MONASH University

MONASH
PUBLIC HEALTH AND
PREVENTIVE MEDICINE

Epidemiology for Occupational & Environmental Medicine Trainees

Karen Walker-Bone

Learning outcomes

- To understand the key role of the research question
- To know the main research study designs
- To be able to explain why you might use these study designs
- To be able to explain the benefits and limitations of each method
- To know how to define key measures and measure risk
- To know the principles of assessing quality of evidence

Plan

- Evidence-based medicine
- Types of research study
  - Qualitative
  - Quantitative
    - Experimental
    - Observational
      - Cross-sectional
      - Cohort
      - Case-control
- Association
  - Bias
  - Confounding
- Measuring risk
- Reading papers critically

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Evidence-based medicine

Decreasing bias

Eminence-based medicine

Research question

- The most important part of any study
- Leads to the appropriate study to undertake
- Should be as SPECIFIC as possible
- Should be clearly laid out in any paper you are reading
- PICO /PECO
  - Population
  - Intervention or Exposure
  - Control
  - Outcome

Study Methodology

- Dependent upon the question…

….. And some other practicalities:

- Time and urgency
- Resources
- Ethical considerations

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Research question dictates study design

• Prevalence /freq of factor	**Cross-sectional**
• Hypotheses about possible causes	**Ecological**
• Causes/risk factors	**Case-Control**
• Harm (or causes)	**Cohort**
• Experience of illness	**Qualitative**
• Efficacy (harm)	**RCT**

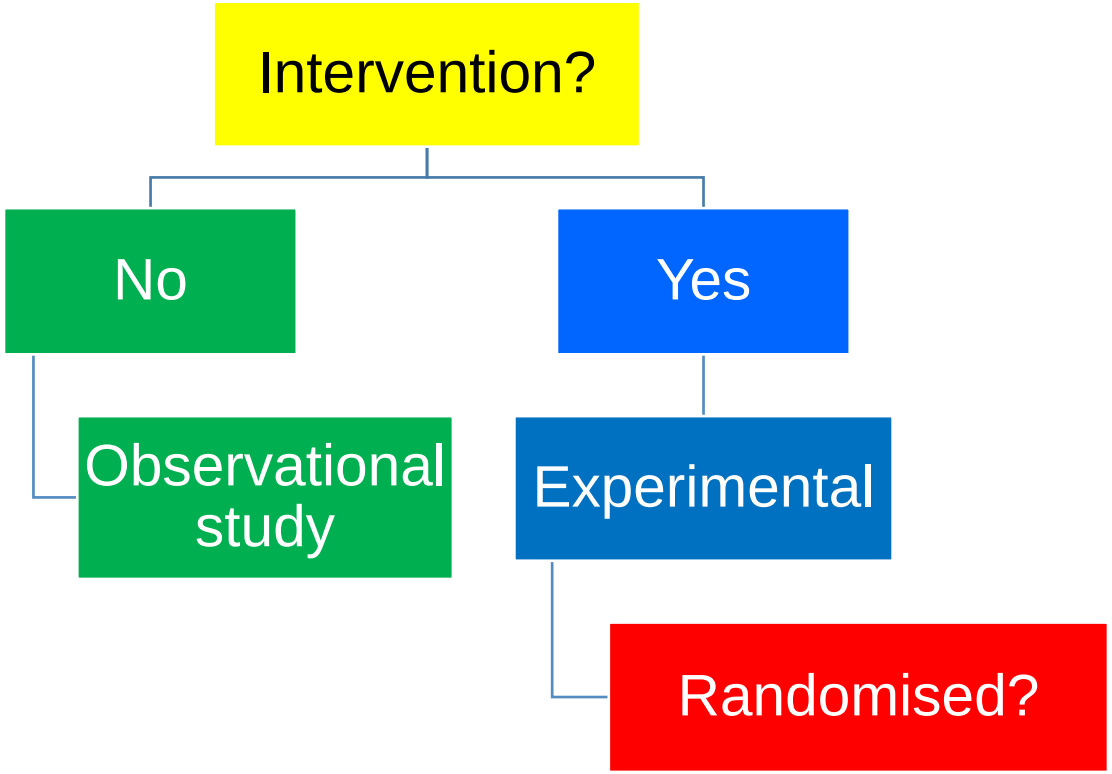
Qualitative research

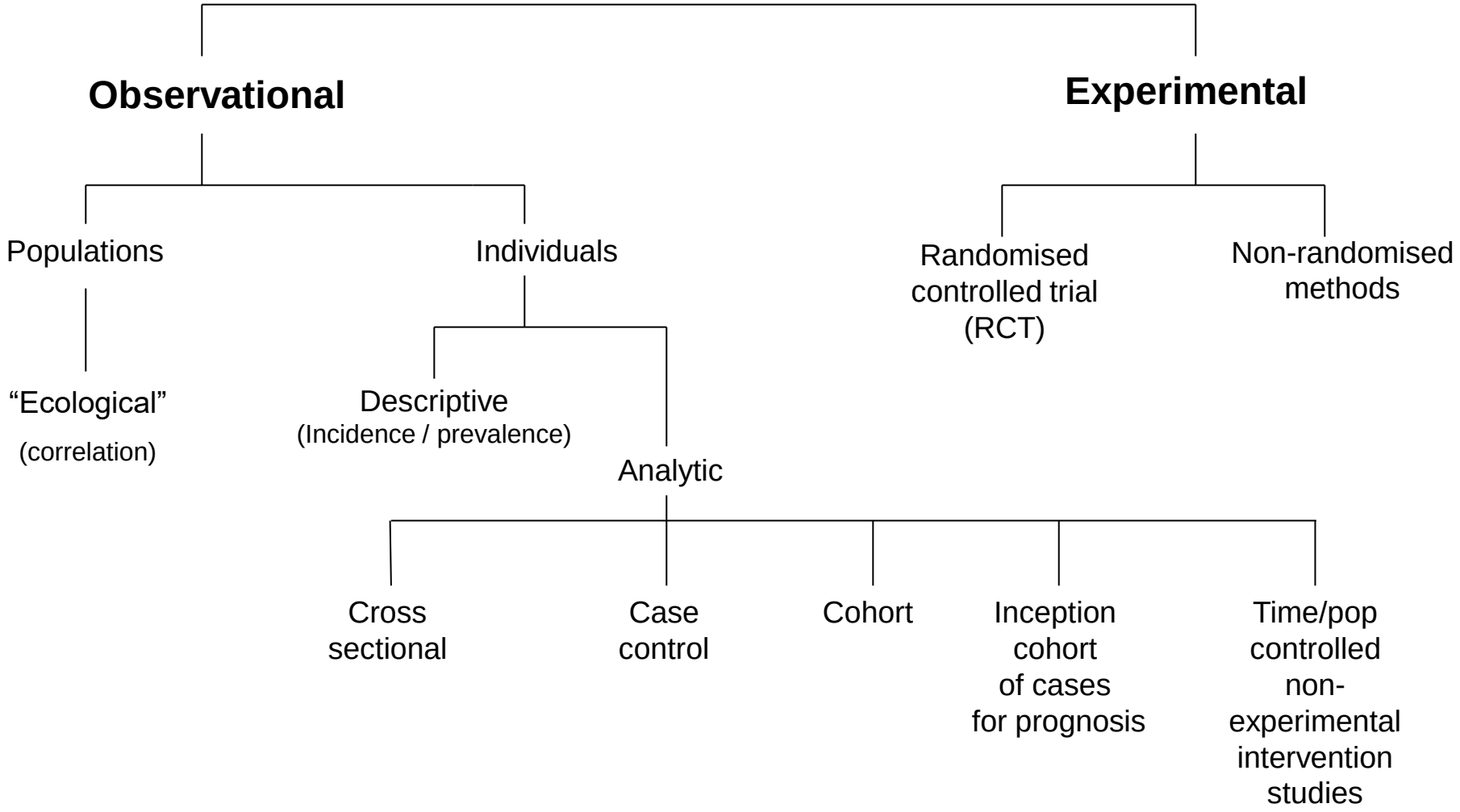
- Perceptions, beliefs and experiences
- Valuable for answering questions about best approaches to planning and delivering interventions
- Can be included in as part of quantitative research

Qualitative studies: methods of data collection and analysis

- Data collection methods
  - Observation
  - Interviews
  - Focus groups
  - Diaries
- Data analysis
  - Themes/Contexts/Categories

