the (causal) explanatory power of the vaccine in regards to COVID-19.***

   b) Do women with breast cancer survive longer than men with prostate cancer? ***No, this is simply a descriptive comparison of the factual survival distributions under different conditioning events.***

   c) Is the life expectancy in Switzerland longer than the life expectancy in Italy? ***No (see above).***

   d) Does drinking 0.5 L beer compared to 0.5 L Coca Cola at 19h00 affect the quality of sleep? ***Yes, see the word *affect*, implying a counterfactual comparison of sleep quality under interventions on beer vs Coca Cola.***

   e) Would drinking a cup of coffee 2 hours before your exam improve your performance? ***Yes - this is a question about outcomes under a hypothetical intervention (or lack thereof).***

2. Based on the definition of a causal effects in the lecture slides, argue whether the following statements about a covariate $L \in \mathbb{R}$, a treatment $A = 0, 1$ and an outcome $Y \in \mathbb{R}$ are right or wrong (there is no guarantee that A is randomly assigned).

   a) $\mathbb{E}(Y^{a=1} \mid L = l) - \mathbb{E}(Y^{a=0} \mid L = l)$ is a causal effect. ***Yes, by linearity of expectations, we re-express as*** $\mathbb{E}(Y^{a=1} - Y^{a=0} \mid L = l)$***, which is the expected individual causal effect among units with*** $L = l$***.***

   b) $\mathbb{E}(Y \mid A = 1, L = l) - \mathbb{E}(Y \mid A = a, L = l)$ is a causal effect. ***No. without additional assumptions, this is simply a contrast of conditional outcome means, representing the association between*** A ***and*** Y ***given*** $L = l$***.***

   c) $\mathbb{E}(Y^{a=1} \mid A = 1, L = l) - \mathbb{E}(Y^{a=0} \mid A = 1, L = l)$ is a causal effect. ***Yes (see part a)).***

   d) $\frac{\mathbb{E}(Y^{a=1})}{\mathbb{E}(Y^{a=0})}$ is an average over individual level (additive) causal effects. ***By counter-example: we know that an individual-level additive causal effect is the random variable*** $Z = Y^{a=1} - Y^{a=0}$ ***which has support in*** $\mathbb{R}$***, and thus the parameter space for its expectation is also*** $\mathbb{R}$***. However,*** $X = \frac{Y^{a=1}}{Y^{a=0}}$ ***is undefined whenever*** $Y^{a=0} = 0$ ***and also*** $\frac{\mathbb{E}(Y^{a=1})}{\mathbb{E}(Y^{a=0})}$ ***is undefined whenever*** $\mathbb{E}(Y^{a=0}) = 0$***.***

3. Translate these English sentences to mathematical (counterfactual) statements.

   a) The average causal effect of receiving a COVID-19 vaccine ($A = 1$) vs placebo ($A = 0$) on mortality after one year ($Y = 1$ is death, $Y = 0$ is alive) in the entire population of interest. ***Answer:*** $\mathbb{E}[Y^{a=1} - Y^{a=0}]$.

   b) The average causal effect of receiving a COVID-19 vaccine ($A = 1$) vs placebo ($A = 0$) on mortality after one year ($Y = 1$ is death, $Y = 0$ is alive) among those who received placebo in the observed (factual) data. ***Answer:*** $\mathbb{E}[Y^{a=1} - Y^{a=0} \mid A = 0]$.

   c) The average causal effect of receiving a COVID-19 vaccine ($A = 1$) vs placebo ($A = 0$) on mortality after one year ($Y = 1$ is death, $Y = 0$ is alive) among those who received treatment in the observed (factual) data. ***Answer:*** $\mathbb{E}[Y^{a=1} - Y^{a=0} \mid A = 1]$.

   d) The average causal effect of receiving a COVID-19 vaccine ($A = 1$) vs placebo ($A = 0$) on mortality after one year ($Y = 1$ is death, $Y = 0$ is alive) in men ($X = 1$). ***Answer:*** $\mathbb{E}[Y^{a=1} - Y^{a=0} \mid X = 1]$.

e) Are your answers in a)-d) estimands, estimators or estimates? ***Estimands.***

4. Suppose investigators had access to data from a study in which they observed for each patient a binary outcome Y, a binary treatment A and a 4-level baseline covariate L. The parameters of the joint density of (L, A, Y) were computed from the data and summarized in Table 1 (where we suppose that the sample size was so large, that sampling variability is not a concern).

   a) From the parameters in Table 1, compute $\mathbb{E}[Y]$.

