Epidemiologické metody

Epidemiology

- The study of the **distribution** and **determinants** of the **frequency** of health-related outcomes in specified populations

- Quantitative discipline

- Measurement of disease / condition / risk factor frequency is central to epidemiology

- Comparisons require measurements

Much of epidemiological research is taken up trying

- to establish associations between exposures and disease rates
- to measure the extent to which risk changes as the level of exposure changes
- to establish whether the associations observed may be truly causal (rather than being just consequence of bias or chance)

- Epidemiology has a major role in developing appropriate strategies to improve public health through prevention
  - public health has wider meaning in this sense; it is about the health of the whole population.
  - it does not cover only classic areas, such as immunization or monitoring of diseases, it also covers factors such as poverty, smoking, nutrition
- In this sense, epidemiology has a crucial role in trying to put into perspective the effects on population health of different risk factors.

Measures of association

- Risk of disease, rate of disease in different groups of population
- Comparison of risks/rates

Measures of effect

We have 2 groups of individuals:

- An **exposed** group (group with risk factor of interest) and **unexposed** group (without such factor of interest)
- We are interested in comparing the amount of disease (mortality or other health outcome) in the exposed group to that in the unexposed group

Risk ratio

- we calculate the risk ratio (RR) as:

$$RR=r_1/r_0$$

Risk difference

- the absolute difference between two risks (or rates)

$$RD = r_1 - r_0$$

Example: cohort study of oral contraceptive use and heart attack

	Myocardial infarction		
	Yes	No	Total
OC use			
Yes	25	400	425
No	75	1500	1575
Total	100	1900	2000

Risk (exposed) = 25/425=0.059
Risk (unexposed) = 75/1575=0.048

Relative risk = 0.059/0.048 = 1.23

Odds ratio

- Alternative measure of risk

The odds of disease is the number of cases divided by the number of non-cases

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         Cases
Odds = ------------
        Non cases
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Odds ratio (**OR**) is ratio of odds of disease among exposed ($odds_{exp}$) and odds of disease among unexposed ($odds_{unexp}$)

$$\mathbf{OR = odds_{exp} / odds_{unexp}}$$

	Myocardial infarction		
	Yes	No	Total
OC use			
Yes	25	400	425
No	75	1500	1575
Total	100	1900	2000

We can calculate

- Odds (exposed) $O_{exp}=25/400$
- Odds (unexposed) $O_{unexp}=75/1500$

- Odds ratio $OR = O_{exp} / O_{unexp}$ = 1.25

Odds ratio as an approximation to the risk ratio

- For a rare disease, odds ratio is approximately equal to the risk ratio (because denumerators are very similar)
- For a common conditions, OR overestimates the true RR

Measures of population impact

- **Population attributable risk (PAR)** is the absolute difference between the risk (or rate) in the whole population and the risk or rate in the unexposed group

$$PAR = r - r_0$$

Population attributable risk fraction (PARF or PAR%)

- It is a measure of the proportion of all cases in the study population (exposed and unexposed) that may be attributed to the exposure, on the assumption of a causal association
- It is also called the aetiologic fraction, the percentage population attributable risk or the attributable fraction

- If r is rate in the total population

$$\mathbf{PAF = PAR/r}$$

$$\mathbf{PAR = r - r_0}$$

$$\mathbf{PAF = (r\text{-}r_0)/r}$$

Risk or rate difference

Measure of the absolute effect

the absolute difference between two risks (or rates)

$$RD = r_1 - r_0$$

Similar for rates = rate difference = incidence rate in exposed – incidence rate in unexposed

<table>
<tr><th>Measure of effect</th><th>Use of the measure</th><th>How to interpret results</th></tr>
<tr><td>Risk Difference</td><td>Public Health
Interested in excess disease burden due to factor (“Attributable risk”)</td><td>Close to 0 = little effect
Large difference = large effect</td></tr>
<tr><td>Risk Ratio</td><td>Epidemiology
Causation
“This factor doubles the risk of the disease”</td><td rowspan="2">Close to 1 = little effect
Large ratio = large effect
Close to 0 = large effect!</td></tr>
<tr><td>Odds Ratio</td><td>As for Risk Ratio
“This factor doubles the odds of the disease”
Only possibility (case-control study)
More advanced statistical methods (logistic regression)</td></tr>
</table>

Three major issues in interpretation of results in any epidemiological study

- **Chance (random variation) – statistics**
- Confounding
- Bias (i.e. systematic error)