Types of quantitative research studies

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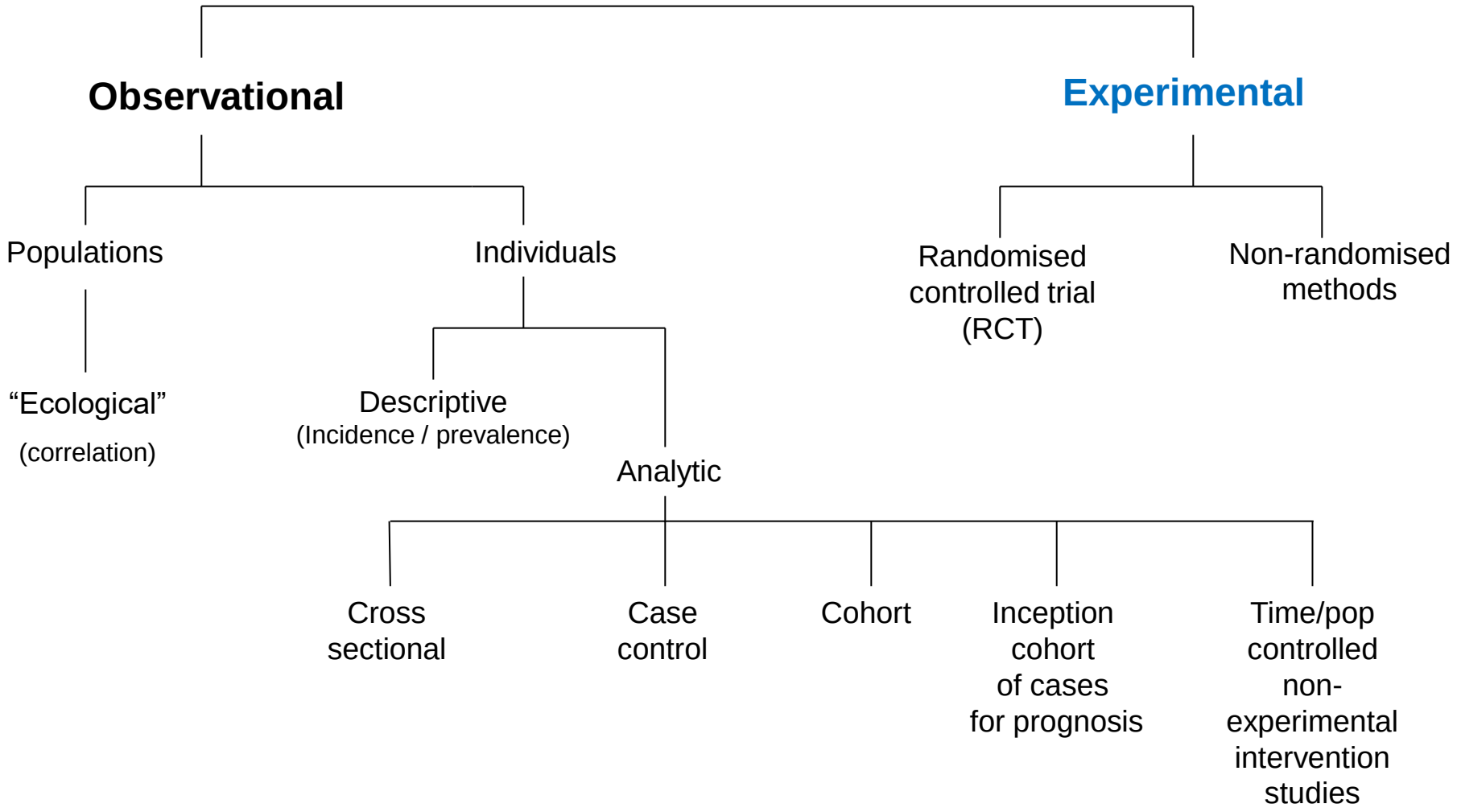
Time/pop controlled non-experimental intervention studies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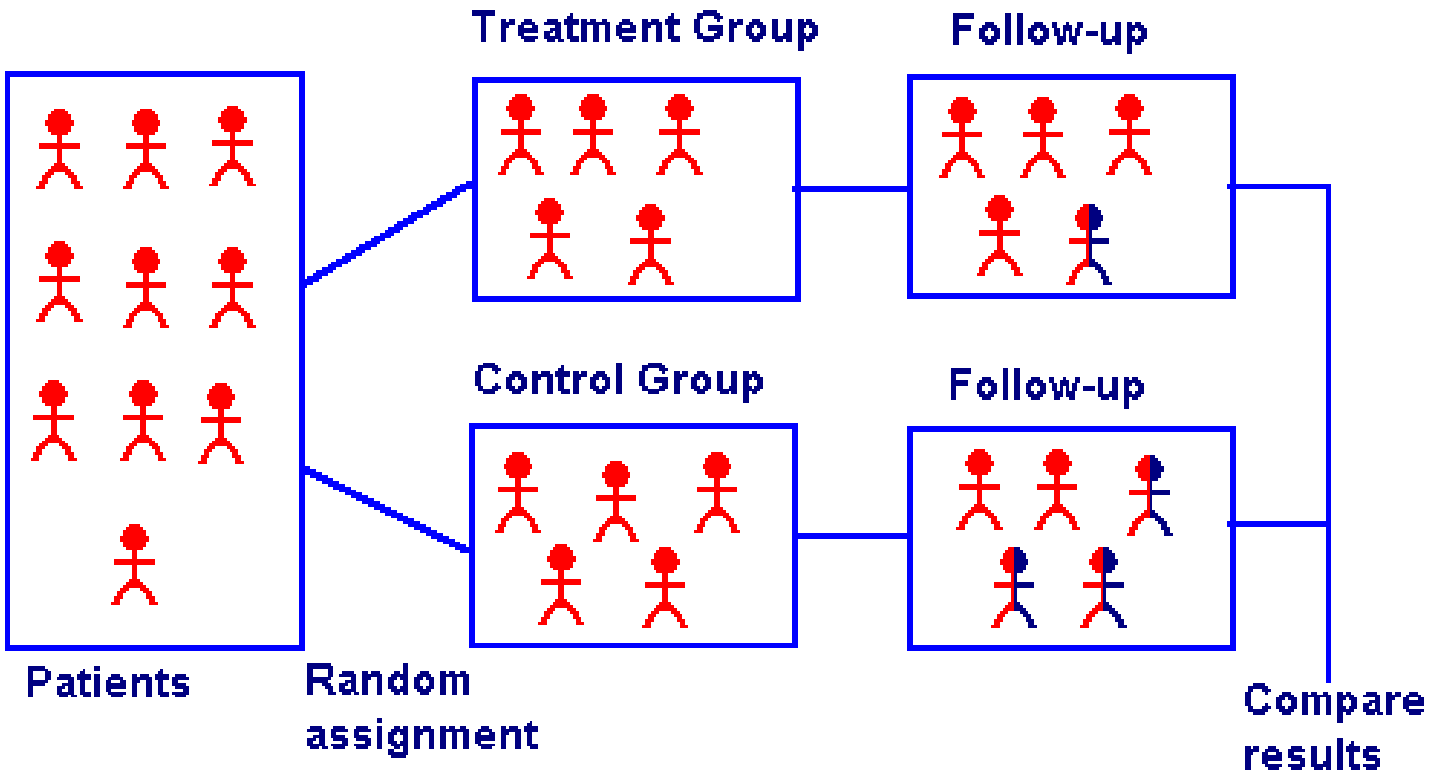
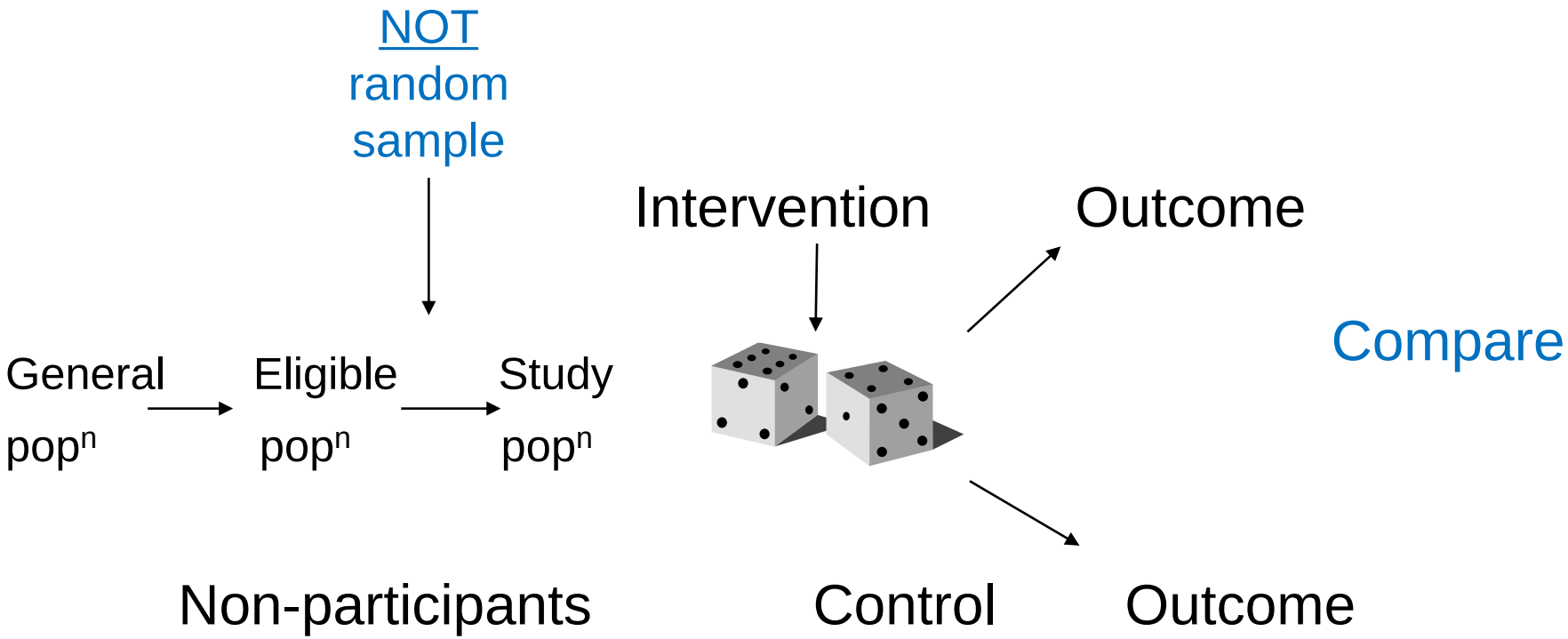
Experimental studies

