Epidemiology starter kit

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Learning objectives

Definitions and background

• Define epidemiology and describe the role of epidemiology in public health

• Explain the role of populations, samples and individuals in quantitative epidemiological research

Interpreting epidemiology

• Distinguish between ideas of association and causation

• Interpret the effect of bias, confounding and chance on causal inference in epidemiology

• Interpret basic measures of disease frequency and measures of association and impact

Study designs

• Compare strengths and weaknesses of common epidemiological study designs

• Begin to critically evaluate epidemiological findings from published research

But NOT looking at infectious diseases, that is the scope of the next session from Andrew Lee.

Group activities

Time out to think or discuss – look for the slides with this background

Say hi in the chat box and give a quick yes or no on have you studied or used epidemiology before?

Definitions and background

- Define epidemiology and describe the role of epidemiology in public health

 Explain the role of populations, samples and individuals in quantitative epidemiological research

Definition of epidemiology

The study of the frequency, distribution and determinants of diseases and health-related states in populations in order to prevent and control diseases

Epidemiology is about revealing unbiased relationships between
exposures e.g. alcohol, smoking, chemicals, stress, genes, etc..
and *health outcomes* e.g. mortality or morbidity, admission rates, etc...

Who? What? Where? When? How? (time, place, person)

Epidemiologists seek to establish cause-effect relationships, evaluate information, and make good decisions that will improve outcomes

Aims of epidemiology

The plural of 'anecdote' is not 'data'

Disease does not occur at random; the likelihood of developing disease is determined by underlying factors

These underlying factors can cause or help to prevent disease and we can identify them through a systematic investigation of populations.

We can:

•Set priorities

•Manage resources

•Make decisions

•Evaluate treatments

What do we mean by cause? What is a causal relationship?
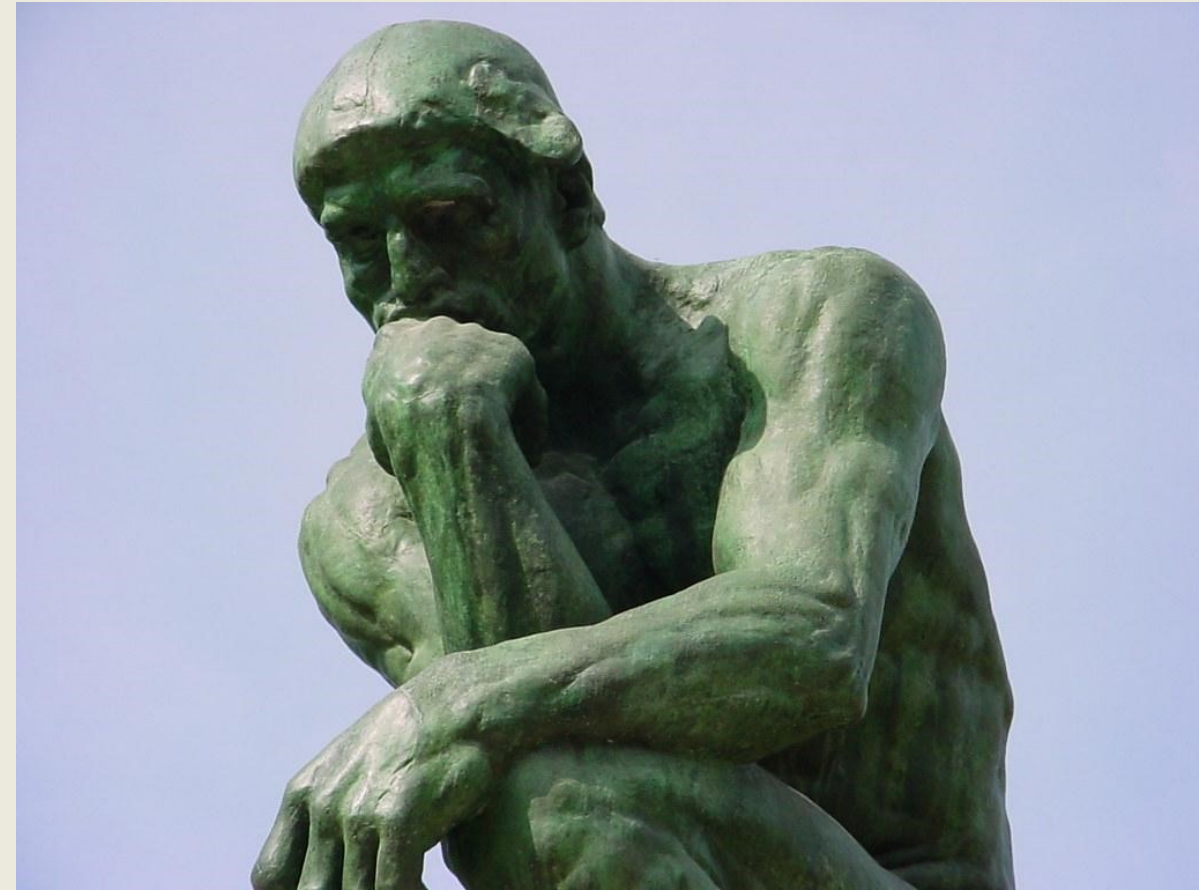
Most health claims on formula milk 'not backed by evidence'

BMJ report found nutritional benefits cited by multibillion-pound industry lacked scientific references
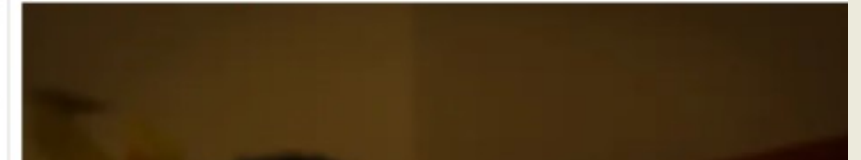
Andrew Gregory *Health editor*

🐦 @andrewgregory

Wed 15 Feb 2023 23.30 GMT

f 🐦 ✉

Health

Good quality sleep can add years to people's lives, study suggests

Researchers say findings indicate quantity of sleep alone is not enough to benefit; quality is key

Kevin Rawlinson

Thu 23 Feb 2023 19.03 GMT

f 🐦 ✉

Air pollution

Cutting air pollution improves children's lung development, study shows

Conclusions from long-term survey in Sweden come days after 10th anniversary of Ella Kissi-Debrah's death in London

Nicola Davis *Science correspondent*

🐦 @NicolaKSDavis

Thu 23 Feb 2023 16.51 GMT

f 🐦 ✉

The Observer
Alzheimer's

Could Alzheimer's be caused by an infection?

David Cox

Sun 19 Feb 2023 11.00 GMT

f 🐦 ✉ 💬 191

Cannabis

Oxford study to trial cannabis-based medicine as treatment for psychosis

CBD is currently only prescribed for a small number of conditions such as rare, severe epilepsy

Andrew Gregory *Health editor*

🐦 @andrewgregory

Thu 16 Feb 2023 06.00 GMT

f 🐦 ✉

Access to green space

RHS developing 'wellbeing blueprint' to enhance health benefits of gardens

Scientists conducting tests at experimental garden in Surrey to determine effects plants and flowers have on people

Helena Horton
Environment reporter

Tue 21 Feb 2023 17.28 GMT

f 🐦 ✉

This research explored why residents engaged with gardening and the extent to which they recognised any health benefits from the activity. A **questionnaire was distributed** electronically within the UK, with 5766 gardeners and 249 non-gardeners responding. Data were collated on factors including garden typology, frequency of gardening and individual perceptions of health and well-being. Significant associations were found between improvements in well-being, perceived stress and physical activity and more frequent gardening.

Methods: We used **individual participant data of 150 090 children** primarily from the EU Child Cohort Network to examine the associations of upper and lower respiratory tract infections from age 6 months to 5 years with forced expiratory volume in 1 s (FEV1), forced vital capacity (FVC), FEV1/FVC, forced expiratory flow at 75% of FVC (FEF75%) and asthma at a median (range) age of 7 (4-15) years.

