## CAUSAL INFERENCE

BY: MIGUEL A. HERNÁN AND JAMES M. ROBINS

Part I: Causal inference without models

Chapter 5: Interaction



12th December, 2014

## OUTLINE

- **1** Chapter 1: A definition of causal effect
- **2** Chapter 2: Randomized experiments
- **3** Chapter 3: Observational studies
- **4** Chapter 4: Effect modification
- **5** Chapter 5: Interaction
  - 5.1 Interaction requires a joint intervention
  - 5.2 Identifying interaction
  - 5.3 Counterfactual response types and interaction
  - 5.4 Sufficient causes
  - 5.5 Sufficient cause interaction
  - 5.6 Counterfactuals or sufficient-component causes?

## Chapter 1.1: Individual causal effects

"The purpose of this chapter is to introduce mathematical notation that formalizes the causal intuition that you already possess."

### Some notation

- Dichotomous treatment variable: A (1: treated; 0: untreated)
- Dichotomous outcome variable: Y (1: death; 0: survival)
- $Y^{a=i}$ : Outcome under treatment a = i,  $i \in \{0, 1\}$ .

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What we would like to observe:

$$\begin{aligned} & \Pr(Y^{a=1} = 1) - \Pr(Y^{a=0} = 1) & \text{(Causal risk difference)} \\ & \frac{\Pr(Y^{a=1} = 1)}{\Pr(Y^{a=0} = 1)} & \text{(Causal risk ratio)} \\ & \frac{\Pr(Y^{a=1} = 1)/\Pr(Y^{a=1} = 0)}{\Pr(Y^{a=0} = 1)/\Pr(Y^{a=0} = 0)} & \text{(Causal odds ratio)} \end{aligned}$$

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### What we can estimate:

Pr(Y = 1|A = 1) - Pr(Y = 1|A = 0)(Associational risk difference)  $\frac{Pr(Y = 1|A = 1)}{Pr(Y = 1|A = 0)}$ (Associational risk ratio)  $\frac{Pr(Y = 1|A = 1)/Pr(Y = 0|A = 1)}{Pr(Y = 1|A = 0)/Pr(Y = 0|A = 0)}$ (Associational odds ratio)

Chapter 1.5: Causation versus association

 $\Pr(Y = 1 | A = 1)$  is a conditional,  $\Pr(Y^a = 1)$  an unconditional probability.

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CHAPTER 1.5: CAUSATION VERSUS ASSOCIATION Pr(Y = 1|A = 1) is a conditional,  $Pr(Y^a = 1)$  an unconditional probability.



FIGURE : Association-causation difference (Figure 1.1 in the book)

Part 1 (Hernán & Robins)

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### EXCHANGEABILITY

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- Means that the outcome would be the same in both study groups if both received the treatment or if both did not receive it.
- Formally: Exchangeability,  $Y^a \coprod A$  for  $a \in \{0, 1\}$ , holds if

$$\Pr(Y^{a=0} = 1) = \underbrace{\Pr(Y^{a=0} = 1 | A = 0)}_{\text{Observable}} = \underbrace{\Pr(Y^{a=0} = 1 | A = 1)}_{\text{Counterfactual}},$$
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- Standardization

$$CRR = \frac{\Pr(Y^{a=1} = 1)}{\Pr(Y^{a=0} = 1)} = \frac{\sum_{I} \Pr(Y = 1 | L = I, A = 1) \Pr(L = I)}{\sum_{I} \Pr(Y = 1 | L = I, A = 0) \Pr(L = I)}$$

# CHAPTER 3: OBSERVATIONAL STUDIES

#### IDENTIFIABILITY CONDITIONS FOR CAUSAL INFERENCE

Three conditions must hold so that an observational study can be conceptualized as a conditionally randomized experiment:

- The values of treatment under comparison correspond to well-defined interventions.
- 2 The conditional probability of receiving every value of treatment, though not decided by the investigators, depends only on the measured covariates.
- The conditional probability of receiving every value of treatment is greater than zero, i.e., positive.

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- The conditional probability of receiving every value of treatment is greater than zero, i.e., positive.