- If participants are assigned to the intervention randomly then its a randomised controlled trial (RCT)
- If NOT randomly assigned, can be quasi-experimental or ‘open label’

A randomised controlled trial



The randomised controlled trial



Randomised controlled trial

Advantages:

- unbiased distribution of known & unknown confounders
- blinding more likely to be possible
- randomisation facilitates statistical analysis

Randomised controlled trial

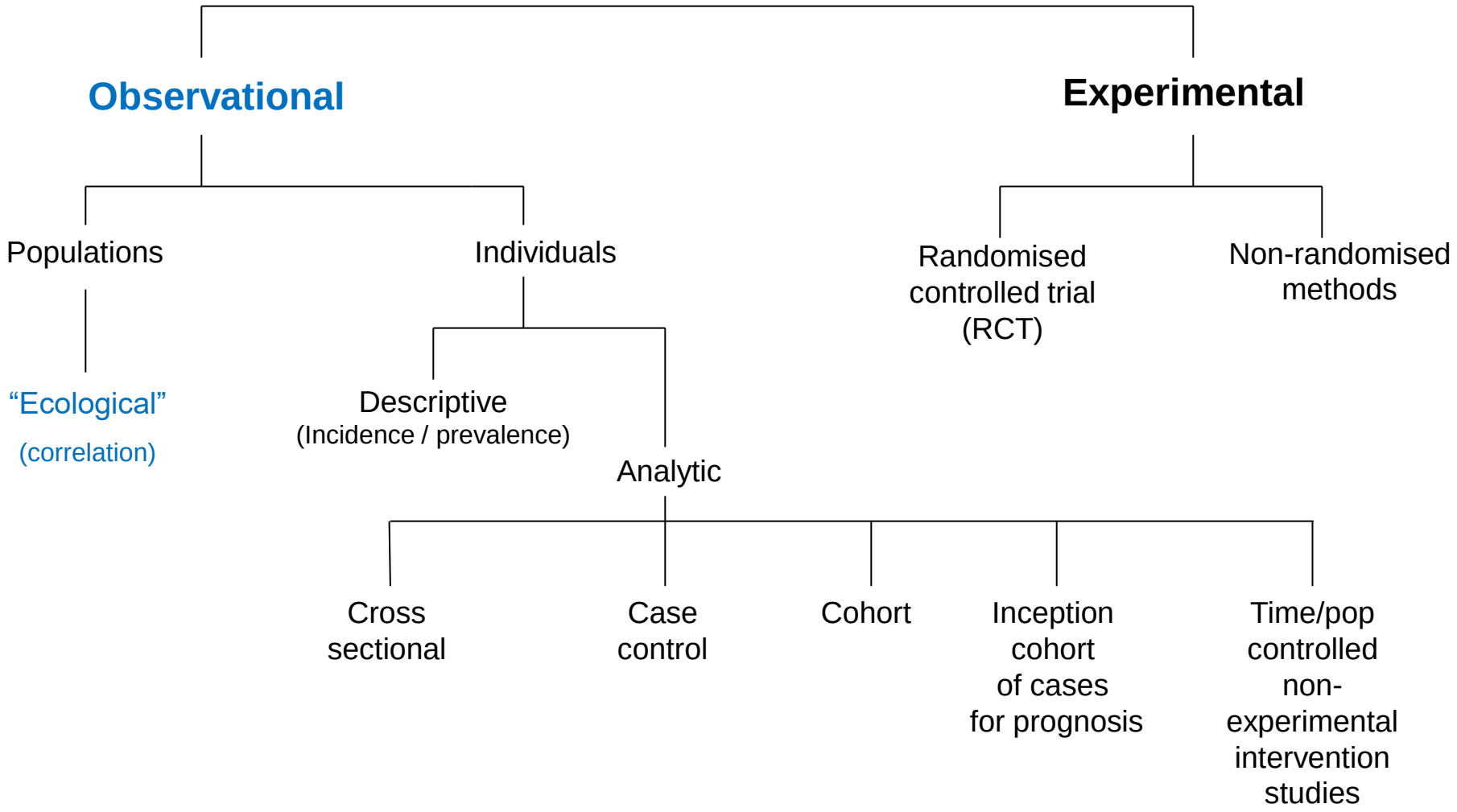
Disadvantages

- expensive: time and money
- volunteer bias
- ethically problematic at times
- recruitment difficulty-clinician /patient
- may not be appropriate method as inappropriate for the question, timescales too long to reach answer, no clinical uncertainty

What questions cannot be answered with a randomised controlled trial?

- How common is pneumoconiosis in coalminers? **Prevalence Incidence**
- Is there more occupational disease amongst migrant workers? **Inequalities**
- Is there more silicosis among stone benchtop workers? **Risk factors**
- Is mesothelioma increasing or decreasing? **Time trends**
- What is the prognosis of melanoma? **Long term outcomes Risk factors**
- What factors influence prognosis?

- all very important questions for health services, prevention efforts and policy makers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Ecological studies

- Exposure and disease measured at population/group level not at individual
  - Alcohol consumption and RTA
  - Staffing levels health centres and vaccination rates
  - Water fluoridation and hip fracture
- Correlate exposure and disease
- Often these studies use routine data collected for other purpose

