Week 6

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Potential Outcome

- Causal Effect
- Randomized Experiment
- Observation Studies
- Effect modification
- Confounding

1. A definition of causal effect

1.1 Individual causal effects

1.2 Average causal effects

1.3 Measures of causal effect

1.4 Random variability

1.1 Individual causal effects

- A formal definition of a causal effect for an individual:

We can now provide a formal definition of a *causal effect for an individual*: The treatment A has a causal effect on an individual's outcome Y if $Y^{a=1} \neq Y^{a=0}$ for the individual. Thus, the treatment has a causal effect on Zeus's outcome because $Y^{a=1} = 1 \neq 0 = Y^{a=0}$, but not on Hera's outcome because $Y^{a=1} = 0 = Y^{a=0}$. The variables $Y^{a=1}$ and $Y^{a=0}$ are referred to as *potential outcomes* or as *counterfactual outcomes*. Some authors prefer the

1.2 Average causal effects

- The average causal effect (ACE) is a measure that quantifies the average treatment effect in a population. It provides an estimation of the average difference in outcomes between the treated and control groups, taking into account the potential outcomes under each treatment condition.
- Formally, the average causal effect is defined as:
- **ACE = E[Y(1) - Y(0)]**
- where E represents the expectation or average over the entire population. Y(1) represents the potential outcome if an individual receives the treatment, and Y(0) represents the potential outcome if the individual does not receive the treatment.

1.3 Measures of causal effect

(i) $\Pr[Y^{a=1}=1]-\Pr[Y^{a=0}=1]=0$ causal risk difference

(ii) $\dfrac{\Pr[Y^{a=1}=1]}{\Pr[Y^{a=0}=1]}=1$ risk ratio

(iii) $\dfrac{\Pr[Y^{a=1}=1]/\Pr[Y^{a=1}=0]}{\Pr[Y^{a=0}=1]/\Pr[Y^{a=0}=0]}=1$ odds ratio

where the left-hand side of the equalities (i), (ii), and (iii) is the causal risk difference, risk ratio, and odds ratio, respectively. we refer to them as effect measures.

The causal risk ratio (multiplicative scale) is used to compute how many times treatment, relative to no treatment, increases the disease risk.

The causal risk difference (additive scale) is used to compute the absolute number of cases of the disease attributable to the treatment.

The use of either the multiplicative or additive scale will depend on the goal of the inference.

1.4 Random variability

- sampling variability :
- Investigators only collect information on a sample of the population of interest. Even if the counterfactual outcomes of all study individuals were known, working with samples prevents one from obtaining the exact proportion of individuals in the population who had the outcome under treatment value a the probability of death under no treatment Pr[Y a=0 = 1] cannot be directly computed. One can only estimate this probability.

- inherently nondeterministic outcome
- In this scenario, the counterfactual outcomes are stochastic or nondeterministic because Zeus's probabilities of dying under treatment (0.9) and under no treatment (0.1) are neither zero nor one. Further, one would expect that these probabilities vary across individuals because not all individuals are equally susceptible to develop the outcome.

2. Randomised Experiment

- 2.1 Randomisation
- 2.2 Conditional randomisation
- 2.3 Standardisation
- 2.4 Inverse probability weighting

2.1 Randomisation and Conditional randomisation

- Randomized experiments, like any other real world study, generate data with missing values of the counterfactual outcomes. However, randomization ensures that those missing values occurred by chance. As a result, effect measures can be computed —or, more rigorously, consistently estimated—in randomized experiments despite the missing data. Let us be more precise.