Participants will be assessed before and after treatment using a range of clinical, digital, cognitive, neuroimaging and blood measures to clarify how cannabidiol acts to produce its effects and to identify factors that predict the response to treatment.

In order to correctly measure the effect of cannabidiol, **half of the participants will be treated with placebo and the other half will receive cannabidiol**. Cannabidiol or placebo will be administered alongside the standard medical treatments for psychosis.

Cause and effect

Things the daily mail says cause cancer…

https://youtu.be/q3chJN9DCGg

Group activities

Take a couple of minutes to read the infographic on the next slide

Think about what kind of questions it raises – do you believe the results? What information is missing? What else would you like to know?

How could you investigate whether walking really does improve mental health?

Populations, samples and individuals

Populations & samples
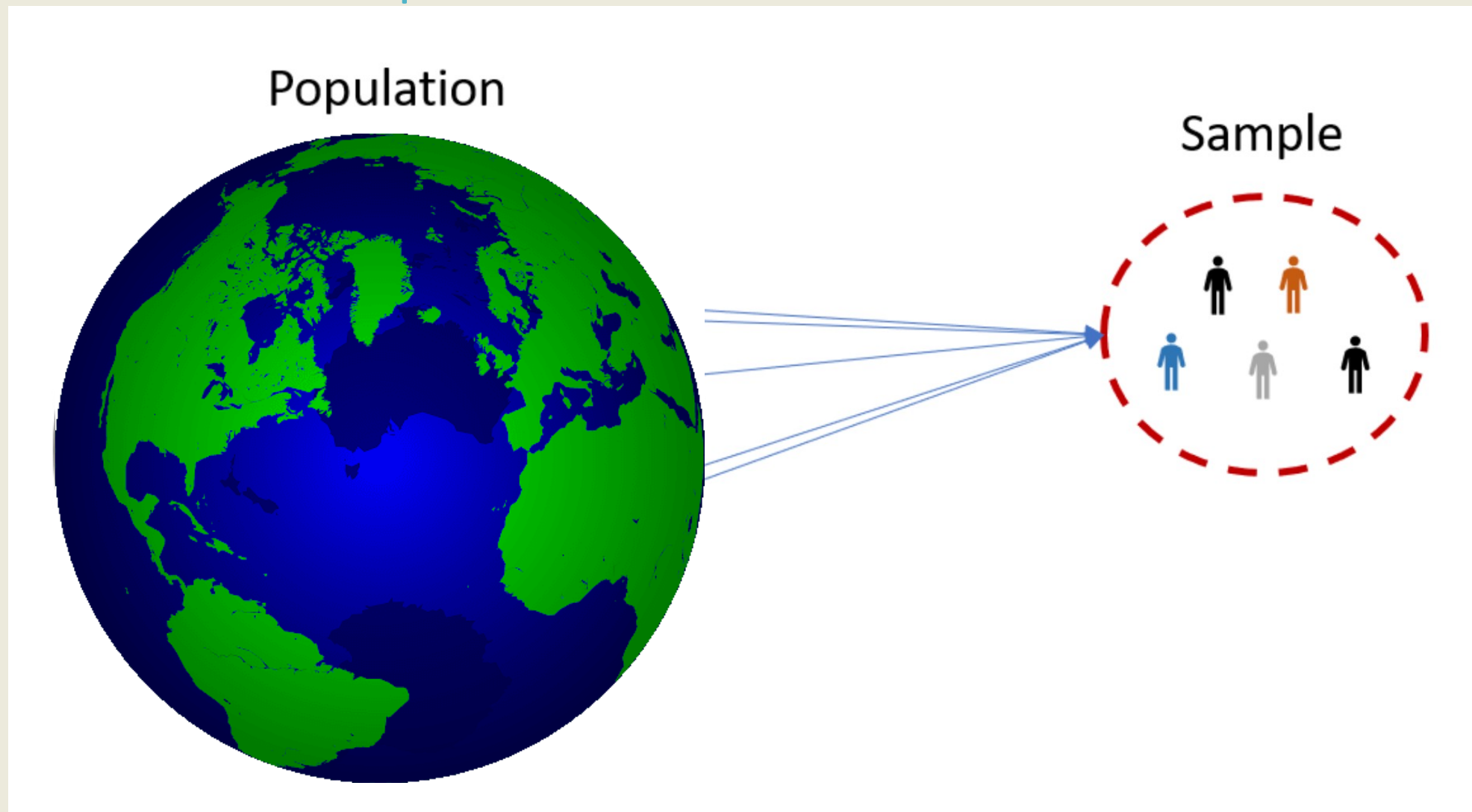
Sampling: the case of the 1936 poll

What happened?

In **1936** the 'Literary Digest', an American magazine, ran a poll to try and predict the outcome of the upcoming election.

It was HUGE – **10 million 'ballots'** were mailed out to people identified through phone directory lists and car ownership registrations.

The prediction was (badly) wrong. The two candidates were Alf Landon, and Franklin Delano Roosevelt.

There was an overwhelming vote in favour of the Republican candidate, Landon. The winner was the sitting president, Roosevelt.
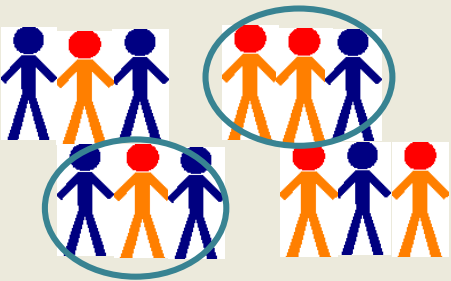
The poll predicted 41% of the vote for Roosevelt. He actually got 61%

What went wrong?

Group activities

The case study of magazine 'presidential poll', what went wrong? Why were the results so far out?

Sampling
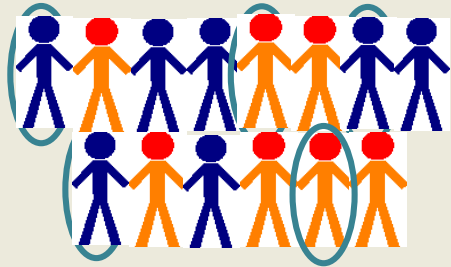
- Simple random sample
- Stratified sample
- Cluster sample
- Systematic sample
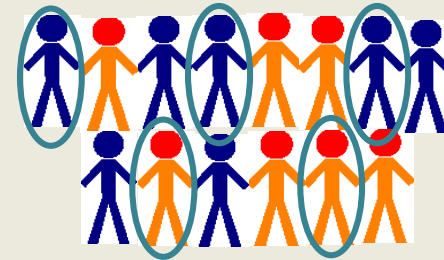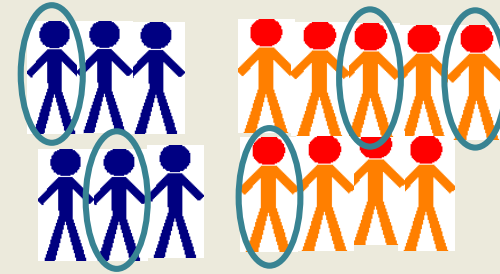
be clear about what it is you are counting

Case definition

Why is it important to have a consistent definition?

Where does it go wrong?

Different times

Different groups

Different questions

Different technologies….

(Similarly, what is a risk? What is an exposure?)

Count events accurately

What is easy to count?

What is more difficult?

Image: https://publicparticipationpartners.com/reaching-the-hard-to-reach/

Validity

"measures which lack validity do not mean what we think they mean"

Face validity

Does that look OK to you?

Content validity

A judgement. Does the measure cover all the aspects of the construct? More rigorous than face validity. Maybe go and look at the literature or ask experts?