### If these three (identifiability) conditions hold,

"... causal effects can be identified from observational studies by using IP weighting or standardization."

# CHAPTER 4: EFFECT MODIFICATION

### EFFECT MODIFICATION (EM)

- We say that *M* is a modifier of the effect of *A* on *Y* when the average causal effect of *A* on *Y* varies across levels of *M*.
- 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:

Additive EM: 
$$E(Y^{a=1} - Y^{a=0}|M = 1)$$
  
 $\neq E(Y^{a=1} - Y^{a=0}|M = 0)$   
Multiplicative EM:  $\frac{E(Y^{a=1}|M = 1)}{E(Y^{a=0}|M = 1)} \neq \frac{E(Y^{a=1}|M = 0)}{E(Y^{a=0}|M = 0)}$ 

# HERNÁN & ROBINS: CAUSAL INFERENCE.

### CHAPTER 5: INTERACTION

- $5.1\,$  Interaction requires a joint intervention
- 5.2 Identifying interaction
- 5.3 Counterfactual response types and interaction
- 5.4 Sufficient causes
- 5.5 Sufficient cause interaction
- 5.6 Counterfactuals or sufficient-component causes?



"Does one's looking up at the sky make other pedestrians look up too?"



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"This chapter provides a formal definition of interaction between two treatments, both within our (...) counterfactual framework and within the sufficient-component-cause framework."

## 5.1 INTERACTION REQUIRES A JOINT INTERVENTION

#### JOINT INTERVENTIONS

Interventions on two or more treatments.

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- There are 4 counterfactual observations:

$$Y^{a=1,e=1}, Y^{a=1,e=0}, Y^{a=0,e=1}, Y^{a=0,e=0}$$

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### DEFINITION

There is **interaction** between A and E if the causal effect of A differs from E = 0 to E = 1 (and viceversa).

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INTERACTION ON THE ADDITIVE SCALE

There is interaction on the additive scale if

$$\Pr(Y^{a=1,e=1} = 1) - \Pr(Y^{a=0,e=1} = 1) \neq \Pr(Y^{a=1,e=0} = 1) - \Pr(Y^{a=0,e=0} = 1),$$

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which is equivalent to

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INTERACTION ON THE MULTIPLICATIVE SCALE

$$\frac{\Pr(Y^{a=1,e=1}=1)}{\Pr(Y^{a=0,e=0}=1)} \neq \frac{\Pr(Y^{a=0,e=1}=1)}{\Pr(Y^{a=0,e=0}=1)} \times \frac{\Pr(Y^{a=1,e=0}=1)}{\Pr(Y^{a=0,e=0}=1)}$$

Part 1 (Hernán & Robins)

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Difference between effect modification and interaction:
A and M are not variables of equal status; only A can be intervened.
There are no counterfactual observations Y<sup>a,m</sup>.

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"... identifying interaction requires exchangeability, positivity, and well-defined interventions for both treatments." In case *E* is randomly assigned, E = 1 and E = 0 are expected to be exchangeable and

$$\Pr(Y^{a=1,e=1} = 1) = \Pr(Y^{a=1} = 1|E = 1).$$

"... identifying interaction requires exchangeability, positivity, and well-defined interventions for both treatments." In case E is randomly assigned, E = 1 and E = 0 are expected to be exchangeable and

$$\Pr(Y^{a=1,e=1} = 1) = \Pr(Y^{a=1} = 1|E = 1).$$

Hence, the definition of interaction on the additive scale can be rewritten:

$$\begin{aligned} \mathsf{Pr}(Y^{a=1} = 1 | E = 1) - \mathsf{Pr}(Y^{a=0} = 1 | E = 1) \\ \neq \mathsf{Pr}(Y^{a=1} = 1 | E = 0) - \mathsf{Pr}(Y^{a=0} = 1 | E = 0). \end{aligned}$$

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That is, "... when treatment E is randomly assigned, then the concepts of interaction and effect modification coincide."

Part 1 (Hernán & Robins)

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- A and E can be seen as a combined treatment with 4 possible levels.
- Identification of interaction is not different from the identification of the causal effect of one treatment.