- **Ignorability/Exchangeability**

Assumption 2.1 (Ignorability / Exchangeability)

$$(Y(1), Y(0)) \perp\!\!\!\perp T$$

- **Conditional Exchangeability / Unconfoundedness**

Assumption 2.2 (Conditional Exchangeability / Unconfoundedness)

$$(Y(1), Y(0)) \perp\!\!\!\perp T \mid X$$

2.2 Standardisation

- **Standardisation**

This method is known in epidemiology, demography, and other disciplines as *standardization*. For example, the numerator $\sum_l \Pr[Y = 1|L = l, A = 1] \Pr[L = l]$ of the causal risk ratio is the standardized risk in the treated using the population as the standard. Under conditional exchangeability, this standardized risk can be interpreted as the (counterfactual) risk that would have been observed had all the individuals in the population been treated.

- **Standardized risk**

The standardized risks in the treated and the untreated are equal to the counterfactual risks under treatment and no treatment, respectively. Therefore, the causal risk ratio $\frac{\Pr[Y^{a=1} = 1]}{\Pr[Y^{a=0} = 1]}$ can be computed by standardization as $\frac{\sum_l \Pr[Y = 1|L = l, A = 1] \Pr[L = l]}{\sum_l \Pr[Y = 1|L = l, A = 0] \Pr[L = l]}$.

2.3 Inverse probability weighting

- Inverse Probability Weighting (IPW) is a statistical method commonly used in causal inference to address confounding factors and selection bias. It utilizes the concept of propensity scores to adjust for comparisons between treatment and control groups, aiming to obtain more accurate causal estimates.

IP weight: $W^A = 1/f[A|L]$

Formal definition of IP weights. An individual's IP weight depends on the individual's values of treatment A and covariate L. For example, a treated individual with $L = l$ receives the weight $1/\Pr[A = 1|L = l]$, whereas an untreated individual with $L = l'$ receives the weight $1/\Pr[A = 0|L = l']$. We can express these weights using a single expression for all individuals—regardless of their individual treatment and covariate values—by using the probability density function (pdf) of A rather than the probability of A. The conditional pdf of A given L evaluated at the values a and l is represented by $f_{A|L}[a|l]$, or simply as $f[a|l]$. For discrete variables A and L, $f[a|l]$ is the conditional probability $\Pr[A = a|L = l]$. In a conditionally randomized experiment, $f[a|l]$ is positive for all l such that $\Pr[L = l]$ is nonzero.

Since the denominator of the weight for each individual is the conditional density evaluated at the individual's own values of A and L, it can be expressed as the conditional density evaluated at the random arguments A and L (as opposed to the fixed arguments a and l), that is, as $f[A|L]$. This notation, which appeared in Figure 2.3, is used to define the IP weights $W^A = 1/f[A|L]$. It is needed to have a unified notation for the weights because $\Pr[A = A|L = L]$ is tautologically equal to 1 and thus not considered proper notation.

As explained in the main text, the mean of the outcome in the pseudo-population $\mathrm{E}_{ps}[Y|A = a]$ equals the IP weighted mean of the outcome in the population, $\mathrm{E}[Y\,\mathrm{I}(A = a)/\Pr(A = a|L)]$, where $\mathrm{I}(A = a)$ is 1 when $A = a$ and 0 otherwise. A proof follows:

$\mathrm{E}_{ps}[Y|A = a] = \mathrm{E}_{ps}[Y\,\mathrm{I}(A = a)]/\mathrm{E}_{ps}[\mathrm{I}(A = a)]$ (by the laws of probability)
$= \mathrm{E}\left[W^A Y\,\mathrm{I}(A = a)\right]/\mathrm{E}\left[\mathrm{I}(A = a)\,W^A\right]$ (by definition of E_{ps})
$= \mathrm{E}[Y\,\mathrm{I}(A = a)/\Pr(A = a|L)]/\mathrm{E}[\mathrm{I}(A = a)/\Pr(A = a|L)]$ (because $\mathrm{I}(A = a)/f(A|L) = \mathrm{I}(A = a)/f(a|L)$)
$= \mathrm{E}[Y\,\mathrm{I}(A = a)/\Pr(A = a|L)]$ (because $\mathrm{E}[\mathrm{I}(A = a)/\Pr(A = a|L)\,|L] = 1$).

