Yarmouk University

Community Medicine

Lec. 7 - Association VS Causation (Part 2)

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Association Vs Causation

Lec. 7

MED 410

Dr. Ola Soudah

Threats: Bias, Confounding, and Interaction

They are called the threats of validity , if one or more of them is found in a research, the research is invalid, as a result the research wont be accepted.

Bias

- **Bias has been defined as** "any systematic error in the design, conduct or analysis of a study that results in a mistaken estimate of an exposure's effect on the risk of disease".

- **Types of Bias Common in Epidemiologic Studies:**
  - Selection Bias.
  - Informational Bias.

- Bias: is a systematic error in the design or in the sampling (unequal groups, their characteristics dramatically differ) .
- Example: in a clinical trial, group A is the control group and are given the placebo drug, group B are given a treatment, the goal of the study is to see weather the treatment given to group B drops the symptoms of the disease.
- Bias in this example occurs if group A were healthier and having lesser symptoms than group B.
- another example: 2 groups of diabetic patients were given a drug to reduces Hb1C, bias occurs if group B in this example were having the disease for a longer duration than group A, the drug is going to give better results in group A because their bodies are less resistance to DM drugs.
- Again Bias is a systematic error, that is usually cant be avoided, the only way to decrease its effect is by using strong study design.

SELECTION BIAS

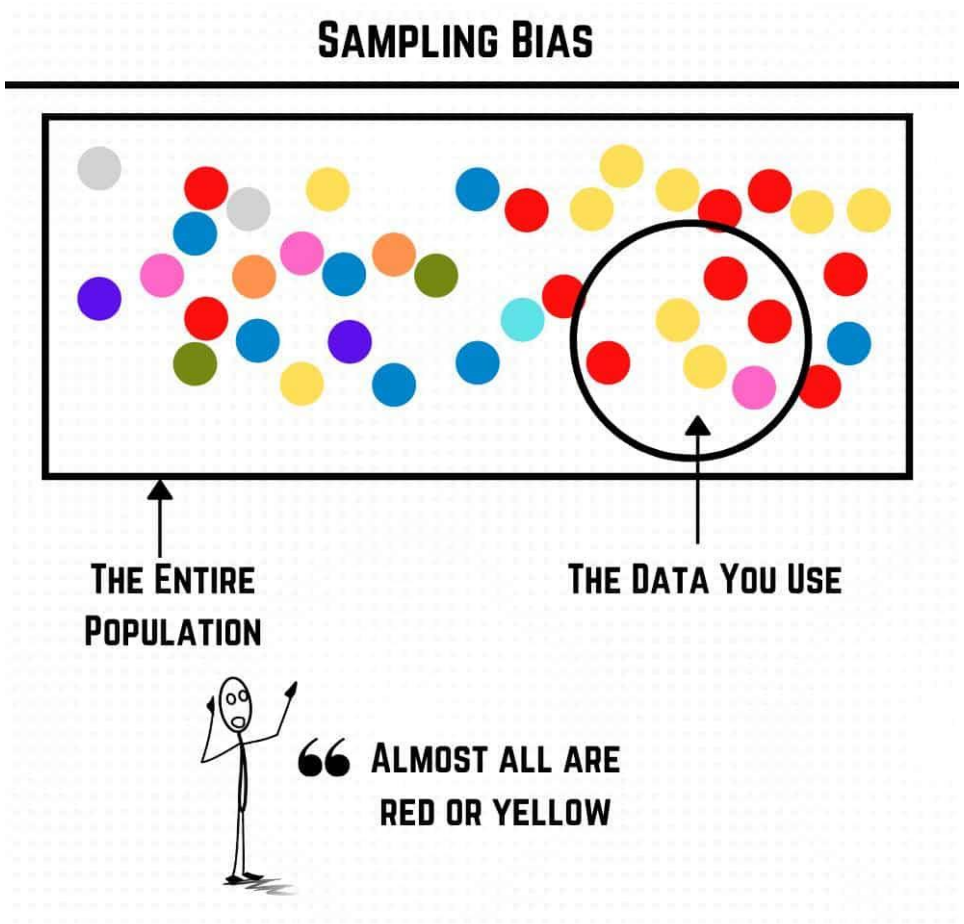
Selection have 2 ways, depending on study type:
1- in clinical trials: assortment
2- in epidemiological (observational) studies: sampling

- **Selection bias.** Stem from the way in which **individuals, were selected** is such that an apparent association is observed—even if, in reality, exposure and disease are not associated.