Ecological studies

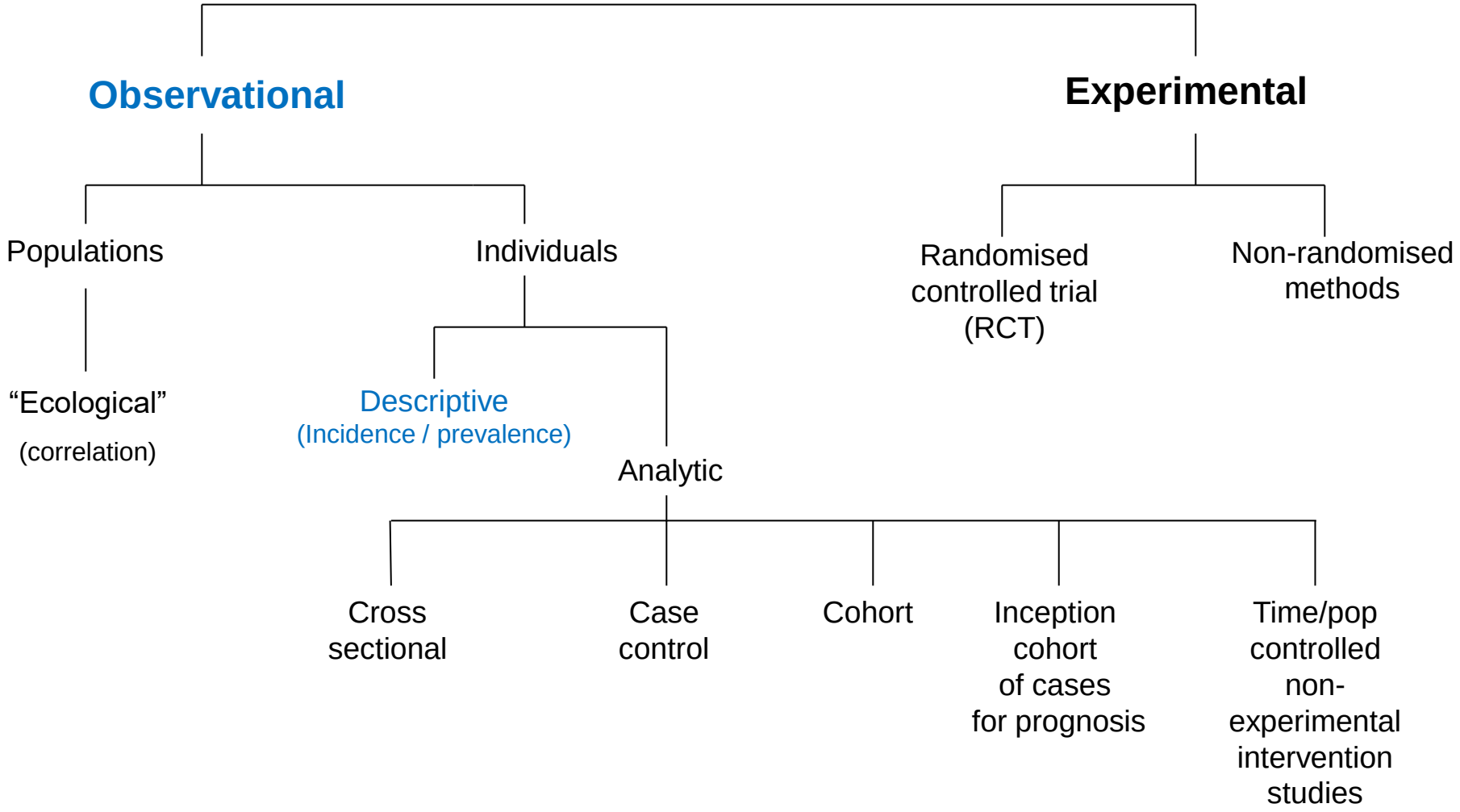
Advantages

- Relatively cheap
- May be only feasible way to evaluate effects of health care programmes where individual data unavailable
- Results obtained quickly
- Can generate interesting hypotheses
- Can be used to investigate outcomes and exposures that show a variety of trends over time

Ecological studies

Disadvantages

- NO causality
- Ecological fallacy
  - The bias that may occur because an association observed between variables on a group level does not necessarily represent the association that exists at an individual level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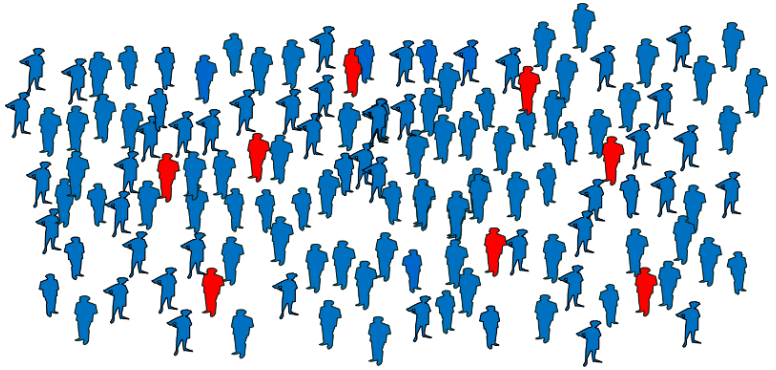
Prevalence

- Prevalence is the proportion of a population who have a specific characteristic in a given time period
- Point prevalence (today, now, at a point in time)
- Period prevalence (cases in last week, month, year, lifetime..)
- Expressed as % (5%, 10%, 90%) or as number of cases per 10,000 or 100,000 per head of population



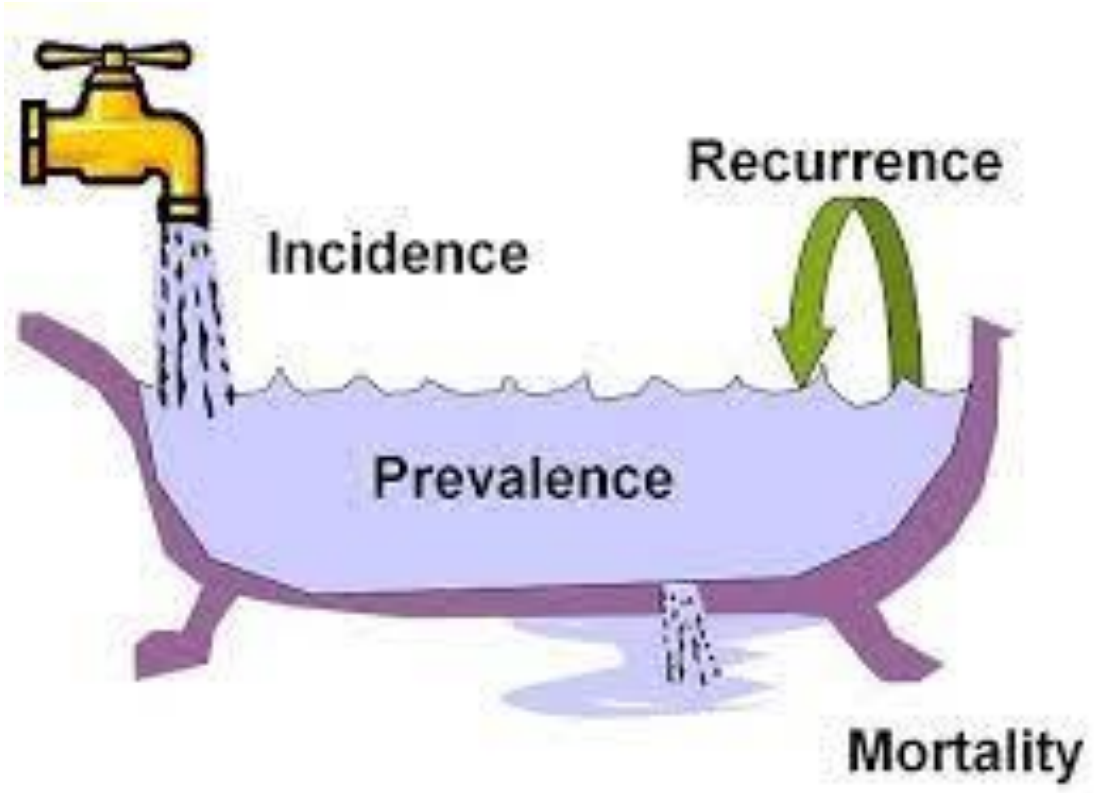
Incidence

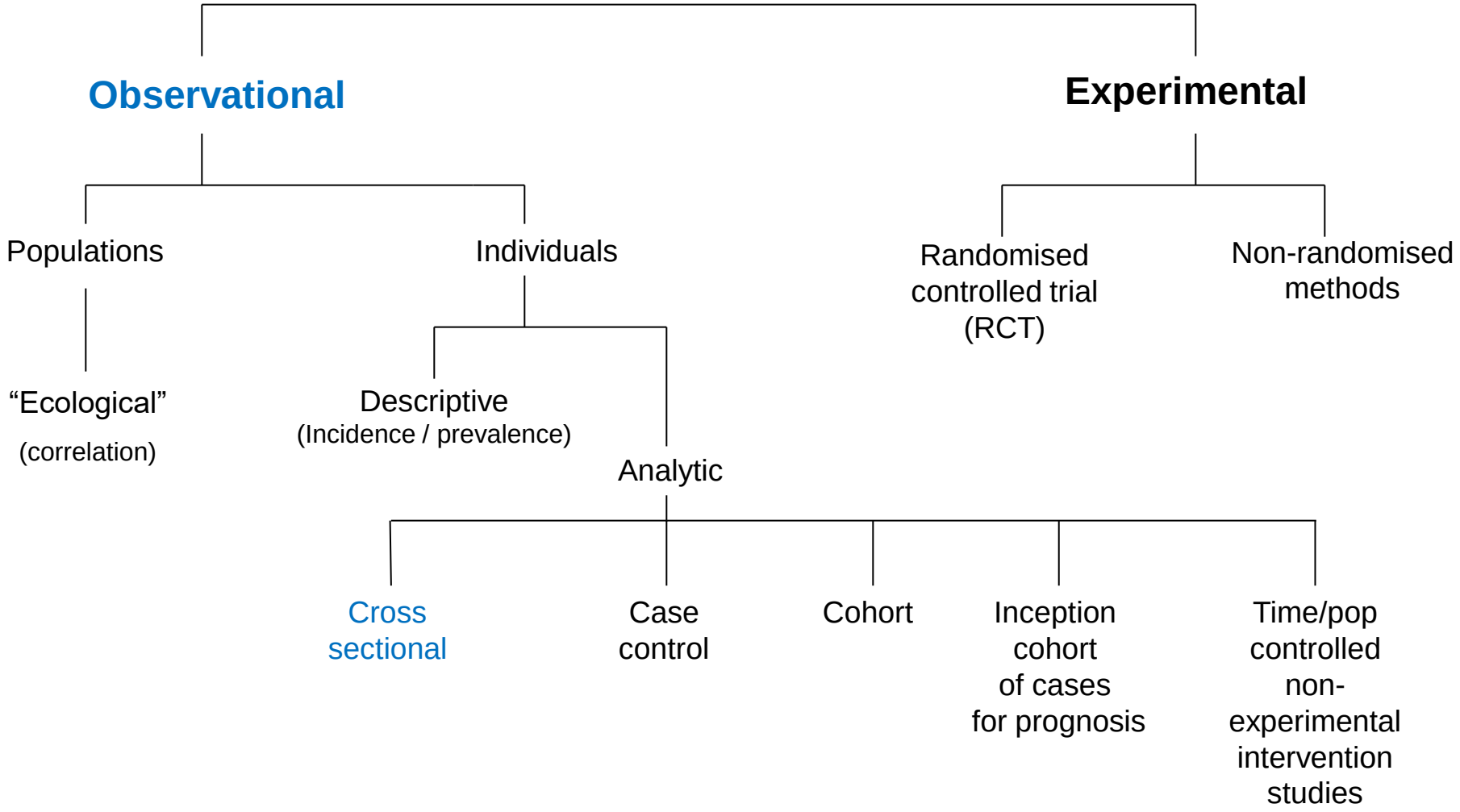
- Incidence is NEW cases over a specified period of time
- Estimated as:

$$\frac{\textbf{Number of new cases of carpal tunnel syndrome over one year}}{\textbf{Total population at risk over one year}}$$