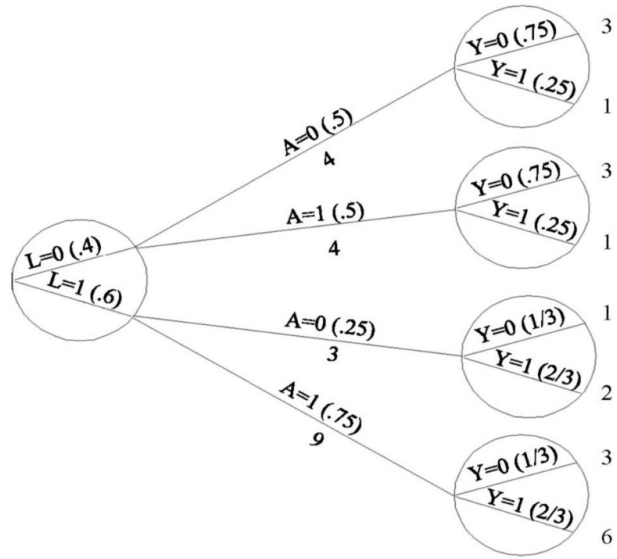
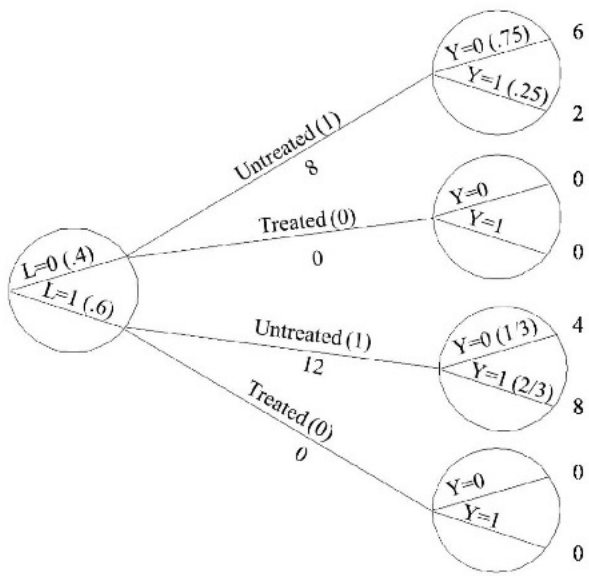
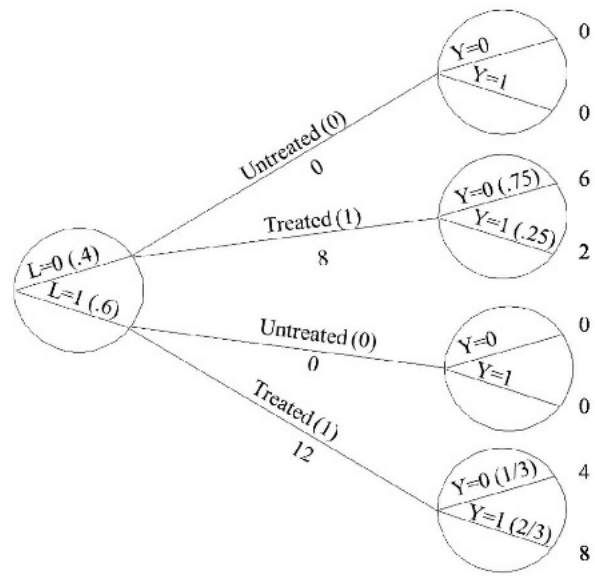


Figure 2.1





$$\frac{\Pr[Y^{a=1} = 1]}{\Pr[Y^{a=0} = 1]}$$

3. Observation Studies

- Identifiability conditions

- Informally, an observational study can be conceptualized as a conditionally randomized experiment if the following conditions hold:

1. **Consistency**, the values of treatment under comparison correspond to well-defined in- terventions that, in turn, correspond to the versions of treatment in the data
2. **Exchangeability**, the conditional probability of receiving every value of treatment, though not decided by the investigators, depends only on measured covariates L
3. **Positivity**: the probability of receiving every value of treatment conditional on L is greater than zero, i.e., positive