- It occurs when there is a **systematic difference between the characteristics of the people**
  - Who participate in the study and those who do not (affecting generalizability) .. **External validity.**
  - Who receiving treatment and those in the control group (affecting comparability between groups)… **Internal validity.**

- Example on: **External validity :** a study about Jordanian students English proficiency level. Bias occurs if the sample is made of medical students only.
- **Random selection** is a technique in the sampling method used in order to get a representative sample.

Types of selection bias



Selection bias
Ascertainment bias
Sampling bias
Competing risks bias
Volunteer bias
Nonresponse bias
Loss to follow-up bias
Attrition bias
Prevalence-incidence (Neyman) bias
Survivor treatment selection bias
Overmatching bias

INFORMATION BIAS

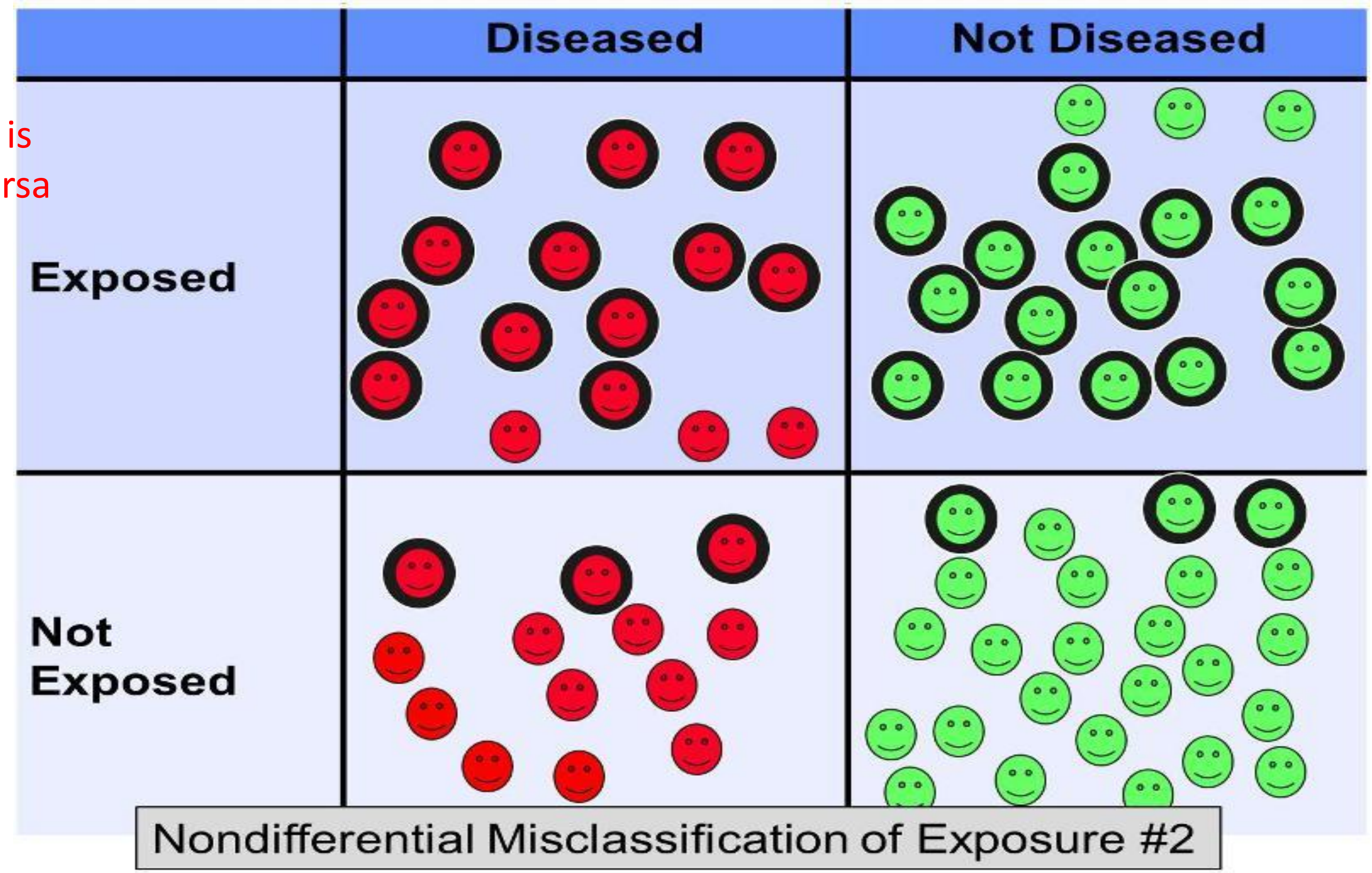
- **Information bias can occur** when the **means for obtaining information (data collection)** about the subjects in the study are flawed so that some of the information gathered regarding exposures and/or disease outcomes is incorrect.