Criterion validity

How does this measure perform when compared to other ones (ie other criteria)? Does it work in practice?

Construct validity

What is a construct?

Fitting the measure to the construct, the theory

Reliability

Inter-rater (or inter-observer) reliability
Does this [instrument] work the same for both of us?

Intra-rater (or intra-observer) reliability
Does it work the same every time I use it? (Cohen's kappa >0.6)

Inter-method reliability
Does it agree with another method?

Internal consistency reliability
This is the degree of agreement, or consistency, between different parts of a single instrument (Cronbach's alpha >0.7)

Take home concepts

✓Epidemiology deals with populations, not individuals. You are comparing outcomes and risks in groups, to find differences in time, place and person

✓ You need to know who your 'population' are

✓ You have to be very clear about what it is you are counting (case definition)

✓ You have to be able to count events accurately

There are almost certainly other explanations for what you observe

You must be able to distinguish between a risk and a cause

It is very easy to count, observe and interpret things inaccurately – how you deal with that is important

Different study designs are useful in different ways. The 'best' depends on what you are trying to do

Take a break

Interpreting epidemiology

Interpret the effect of bias, confounding and chance on causal inference in epidemiology

Causality, and other explanations for what you observe

Public health classics

Association or causation: evaluating links between environment and disease

Cause and effect: state your position

Koch – the necessary role of germs (Koch's postulates)

Hill – criteria for causality (paper)

Rothman – necessary and sufficient cause (paper) How often does one cause lead to one outcome?

Susser – considered the role of society as well as the individual behaviour in 'cause'. Not a simple path. Ask 'why else might this be so' and try to show 'why not' (paper)

Counterfactuals – cause follows effect. The counterfactual is that if the cause did not happen, the effect would not happen either.

Association =/= causation
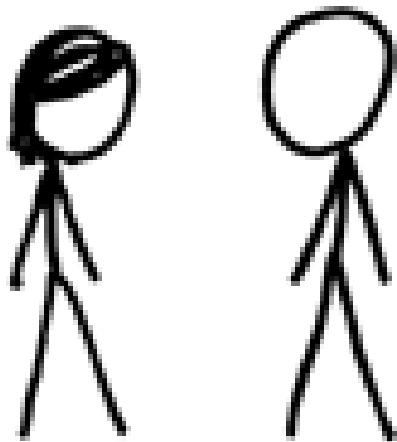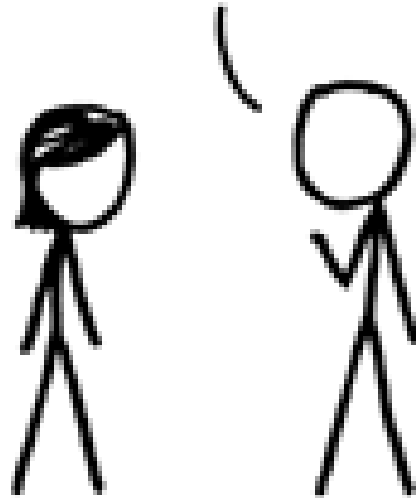
What is a risk and what is a cause?

To be a cause, the factor:

Must precede the effect

Can be a host *or* environmental factor

Can be positive (causative exposure) or negative (lack of a preventive exposure)

A risk factor is not necessarily a cause. It could be a surrogate for an underlying cause. For example, place of birth or socioeconomic status don't *cause* ill health, but are linked with a wide range of poorer health outcomes

"Criteria" for causality (or factors to consider when assessing causality)
the 'Bradford Hill' criteria

Strength of association

the magnitude of the relative risk

Dose-response

the higher the exposure, the higher the risk of disease

Consistency

similar results from different researchers using various study designs

Temporality

does exposure precede the outcome?

Reversibility (experiment)

removal of exposure reduces risk of disease

Biological plausibility

biological mechanisms explaining the link

Group activities

Applying causality:

Thinking about the link between smoking and cancer, think of something for as many of Bradford Hill's criteria as possible

Now try the same exercise for the link between spending time in nature and good mental health

The fact that the association between cigarette smoking and lung cancer meets each of these criteria provides powerful evidence that indeed smoking causes cancer:

➢ the association is strong: the risk of a smoker dying of lung cancer is 25 times that of a non-smoker;

➢ the association is graded: the more you smoke, the greater the risk of cancer;

➢ the association stands independent of confounding variables, such as class, gender, race, occupation;

➢ the association is consistent: it has been observed in different types of study, in different study populations;

➢ the association is reversible: if you stop smoking, your risk of cancer declines;

➢ the association is plausible: cigarette smoke is known to contain substances that cause cancer (carcinogens).

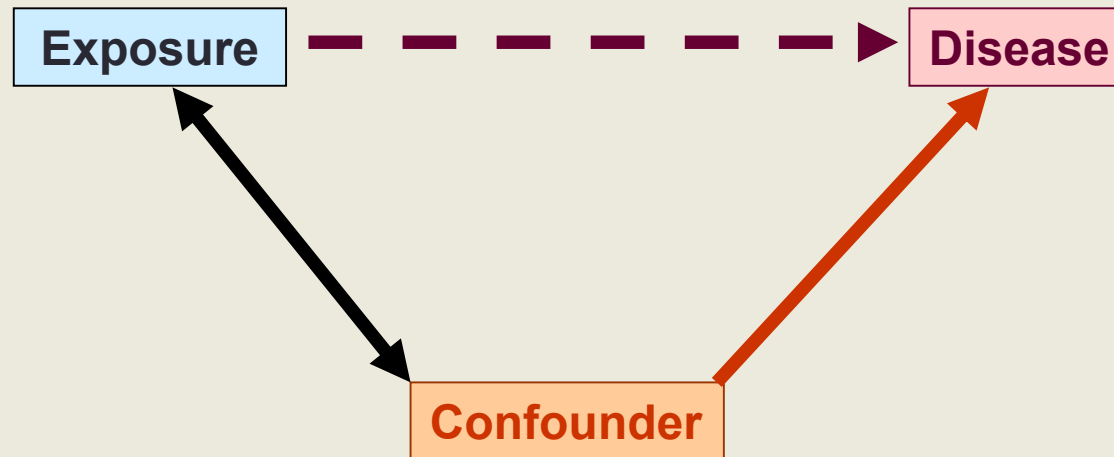# Association and causation: what else links risk to outcome?

Bias

Chance

Confounding

Reverse causality?

"Criteria" for causality

What is confounding?

- The situation where
  - a factor is associated with the exposure of interest
  - it independently influences the outcome
  - but does not lie on the causal pathway

