BSc Global Health
Practical Session

Case-Control Study on Cardiovascular Disease

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Aims and Objectives

- Aims
  - To provide the skills necessary to interpret and critically appraise findings
- Objectives
  - Epidemiology study design, case-control study
  - Risk factors and CVD

Epidemiology

- Is the study of the *distribution* and *determinants* of health and disease in populations
- Epidemiology can be used to identify
  - patterns of disease (e.g., spatial, temporal)
  - risk factors
  - therapeutic targets
- Can guide
  - health service provision
  - public health policy
  - clinical practice

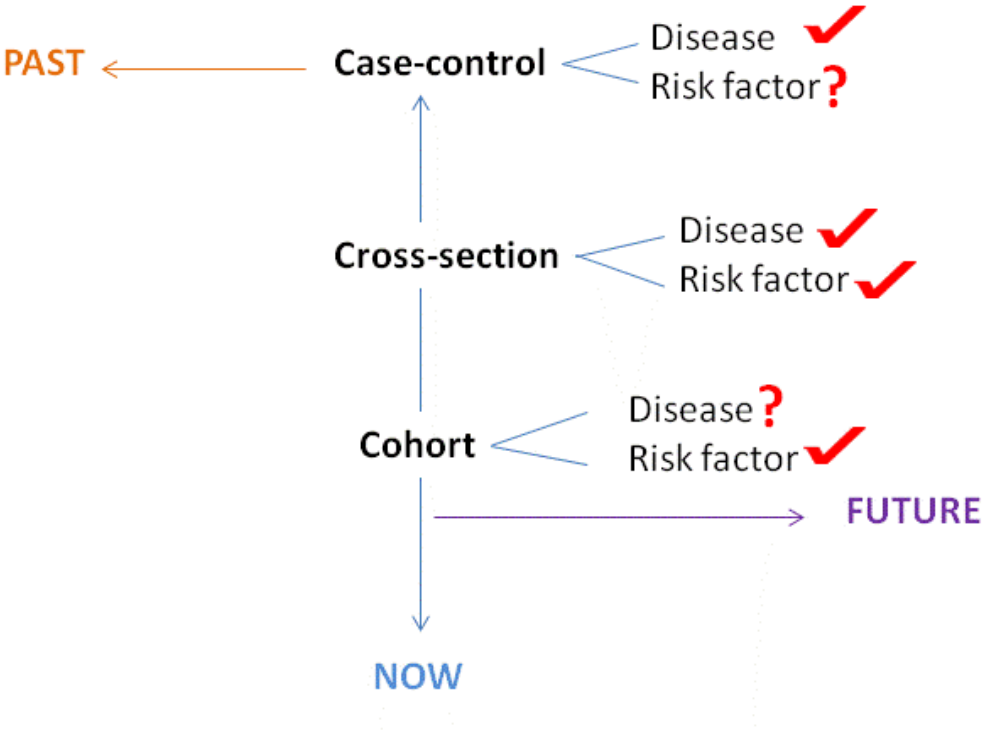
Observational studies

Design

- Case-control study
- Cross sectional study
- Cohort study

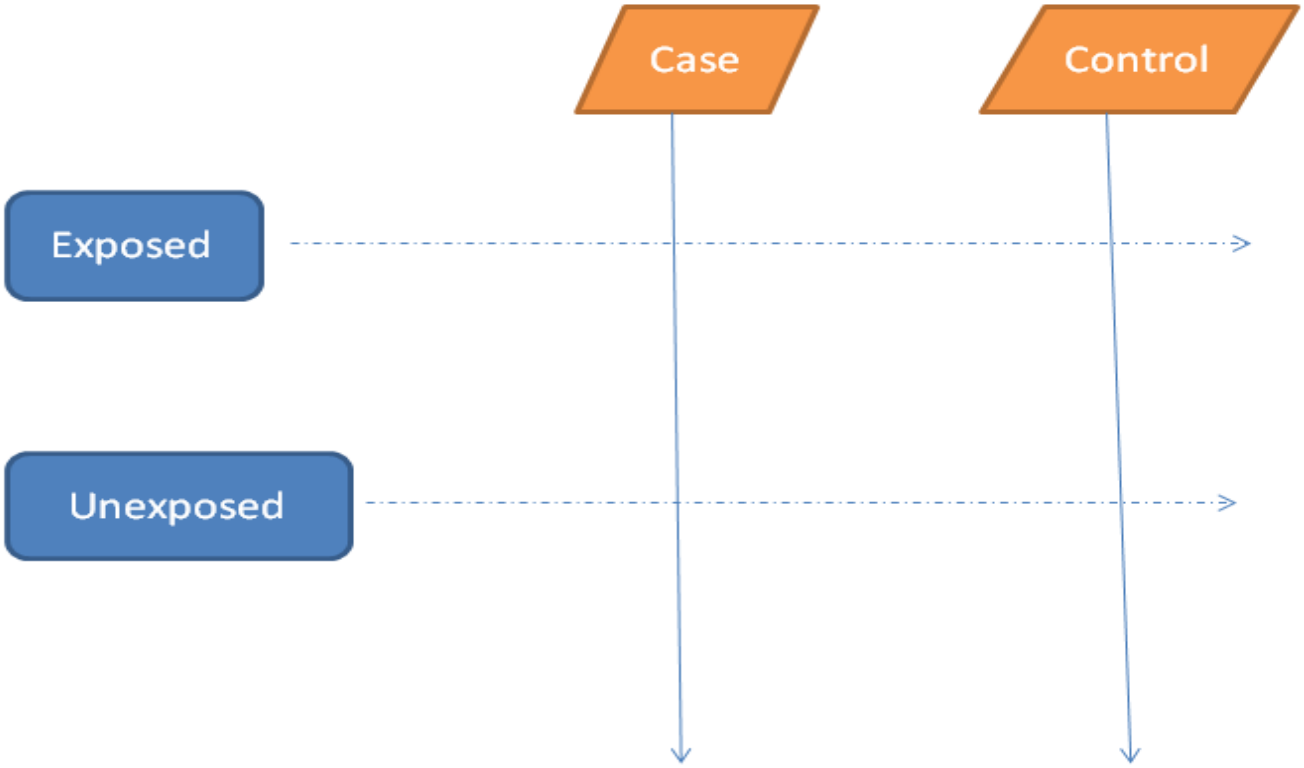
Objectives

- Cause
- Prevalence, cause
- Incidence, cause, prognosis



Case-Control Study

- *Case* people with the disease
- *Control* people free of the disease



Case-Control Study Design

- Case selection
- Control selection
- Exposure evaluation
- Analysis
- Interpretation

Example: Case-Control Study

Effect of potentially modifiable risk factors associated with myocardial infarction in 52 countries (the INTERHEART study): case-control study

*Salim Yusuf, Steven Hawken, Stephanie Ôunpuu, Tony Dans, Alvaro Avezum, Fernando Lanas, Matthew McQueen, Andrzej Budaj, Prem Pais, John Varigos, Liu Lisheng, on behalf of the INTERHEART Study Investigators**

Summary

Background Although more than 80% of the global burden of cardiovascular disease occurs in low-income and middle-income countries, knowledge of the importance of risk factors is largely derived from developed countries. Therefore, the effect of such factors on risk of coronary heart disease in most regions of the world is unknown.