BOX 15.1 SOME TYPES AND SOURCES OF INFORMATION BIAS

Bias in abstracting records
Bias in interviewing Asking the question in a way the researcher get the wanted piece of information
Bias from surrogate interviews Asking a person about another person's information
Surveillance bias
Recall bias Asking about past information
Reporting bias

- Given inaccuracies in methods of data acquisition, we may at times misclassify subjects and thereby introduce a misclassification bias.

Depends on how I
Classify patients.
Example: When a patient is
misdiagnosed and vise versa



Approaches to handle Bias

- Strong study design
- Strong , validated data collection tool.
- Sensitivity analysis.
- Blinding.
- Data monitoring Unit.

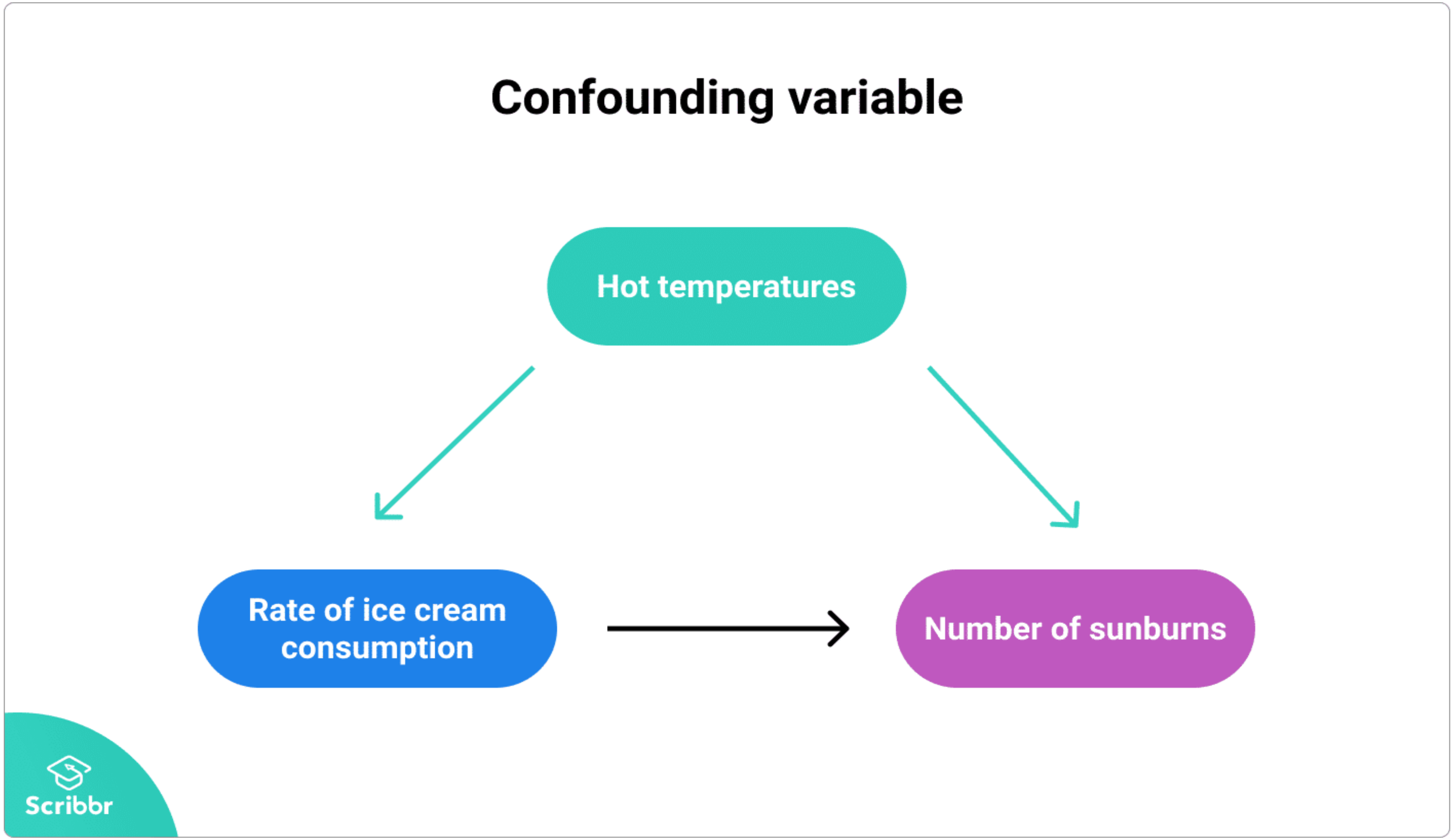
* Example on Sensitivity analysis:
If the sample for a certain study was 1000, after analyzing the results RR was 1.5. to see if severe cases in this study have biased the Results, I remove them and reanalyze the data, If the RR was 1.3 after reanalysis, the difference between Results before and after removing the severe Cases is **not huge** : so the result is stable.
But if the result after reanalysis was 1, then the severe cases had biased my Results and they are not stable.

Confounding

Extra factor has effect on the outcome

You get them from the literature review

- **What do we mean by confounding?**
- In a study of whether exposure A is a cause of disease B, we say that a third factor, factor X, is a confounder if the following are true:
    1. Factor X is a known risk factor for disease B.
    2. Factor X is associated with exposure A, but is not a result of exposure A.


Confounding variable
Hot temperatures
Rate of ice cream consumption
Number of sunburns
Scribbr