$$\mathbb{E}[Y] = \sum_{l,a} P(Y = 1 \mid A = a, L = l)P(A = a \mid L = l)P(L = l) = 0.5$$

   b) Suppose now that the data did not in fact arise from a regular observational study, but had instead come from a special trial. Upon recruitment into the study, each patient's covariate L is measured and then they are sorted into groups based on that covariate's value. In each group, the investigators conduct a separate experiment, which are identical except they use a special coin to randomize patients to either treatment ($a = 1$) or control ($a = 0$), with "heads" corresponding to treatment and "tails" corresponding to control. The probabilities for heads for each of these sub-trials is given by the column labeled $P(A = 1 \mid L = l)$. Assume consistency holds ($Y^A = Y$), and that patients perfectly complied with their assignments. With the information in the table, compute the effect of treatment $\mathbb{E}[Y^{a=1} - Y^{a=0} \mid L = l]$ for each subgroup $L = l$ that was targeted in each of the sub-trials. What additional assumptions did you use along the way, that was justified given the source of the data?

$$\mathbb{E}[Y^a \mid L = l] = P(Y = 1 \mid A = a, L = l)$$

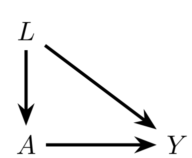
By consistency and by the exchangeability $Y^a \perp\!\!\!\perp A = a \mid L = l$ ***justified by the conditional randomization in the trial for which, by design,*** $(Y^{a=0}, Y^{a=1}) \perp\!\!\!\perp A \mid L$***.***

	$E(Y^{a=1} \mid L = l)$	$E(Y^{a=0} \mid L = l)$	$E(Y^{a=1} - Y^{a=0} \mid L = l)$
$l = 1$	.1	.8	-.7
$l = 2$	.2	.7	-.5
$l = 3$	.3	.6	-.3
$l = 4$	.4	.5	-.1

   c) From the quantities computed in part a), use laws of probability to compute the average treatment effect, among the whole population, $\mathbb{E}[Y^{a=1} - Y^{a=0}]$.

$$\mathbb{E}[Y^a \mid L = l] = \sum_{l} \mathbb{E}[Y^a \mid L = l]P(L = l) = -0.4$$

   d) Draw a directed acyclic graph (DAG) that could depict the mechanism that generated the observed data.



   e)

f) The data analyst for the study approaches you and said they made a terrible mistake: when preparing the column $P(A = 1 \mid L = l)$ in Table 1, they reverse coded the treatment variable, so in fact the true values of the treatment propensities are 1 minus those listed in the table. What will be the values of the previously computed parameters, and explain in words why these changes did (or did not occur).

Only the factual marginal expectation of Y will change - the other parameters are not functions of the propensities.

	$P(Y = 1 \mid A = a, L = l)$		$P(A = 1 \mid L = l)$	$P(L = l)$
	$a = 1$	$a = 0$		
$l = 1$	.1	.8	.2	.2
$l = 2$	.2	.7	.4	.4
$l = 3$	.3	.6	.6	.1
$l = 4$	.4	.5	.8	.3

Table 1: Parameters of $P_{L,A,Y}$ observed in the conditionally randomized trial.

5. Consider a covariate $L \in \mathbb{R}$, a treatment $A = 0, 1$ and an outcome $Y \in \mathbb{R}$.

a) Investigator 1 claims that $A \perp\!\!\!\perp Y \implies A \perp\!\!\!\perp Y \mid L$. Show that the statement is wrong.

Consider the following joint distribution with binary L, A, Y:

	$P(Y = 1 \mid A = a)$		$P(Y = 1 \mid A = a, L = l)$		$P(L = l \mid A = a)$	
	$a = 1$	$a = 0$	$a = 1$	$a = 0$	$a = 1$	$a = 0$
$l = 1$	.5	.5	.25	.75	.5	.5
$l = 2$			.75	.25	.5	.5

b) Investigator 2 claims that $A \perp\!\!\!\perp Y \mid L \implies A \perp\!\!\!\perp Y$. Show that the statement is wrong.

Consider the following joint distribution with binary L, A, Y:

	$P(Y = 1 \mid A = a)$		$P(Y = 1 \mid A = a, L = l)$		$P(L = l \mid A = a)$	
	$a = 1$	$a = 0$	$a = 1$	$a = 0$	$a = 1$	$a = 0$
$l = 1$	.65	.5	.2	.2	.25	.5
$l = 2$			.8	.8	.75	.5