# CaUsAL Inference <br> By: Miguel A. Hernán and James M. Robins 

Part I: Causal inference without models
Chapter 5: Interaction
$12^{\text {th }}$ 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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However, in general, individual effects cannot be identified.

## Chapter 1.2: Average causal effects

## Definition

Average causal effect is present if

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What we would like to observe:

$$
\begin{array}{ll}
\operatorname{Pr}\left(Y^{a=1}=1\right)-\operatorname{Pr}\left(Y^{a=0}=1\right) & \text { (Causal risk difference) } \\
\frac{\operatorname{Pr}\left(Y^{a=1}=1\right)}{\operatorname{Pr}\left(Y^{a=0}=1\right)} & \text { (Causal risk ratio) } \\
\frac{\operatorname{Pr}\left(Y^{a=1}=1\right) / \operatorname{Pr}\left(Y^{a=1}=0\right)}{\operatorname{Pr}\left(Y^{a=0}=1\right) / \operatorname{Pr}\left(Y^{a=0}=0\right)} & \text { (Causal odds ratio) }
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## What we can estimate:

$$
\begin{array}{ll}
\operatorname{Pr}(Y=1 \mid A=1)-\operatorname{Pr}(Y=1 \mid A=0) & \text { (Associational risk differen } \\
\frac{\operatorname{Pr}(Y=1 \mid A=1)}{\operatorname{Pr}(Y=1 \mid A=0)} & \text { (Associational risk ratio) } \\
\frac{\operatorname{Pr}(Y=1 \mid A=1) / \operatorname{Pr}(Y=0 \mid A=1)}{\operatorname{Pr}(Y=1 \mid A=0) / \operatorname{Pr}(Y=0 \mid A=0)} & \text { (Associational odds ratio) }
\end{array}
$$

## Chapter 1.5: Causation versus association

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

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## ExCHANGEABILITY

- 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

$$
\begin{aligned}
& \operatorname{Pr}\left(Y^{a=0}=1\right)=\underbrace{\operatorname{Pr}\left(Y^{a=0}=1 \mid A=0\right)}_{\text {Observable }}=\underbrace{\operatorname{Pr}\left(Y^{a=0}=1 \mid A=1\right)}_{\text {Counterfactual }}, \\
& \operatorname{Pr}\left(Y^{a=1}=1\right)=\underbrace{\operatorname{Pr}\left(Y^{a=1}=1 \mid A=0\right)}_{\text {Counterfactual }}=\underbrace{\operatorname{Pr}\left(Y^{a=1}=1 \mid A=1\right)}_{\text {Observable }} .
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- Standardization

$$
\mathrm{CRR}=\frac{\operatorname{Pr}\left(Y^{a=1}=1\right)}{\operatorname{Pr}\left(Y^{a=0}=1\right)}=\frac{\sum_{l} \operatorname{Pr}(Y=1 \mid L=I, A=1) \operatorname{Pr}(L=I)}{\sum_{I} \operatorname{Pr}(Y=1 \mid L=I, A=0) \operatorname{Pr}(L=I)}
$$

## 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:
(1) 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.
(3) The conditional probability of receiving every value of treatment is greater than zero, i.e., positive.

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(3) 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: $\quad \mathrm{E}\left(Y^{a=1}-Y^{a=0} \mid M=1\right)$

$$
\neq \mathrm{E}\left(Y^{a=1}-Y^{a=0} \mid M=0\right)
$$

Multiplicative EM: $\quad \frac{\mathrm{E}\left(Y^{a=1} \mid M=1\right)}{\mathrm{E}\left(Y^{a=0} \mid M=1\right)} \neq \frac{\mathrm{E}\left(Y^{a=1} \mid M=0\right)}{\mathrm{E}\left(Y^{a=0} \mid M=0\right)}$

## Hernán \& Robins: Causal Inference.

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5.2 Identifying interaction
5.3 Counterfactual response types and interaction
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## "Looking up at the sky": Version III <br> 

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- Random assignment of you looking up.
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- Random assignment of you looking up.
- Random assignment of you standing in the street dressed or naked.
- If causal effect of you looking up differs from being dressed to being naked $\rightsquigarrow$ Both "treatments" interact.
"This chapter provides a formal definition of interaction between two treatments, both within our (...) counterfactual framework and within the sufficient-component-cause framework."


