Designing a Research Study

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Abstract. There are 10 steps to consider in any research study. These steps can be used to perform a critical appraisal of a published paper, or to design your study in the first place. The use of a simple system such as this can ensure that biases in study design are avoided and that an appropriate study is developed.

(1) What is the study hypothesis? (2) What is the study type? (3) What are the outcome measures? Is their measurement biased in any way? (4). What is the study factor (the intervention being offered to the children)? Is there bias in this? (5) Is there a possibility of confounding? (6) What are the reference population, source population and study sample? How have the sampling and selection into the study been performed? (7) Study methods that might threaten the internal validity of the study. (8) Statistical considerations. (9) Are the results clinically and socially significant? (10) Will the conclusions of the study be relevant to the kind of patients you see, or communities you work with? **(Indian J Pediatr 2000; 66 : 39-41)**

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We read research articles in a variety of journals such as this, and they all have one thing in common - someone has designed them! The Editor, however, might have questions sometimes about the way the studies have been designed. It is quite clear to those of us in academic medicine that the best journal articles (and the ones most easily accepted for publication) are those that have been properly designed.

There is no magic to this - just a question of using a system and working hard at filling in all the parts of the system. Described below is a method that we have been using here in the Centre for Clinical Epidemiology and Biostatistics in Newcastle, Australia for many years. It is based on a published way of assessing a journal article by critical appraisal. We have developed a 'Critical Appraisal Worksheet' which takes readers through each step of assessing the quality of what is published. Since this covers the methodology of the end result of a research study - the publication - it is also very suitable for use in designing the study in the first place.

Ten steps are involved, and illustrated by examples how each step might work.

(1) What is the Study Hypothesis?

This is the most difficult of all the steps in designing a study. You cannot start to design the study with the hypothesis; you usually come back to it after you have got the rest of it straight, but at some stage you must have a clear hypothesis, which can actually be tested.

The development of the hypothesis comes after you have had the idea for the research, thought about the type of question you want to ask and performed a careful literature search. The literature search is to see what others have done and how your study can be justified on the basis of, and can build on, previous work.

The hypothesis should be stated in a way that will demonstrate how the study will be carried out. Here is an example.

The idea : We know that coronary heart disease runs in families due to the aggregation of risk factors in families. If we used people who have had a heart attack as a prompt, could we change the behaviour of children of those who have had a heart attack so that they will adopt a healthy lifestyle from an early age and prevent their own heart disease when they become adults?

The literature search : This confirms that heart disease does run in families due to risk factor aggregation, and that it is possible to give advice to children that targets their risk behaviours. No previous study along the lines you have in mind has been performed in a population such as yours.

The hypothesis : Among the children of men who have been admitted to hospital with a heart attack, advice given by a specially trained nurse will lead to a change in saturated fat intake and cigarette smoking in comparison with a group of children not given the advice. (Note : this still needs to be

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confirmed later as we decide what type of study to perform, the details of the intervention and the expected outcomes. We should return to the hypothesis when all these have been decided).

(2) What is the Study Type?

In order to ensure that the intervention is producing the outcome you are measuring, perform a randomised controlled trial. Here, we allocate children, or families, at random and make comparisons at the start and end of the study. There are other study types that can be done to answer the question we have in mind, but they are always going to be inferior to the randomised controlled trial.

(3) What are the Outcome Measures? Is Their Measurement Biased in Any Way?

The outcome measures are the study end - points and reflect what we want to achieve. Of course we would rather be able to measure the reduction in heart disease, but this would take too long to study and so we must settle for some interim way of assessing the success of our intervention. Here we have chosen two of the well known risk factors for heart disease, diet and cigarette smoking. We would also like to know if any change we produce is carried on into adult life, but again we will have to settle for a time period that is feasible to study!

Measurement bias is very important. We must know if the way the outcome is assessed is biased in any way. One method to ensure this is to make the person assessing the outcome 'blind' as to the group the study subject is in. We will have to use questionnaires to measure the outcomes of diet and cigarette smoking presumably, and these may be biased by the subjects who have been in our intervention group wanting to please the researchers by reporting to have made the changes asked of them. We will need some way of verifying the answers, and of making the person coding the answers and analysing the results blind as to the group to which the subjects belong.

(4) What is the Study Factor (Here the Intervention Being Offered to the Children)? Is There Bias in This?

The intervention will need to be spelt out clearly in the study protocol. We have said in our hypothesis that we want to use nurses to provide the intervention. Our literature search should try to find evidence for the success of nurses in giving advice to children, and whether there should be a time delay between the time the parent is in hospital and the timing of the intervention. Often, literature in a related field can be used, even if a similar study has not been performed. We may need to change our minds about how best to deliver the intervention.