Could be general population
Could be people at work in e.g. meat processing factory
(Total number of person-years of observation)

Epidemiologist's bathtub

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Cross-sectional studies

- Usually a **survey** of a ‘population’ of interest
- Measure exposure and/or disease at **one point in time**
- Measures **prevalence** not incidence
- No temporal relation of exposure and disease so not good for investigating causal relations
- Widely used for biochemical, pathophysiological, lifestyle measures

Cross-sectional studies

- Descriptive: frequency and distribution of health related exposures or outcomes
  - **Survey (prevalence of silicosis amongst stone benchtop workers in Victoria)**
- Analytical: Measure association between exposure to risk factors and outcome
  - **Association between ever working in aluminium production and prevalence of mesothelioma**

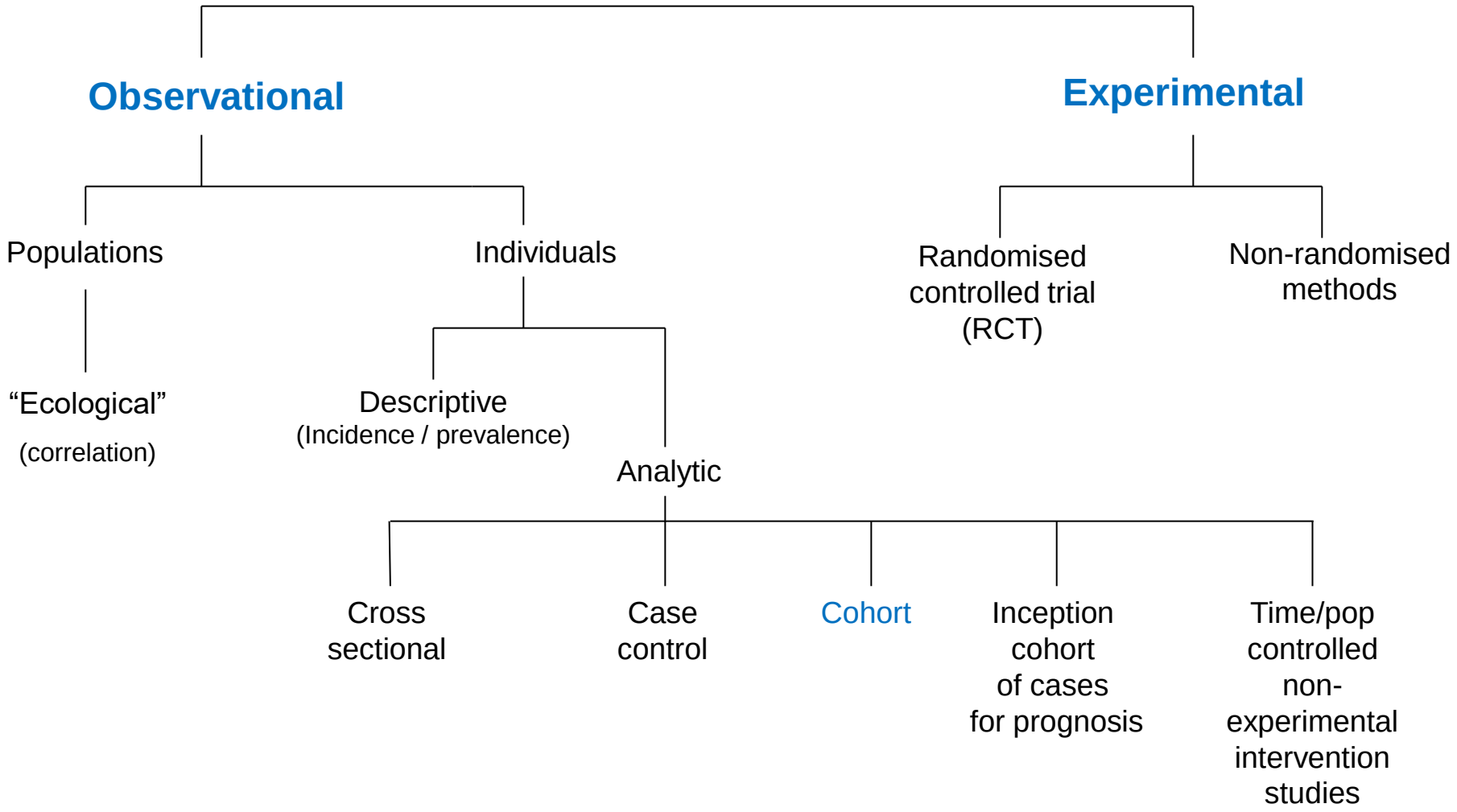
Cross sectional studies

STRENGTHS

- Relatively quick and easy (cheap)
- Useful for measuring prevalence of disease, risk factors for disease and patterns of disease in a population
- Repeated studies can provide data on change in disease or risk factors over time
- Hypothesis generation
- Ethically safe