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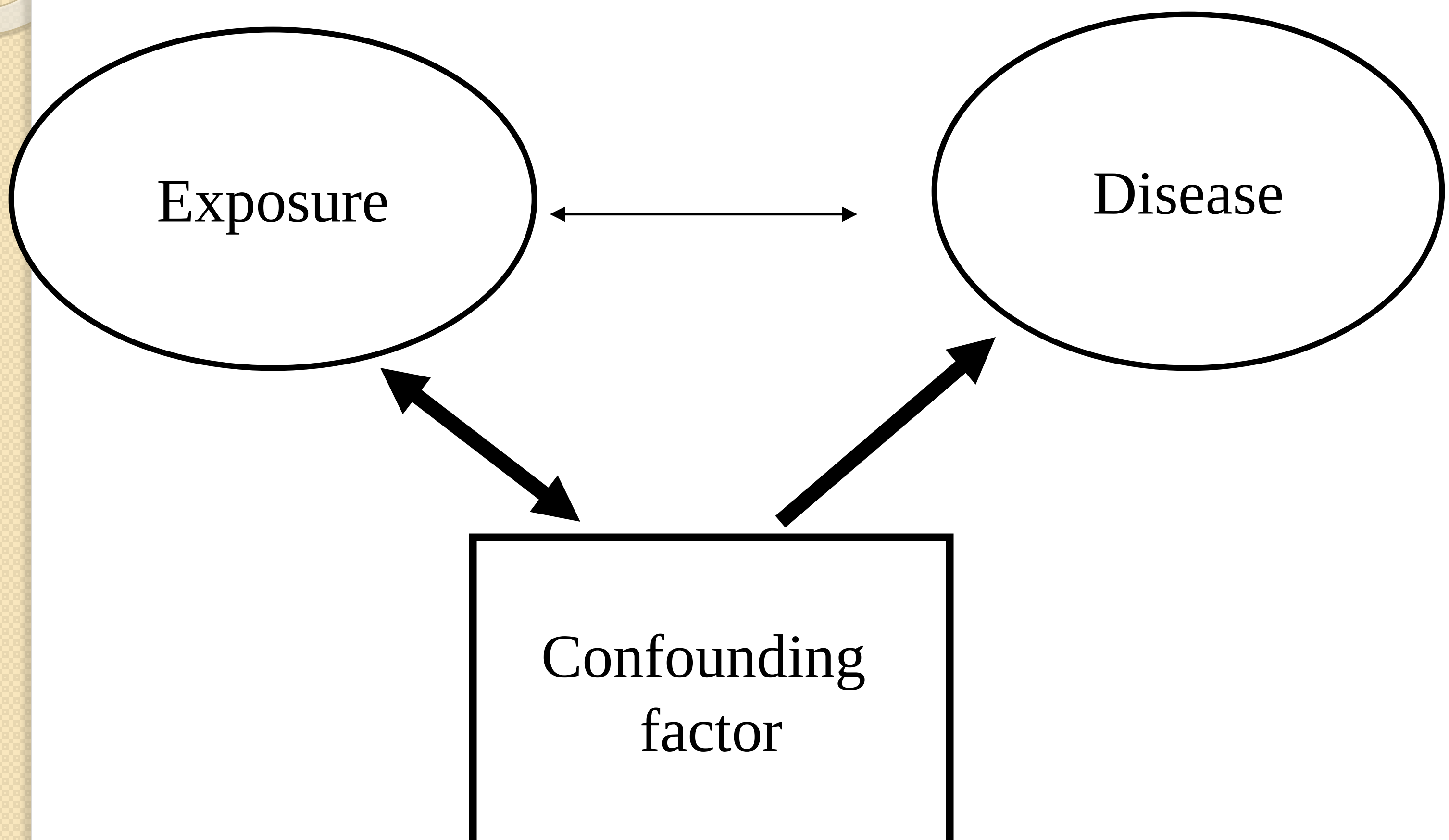
Confounding

- Situation when a third factor is associated with both exposure and disease

- Association between exposure and disease may not be causal; instead, it is due to a third factor which is associated with both exposure and disease.