Coffee consumption and pancreatic cancer

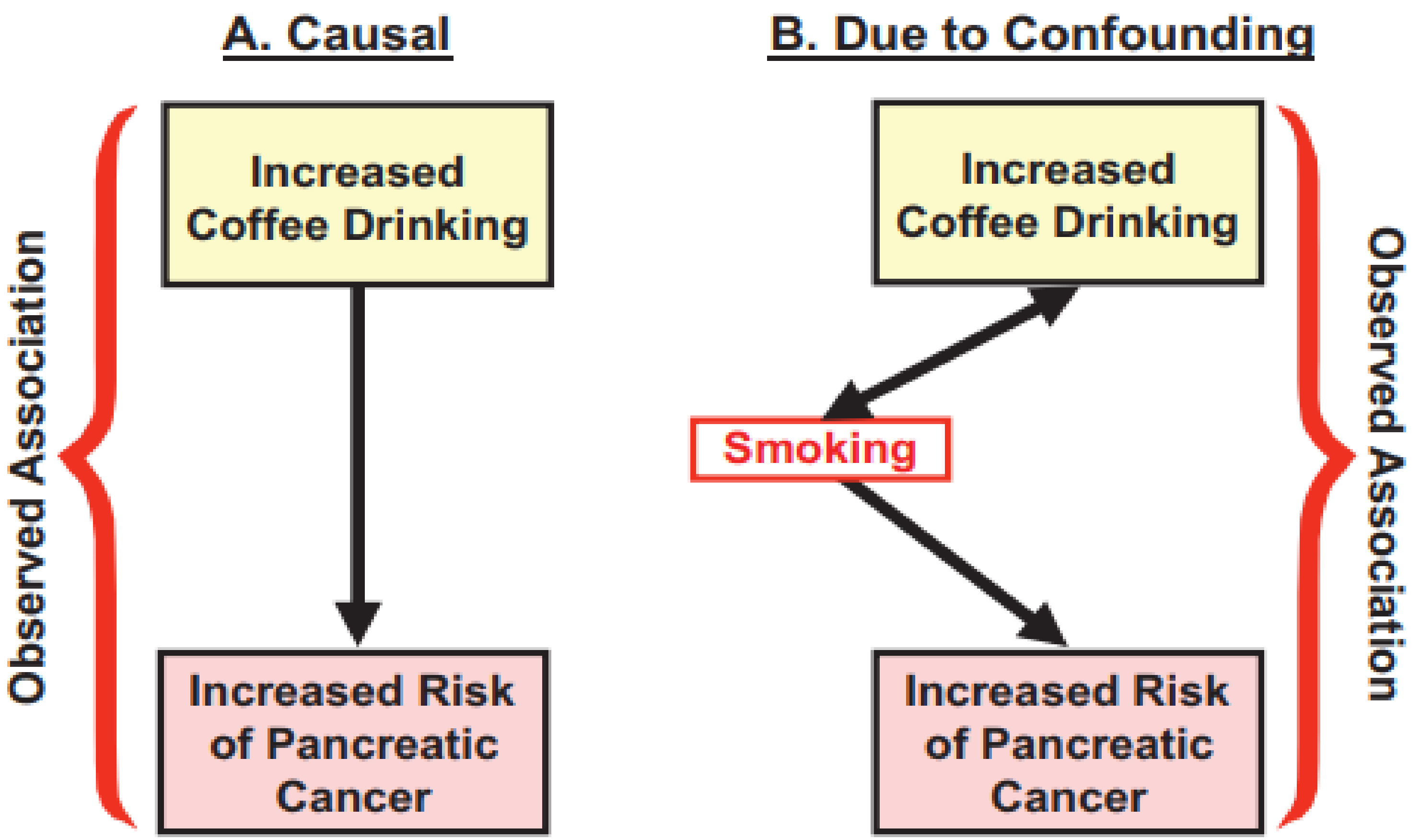


Fig. 14.5 Interpreting an observed association between increased coffee drinking and increased risk of pancreatic cancer.

Is there an association between exposure and the disease?

RR= 1.95 > 1

???

Yes

TABLE 15.3 Hypothetical Example of Confounding in an Unmatched Case-Control Study: I. Numbers of Exposed and Nonexposed Cases and Controls

Exposed	Cases	Controls
Yes	30	18
No	70	82
Total	100	100

$$\text{Odds ratio} = \frac{30 \times 82}{70 \times 18} = 1.95$$

Wait …..

- Is this association of the exposure with the disease a causal one, or could it have resulted from differences in the age distributions of the cases and controls **(outcome)?**

TABLE 15.4 Hypothetical Example of Confounding in an Unmatched Case-Control Study: II. Distribution of Cases and Controls by Age

Age (yr)	Cases	Controls
<40	50	80
≥40	50	20
Total	100	100

Because controls younger than 40 are 80
and controls older than 40 are 20
we say that there is a baseline difference depending on age.

Is this association of the exposure with the disease a causal one, or could it have resulted from differences in the age distributions of the exposed and unexposed group **(Independent Variable)?**

TABLE 15.5 Hypothetical Example of Confounding in an Unmatched Case-Control Study: III. Relationship of Exposure to Age

Age (yr)	Total	Exposed	Not Exposed	% Exposed
<40	130	13	117	10
≥40	70	35	35	50

We did stratify the analysis by age group (we did two separate analysis for each age group).