WEAKNESSES

- Establishes association at most, not causality
- Retrospective exposure so risk of **recall bias**
- Non-response to survey
- Single measures (chronicity?)
- Measures prevalent rather than incident cases
- Prevalent cases are survivors
  - may miss acute fatal illnesses
  - or those with not recovered or more severe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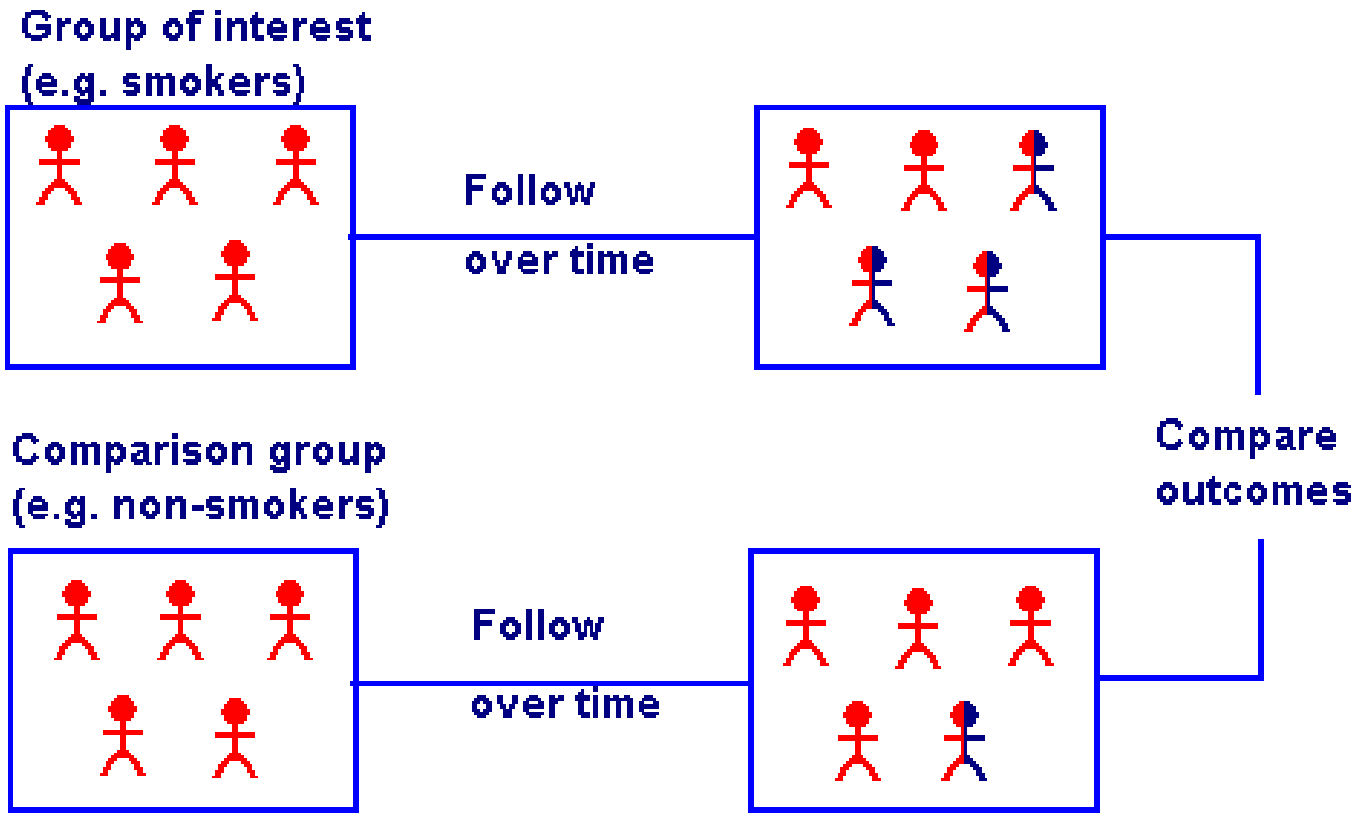
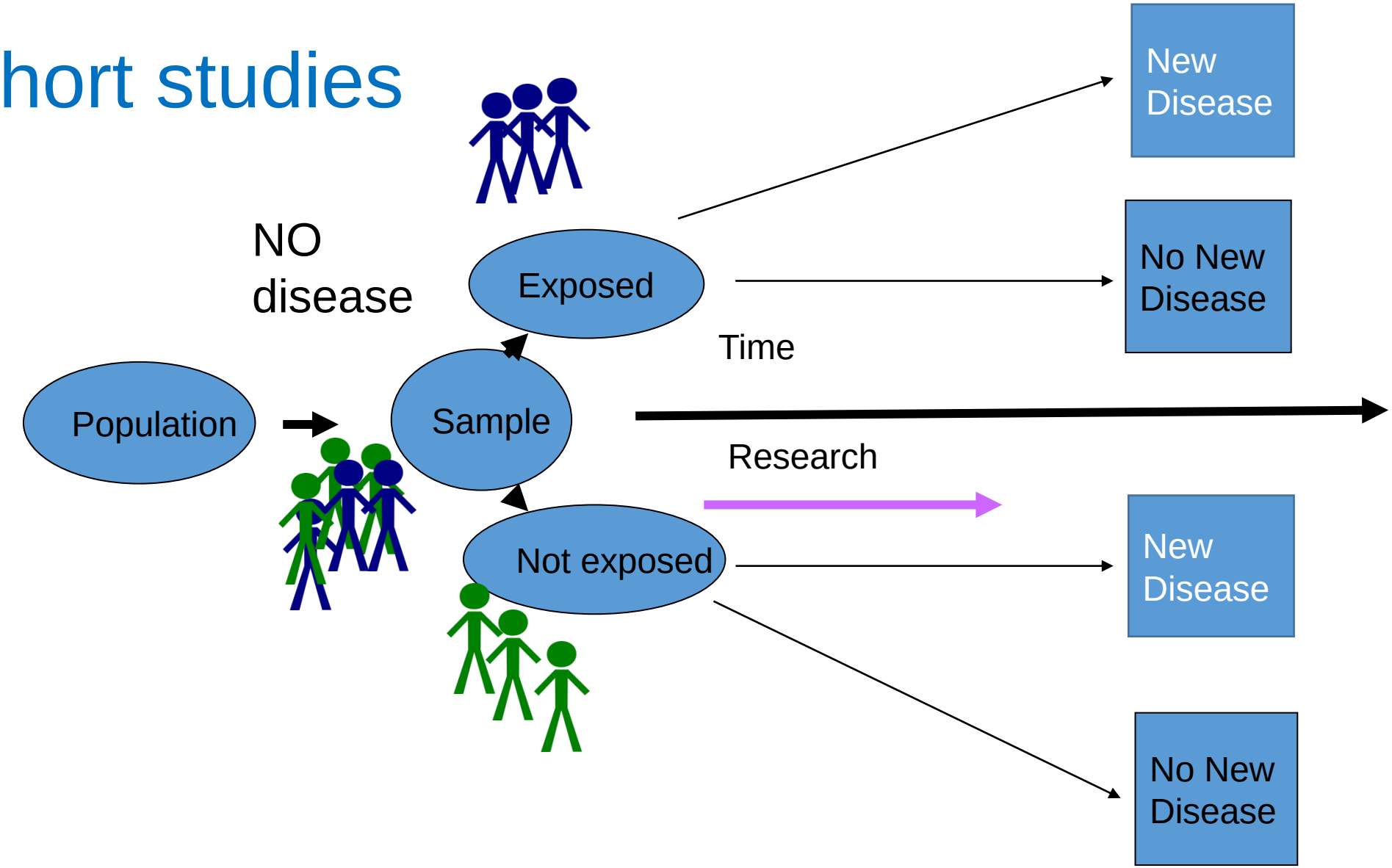
Cohort studies



Cohort studies

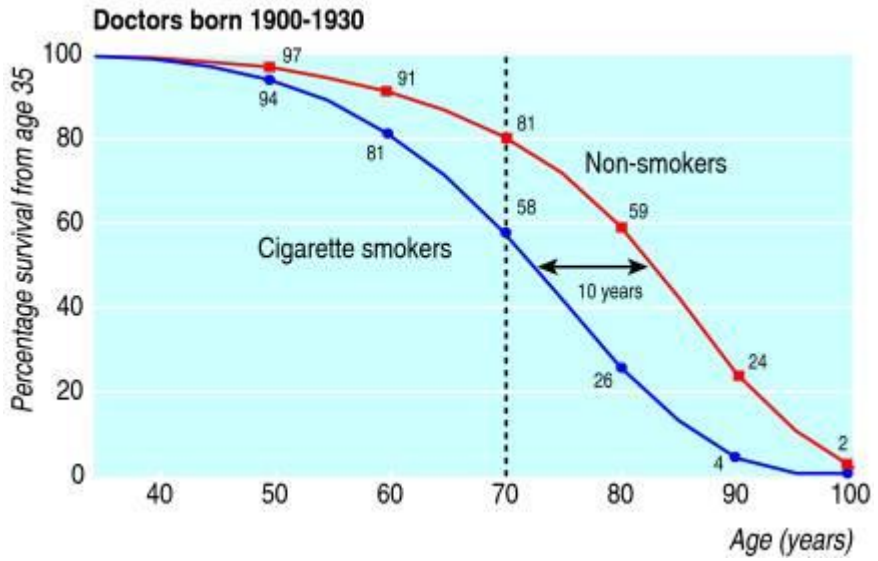
- Define population group with a common characteristic e.g. workers from a factory/individuals without outcome of interest
- Measure exposure then follow-up over time to see who gets disease
- Can be prospective or retrospective (esp occupational/clinical)
- Exposure can be an intervention
- Cohort can be people with disease followed to determine prognostic factors
- Good for rare exposures
- NB Healthy worker effect need to be careful in occupational cohort studies

Cohort studies



Famous cohort study

Hazards of cigarette smoking in a cohort of nearly 35,000 British doctors 1951 onwards



Survival from age 35 for continuing cigarette smokers and lifelong non-smokers among UK male doctors born 1900-1930, with percentages alive at each decade of age

Doll R, et al. Mortality in relation to smoking: 50 years' observations on male British doctors BMJ 2004;328:1519