Confounding and associations

OBSERVED RELATIONSHIP
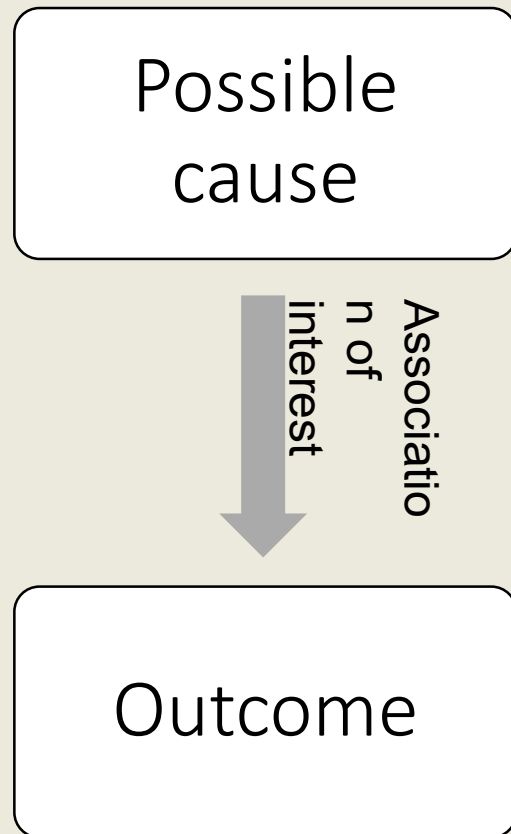
CONFOUNDER
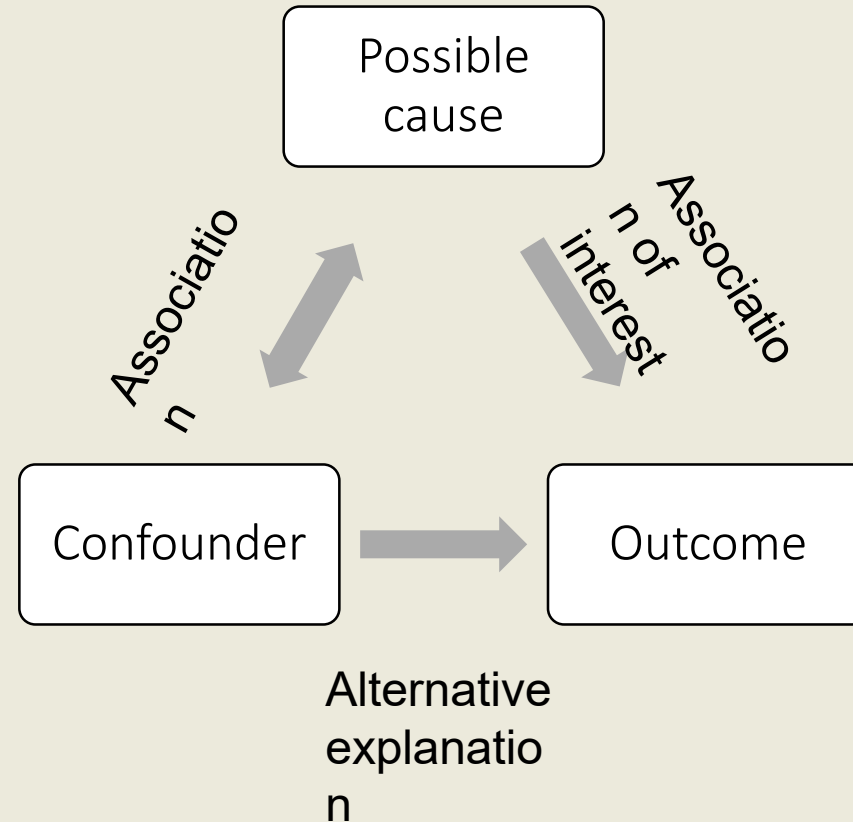
Example: bedsores in hip fracture patients[1]

DATA

Feature	Number
Had bedsore, died	79
Had bedsore, alive	745
Had bedsore (all)	824
Proportion who died?	9.6%
No bedsore, died	286
No bedsore, alive	8290
No bedsore (all)	8576
Proportion who died?	3.3%
Relative risk?	2.9

OBSERVED RELATIONSHIP

Bedsores

Death in hospital
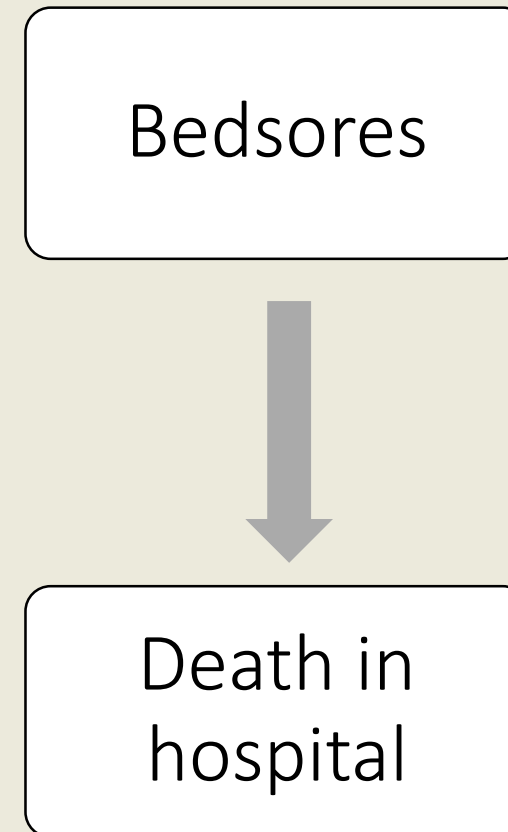
[1] Data taken from **Confounding in Epidemiology,** Baumgarten & Olsen (available from *www.collegeboard.com*)

Group activities

Confounding – 10 min time out to think and come back

What was an alternative explanation for the deaths in hip fracture patients?

What effect would better prevention of bedsores have had on the death rate in this population?

Bedsores in hip fracture, and death in hospital

OBSERVED RELATIONSHIP

Bedsores

Death in hospital

CONFOUNDER

Bedsores

Medical severity of fracture

Death in hospital
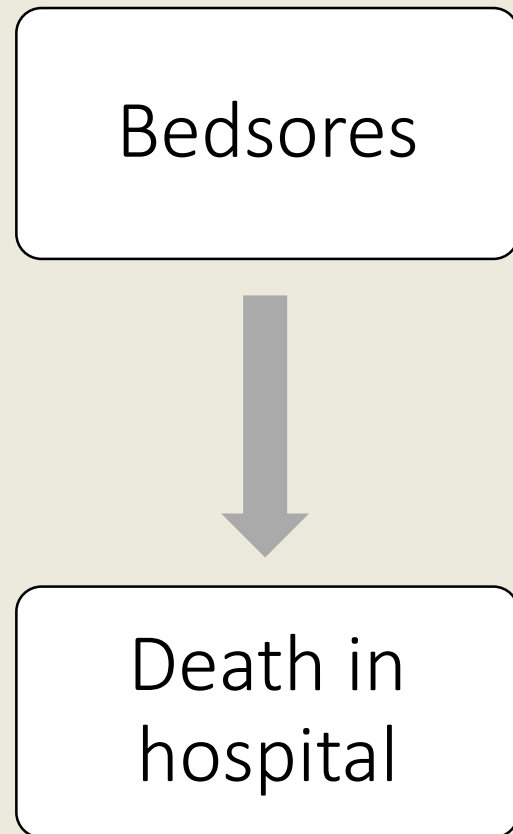
Looking at a confounder: stratifying

HIGH MEDICAL SEVERITY GROUP

	Died	Did not die	total
Bedsore	55	51	106
No bedsore	5	5	10
Total	60	56	116

LOW MEDICAL SEVERITY GROUP

	Died	Did not die	total
Bedsore	24	694	718
No bedsore	281	8285	8566
Total	305	8979	9284

Relative risk of death in those with bedsores compared to those without?
(55/106) / (5/10)
1.03

Relative risk of death in those with bedsores compared to those without?
(24/718) / (281/8566)
1.01

Managing confounding

Stratifying – manage the participants in separate groups

Matching – if you are comparing, make sure each 'case' has a 'control' with similar characteristics

Randomising – allocate people at random and hope that the confounders are distributed randomly as well, so they don't make the groups too different from one another

Standardise – essentially summarising a stratified analysis

Regression – allows you to cope with several confounders at once.

Choosing and measuring – what is bias and why avoid it?

Systematic error

Is bigger, better when you are taking a sample?