Assumption 2.5 (Consistency) *If the treatment is T, then the observed outcome Y is the potential outcome under treatment T. Formally,*

$$T = t \implies Y = Y(t) \tag{2.12}$$

We could write this equivalently as follow:

$$Y = Y(T) \tag{2.13}$$

Assumption 2.3 (Positivity / Overlap / Common Support) *For all values of covariates x present in the population of interest (i.e. x such that $P(X = x) > 0$),*

$$0 < P(T = 1 \mid X = x) < 1$$

Assumption 2.2 (Conditional Exchangeability / Unconfoundedness)

$$(Y(1), Y(0)) \perp\!\!\!\perp T \mid X$$

4. Effect modification

- Definition
- V is a modifier of the effect of A on Y when the average causal effect of A on Y varies across levels of V . Since the average causal effect can be measured using different effect measures (e.g., risk difference, risk ratio), the presence of effect modification depends on the effect measure being used.

- qualitative effect modification
- There is qualitative effect modification because the average causal effects in the subsets V = 1 and V = 0 are in the opposite direction. In the presence of qualitative effect modification, additive effect modification implies multiplicative effect modification, and vice versa. In the absence of qualitative effect modification, however, one can find effect modification on one scale (e.g., multiplicative) but not on the other (e.g., additive).

Effect modification on additive $\mathrm{E}\left[Y^{a=1} - Y^{a=0} \mid V = 1\right] \neq \mathrm{E}\left[Y^{a=1} - Y^{a=0} \mid V = 0\right]$

Effect modification on multiplicative $\dfrac{\mathrm{E}\left[Y^{a=1} \mid V = 1\right]}{\mathrm{E}\left[Y^{a=0} \mid V = 1\right]} \neq \dfrac{\mathrm{E}\left[Y^{a=1} \mid V = 0\right]}{\mathrm{E}\left[Y^{a=0} \mid V = 0\right]}$)

Stratification as a form of adjustment

Stratification: the causal effect of A on Y is computed in each stratum of V. For dichotomous V, the stratified causal risk differences are:
$\Pr[Y^{a=1} = 1|V = 1] -$
$\Pr[Y^{a=0} = 1|V = 1]$
and
$\Pr[Y^{a=1} = 1|V = 0] -$
$\Pr[Y^{a=0} = 1|V = 0]$

A stratified analysis is the natural way to identify effect modification. To determine whether V modifies the causal effect of A on Y , one computes the causal effect of A on Y in each level (stratum) of the variable V .

The procedure to compute the conditional risks $\Pr[Y^{a=1} = 1|V = v]$ and $\Pr[Y^{a=0} = 1|V = v]$ in each stratum v has two stages: 1) stratification by V, and 2) standardization by L (or, equivalently, IP weighting with weights depending on L). We computed the standardized risks in the Greek stratum

Matching as another form of adjustment

Matching is another form of adjustment used in causal inference to control for confounding variables and reduce bias. It involves creating pairs or groups of individuals with similar characteristics, based on the confounding variables, in order to compare their treatment effects.

Effect modification and adjustment methods

- Standardization, IP weighting, stratification/restriction, and matching are different approaches to estimate average causal effects, but they estimate different types of causal effects. These four approaches can be divided into two groups according to the type of effect they estimate:

  1. standardization and IP weighting can be used to compute either marginal or conditional effects,
  2. stratification/restriction and matching can only be used to compute conditional effects in certain subsets of the population.

- All four approaches req uire exchangeability and positivity but the subsets of the population in which these conditions need to hold depend on the causal effect of interest.