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Following, the concepts reviewed require that counterfactuals

"(...) are assumed to be deterministic, and that treatments and outcomes are dichotomous. This oversimplification, though not necessary, makes the study of these concepts manageable and helps clarify some issues ...."

Classification of individuals according to their counterfactual responses:

Туре	$\mathbf{Y}^{a=0}$	Y <sup>a=1</sup>		
Doomed	1	1		
Preventative	1	0		
Causative	0	1		
Immune	0	0		

Table 5.1Possible response types

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Table 5.1Possible response types

In case of two dichotomous treatments, there are 16 possible response types.

Туре	1,1	0,1	1,0	0,0	Туре	1,1	0,1	1,0	0,0
1	1	1	1	1	9	0	1	1	1
2	1	1	1	0	10	0	1	1	0
3	1	1	0	1	11	0	1	0	1
4	1	1	0	0	12	0	1	0	0
5	1	0	1	1	13	0	0	1	1
6	1	0	1	0	14	0	0	1	0
7	1	0	0	1	15	0	0	0	1
8	1	0	0	0	16	0	0	0	0

**Table 5.2** Responses  $Y^{a,e}$  for each a, e value

Classification of response types:

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► Type 7 (
$$Y^{a=1,e=1} = 1$$
,  $Y^{a=0,e=0} = 1$ ,  $Y = 0$  otherwise),  
Type 10 ( $Y^{a=1,e=0} = 1$ ,  $Y^{a=0,e=1} = 1$ ,  $Y = 0$  otherwise).

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  - ► Type 7 (Y<sup>a=1,e=1</sup> = 1, Y<sup>a=0,e=0</sup> = 1, Y = 0 otherwise), Type 10 (Y<sup>a=1,e=0</sup> = 1, Y<sup>a=0,e=1</sup> = 1, Y = 0 otherwise).
  - Types 2, 3, 5, 9: Y = 1 under 3 of the 4 treatment combinations.

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FIGURE : Hernán & Robins: Figure 5.1

In case of two treatments, there are nine possible sufficient causes (not all of them exist necessarily):



FIGURE : Hernán & Robins: Figure 5.2

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- The previous example is equivalent to the presence of individuals with  $Y^{a=1,e=1} = 1$  and  $Y^{a=1,e=0} = Y^{a=0,e=1} = 0$ .
#### 5.5 Sufficient cause interaction

- "... the definition of interaction within the counterfactual framework does not require any knowledge about those mechanisms nor even that the treatments work together."
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- The previous example is equivalent to the presence of individuals with  $Y^{a=1,e=1} = 1$  and  $Y^{a=1,e=0} = Y^{a=0,e=1} = 0$ .
- "Unlike the counterfactual definition of interaction, sufficient cause interaction makes explicit reference to the causal mechanisms involving the treatments."

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- "Though the sufficient-component-cause framework is useful from a pedagogic standpoint, its relevance to actual data analysis is yet to be determined. In its classical form, the sufficient-component-cause framework is deterministic, its conclusions depend on the coding on the outcome, and is by definition limited to dichotomous treatments and outcomes."

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- "Though the sufficient-component-cause framework is useful from a pedagogic standpoint, its relevance to actual data analysis is yet to be determined. In its classical form, the sufficient-component-cause framework is deterministic, its conclusions depend on the coding on the outcome, and is by definition limited to dichotomous treatments and outcomes."
- "To estimate causal effects more generally, the counterfactual framework will likely continue to be the one most often employed.".

- "The sufficient-component-cause framework and the counterfactual (potential outcomes) framework address different questions."
- The counterfactual approach addresses the question "What happens?", the sufficient-component-cause, "How does it happen?"
- "Though the sufficient-component-cause framework is useful from a pedagogic standpoint, its relevance to actual data analysis is yet to be determined. In its classical form, the sufficient-component-cause framework is deterministic, its conclusions depend on the coding on the outcome, and is by definition limited to dichotomous treatments and outcomes."
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#### CONTINUARÁ..