Improving the quality of small RCTs nested in routine clinical practice

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Abstract

Conducting small randomised controlled trials (RCTs) 'nested' in routine clinical practice is ideal for family practitioners, non-academics and young researchers, who often are required to complete a 'small-scale' research project for their master's (MMed) theses. These trials have the potential to produce good outcomes that could promptly change clinical practice and behaviour. In this paper, the author discusses the advantages and disadvantages of conducting RCTs nested in routine clinical practice, as well as ways of improving their quality.

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Introduction

Conducting small randomised controlled trials (RCTs) 'nested' in routine clinical practice is ideal for family practitioners, non-academics and young researchers, who are often required to complete a 'small-scale' research project for their master's (MMed) theses.[1,2] RCTs 'nested' in routine clinical practice are clinical trials (studies) that usually are conducted within the context or framework of day-to-day clinical practice, often with no external funding. These trials have the potential to produce good outcomes that could promptly change clinical practice and behaviour. However, they often lack the luxury of a trial manager, programmer, data clerk, trial pharmacist, statistician, secretary and large amounts of money that are available to multicentred RCTs.

Advantages of small RCTs

Recruitment: It is relatively easy to recruit the required numbers for a trial because the practice has access to patients coming for consultations. In the case of hospitals, there are opportunities for using referral systems, and it is easier to do follow-ups.

Facilities: Established practices have facilities that could be used for the trial. These include refrigerators, storage space and security systems.

Trial medication and staff: If the trial compares the 'effectiveness' of medicines already in use, then there is no need to spend money on 'trial medication'. People working in the institution can also participate in the trial as researchers, clerks or administrators, and this reduces the costs.

Changing clinical practice and/or behaviour: The findings of small trials, even when they are not generalisable, are more likely to be implemented at the study location.

Disadvantages of small RCTs

Decision making: Senior institution managers or chief executive officers, in the event of group practices, are the major decision makers with regard to the day-to-day running of the institution. At times they could make decisions that are detrimental to the success of the trial. These include closure of the unit where the research is taking place, and termination of the service that the trial is assessing as a result of financial or other managerial issues.

Disciplinary issues: Practitioners and nurses working in general practices or hospitals often have no contractual obligation to participate in research. It might, therefore, be difficult to discipline staff members who are intentionally or unintentionally violating the research protocol.

Blinding might be very difficult in small trials, mainly due to lack of assistance. The principal researcher often has to do practically everything, especially when there are demands from the university for that person to work independently in order for a Master's degree to be awarded.

Apathetic team: If the research does not have obvious and imminent benefits for the staff and patients, the team might be apathetic and disruptive. In extreme instances, some staff members might even dissuade patients from participating.

Coercion: When doctor-patient or nurse-patient relationships have been formed, it might be difficult for the participants to 'refuse' to participate in the study. They might even participate in the trial to 'please' their practitioner. In addition, patients may provide the

information that they think would satisfy their practitioner, because the doctor-patient relationship may far outweigh the researcher-participant relationship.

Representation: It often is difficult to recruit a representative sample from just one general practice because the patients coming to that particular practice might have similar characteristics. Therefore, the findings may not be widely generalisable.

Ways of improving the quality of RCTs nested in routine clinical practice

Trial-related issues: To enhance internal validity, the research protocol should be adhered to strictly and only 'validated questionnaires' should be used. Measures should be put in place to identify issues that could cause high drop-out rates or absconding.[3,4]

Recruitment: To avoid bias and coercion during the recruitment phase, an independent nurse (researcher) should be used if the practitioner providing the service is also the principal researcher. The practitioner may not use his or her personnel (e.g. receptionist), because the patients who know the receptionist may feel obliged to participate.

The principal researcher: Researchers should keep in touch with the situation on the ground for the trial to happen. Staff members used as research assistants should be encouraged by the principal researcher, who regularly has to monitor progress and solve urgent issues related to the trial.

Randomisation, blinding and concealment of allocation: The practitioner should be blinded to the treatment that his/her patients (participants) are receiving. Blinding will reduce bias, especially when making clinical decisions that may impact on the findings of the trial.[5]

Sample size and power: If time and resources are unlimited, it is favourable to collect data from as many participants as possible. Remember, as the sample size increases, the 'confidence intervals' narrow and the effect is being measured with greater precision. However, it is often necessary to estimate how many participants are needed for a study. For example, if 500 patients are needed to make the study worthwhile, but the maximum that could be recruited is 50, it would not be ethical to waste scarce resources on a study that is unlikely to answer the research question. Resources are limited and therefore it always is vital to make an estimation of the minimum size at which a study would be acceptable or statistically significant. The commonly used cut-off point for significance (p value) is 5% (0.05).[6] The power (usually 80% or 90%) of a study is the ability (probability) to detect, as statistically significant, a difference of a particular size – if that difference truly exists. Estimating a sample size is relatively easy, even though this frightens many family practitioners involved in research. For example, a statistical package could be used, for example Epi Info, which is available free of charge from the Centre for Disease Control and Prevention in the USA, gives a range of values in each group and a total sample size.[7] Alternatively, Altman's Nomogram could be used without or with a little help from a statistician.[8]

Placebos: Placebos should be avoided in RCTs nested in routine clinical practice, because a more rigorous protocol adherence will be required. Nevertheless, placebos are less likely to be used in routine clinical practice.

Institution: The 'host institution' should make a commitment to maintain, for the duration of the trial, key disciplines for all aspects of the design and implementation of the trial. Furthermore, researchers should, whenever possible, make preliminary reports available to the managers of the institution.[9]

Ethical issues: Patients must be informed of all aspects of a trial, be competent to give consent, and give such consent voluntarily.[5]

In conclusion, it is not impossible to conduct small RCTs nested in routine practice. The trials that are most likely to succeed and change clinical practice are those that (i) minimise disruption of the normal working environment, (ii) compensate general practitioners, nurses and administration staff for additional time spent on the project and for their commitment, and (iii) adhere to the "guidelines for good clinical practice in clinical trials".[10,11,12]

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