Assessing Research Protocols: Introduction to Randomized Controlled Trials (RCTs)

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Overview

A randomized controlled trial is one of the most powerful tools of research. In essence, the randomized controlled trial is a study in which people are allocated at random to receive one of several clinical interventions[1]. On most occasions, the term "intervention" refers to treatment, but it should be used in a much wider sense to include any clinical maneuver offered to study participants that may have an effect on their health status. Such clinical maneuvers include prevention strategies, screening programs, diagnostic tests, interventional procedures, the setting in which health care is provided, and educational models.

Randomized controlled trials are used to examine the effect of interventions on particular outcomes such as death or the recurrence of disease. Some consider randomized controlled trials to be the best of all research designs, or "the most powerful tool in modern clinical research", mainly because the act of randomizing patients to receive or not receive the intervention ensures that, on average, all other possible causes are equal between the two groups. Thus, any significant differences between groups in the outcome event can be attributed to the intervention and not to some other unidentified factor. However, randomized controlled trials are not a panacea to answer all clinical questions; for example, the effect of a risk factor such as smoking cannot ethically be addressed with randomized controlled trials. Furthermore, in many situations randomized controlled trials are not feasible, necessary, appropriate, or even sufficient to help solve important problems[1].

Randomized controlled trials may not be appropriate for the assessment of interventions that have rare outcomes or effects that take a long time to develop. In such instances, other study designs such as case-control studies or cohort studies are more appropriate. In other cases, randomized controlled trials may not be feasible because of financial constraints or because of the expectation of low compliance or high drop-out rates.

Many randomized controlled trials involve large sample sizes because many treatments have relatively small effects. The size of the expected effect of the intervention is the main determinant of the sample size necessary to conduct a successful randomized controlled trial. Obtaining statistically significant differences between two samples is easy if large differences are expected. However, the smaller the expected effect of the intervention, the larger the sample size needed to be able to conclude, with enough power, that the differences are unlikely to be due to chance. For example, if we wish to study two groups of

patients who will undergo different interventions, one of which is a new procedure. We expect a 10% decrease in the morbidity rate with the new procedure. To be able to detect this difference with a probability (power) of 80%, we need 80 patients in each treatment arm. If the expected difference in effect between the two groups increases to 20%, the number of patient required per arm decreases to 40. Conversely, if the difference between the groups is expected to be only 1%, the study population must increase to 8,000 per treatment arm. The sample size required to achieve power in a study is inversely proportional to the treatment effect squared[2]. Standard formulas are available to calculate the approximate sample size necessary when designing a randomized controlled trial[3,4].

In summary, randomized controlled trials are quantitative, comparative, controlled experiments in which a group of investigators studies two or more interventions by administering them to groups of individuals who have been randomly assigned to receive each intervention. Alternatively, each individual might receive a series of interventions in random order (crossover design) if the outcome can be uniquely associated with each intervention through the use of a "washout" period. This step ensures that the effects from one test are not carried over to the next one and subsequently affect the independent evaluation of the second test administered. Apart from random allocation to comparison groups, the elements of a randomized controlled trial are no different from those of any other type of prospective, comparative, quantitative study.

Critical Appraisal of RCTs

Critical appraisal is an integral process in Evidence Based Practice. Critical appraisal aims to identify methodological flaws in the literature and provide consumers of research evidence the opportunity to make informed decisions about the quality of research evidence. Below is a list of critical appraisal tools commonly used for RCTs.

1. CASP: Randomised Controlled Trial Appraisal Tool

Summary: Critical Appraisal Skills Program (CASP is a methodological checklist which provides key criteria relevant to randomised controlled trials. This tool was developed by Public Health Resource Unit, National Health Service, United Kingdom. Website: http://www.caspinternational.org/mod_product/uploads/CASP%20Randomised%20Controlled%20Trial%20Checklist%2031.05.13.pdf

2. The CONSORT Statement

Summary: The Consolidated Standards of Reporting Trials (CONSORT) Statement is a detailed document which outlines an explanation and elaboration of the CONSORT statement for reporting randomized controlled trials. It also includes (in table two) the critical appraisal tool. This tool was developed by The CONSORT Group, Canada. Website: http://www.consort-statement.org/consort-statement/