Cohort studies

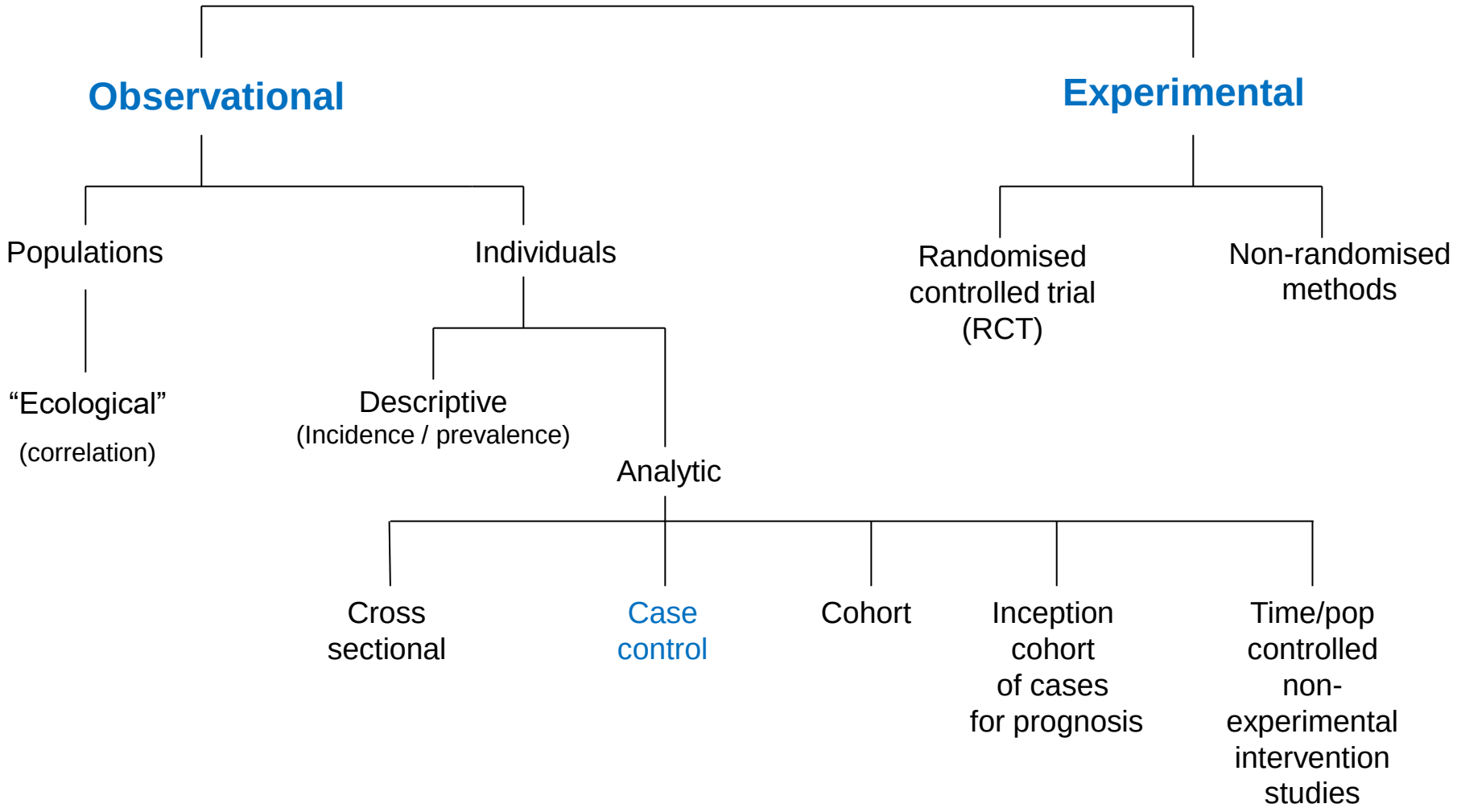
Advantages

- Rare exposures can be studied
- Multiple outcomes can be studied for one exposure
- Retrospective cohorts can produce relatively quick results on longer term outcomes
- Time sequence of intervention and outcomes can be measured
- Can measure incidence and prevalence

Cohort studies

Weaknesses

- Loss to follow up can cause bias- if drop out is related to outcome
- Observation bias a problem if exposure status known by person assessing outcome
- No mechanism to deal with unknown confounders
- Need large number of participants especially if disease is rare
- Cost of data collection and of long duration of follow up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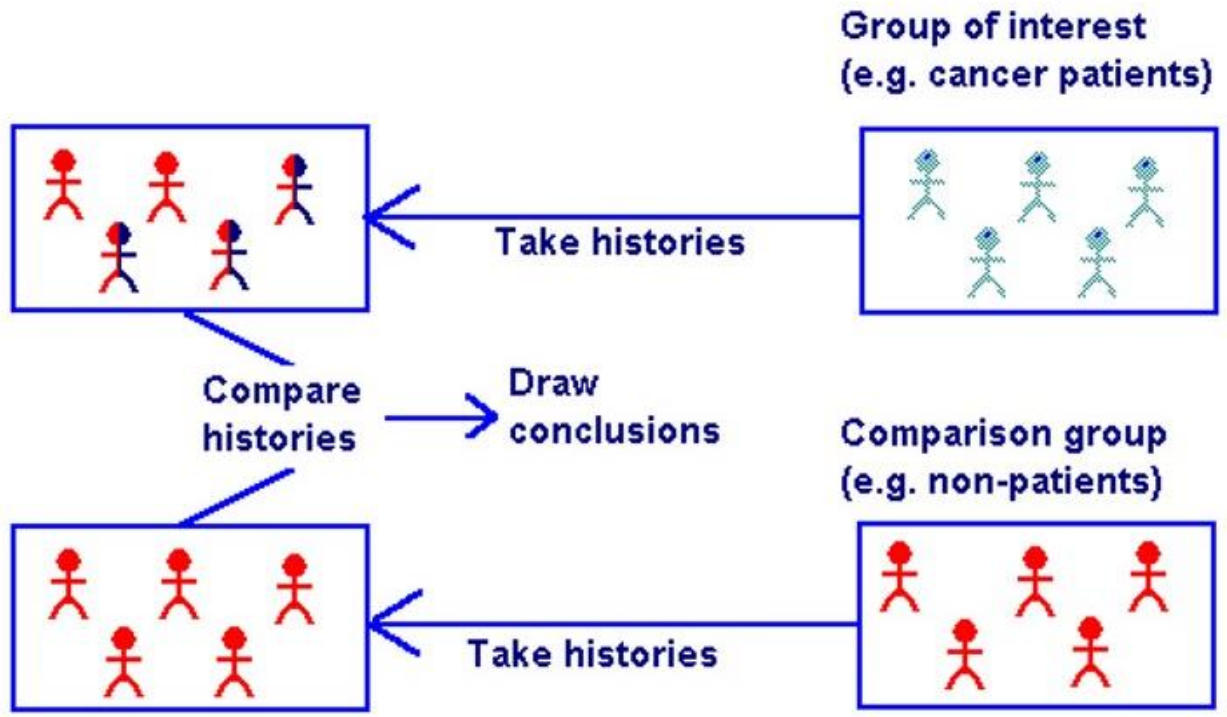
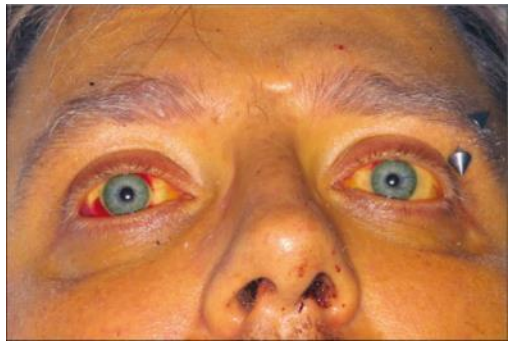
Case-control studies

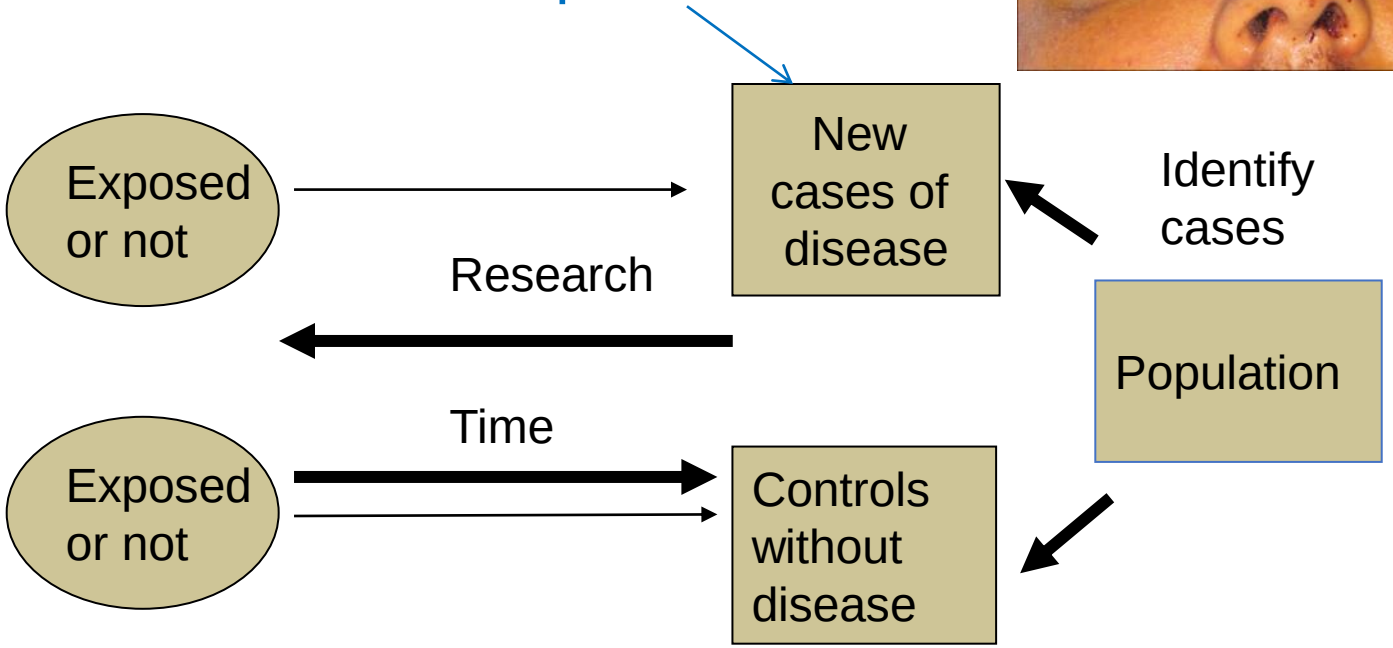


Case-control studies

- Study population defined by outcome not exposure
  - find new cases of disease
- Then find controls with no disease
- Cases compared to controls to assess whether they are different in terms of their historical exposure to particular risk factors



Case definition:
Incident/prevalent



Case-control studies

Advantages

- Quicker and cheaper than cohort studies
- Good for study of rare diseases
- Can be used to study multiple risk factors/exposures
- Can be used as initial study to establish an association

Case-control studies

Disadvantages

- Recall bias
- Selection bias especially controls
- Observer bias (especially if unblinded)
- Not good at investigating rare exposures
- Only one outcome can be investigated
- Cannot be used to estimate incidence
- Reverse causality ensure risk factor occurred before disease diagnosis (particularly if long latent period)

Case-control studies

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Hospital controls vs community controls

Convenient, cheap, available (in bed)

More likely to participate

BUT: they are ill

More likely biased sample

May not be representative of the study sample

Beware if similar risk factors e.g. COPD and lung cancer cases..

