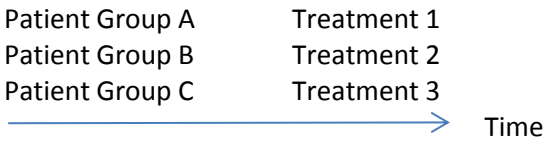
AN INTRODUCTION TO RANDOMISED CONTROLLED TRIALS

A clinical trial is a method for comparing objectively, by a prospective study, the results of two or more therapeutic procedures. It aims to compare the response of a test group of patients receiving a new treatment with that of a control group who are receiving a standard treatment (or existing treatment) or occasionally a placebo or no treatment at all. The use of controls is important o substantiate claims of therapeutic efficacy for a procedure.

What is a randomised controlled trial?

Randomised controlled trials (RCTs) are one type of clinical trial design and are regarded by the scientific community to provide the 'gold standard' in terms of evidence when conducting primary research to study healthcare interventions. RCTs are commonly associated with pharmaceutical research and are less easily adaptable to the study of complex interventions such as chiropractic.

RCTs can use either a parallel design or a crossover design. The most common design is a parallel design. A parallel design is more likely to require larger numbers of patients than a crossover design but is suitable for looking at both short and longer term conditions and is less likely to be affected by complications and patients dropping out than in crossover designs. A parallel design uses two or more groups of patients who are studied concurrently; each group receives one of the possible treatment interventions being studied. The parallel design can be demonstrated:



Why are randomised controlled trials needed?

If a simple trial is conducted with no comparison group, the outcome observed cannot be attributed to the treatment intervention with any great degree of confidence.

When **non-randomised controlled trials** are used, they may be difficult to interpret since not all of the subjects have the same chance to receive the treatment intervention; the control and intervention group may differ in terms of age, gender, height, weight or other features which will be relevant to the final outcome of the study. **Random allocation** attempts to make the intervention groups as similar as possible in terms of these factors. Random allocation is achieved using tables of random numbers or computer generated random numbers e.g. using sites such as www.random.org.

Concern inevitably arises over the ethical issues of assiugning patients at random to an untreated group when a test treatment is believed to be advantageous. **Randomisation** is essential to avoid bias in assigning individual patients to test or control groups. Hence the randomised controlled trial is now regarded as the essential tool for assessing clinical efficacy.

Randomisation is one of two main strategies to minimise bias in clinical trials; the **double blind technique** is another method to minimise bias. HOwever, in small groups of patients, groups can still end up being poorly matched and a compromise solution is to split the series into bloacks of, for example, eight patients within each block consisting of four patients for group A and four for group B. Another difficulty with **simple randomisation** is that the two groups can turn out to be ill-matched

with respect to a variety of characteristics including age, gender or disease severity. The chance of mismatch decreased as the size of the series increases. In small scale trials **stratified randomisation** is used to avoid this difficulty. The subjects might be divided into categories and random allocation to each group can be used within each category.

How is an RCT conducted?

Identification of treatment intervention

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Selection of study population

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Obtain ethical approval

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Provide information concerning the treatment intervention and risks

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Randomise members of study population to control of treatment intervention groups.
Provide the treatment intervention employing blinding/masking to either study subject OR therapist (single blind) or study subject AND therapist (double blind).

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Measure outcomes at time intervals as defined in the study protocol using a blinded/masked/independent assessor

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Follow up any losses from the study population

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Analysis of all outcomes using a blinded/masked/independent analyst

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Write up findings

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Dissemination of findings to suitable audiences e.g. conferences, patient groups, peer reviewed journals.

Terminology

Blinding/masking. This is the method of concealing the allocation of a sample of people, for example, to an experimental group or a control group during the research process. This concealment can be from the individuals involved in the research process (**single blind**) or concealment from both researchers and research participants (**double blind**). The term masking is now commonly used to replace the use of the term blinding.

Consent. The process whereby a patient freely agrees without coercion or pressure to be involved in a research project. Consent can only be given where a full explanation of the process, potential risks and rewards have been fully explained to the patient and presented to them as a ormal document in a form in which they are able to understand (translated from another language, Braille or auditory version). Written consent is required from all participants in a research study. If this cannot be given by the patient involved, it can be given by a legal representative, guardian or other responsible appointed adult at the participant's behest.

Control group. The group in an experimental process that is not exposed to an intervention/treatment. This group can then be compared to the experiemental group receiving treatment to study the effects of the intervention.