3. The JADAD Score

Summary: The Jadad scale assesses the quality of published clinical trials based methods relevant to random assignment, double blinding, and the flow of patients. There are 7 items in the scale, scored with a yes scoring 1 and a no scoring zero. The last 2 questions attract a negative score, which means that the range of possible scores is 0 (bad) to 5 (good). Website: http://onlinelibrary.wiley.com/doi/10.1002/9780470988343.app1/pdf

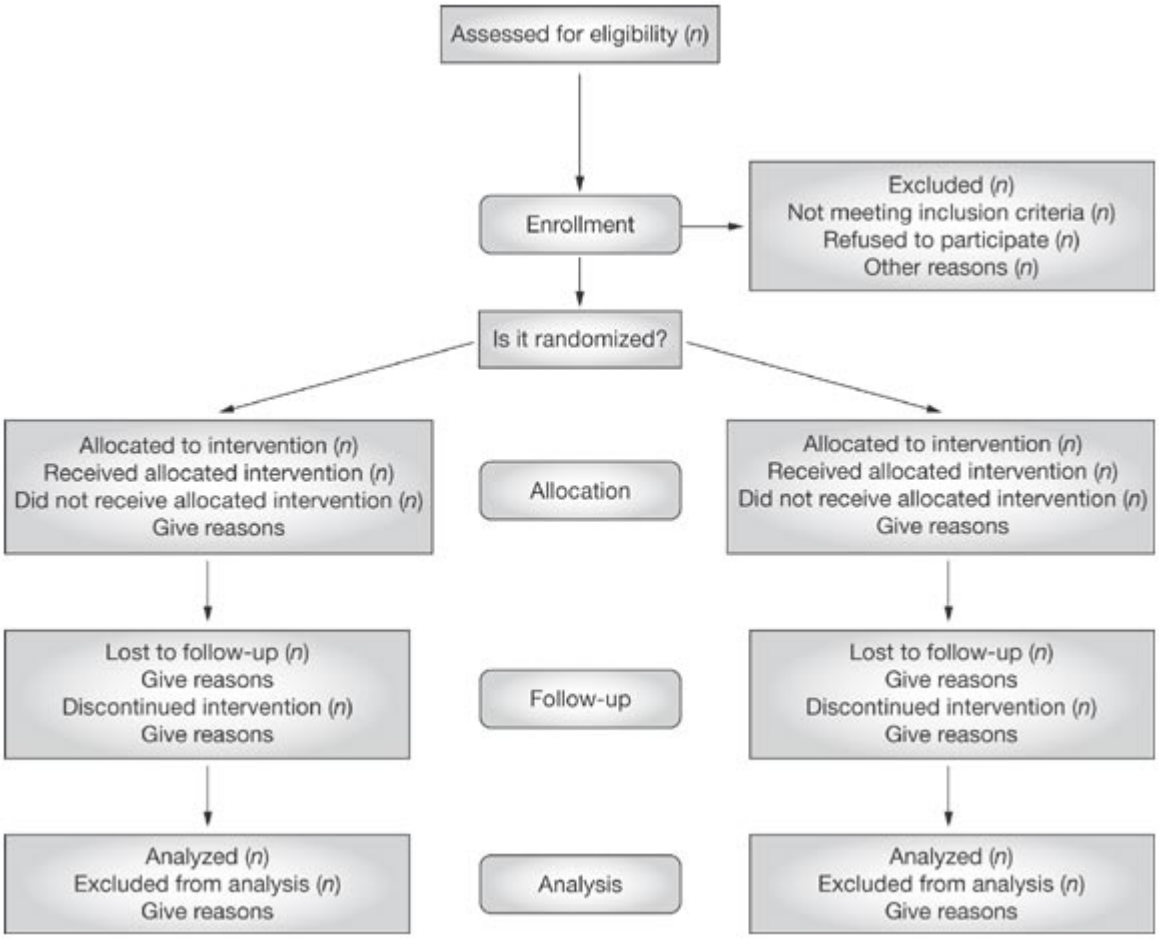

Figure 1. Consolidated standards of reporting trials (CONSORT) statement flowchart for the standard reporting and appraisal of randomized controlled trials[5].

References

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