Methods We established a standardised case-control study of acute myocardial infarction in 52 countries, representing every inhabited continent. 15 152 cases and 14 820 controls were enrolled. The relation of smoking, history of hypertension or diabetes, waist/hip ratio, dietary patterns, physical activity, consumption of alcohol, blood apolipoproteins (Apo), and psychosocial factors to myocardial infarction are reported here. Odds ratios and their 99% CIs for the association of risk factors to myocardial infarction and their population attributable risks (PAR) were calculated.

Example: INTERHEART Study

Case Selection

Specific definitions

Inclusion? Exclusion?

Incident/prevalent?

Hospital/population based?

Control Selection

How many? - power calculation

Matching – individual or group?

Exposure Evaluation

What risk factors?

How to measure?

Analysis & Interpretation

Example: Exposure to risk factor

- Smoking
- Lipids (apolipoproteins ratio)
- History of hypertension
- History of diabetes mellitus
- Abdominal obesity (waist/hip ratio)
- Psychosocial index
- Exercise
- Vegetable and fruit intake
- Alcohol intake

Case-Control Study: Analysis

Un-matched

	Case	Control
Exposed	a	b
Unexposed	c	d

$$OR = \frac{a/b}{c/d} = \frac{ad}{bc} \approx RR$$

Relative Risk (RR)

Matched

		Control	
		Exposed	Unexposed
Case	Exposed	a	b
	Unexposed	c	d

$$OR = \frac{b}{c}$$

Odd Ratio (OR)

Interpretation: Association

- *Association* implies a statistical link between exposure and outcome
- Significant association due to:
  - Causation
  - Chance
  - Confounding
  - Bias

Causation

- *Causality* implies that the exposure causes the outcome
- Association *does not equal* causation
  - e.g., there is an association between ice cream consumption and hot weather, but eating ice-cream does not cause hot weather!