Image: https://sketchplanations.com/sampling-bias
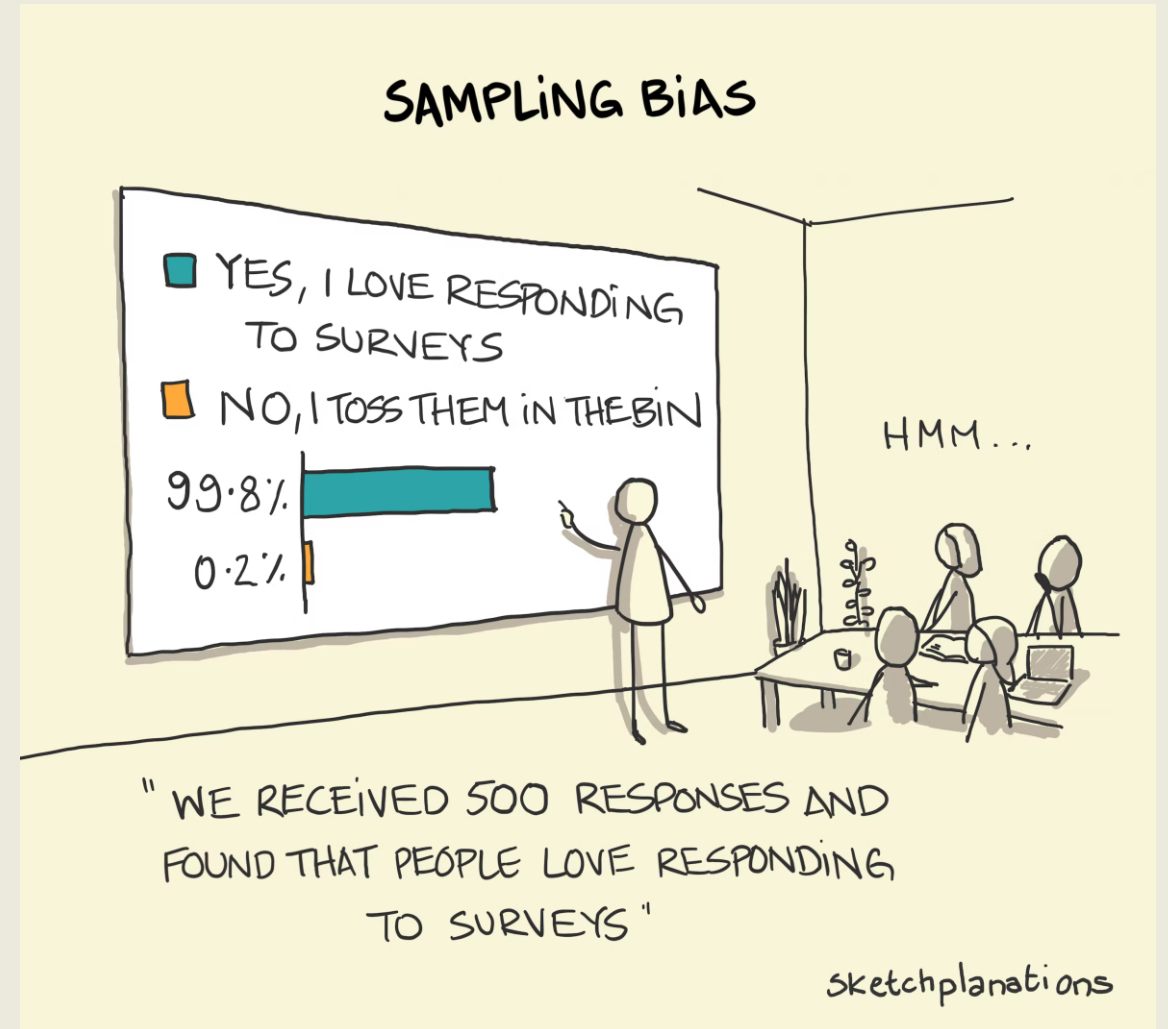
Two main groups of bias

Selection bias

A systematic error in selecting study participants

What if they don't represent the wider population?

A systematic error in allocating participants to comparison groups

What if you introduce differences between the groups?

Information bias

A systematic error in the measurement or classification of

Exposure (risk)

Outcome

What is the problem with bias?

What are two or three impacts that you think bias might have?

Chance

Whole purpose of carrying out statistical tests is to find out if the results of a study has occurred purely by chance.

Hypothesis: There is a difference in those who take Drug A versus those who don't

Null hypothesis: No difference

Type 1 error: Finding a difference when there is none

Type 2 error: Finding no difference when there is one

p=0.05 means there is a 5% likelihood that the difference found has occurred by chance.

Confidence intervals

E.g.

A study quoted an effect size of RR 2.4, 95% CI 1.9 to 3.2

Study population is only a sample of the whole population.

Observed effect in this sample was 2.4

There is a 95% chance that the true, real population effect lies between 1.9 to 3.2.

Larger sample, narrower CI as approximates population more, and vice versa.

Reverse causality

'Chicken and egg' scenario

Describes the situation where the order of exposure and outcome is mixed up.

E.g.

Alcohol abuse (*exposure*) → Depression (*outcome*)

or is it

Depression (*exposure*) → Alcohol abuse (*outcome*)

Take home concepts

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Different study designs are useful in different ways. The 'best' depends on what you are trying to do

Interpret basic measures of disease frequency and measures of association and impact

The statistics bit…

Incidence & Prevalence

Incidence = Rate at which new cases occur in a population in a certain time period

= number of new cases
Population at risk
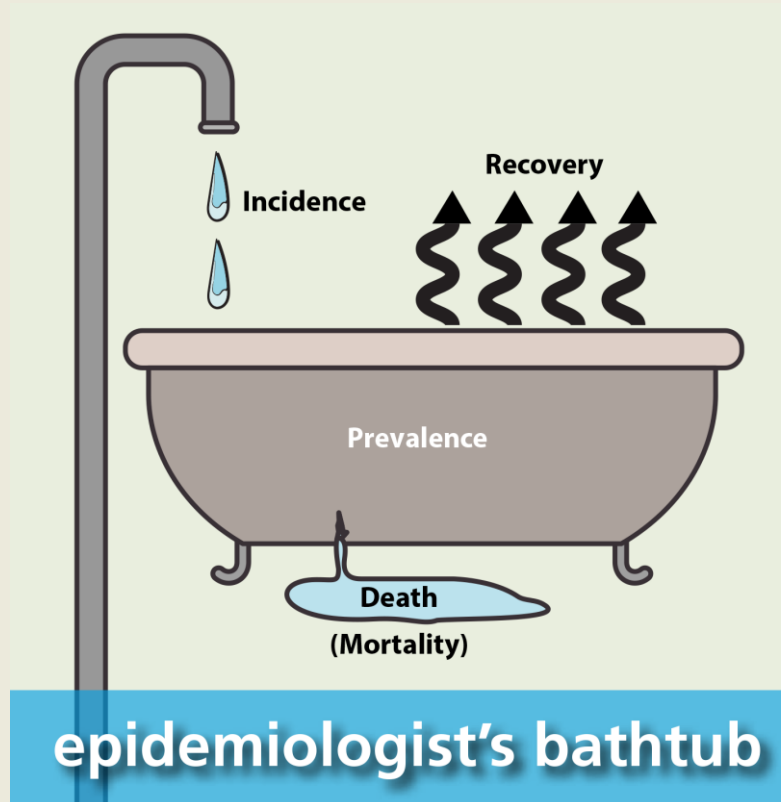
Prevalence = Proportion of a population with a disease/condition at a point in time

= number of cases at a point in time
total population

epidemiologist's bathtub

Incidence

Recovery

Prevalence

Death
(Mortality)

https://www.publichealth.hscni.net/node/5277

Comparing outcomes and risks in groups

Risks, rates and odds

Relative measures

Differences

Frequency Measures: how much?

Risk measures refer to the population fraction affected by the condition.

Rate measures are used to understand how fast the condition is occurring by having the sum of the times at risk in the denominator but keeping the same numerator as risk measures.