Confounding



Case-control study of alcohol and lung cancer

	Alcohol	No alcohol
Cases	450	300
Controls	200	250

Estimated odds ratio =1.9

The same data stratified by smoking:

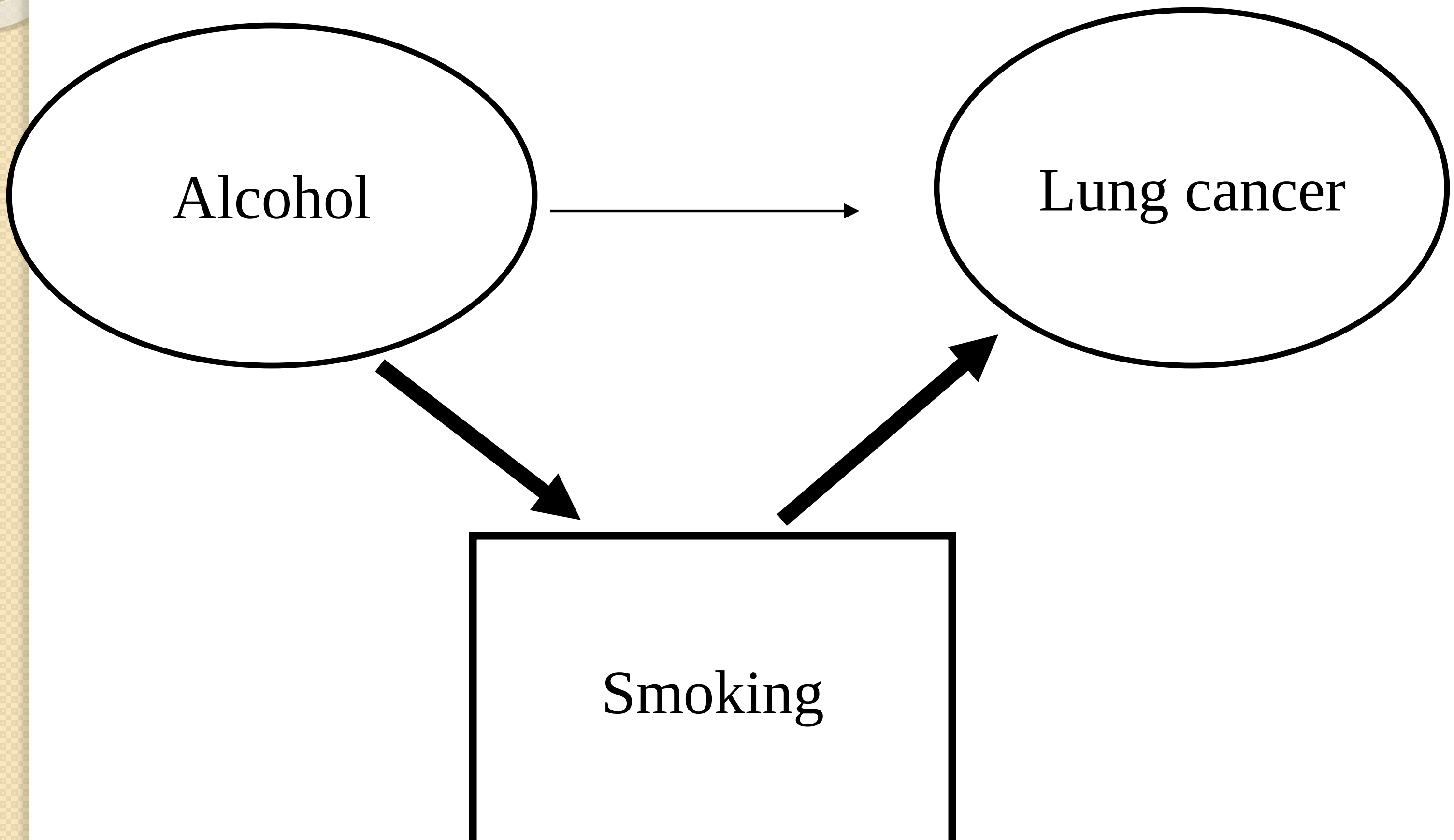
	Non-smokers		Smokers	
	Alcohol	No alcohol	Alcohol	No alcohol
Cases	50	100	400	200
Controls	100	200	100	50
Estimated odds ratio	1.0		1.0	

Alcohol and smoking in controls

	Alcohol	No alcohol
Smokers	100	50
Non-smokers	100	200

Non-drinkers: 1 in 5 were smokers,
Drinkers: 1 in 2 were smokers.