7. Confounding

- **7.1 The structure of confounding**
- **7.2 Confounding and exchangeability**
- **7.3 Confounding and the backdoor criterion**
- **7.4 Single-world intervention graphs**
- **7.5 Confounding adjustment**

7.1 The structure of confounding

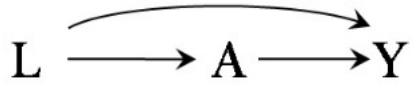


Figure 7.1

Occupational factors: The effect of working as a firefighter A on the risk of death Y will be confounded if "being physically fit" L is a cause of both being an active firefighter and having a lower mortality risk.

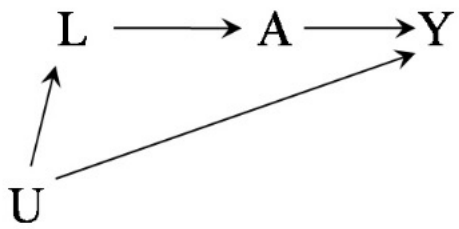


Figure 7.2

Clinical decisions: The effect of drug A (say, aspirin) on the risk of disease Y (say, stroke) will be confounded if the drug is more likely to be prescribed to individuals with certain condition L (say, heart disease) that is both an indication for treatment and a risk factor for the disease.

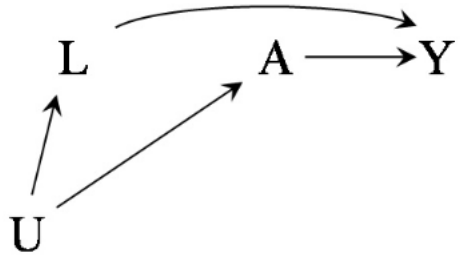


Figure 7.3

Lifestyle: The effect of behavior A (say, exercise) on the risk of Y (say, death) will be confounded if the behavior is associated with another behavior L (say, cigarette smoking) that has a causal effect on Y and tends to co-occur with A.

7.2 Confounding and exchangeability

- We now link the concept of confounding, which we have defined using causal diagrams, with the concept of exchangeability,

Let us now relate the backdoor criterion (i.e., exchangeability) to confounding. The two settings in which the backdoor criterion is satisfied are

1. *No common causes of treatment and outcome.* In Figure 6.2, there are no common causes of treatment and outcome, and hence no backdoor paths that need to be blocked. Then the set of variables that satisfies the backdoor criterion is the empty set and we say that there is no confounding.

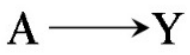


Figure 6.2

2. *Common causes of treatment and outcome but a subset L of measured non-descendants of A suffices to block all backdoor paths.* In Figure 7.1, the set of variables that satisfies the backdoor criterion is L. Thus, we say that there is confounding, but that there is no residual confounding whose elimination would require adjustment for unmeasured variables (which, of course, is not possible). For brevity, we say that there is *no unmeasured confounding*.