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- $Y$ : Death (1: yes; 0: no),
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- E: Multivitamin complex (1: yes; 0: no)
- 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).

### 5.1 Interaction Requires a Joint intervention

## Interaction on the additive scale

There is interaction on the additive scale if

$$
\operatorname{Pr}\left(Y^{a=1, e=1}=1\right)-\operatorname{Pr}\left(Y^{a=0, e=1}=1\right) \neq \operatorname{Pr}\left(Y^{a=1, e=0}=1\right)-\operatorname{Pr}\left(Y^{a=0, e=0}=1\right)
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which is equivalent to

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Interaction on the multiplicative scale

$$
\frac{\operatorname{Pr}\left(Y^{a=1, e=1}=1\right)}{\operatorname{Pr}\left(Y^{a=0, e=0}=1\right)} \neq \frac{\operatorname{Pr}\left(Y^{a=0, e=1}=1\right)}{\operatorname{Pr}\left(Y^{a=0, e=0}=1\right)} \times \frac{\operatorname{Pr}\left(Y^{a=1, e=0}=1\right)}{\operatorname{Pr}\left(Y^{a=0, e=0}=1\right)} .
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- Difference between effect modification and interaction:


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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 $Y^{a, m}$.


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In case $E$ is randomly assigned, $E=1$ and $E=0$ are expected to be exchangeable and

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

$$
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\operatorname{Pr}\left(Y^{a=1}=1 \mid E=1\right)-\operatorname{Pr}\left(Y^{a=0}\right. & =1 \mid E=1) \\
& \neq \operatorname{Pr}\left(Y^{a=1}=1 \mid E=0\right)-\operatorname{Pr}\left(Y^{a=0}=1 \mid E=0\right) .
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That is, ". . . when treatment $E$ is randomly assigned, then the concepts of interaction and effect modification coincide."

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- Can be done "under the usual identifying assumptions, by standardization or IP weighting conditional on the measured covariates."
- $A$ 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.


### 5.2 IDENTIFYING INTERACTION

If exchangeability can be assumed for $A$ but not for $E$

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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 ...."

### 5.3 Counterfactual Response types and INTERACTION

Classification of individuals according to their counterfactual responses:
Table 5.1 Possible response types

| Type | $\mathbf{Y}^{\mathbf{a}=\mathbf{0}}$ | $\mathbf{Y}^{\mathbf{a}=\mathbf{1}}$ |
| :--- | :---: | :---: |
| Doomed | 1 | 1 |
| Preventative | 1 | 0 |
| Causative | 0 | 1 |
| Immune | 0 | 0 |

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

### 5.3 Counterfactual Response types and INTERACTION

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

| Type | $\mathbf{1 , 1}$ | $\mathbf{0 , 1}$ | $\mathbf{1 , 0}$ | $\mathbf{0 , 0}$ | Type | $\mathbf{1 , 1}$ | $\mathbf{0 , 1}$ | $\mathbf{1 , 0}$ | $\mathbf{0 , 0}$ |
| :--- | :---: | :---: | :---: | :---: | :--- | :---: | :---: | :---: | :---: |
| 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 |

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- Types $8,12,14,15: Y=1$ under 1 of the 4 treatment combinations.
- Type $7\left(Y^{a=1, e=1}=1, Y^{a=0, e=0}=1, Y=0\right.$ otherwise $)$, Type $10\left(Y^{a=1, e=0}=1, Y^{a=0, e=1}=1, Y=0\right.$ otherwise $)$.


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- Types 4, 6, 11, and 13: Causal effects of $A$ and $E$ are independent.
- If the population only consisted of types $1,4,6,11,13$, and 16 , there would be no interaction between $A$ and $E$ on the additive scale.
- For interaction to be present there must be individuals in, at least, one of the following classes:
- Types $8,12,14,15: Y=1$ under 1 of the 4 treatment combinations.
- Type $7\left(Y^{a=1, e=1}=1, Y^{a=0, e=0}=1, Y=0\right.$ otherwise $)$, Type $10\left(Y^{a=1, e=0}=1, Y^{a=0, e=1}=1, Y=0\right.$ 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

### 5.4 SuFficient causes

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







Figure: Hernán \& Robins: Figure 5.2

### 5.5 SUFFICIENT CAUSE INTERACTION

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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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## CONTINUARÁ...