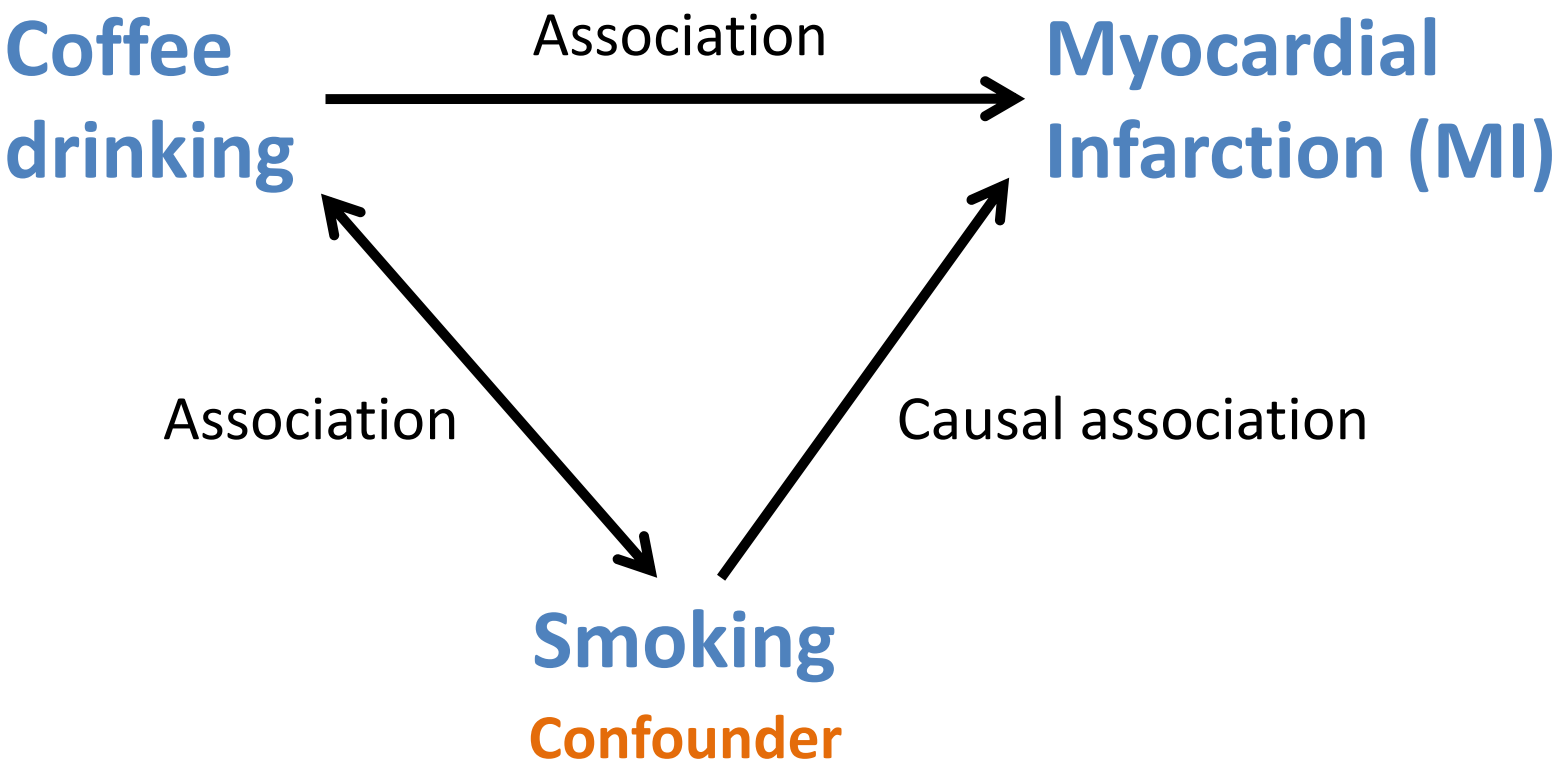
Chance

- The *null hypothesis* states that the association observed in the sample is due to chance alone
- The probability that the null hypothesis is true is usually reported as a *p value*
- If the *p* value is sufficiently low (often $p < 0.05$) then we may *reject the null hypothesis*, and *accept the alternate hypothesis*: that the association observed in the sample exists in the wider population
  - If $p < 0.05$ we can be 95% certain that the observed association is not due to chance

Confounding

- This occurs when an association between an exposure and an outcome is distorted by the presence of a confounder
- A confounder is a variable that is associated with both the exposure and the outcome

Confounding



Bias

- Bias is a systematic error, e.g., in the measurement of exposure or outcome
  - *Misclassification bias* (e.g., 10% of smokers deny their habit)
  - *Selection bias* (e.g., healthy worker effect, volunteer bias, follow-up bias)
  - *Measurement bias* (e.g., instrument bias, recall bias, observer bias)

Advantages: case-control study

- Quicker and cheaper than cohort studies
- Efficient (small sample sizes)
- Useful for studying infrequent events
- Wide screen possible
- Many risk factors can be studied simultaneously
- No drop out
- Consistent techniques

Disadvantages: case-control study

- Bias
- No incidence data
- Only one outcome
- Temporal sequence difficulties
- False negative potential

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Thank you

Example: number of case and control

- How many cases and controls do you need assuming…
  - 80% statistical power, Z_β=.84
  - 0.05 significance level, Z_α=1.96
  - an equal number of cases and controls (r=1)
  - standard deviation (σ=10.0)
  - a difference in characteristic of 5.0 (0.5 x σ)

$$n = \left(\frac{r+1}{r}\right)\frac{\sigma^2(Z_\beta + Z_{\alpha/2})^2}{(\mathit{d}\text{ifference})^2}$$

$$n = (2)\frac{10^2(7.84)}{(5)^2} = (2)2^2(7.84) = 63$$