statstutor

community project

encouraging academics to share statistics support resources

stcp-rothwell-types_of_trials

The following resources are associated:
Statistical Hypothesis testing, Medical Statistics

Types of Trials

There are a number of different ways that a hypothesis can be investigated and this sheet aims to provide an overview of the various trial types that can be conducted. The terms factor or hazard are used in this sheet and these are classed as exposures. For example, consider exposure to second-hand cigarette smoke, or intense sun exposure as a hazard or factor. They are something that could cause harm and are generally the factor which the researcher is interested in investigating.

Randomised Controlled Trials

Randomised controlled trials (RCTs) are the typical clinical trial or research study used to test a particular intervention (such as a drug or diet). Generally there is an experimental intervention of interest being tested against a standard intervention, often referred to as a control (such as current treatment or usual care), or a placebo (an intervention with no active properties). The format of these RCTs can vary, but there are two main types which are parallel group trials and cross over trials.

Parallel Group Trials

In a parallel group trial patients are randomly assigned to one of two treatment groups. The ideal scenario is that all other baseline characteristics of the patients are roughly similar in each group (i.e. equal number of males and females, location of hospital, patient ages, etc.). Randomisation of patients to treatment allocation is used to try to balance out the patient characteristics and this can be stratified by the characteristics that are deemed to be the most important or influential. If we consider a diagram of a parallel group trial, it would look like this:

These trials are typically used to test two, or more, different interventions on separate groups of people and is the most common design.

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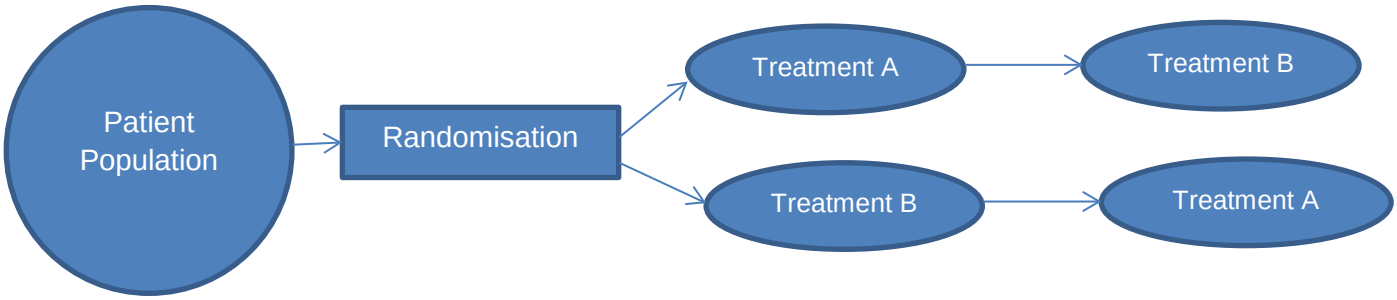
Cross over trials

In cross over trials the aim is that all patients experience all treatments (Treatment A and Treatment B). This is done by randomly allocating the patients to different treatment sequences, for two period cross-over studies these would be A **followed by B (AB)** or **B followed by A (**BA**)**. Thus, each group has a different order of treatments assigned to it. If we consider a diagram of a cross over trial, it would look like this:



These trials are commonly used for chronic conditions such as asthma or eczema. The conditions should be non-degenerative as this type of trial relies on the disease status returning to baseline between treatments in order to perform a fair trial. Occasionally there is a “wash-out” period between the two treatments to allow the first treatment to be flushed out of the body and the patients to return as close to baseline as possible.

Another consideration for all RCTs is what type of trial is to be performed. There are a number of options including superiority trials (showing one treatment is better than the other), non-inferiority trials (showing a new clinical approach is no worse than the current one) and equivalence trials (showing two treatment methods result in the same response).

Prospective Studies

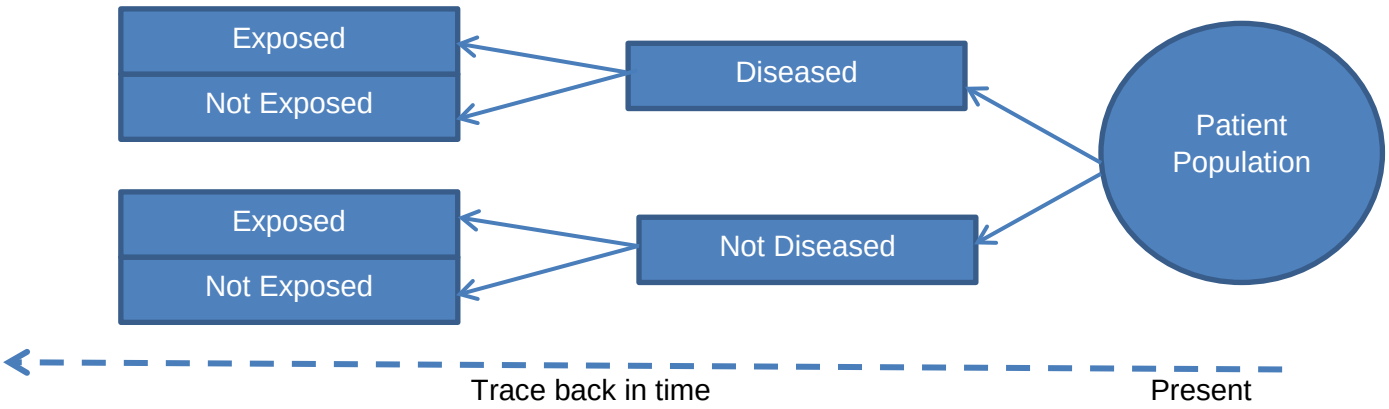
Prospective studies move forward in time. The easiest way to think of them is to think you are taking a random sample of people and following them from the present to see if they become ill or not. Alternatively, patients with a particular condition selected and followed up to see if there is an improvement over time. These studies can be extremely time-consuming and are the opposite of retrospective studies.

