Choosing the right study design
Main types of study design

- Randomised controlled trial (RCT)
- Cohort study
- Case-control study
- Cross-sectional study
- Case series/case note review
- ‘Expert’ opinion
Experimental vs. Observational

**Experimental study**

Investigator *intervenes* in the care of the patient in a pre-planned, experimental way and records the outcome.

**Observational study**

Investigator does not intervene in the care of a patient in any way, other than what is routine clinical care; investigator simply *records* what happens.
Cross-sectional vs. Longitudinal

**Cross-sectional study**

Patients are studied at a *single time-point only* (e.g. patients are surveyed on a single day, patients are interviewed at the start of therapy)

**Longitudinal study**

Patients are followed over a *period of time* (days, months, years...
Assessing causality (Bradford Hill criteria)

- Cause should precede effect
- Association should be plausible (i.e. biologically sensible)
- Results from different studies should be consistent
- Association should be strong
- Should be a dose-response relationship between the cause and effect
- Removal of cause should reduce risk of the effect
Incidence vs. prevalence

**Incidence:** proportion of patients *without the event of interest* who *develop the event* over the study period
- Can only estimate from a longitudinal study
- Must exclude those who have the event at start of study from the calculation

**Prevalence:** proportion of *all patients in study* who have the event *at a particular point in time*
- Can estimate prevalence from longitudinal or cross-sectional studies
- Generally include all patients in calculation
Randomised controlled trials (RCTs)

- **Experimental** and **longitudinal**
- **Comparative** – comparison of two or more treatment strategies (e.g. new regimen vs. existing regimen)
- Control group allows us to conclude that any improvement in outcome is due to the test treatment rather than some other factor
- Where no existing regimen exists, control group may consist of untreated patients (usually receive a **placebo**)
Randomised controlled trials (RCTs)

- Subjects allocated to treatment groups by process known as **randomisation**
- Ensures that treatment groups are similar at start of trial; any differences are due to chance only
- Randomisation is most important feature of a RCT and is why RCTs are perceived to be the gold-standard approach to obtaining evidence of a treatment effect
- If you can randomise you should – however, randomisation is not always possible or feasible
Cohort studies

- **Observational** and **longitudinal**
- Follow a group of individuals over time to assess the **incidence** of a disease (or some other outcome)
- Can look at the effect of exposure to a number of factors of interest (potential risk factors) on the incidence of the outcome
Cohort studies

Disease-free

Exposed to factor
  - Develop disease
  - Do not develop disease

Not exposed to factor
  - Develop disease
  - Do not develop disease

Starting point
Present time
Follow individuals
Future time
Pros and cons of cohort studies

Advantages

- Can assess **temporal relationship** between exposure and disease (i.e. we know which event occurs first)
- Can make some attempt to assess cause and effect

Disadvantages

- If the disease is rare then cohort may have to be very large and follow-up long (i.e. expensive)
- May be problem with **loss-to-follow-up**
- Potential for bias due to **confounding**
Example: Royal Free Hospital (RFH) Haemophilia Cohort

- 111 men with haemophilia registered at RFH Haemophilia Centre became infected with HIV between 1979 and 1985
- Men were followed for over 25 years to describe the natural history of HIV infection
- Information collected on demographics, clinical events, laboratory data and treatment information
- When follow-up ended (Dec 2005), 39 men remained alive and 28 were under follow-up at the hospital
Case-control studies

- **Observational** and **longitudinal** (retrospective)
- Group of patients with a disease (cases) are compared to group of patients without the disease (controls)
- Aim: has exposure to any factor occurred more or less frequently *in the past* in cases than in controls?
- Cases and controls may often be **matched** on basic demographic information (e.g. sex and age) to make the two groups as similar as possible
Case-control studies

Exposed to factor

Disease (cases)

No disease (controls)

Exposed to factor

Not exposed to factor

Exposed to factor

Not exposed to factor

Compare cases and controls

Starting point

Past time

Trace individuals
Pros and cons of case-control studies

Advantages

- Relatively cheap, quick and easy to conduct
- No loss-to-follow-up
- Suitable for rare events

Disadvantages

- Potential for recall bias
- Timing of events cannot be reliably established – therefore more difficult to assess causality
- Cannot assess incidence (proportion with disease is fixed as part of the study design)
Example: Predictive factors for HIV seroconversion

**Cases:** Persons attending a Spanish HIV unit who seroconverted to HIV >3 months after their first visit following a specific risk of HIV (n=69)

**Controls:** Persons attending same unit after a risk of HIV who did not seroconvert, matched by gender, birthdate and date (n=69)

**Variables:** Demographics, serostatus of partner, exposure risk, previous PEP and STI, PEP regimen, previous HIV testing and presence of STI at baseline

**Conclusions:** Being MSM, having had previous PEP, an HIV-positive sexual partner and previous STI were all predictive factors for HIV seroconversion

Leal L et al. AIDS Res Hum Retroviruses (2016); in press.
Cross-sectional studies

- Carried out at a **single point in time** – no follow-up
- Often used to assess the prevalence of a condition, to describe the current situation or to assess attitudes and beliefs
- Advantages – relatively cheap and quick
- Disadvantages – not possible to estimate incidence of disease, but can assess prevalence
Cross-sectional study of 2230 HIV+ve patients in three primary care clinics in Pretoria; 25.1% reported hazardous or harmful drinking (2.0% had possible alcohol dependence)

In multivariable analyses, high-risk drinking associated with male gender, never being married, tobacco use, a higher level of independence and more depressive symptoms

Authors recommend routine screening for alcohol use and harm reduction interventions, taking into account associated factors

Huis In’t Veld D et al. Int J STD AIDS (2016); in press.
Case series / case-note review

- Fairly low form of evidence but can provide useful preliminary data
- Useful as a descriptive tool – i.e. to define the natural history of disease or to describe current practices
- No comparative element – therefore not possible to show a link between exposure and disease
- Usually retrospective – therefore potential for problems with historical data
Choosing an appropriate study design

- The hypotheses that can be tested in any study, particularly regarding ‘cause and effect’, will depend on the study design.
- Some study designs may offer ‘benefits’ in terms of cost, time and administrative effort, but in general, studies that are quicker and cheaper to perform will provide weaker evidence.
- Must have a clear idea of the hypotheses being tested before choosing the optimal study design.
Summary

- The hypotheses that can be tested in any study, particularly regarding ‘cause and effect’, will depend on the study design.
- Some study designs may ‘offer’ benefits in terms of cost, time and administrative effort – these are likely to provide weaker evidence.
- All studies involve the selection of a sample – if the sample is not representative, the results of the study may be biased.