Odds measures are used when the population denominator isn't available and are a measure of the (number of event A occurring / no. of event A **not** occurring)
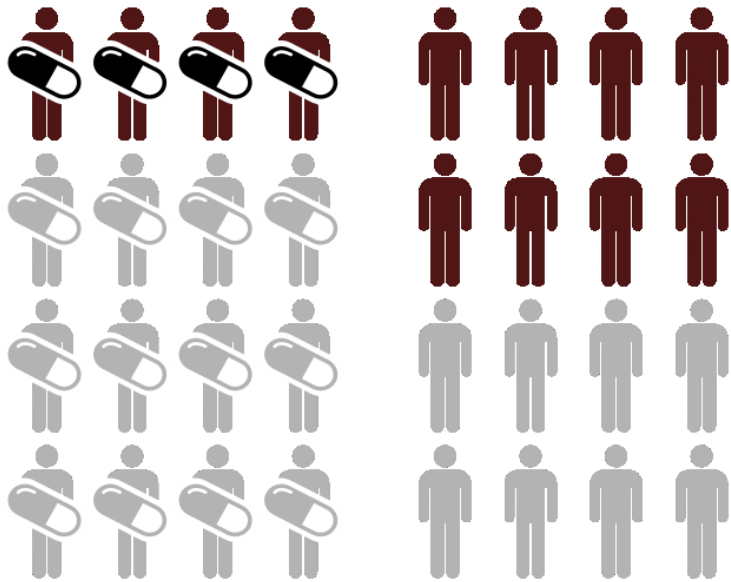
(Image: Parksa (CC BY-SA 4.0))

Risk of disease in the treatment group = 4/16 = 0.25
Rate of disease in the treatment group = 25 cases per 100 person-years
Odds of disease in the treatment group = 4/12 = 0.33

Relative measures of association: risk, rate and odds

Risk in one category relative to another

Gives some idea of the strength of *association* between risk factor and disease

No units!

Risk of bladder cancer in smokers (R_1) is 18.0 per 100,000

Risk of bladder ca. in non-smokers (R_2) is 6.0 per 100,000
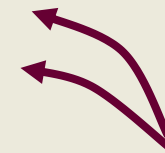
These are *absolute risks*!

Therefore, the *relative risk* of smokers developing bladder cancer compared to non-smokers is R_1/R_2 = 3.0

Measures of Impact: Absolute risk

Gives a feel for actual numbers involved

The likelihood or chance of an event happening – a measure of **impact**

E.g. if 18 people are diagnosed with bladder cancer each year in a town with a population of 200,000,

→ the *absolute risk* of developing bladder cancer each year is 9.0 per 100,000 population

Attributable risk

A measure which tells us how much of a disease is 'attributable to' (caused by) the risk factor we are investigating.

Remember – all diseases have a lot of underlying possible causes. Not all lung cancer is caused by smoking. Not all heart disease is caused by diabetes.

Question – how much of the disease is caused by smoking?

Useful for public health: **Attributable risk** – size of effect in absolute terms i.e. gives a feel for the public health impact (if causality is assumed)

Smokers   Non-smokers
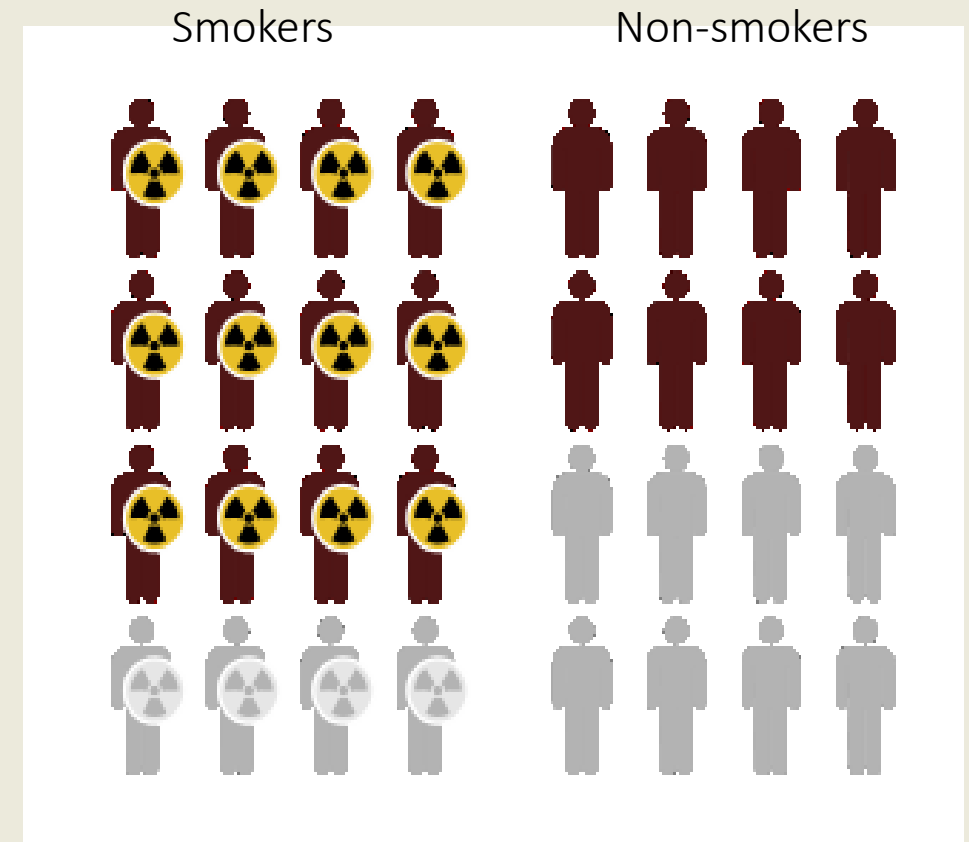
(Image: Parksa (CC BY-SA 4.0))

Absolute risk reduction

Incidence of MI in people given Drug A, 6/1000 pop^n p.a.
Incidence of MI in people on placebo, 10/1000 pop^n p.a

Absolute risk reduction (ARR) = 10/1000 – 6/1000

$$= 4/1000 \text{ pop}^n \text{ p.a.}$$

Relative risk   = $\dfrac{6/1000}{10/1000}$ = 0.6

i.e. if people take drug A, they have only 60% of the risk of an MI compared to those who don't,

Or, put another way, people on drug A have a 40% reduction in their risk of having an MI (*risk reduction* = 0.4)

Number needed to treat (NNT) & relative risk reduction

Incidence of MI in people given Drug A, $6/1000$ pop^n p.a.
Incidence of MI in people on placebo, $10/1000$ pop^n p.a

Number needed to treat = 1/Absolute risk reduction

= 1/ (10/1000 – 6/1000)

= 1/ (4/1000)

= 250

Relative risk reduction = 1 – Relative Risk

= 0.4 (or 40%)

Simplified way of expressing risk reductions

Gives an idea of how many people have to be given a treatment in order to avoid ONE unwanted outcome

DOES NOT MEAN OTHER PEOPLE TAKING TREATMENT NOT RECEIVING SOME BENEFIT!