Retrospective Studies

A retrospective study is one which looks back in history for the exposure. The random sample is acquired then the researcher or the patients themselves think back to establish if they have been exposed to the factor or not. Retrospective studies can introduce recall bias, so patients will remember things differently as time passes. However, they are generally cheaper than prospective studies and take up less time.

Case-Control Studies

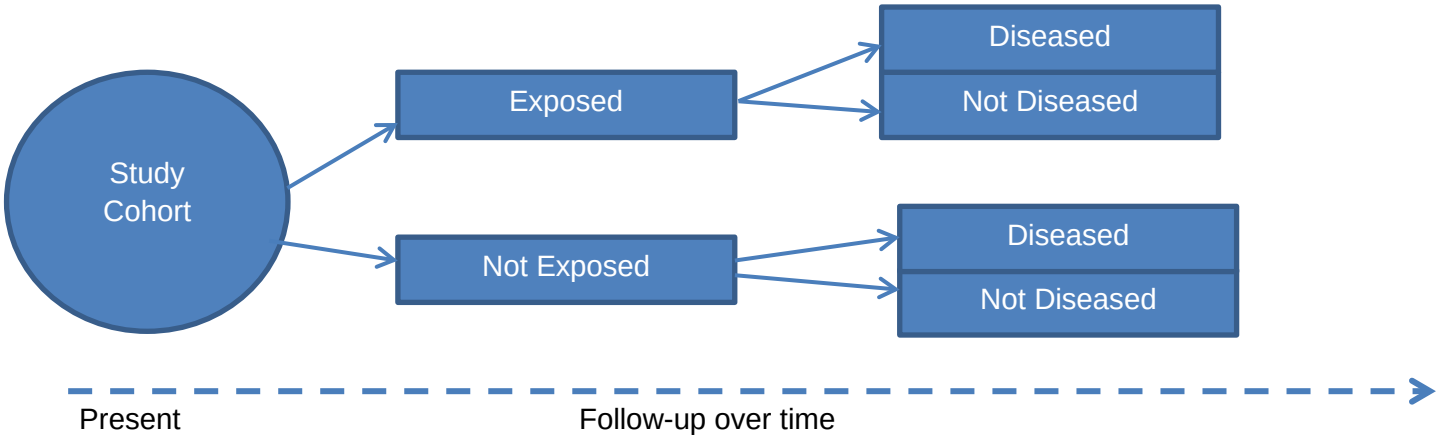
Case-control studies are useful to identify factors that may contribute to a medical condition by comparing individuals who have the condition of interest and those who do not. These studies are retrospective, so they start with the patient population of interest and then establish which patients are diseased or not. From this, the researcher looks back to determine how many patients were exposed or not exposed to a particular hazard or factor in each group. An illustration of how a case-control study works is as follows:



Advantages	Disadvantages
- Good when the disease or condition is rare - Can look at many different exposures or potential factors at once	- As it is retrospective it is open to recall bias - Potential unknown confounding factors

Cohort Studies

A cohort study is a prospective observational study where the cohort or sample is gathered, then it is established whether each participant has been (or is) exposed or not to a factor or hazard at baseline. The patients are followed up over time to see which ones (how many) become diseased or not. An illustration of this is shown below.



Cohort – A defined group of people with a common exposure or characteristic e.g. smokers, obese, people living near a chemicals factory.

Advantages	Disadvantages
- Good when the exposure is rare – identifies and follows up those with specific exposure of interest - Can look at many diseases or outcomes - Longitudinal observation of the individual over time - Data is collected at regular intervals	- Expensive to conduct - Sensitive to people dropping out – this can introduce bias - Takes a long time to generate a worthwhile amount of data - Potential unknown confounding factors

Cross-sectional Studies

A cross-sectional study does exactly what the name suggests. It takes a cross-section (or sample) of the population of interest and establishes which of those patients have a particular disease or condition and which do not, and who is exposed or not exposed to a specific hazard or factor. These studies do not look back or forwards in time, all the investigation occurs simultaneously.