Confounding



Three major issues in interpretation of results in any epidemiological study

- Chance (random variation) – statistics
- Confounding
- **Bias (i.e. systematic error)**

Bias

- is a systematic error in the design of an epidemiological study which leads to a distortion or error in the study results.
- An association will allow to be distorted if error is differential

Two main types of bias

- Selection bias

  due to errors in the way sample is recruited

- Information bias

  due to errors in way in which information collected from the sample

Selection bias

- a distortion that results from procedures used to select subjects or their participation
- resulting in a difference in the characteristics between those who are included in the study and those in study population but not included in the study sample

Information bias

- Errors in the way information about exposure or disease collected
- Misclassification - putting subjects in wrong category
- Eg exposed as unexposed, case as control

Misclassification may be

- Random - above / below
- Systematic – all in one direction

- Non–differential (error in one variable not related to / dependent on the value of other variables)
- Differential (error in one variable is related to value of other variable

Assessment of bias

- Non-responders questionnaire
- Baseline characteristics of those lost to follow can be analysed and compared to those remaining in study
- Objective validation of self-reported information

Bias: the silent menace

- Cannot be assessed numerically
- No software to identify bias
- If there is flaw in the design of the study increasing numbers will not get rid of it!
- Can only be assessed by careful evaluation of the design

Causality

- 1/ we find an association between exposure and outcome
- 2/ we need to ask whether the association is causal = does the exposure cause the outcome?

What is a cause?

Rothman (1986):

An event, condition, or characteristic that plays an essential role in producing an occurrence of the disease. Source - Modern Epidemiology.

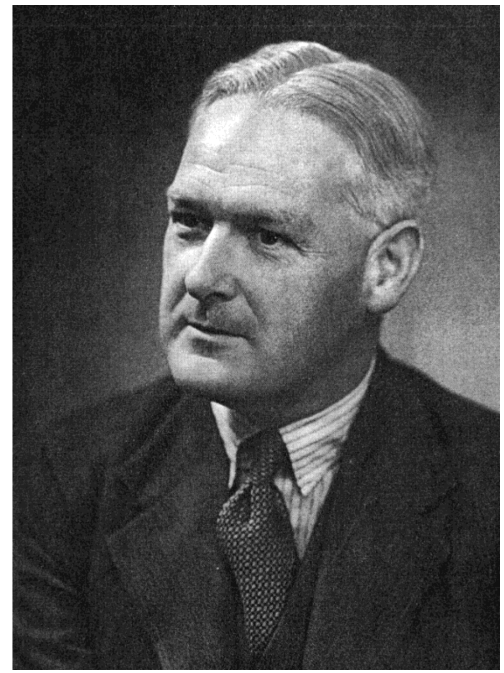
- Something that has an effect
- Alters disease frequency or health status

Association versus Causation

- Epidemiological research aims to discover aetiology of disease
- Epidemiology is the study of the <u>association</u> between a potential cause (risk factor/determinant) and a specific disease (outcome).
- Presence of a valid statistical association does <u>not</u> imply causality
- Association is not the same as causation
- Goes beyond association
- How do we decide whether a given association is causal or not?

Sir Austin Bradford Hill (1897-1991)

Exposure and Disease: Association or Causation?



1. Strength
2. Consistency
3. Specificity
4. Temporality
5. Dose-response
6. Biological plausibility
7. Coherence
8. Reversibility

The Bradford-Hill criteria of causation (J Royal Soc Med 1965; 58: 295-300)

Bradford Hill Closing Remarks (1965)

“I do not believe … that we can usefully lay down some hard-and-fast rules of evidence that must be observed before we accept cause and effect.

None … can bring indisputable evidence for or against the cause and-effect hypothesis and none can be required …

What they can do, with greater or less strength, is to help us to make up our minds on the fundamental question - is there any other way of explaining the set of facts before us, is there any other answer equally, or more, likely than cause and effect?

Causal Inference

- Not just ticking boxes
- Weigh evidence of causal association against other explanations
- Understanding, judgement & interpretation
- Cannot prove a causal association
- Can only be inferred based on evidence
- May change in the light of new evidence

Public health policy

- Ideally based on ‘evidence’ - meta-analyses and systematic reviews
- Considerations of efficiency, cost-effectiveness and harm
- Eradication of poverty for improving health?
- Reduction in social inequality for reducing health inequality?

Summary

- Epidemiology = the study of the distribution and determinants of disease in population
- Measures of association
- Bias, confounding, chance
- Causality