Number needed to treat = 1/ARR (to avoid an event)

Population attributable risk (PAR)

Estimate of the excess rate of disease in the total study population of exposed and non-exposed individuals that is attributable to the exposure

PAR = $I_T - I_0$

PAR = All the disease we can count – the disease which would have happened anyway, even without this risk factor

Where I_T = total incidence of disease in both exposed and non-exposed

I_0 = incidence of disease in non-exposed

Can be worked out using the AR

PAR = AR $_x$ P_e where P_e = proportion of population exposed

Take home concepts

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Different study designs are useful in different ways. The 'best' depends on what you are trying to do
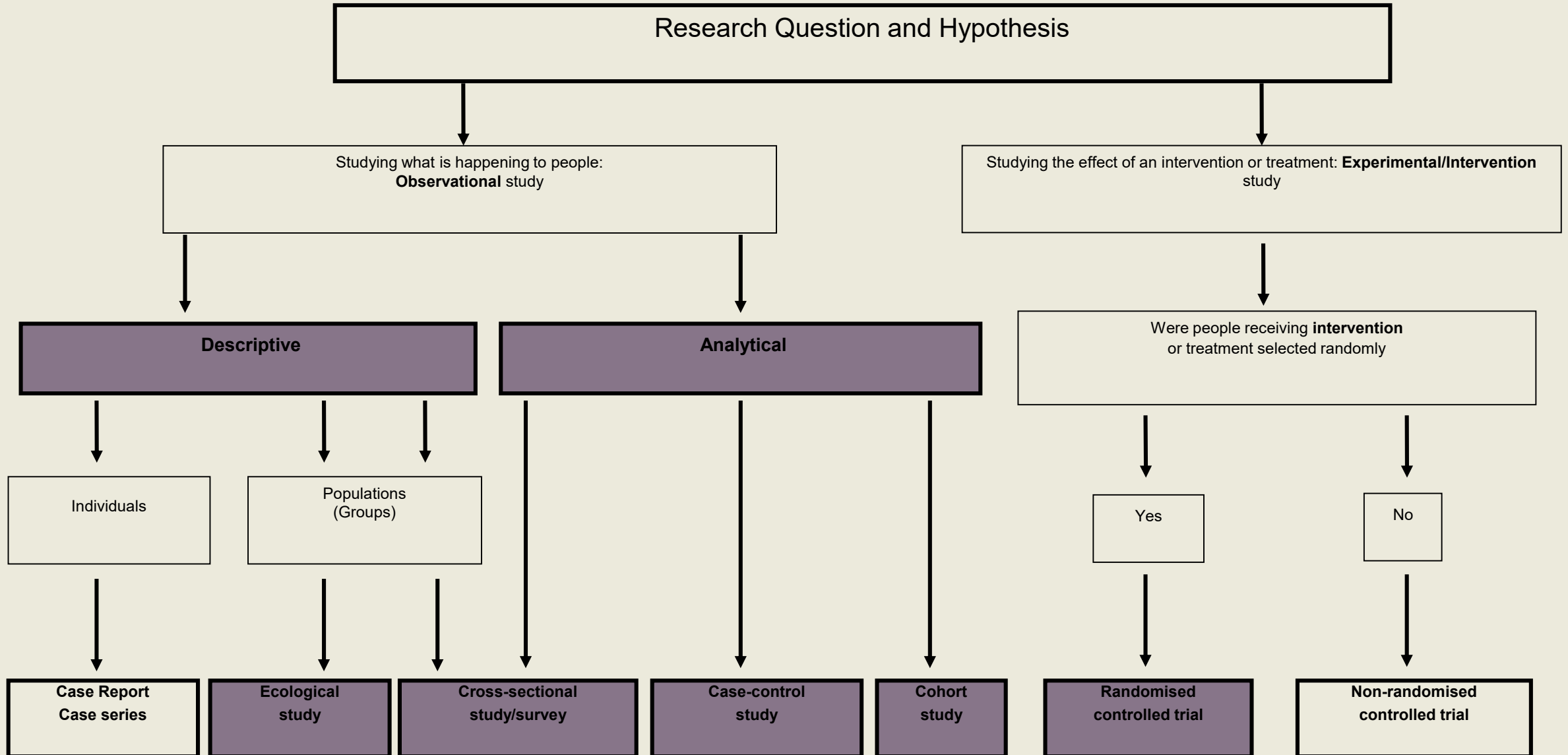
Take a break

Study designs

Compare strengths and weaknesses of common epidemiological study designs

Different study designs are useful in different ways. The 'best' depends on what you are trying to do

Types of Study Design

Ecological studies

Objectives Recent studies have demonstrated worsened mental health in relatively highly developed countries impacted by social inequalities and unemployment. Here, we investigate (1) whether mental health issues are differently or similarly affected by these social factors and (2) whether their effects on mental health are related or unrelated to each other.

Analysis at the country level among Organization for Economic Cooperation and Development (OECD) countries (n=36). Data on social indicators were collected from OECD and the United Nations Development Programme **databases**. Data on the prevalence of mental issues were obtained from the Institute for Health Metrics and Evaluation's **Global Burden of Disease study** 2017.

http://orcid.org/0000-0002-8212-8053

Cross sectional studies

Background: Veterinary surgeons are at elevated risk of suicide ... There has been much speculation regarding possible mechanisms underlying increased suicide risk in the profession but little empirical research. We aimed to assess the contribution of mental health and well-being to the elevated risk, through **a postal questionnaire survey** of a large **stratified random sample** of veterinary surgeons practising within the UK.

Methods: A questionnaire was mailed twice to 3,200 veterinary surgeons. Anxiety and depressive symptoms, alcohol consumption, suicidal ideation, positive mental well-being, perceptions of psychosocial work characteristics, and work-home interaction were assessed using **valid and reliable existing instruments** and a series of bespoke questions previously developed through informal focus groups.

Cohort studies

It is clear that postnatal maternal depression can impair maternal care and may be associated with delayed social, behavioral, cognitive, and physical development in growing children. There also is evidence that adolescent children of depressed fathers are likelier to experience psychopathology. This **longitudinal cohort study**, the Avon Longitudinal Study of Parents and Children (ALSPAC), postulated that **paternal depression postnatally would be associated with a heightened risk of behavioral and emotional problems at age 3.5 years**. Participants included 13,351 mothers and 12,884 fathers, all of them evaluated 8 weeks postnatally using the **Edinburgh Postnatal Depression Scale** (EPDS). The fathers were again assessed when their children were 21 months old. The **Rutter revised preschool scales** served to measure children's emotional and behavioral development. Relevant information was available for 8431 fathers, 11,833 mothers, and 10,024 children.
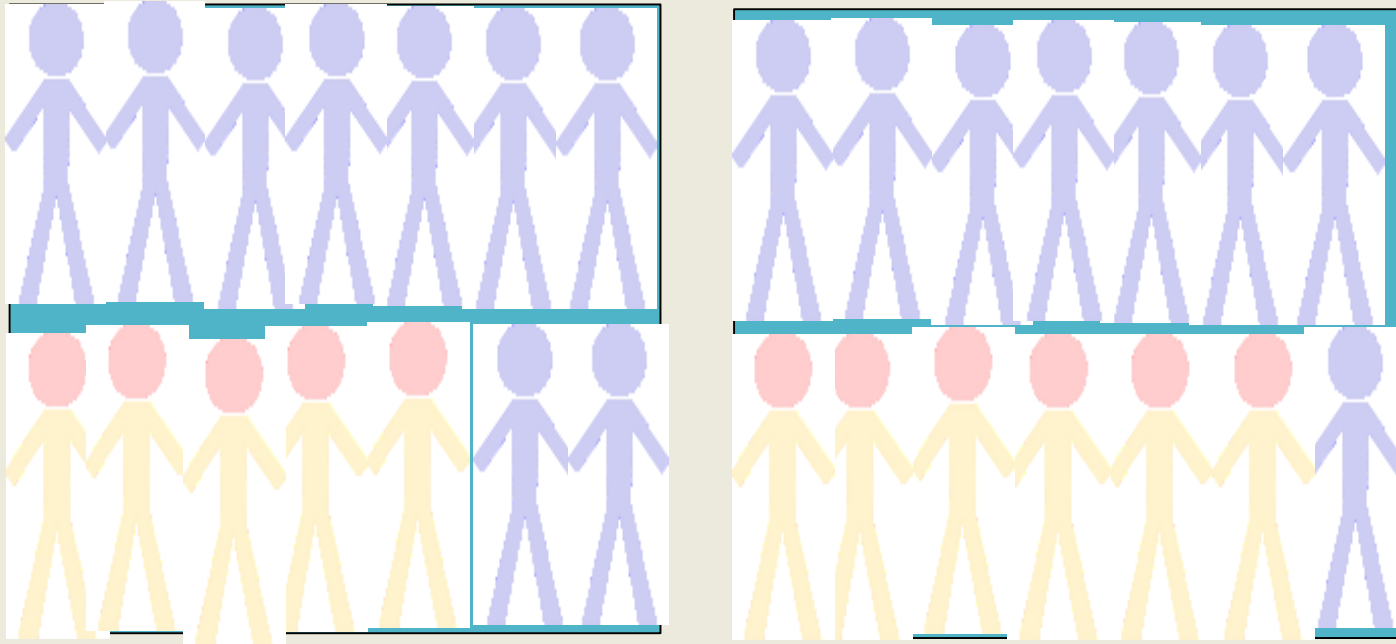doi: 10.1097/01.ogx.0000189166.38069.00.