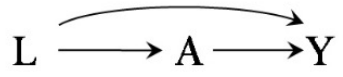


Figure 7.1

7.3 Confounding and the backdoor criterion

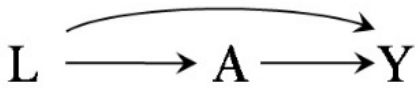


Figure 7.1

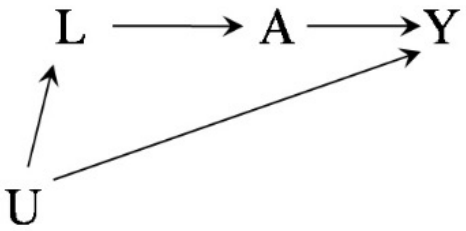


Figure 7.2

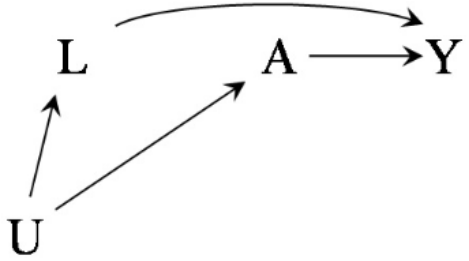


Figure 7.3

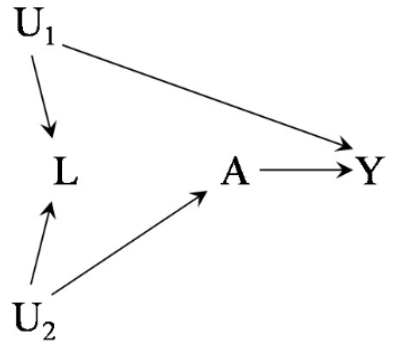


Figure 7.4

Suppose, as in the last four examples, that data on L, A, and Y suffice to identify the causal effect. In such setting we define L to be a confounder if the data on A and Y do not suffice for identification (i.e., we have structural confounding).

7.4 Single-world intervention graphs

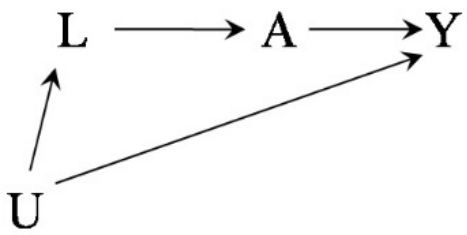


Figure 7.2

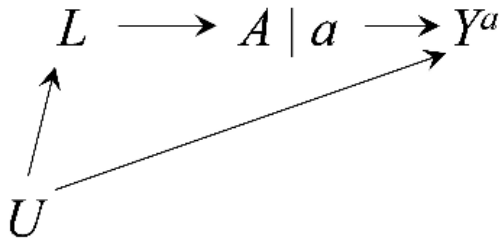


Figure 7.9

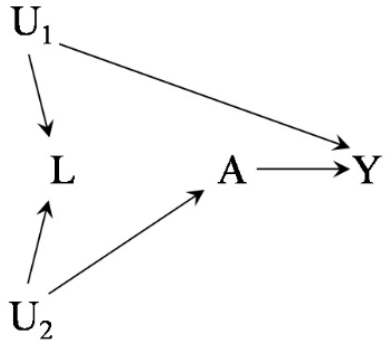


Figure 7.4

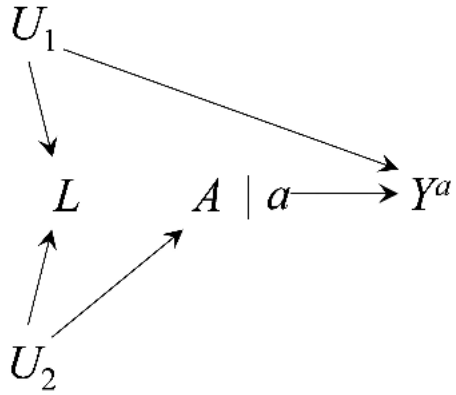


Figure 7.10

7.5 Confounding adjustment

- In the absence of randomization, causal inference relies on the uncheckable assumption that we have measured a set of variables L that is a sufficient set for confounding adjustment, i.e., a set of non-descendants of treatment A that includes enough variables to block all backdoor paths from A to Y .
- Methods that adjust for confounders L can be classified into two broad categories:

  - G-methods: Standardization, IP weighting, and g-estimation. These methods (the 'g' stands for 'generalized') exploit conditional exchangeability given L to estimate the causal effect of A on Y in the entire population or in any subset of the population. In our heart transplant study, we used g-methods to adjust for confounding by disease severity L in Sections 2.4 (standardization) and 2.5 (IP weighting). Part II describes model-based extensions of g-methods: the parametric g-formula (standardization), IP weighting of marginal structural models, and g-estimation of nested structural models.

  - Conventional methods for stratification-based adjustment: Stratification (including restriction) and matching. These methods exploit conditional exchangeability given L to estimate the association between A and Y in subsets defined by L. In our heart transplant study, we used stratification-based methods to adjust for confounding by disease severity L in Sections 4.4 (stratification) and 4.5 (matching). Part II describes the model-based extension of conventional stratification: outcome regression.