What Happen to the RR ??

RR= 1 is there an association? NO

TABLE 15.6 Hypothetical Example of Confounding in an Unmatched Case-Control Study: IV. Calculations of Odds Ratios After Stratifying by Age

Age (yr)	Exposed	Cases	Controls	Odds Ratio
<40	Yes	5	8	$\frac{5 \times 72}{45 \times 8} = \frac{360}{360} = 1.0$
	No	45	72	
	Totals	**50**	**80**	
≥40	Yes	25	10	$\frac{25 \times 10}{25 \times 10} = \frac{250}{250} = 1.0$
	No	25	10	
	Totals	**50**	**20**	

BOX 15.2 APPROACHES TO HANDLING CONFOUNDING

In designing and carrying out the study:

1. Individual matching
2. Group matching

Mostly used in case-control study design

In the analysis of data:

1. Stratification

By doing different analysis to different groups, that are classified depending on the confounder factor

2. Adjustment

Most commonly used method in Regression

By giving the confounder value of 0 in the biostatical sowftware

INTERACTION

- In this section, we ask the question: How do multiple factors interact in causing a disease?

- **What do we mean by interaction?** MacMahon defined interaction as follows: “When the incidence rate of disease in the presence of two or more risk factors differs from the incidence rate expected to result from their individual effects.”

- **Positive interaction (synergism):** The effect can be greater than what we would expect.

- **Negative interaction, (antagonism):** Less than what we would expect (antagonism).

TABLE 15.9 Incidence Rates for Groups Exposed to Neither Risk Factor or to One or Two Risk Factors (Hypothetical Data)

		Factor A	
		–	+
Factor B	–	3.0	9.0
	+	15.0	

TABLE 15.19 Relative Risks of Lung Cancer According to Smoking and Radiation Exposure in Two Populations

Radiation Level	Uranium Workers (Smoking Level)		A-Bomb Survivors (Smoking Level)	
	Low	High	Low	High
Low	1.0	7.7	1.0	9.7
High	18.2	146.8	6.2	14.2

From Blot WJ, Akiba S, Kato H. Ionizing radiation and lung cancer: a review including preliminary results from a case-control study among A-bomb survivors. In: Prentice

- there is an association between cancer and radiation, RR= 18.2
- there is an association between cancer and smoking, RR = 7.7
- there an association between cancer and (smoking + radiation) = 146.8 and this is **synergism**.

- Another example: studying the effect of wearing PPE (personal protective equipment) and radiation level on cancer:

- NO PPE, low radiation, RR =1
- NO PPE, high radiation, RR =18
- PPE, Low radiation, RR = 4
- PPE, high radiation, RR = 14 (18 - 4) : this is **antagonism**

In A-Bomb Workers: we can see the incidence rate of lung cancer for smoking exposure only = 9.7 , & from radiation only =6.2.

From both exposure = 14.2 ~ (9.7 + 6.2 = 15.1)

Additive model of interaction

TABLE 15.19 Relative Risks of Lung Cancer According to Smoking and Radiation Exposure in Two Populations

Radiation Level	URANIUM WORKERS (SMOKING LEVEL) Low	URANIUM WORKERS (SMOKING LEVEL) High	A-BOMB SURVIVORS (SMOKING LEVEL) Low	A-BOMB SURVIVORS (SMOKING LEVEL) High
Low	1.0	7.7	1.0	9.7
High	18.2	146.8	6.2	14.2

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In Uranium Workers: we can see the incidence rate of lung cancer for smoking exposure only = 7.7 , & from radiation only =8.7.

From both exposure = 146.8 ~ (7.7 * 18.2 = 140.14)

Multiplicative model of interaction

TABLE 15.19 Relative Risks of Lung Cancer According to Smoking and Radiation Exposure in Two Populations

Radiation Level	URANIUM WORKERS (SMOKING LEVEL)		A-BOMB SURVIVORS (SMOKING LEVEL)	
	Low	High	Low	High
Low	1.0	7.7	1.0	9.7
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Question