Case control studies

We collected a **12 month consecutive sample of deaths from suicide and probable suicide** (open verdicts) in Greater Manchester. Those people who had had a psychiatric admission in the previous five years were identified by checking against all hospitals in the area. We **examined case records and recorded information** on the last admission before death and care after discharge. The equivalent information was collected on controls, identified by **block randomisation** of hospitals in the area. **Controls were matched** for age, sex, clinical diagnosis, and date of admission. Cases and controls were compared on 18 social and clinical variables (see table).

doi:

Case-control study

Exposed

Not exposed

Exposed

Not exposed

Cases
(people with disease

Controls
(people without disease)

Population

Time course

Direction of enquiry
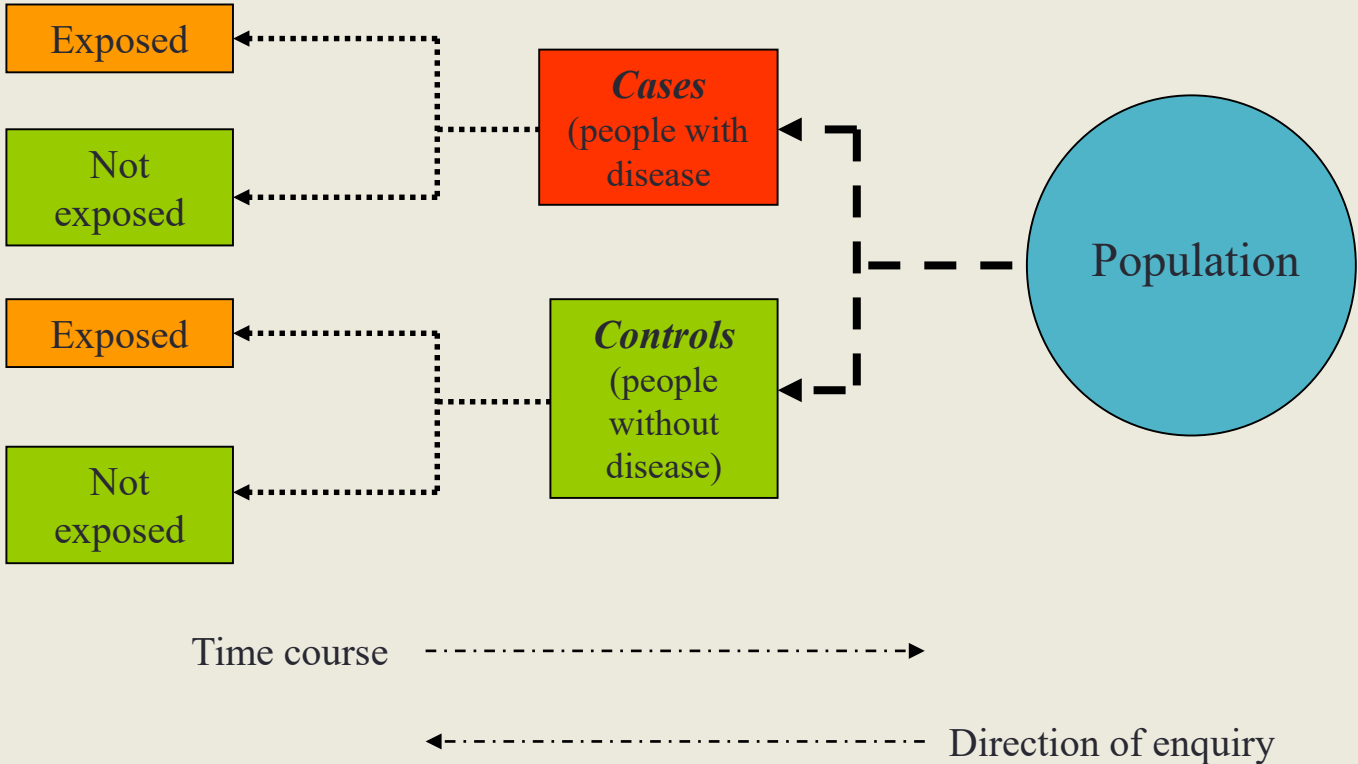
RCTs

Summary points

There are good randomised controlled trials in psychiatry, but as psychological treatments are difficult to standardise and disability is a difficult endpoint to measure, small randomised controlled trials are susceptible to bias

Psychiatry seems nervous about proceeding with the implementation of clinical practice guidelines on the evidence from randomised controlled trials

"…the 22% of the global burden of disease attributed to mental disorders is made up of 21% from morbidity and only 1% from mortality.[6] Measuring morbidity or disability is much more complex than measuring mortality, the usual endpoint in mega-trials of physical disorders"

doi: https://doi-org.sheffield.idm.oclc.org/10.1136/bmj.319.7209.562

RCTs

Involve an INTERVENTION (experimental, not observational)

Allocate the intervention **randomly**

Result in two or more groups for comparison

Known and unknown confounders are evenly distributed between the groups (we hope)

The only difference should be the intervention

Strong evidence of causality

Strong internal validity

Possibly weak generalisability.

What is suitable for an RCT and what isn't?

N-of-1 trials

A single patient is a trial of 1

This uses a crossover design, where the patient is offered both treatment and placebo in a random order

The thing randomised is the treatment order, rather than the participant

The results for each individual are compared in that one case

There will usually be about three cycles to allow for comparisons

Used for chronic and stable conditions not resolved by treatment

Used to determine the best treatment for one patient.

Take home concepts

✓ Epidemiology deals with populations, not individuals. You are comparing outcomes and risks in groups, to find differences in time, place and person

✓ You need to know who your 'population' are

✓ You have to be very clear about what it is you are counting (case definition)

✓ You have to be able to count events accurately

✓ There are almost certainly other explanations for what you observe

✓ You must be able to distinguish between a risk and a cause

✓ It is very easy to count, observe and interpret things inaccurately – how you deal with that is important

✓ Different study designs are useful in different ways. The 'best' depends on what you are trying to do

Group activities

Can you identify the study designs which give the strongest evidence for causality?

What do you need to consider when evaluating epidemiological research?

Can we create a checklist?

Hierarchy of Evidence

Meta-analyses	I*
Randomised controlled trials	I
Non-randomised controlled trials	II
Cohort studies	III
Case-control studies	IV
Cross sectional studies	V

Summary of epidemiological studies

Table 3.3 summarizes the applications of different observational studies and Table 3.4 outlines the advantages and disadvantages of the major types of observational study.

Table 3.3. Applications of different observational study designs [a]

Objective	Ecological	Cross-sectional	Case-control	Cohort
Investigation of rare disease	++++	–	+++++	–
Investigation of rare cause	++	–	–	+++++
Testing multiple effects of cause	+	++	–	+++++
Study of multiple exposures and determinants	++	++	++++	+++
Measurements of time relationship	++	–	+[b]	+++++
Direct measurement of incidence	–	–	+[c]	+++++
Investigation of long latent periods	–	–	+++	–

[a] +...+++++ indicates the general degree of suitability; there are exceptions
  – not suitable.

[b] If prospective.

[c] If population-based.

http://whqlibdoc.who.int/publications/2006/9241547073_eng.pdf