Which study to use when?

- The disease of interest is a rare condition?
  - Case-control study
- We want to assess multiple outcomes?
  - Cohort study
- There is a cost/time constraint?
  - Case-control study
- We want to know prevalence?
  - Cross-sectional

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Associations

Exposure ?→ Outcome

Have you considered

- Chance
- Bias
- Confounding

Bias

- Any process at any stage of study that produces results that depart from the truth
- Two main types:
  - Selection
  - Information

Selection bias

- Identification of subjects into study biased
  - e.g. non responders in a survey? are they the same as responders
- Case control studies
  - Where choice of cases or controls is dependent on exposure
- Cohort studies
  - ‘healthy worker’ in occupational studies

Information bias

- Measurement
  - systematic differences in the way information on exposure or disease is collected between groups
- Observer
  - awareness of exposure affects assessment of disease or vice versa
- Subject
  - recall - patient with disease maybe more likely to remember exposure than control group

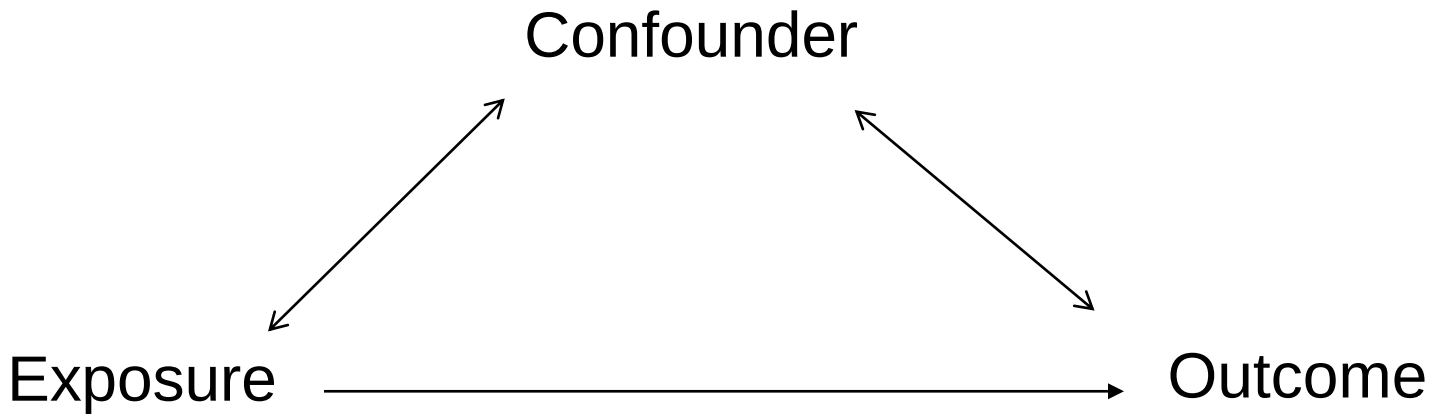
How to deal with bias in research

- Get design as good as possible
- Statistical analysis cannot compensate for design flaws
- Take care in:
  - Selection of cases and controls
  - Assessment of exposures and outcome
  - Follow-up: aim to maximise

GOOD epidemiology relies upon acknowledgement and recognition of bias

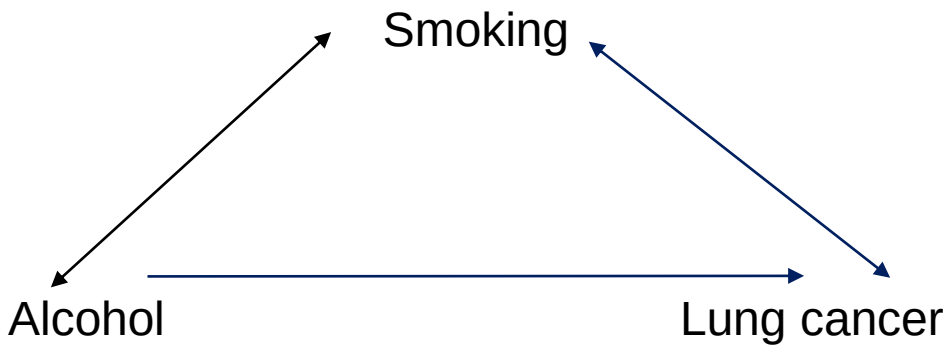
Confounding

- A confounder is a factor that is independently associated with both exposure and outcome



- It provides an alternative explanation for an observed association between exposure and outcome

An example of confounding



How to take confounding into account

- Consider potential confounders
- Design:
  - matching (age/sex)
  - randomisation
- Analysis:
  - stratification
  - multivariate analysis
  - standardisation (usually age sex)

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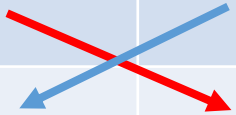
Measuring “risk” (odds ratio)

	Hand dermatitis	No hand dermatitis
Wears latex gloves at work	A	B
Does not wear latex gloves at work	C	D



$$\text{OR} = \frac{\text{Odds that a case was exposed (A/C)}}{\text{Odds that a control was exposed (B/D)}} = \frac{\text{A x D}}{\text{B x C}}$$

Measuring “risk” (odds ratio)

	Hand dermatitis	No hand dermatitis
Wears latex gloves at work	25	25
Does not wear latex gloves at work	250	500

$$\text{OR} = \frac{\text{Odds that a case was exposed (A/C)}}{\text{Odds that a control was exposed (B/D)}} = \frac{25 \times 500}{25 \times 250} = \frac{12500}{6250} = 2.0$$

Relative risk

	Hand dermatitis	No hand dermatitis	
Wears latex gloves at work	A	B	A + B
Does not wear latex gloves at work	C	D	C + D

$$\text{Relative risk} = \frac{A / (A+B)}{C / (C+D)} = \frac{\text{Incidence of disease with exposure}}{\text{Incidence of disease without exposure}}$$

Measurement of the **strength of the association** of the outcome for the exposure

Relative risk

	Hand dermatitis	No hand dermatitis	
Wears latex gloves at work	25	25	50
Does not wear latex gloves at work	250	500	750

$$\text{Relative risk} = \frac{25 / 50}{250 / 750} = \frac{0.5}{0.333} = 1.5$$

Standardised incidence rate ratio (SIR)

- SIR is an estimate of the number of disease cases in a given population compared to what might be “expected” based on a comparison with the disease experience in a larger population.
- It is the ratio of the number of disease cases observed compared to the number expected

	Lung cancer	Person-years without lung cancer
Coalmine worker	60	51477.5
Never coalmine worker	30	54308.7

The rate in those who worked in coalmines was 60 / 51477.5 = 116.6 per 100,000 person-years

The rate in those NOT working in coalmines was 30 / 54308.7 = 55.2 per 100,000 person-years.

= SIR 2.1

Standardised mortality rate (SMR)

- SMR describes whether a specific population (e.g. people who worked in petrochemical industry) are more, less or equally as likely to die than a standard/ reference population (e.g. general population of Australia)
- It is the ratio of the number of observed deaths over the number of expected deaths

$$\frac{\text{The number of observed deaths}}{\text{The number of expected deaths}}$$

SMR < 1.0 indicates there were fewer than expected deaths in the study population
SMR = 1.0 indicates the number of observed deaths equals the number of expected deaths in the study population
SMR >1.0 indicates there were more than expected deaths in the study population (excess deaths)

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Reading papers critically

- Research question (PICO or PECO)
- Research methodology
- Selection of the participants for study
- Selection of the controls (if relevant) for study
- How is exposure assessed –is it reliable and valid?
- Is there blinding of the participants? Researchers?
- How are the data analysed? Is it appropriate?
- What are the outcome(s) – how well are they assessed?
- Have bias and confounding been considered fully and discussed?

Conclusions

- Evidence based medicine is underpinned by high-quality research
- Research questions are pivotal
- Methodology is dependent upon research question and nature of the population, exposure and outcome
- In occupational epidemiology, key study designs are cross-sectional, case control and cohort
- Each method has pros and cons – findings must be interpreted with this in mind
- Rarely is anything DISCOVERED or ESTABLISHED by one study

Learning outcomes

- To understand the key role of the research question
- To know the main research study designs
- To be able to explain why you might use these study designs
- To be able to explain the benefits and limitations of each method
- To know how to define key measures and measure risk
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