Bias is important too. The most important type of bias here is the way the subjects are randomly allocated to the two groups (intervention and control). If there is any way in which one type of child is more likely to be found on one side of the study than the other, then bias may have occurred. Detailed attention to the method of randomisation is crucial.

Another type of bias might occur if care is not taken and children who know each other are assigned to different groups; it is possible that 'contamination' will occur. Here, the intervention might inadvertently be given to the 'control' group as the children of both groups discuss what is going on. There are plenty of other types of biases that can be introduced to the study design at this stage!

(5) Is There a Possibility of Confounding?

This is a very serious type of study bias. A confounder is a variable that is related to both the study factor and the outcome factor. In our example, such a confounder might be age. If the intervention group comprises relatively more older children and older children are more likely to take the advice, age is a confounder because it is related to both the study factor (the intervention) and the outcome factor (measurement of the uptake of advice by change in diet and smoking). Socio - economic status is another, often quoted example of a confounder.

The great advantage of the randomised controlled trial is, that by randomisation, the potential confounders should be equally distributed between both sides of the trial. In this example, if the randomisation has worked well we should see that the intervention and control groups have a similar spread of age and socio - economic status.

(6) What are the Reference Population, Source Population and Study Sample? How Have the Sampling and Selection Been Performed?

This area needs careful attention also, as it will determine the way in which the results are interpreted for others who wish to try to apply these into practice. The 'external validity' of the study is an indication of, to whom may the results be applied - how generalised are the results?

If the patients with heart attack (the source of the children for the study) are found in private hospitals, are the results valid for other types of patients? If the selection process ensures that only families literate enough to be likely to take advantage of the advice are enrolled in the study, how

relevant are the results for all families? You will be able to assess these issues and make a decision whether the study is to be generalised or not. Then decide on what the sampling and selection factors should be for the study sample.

(7) Study Methods that Might Threaten the Internal Validity of the Study

Internal validity describes whether the study has avoided bias in a way that will allow the results to reflect the truth. All of the issues we have considered above are important to consider, however, each type of study has its own critical points to cause bias. In a randomised controlled trial, one of the most important issues is the way the subjects were allocated to groups - did the randomisation process truly avoid bias in the way subjects were assigned. In a longitudinal or cohort study, did a sufficient number of subjects reach the follow - up point? In a case - control study, was the selection of the controls appropriate?

In our study of children of the people with heart attack, we will have to devise a method of random allocation that is truly random. It should involve a decision to include the subject who will have met all selection criteria and none of the exclusion criteria before the random allocation is made. The allocation should be made by some process that produces a decision that is blind to the person dealing with the subjects - a telephone call to a central office saying that a subject is eligible and the office reading a list of random numbers can be a successful method.

(8) Statistical Considerations

There is a need to plan the statistical analysis carefully in advance. The best study protocols include 'dummy' tables. These are blank tables which show how the analysis will be performed. The analysis must reflect the study hypothesis, and take into account any potential confounders.

In designing the study, we must estimate the sample size needed to detect the difference we have stated in our hypothesis. We can use standard programmes to calculate this - they depend on the size of the difference we want to detect, the variation of the measurement used and the significance level and power we select. This will also depend on the study hypothesis.

In our study, we will compare the proportion of cigarette smokers and mean levels of measured dietary intake between the intervention and control groups, with a way of adjusting for differences between the two groups (often using a regression model for this).

The results should be presented in a way that can be clearly understood, and include confidence intervals around any estimate of difference rather than just significance levels. If there is no statistically significant difference between the two sides, then the power of the study to detect a difference should be given.

(9) Are the Results Clinically and Socially Significant?

It is not enough to say that the study is statistically significant–is the size of the difference enough to be clinically or socially relevant? Again, we need to plan appropriately to ensure that the study is going to answer an important question. This might be an appropriate place to reformulate our hypothesis which might be : "Among the children of men admitted to hospital and who survive a heart attack, those allocated at random to receive a nurse administered advice package focusing on diet change and not smoking cigarettes will, one year later, have a lower mean level of saturated fat in their diet (by 20%) and be less likely to smoke cigarettes (by 25%) than those allocated to receive no advice". This tells us most of what we want to know about the study design and the size of the difference we consider important.

(10) Will the Conclusions of the Study be Relevant to the Kind of Patients You See, or Communities You Work with?

When planning the study, again consider the likely value of the results and make sure that the way the study is conducted and the subjects chosen will allow the results to be useful.

These ten easy steps can make designing the study relatively easy. I wish you luck in your research work.

REFERENCE

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