The language of research (part 15): research methodologies: randomised controlled trials (2)

KEY WORDS
- Blinding
- Cause and effect
- Comparison
- Controlled
- Randomised
- Sampling
- Validity

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In the previous paper in this series, we identified that RCTs are a form of experimental study design used to prove cause and effect in the healthcare setting. Furthermore, we defined some of the key principles and terminology used in RCTs like validity, reliability and dependent and independent variables.

In this article, we continue to look at the design features of RCTs and go on to examine other elements of the RCT study methodology, including sampling, blinding, and the use of placebos. These strategies are all important to maintain the integrity of this research methodology.

In the last paper in the series, we identified that RCTs have an experimental and a control arm. The control arm are essentially people who are treated in every way the same as the people in the intervention arm, other than not receiving the drug or therapy under study. This means that at the end of the study one can, in essence, subtract the effect of being in the study in the control arm from the effect of being in the study in the intervention arm and thereby see the impact of the intervention.

Being in a study affects the way people behave, both just because they are in a study and also because they are receiving attention from the study staff. They may be more concordant with their usual care than they otherwise would be, this might mean, for instance, that their wounds heal quicker than normal. Someone in the intervention arm, say trialling a new dressing, will also be more concordant with the wound care advice as well as potentially having the benefit of the new dressing.

If the study is interested in the effect of the new dressing on the rate of wound healing, rather than the impact of extra attention on the rate of wound healing, one would look to the difference in the rate of wound healing between people in the intervention group and those in the control group – the only difference being the dressing used. Hence taking away the rate of healing in the control group from the rate of healing in the intervention group gives you a view of the impact of the new dressing.

In order for this equation to work, three other things must hold true, these are:

- the sample must be broadly homogenous
- ideally, the study subject and researchers should not know what group the study subject is in
- a placebo, or sham intervention, should be used.

SAMPLING

At its simplest, for the study to work, the two group, intervention and control need to be broadly the same at the start of the study. If the groups are not broadly the same, then any differences that arise between the groups at the end of the study may be said to have arisen because of the differences between the groups; that is the outcome could be said to be biased (Woodward, 1999).

One obvious solution to this might be to match the two groups for all the things that we can measure to make sure that they are alike. An example might be if we were testing the usefulness of a new dressing, we could assemble patients with diabetes and leg ulcers and simply divide them into two groups.

Further, we could ensure that the groups had equal numbers of people of particular ages, genders, ethnicities, body mass indexes, and perhaps blood pressures. We might also ensure they had similar forms of diabetes, treated in a similar way (insulin or not) and by doing all this matching we might reasonably claim that the two groups are the same at the start of the study. Indeed some studies report on these sort of measurable criteria, presenting the data in tables and showing statistically that the groups are not statistically significantly different.

If we accept the issues identified as important in determining how people respond to the wound dressing this might seem reasonable. In some smaller studies this is done and is recognised as a pragmatic answer to what is a tricky problem.

In reality, matching in this way is not as useful as it might first appear. What this sort of matching fails to do is to deal with criteria which we cannot see or measure. It also has the potential for splitting the groups by some criteria by some important criteria of which researchers are not aware; that is to say it can inadvertently introduce a selection bias (Ellis, 2016). For example by matching in this way we cannot have any faith in the fact that we are dividing the two groups evenly according to genetics, attitudes, beliefs or other criteria which are undetermined.

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In order to overcome these issues, and a few others, it is usual for such studies to randomly assign people to the study or control arm — hence randomised controlled trials.

This is done by starting the study with participants who all meet the inclusion criteria (age range, disease and presence of the diabetic ulcer) and are therefore similar in many ways. These people are subsequently divided randomly into two groups so variables that can be seen and measured and variables that cannot be seen and measured are likely to be split evenly between the two groups (assuming that the number of participants included in the trial is large enough).

In the real world randomisation may be done using randomisation tables or computerised programmes.

The other approach which some studies use to divide participants into the two groups is to allow the study staff to divide the participants. This approach is prone to selection bias (Pocock, 1997). Selection bias occurs when a researcher places a person in one arm of the study because they, perhaps subconsciously, believe the person will benefit the most from the new intervention and/or that they are likely to show the new intervention in its best light.

BLINDING

If the study sets out to show the difference between the two groups and wants to avoid any chance that this difference is in some way contaminated by the research team knowing which group, intervention or control, a participant is in then the study must find a way of preventing this.

Quite simply this is achieved by ensuring that neither the participant nor the researcher can tell which group any individual participant is in. There are some good reasons for this:

- Participants react differently if they know they are getting a new intervention. Behavioural biases such as changed behaviours (sometimes called the Hawthorne effect) will affect the participant's behaviour and therefore the confidence that can be placed in the study findings
- Researchers can behave differently, either consciously or subconsciously, if they know what arm of a study a participant is in – often because they want to be part of something successful. In our example of the new wound dressing this may lead them to exaggerate the rate of healing using the new dressing.

To avoid such behavioural biases, gold standard RCTs (that is the best RCTs) blind both the researchers and participants as to which arm of the study each participant is on. This blinding (sometimes known as masking) is normally achieved by the use of a placebo in a drug trial or a sham intervention in a treatment trial (Gordis, 2014).

PLACEBOS

A placebo is a drug, tablet or injection, made to look identical to the real drug being trialled. What is different is that the placebo does not contain the active ingredient; the actual drug. In this way the participant and study staff do not know who is taking the trial drug and who is not and theoretically therefore people in the intervention and placebo arms are treated, and behave, in the same way.

Sham interventions are harder to provide; for instance, it is hard to pretend to give to hide which wound dressing is being used. Where this is impossible, for example if one is applying honey to a wound versus not, one way round this is for the person delivering the intervention and the person recording the effectiveness of the intervention to be different. This means that prior knowledge of what treatment a patient is receiving does not bias the measurements being taken.

CONCLUSION

In this paper we have seen that in order to maintain the integrity of an RCT it is necessary for the study subjects to be broadly the same at the start of the study and that the researcher and the participants are best kept blind as to which arm of a study the participant is in. We have seen blinding can be achieved by the use of placebos or sham interventions.

In the next paper in this series, and the third and final paper on RCTs we will look at the methods used to collect data and draw some final conclusions about the usefulness of RCTs as a research methodology. WUK