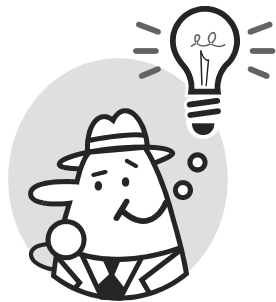




HOW TO DEVELOP A RESEARCH PROTOCOL



Research for
Better Health
Outcomes

Clinical trials should be designed, conducted and analysed according to sound scientific principles so that their objectives can be achieved, and these objectives should be reported appropriately. The primary objectives of any trial should be clear and stated explicitly.

The research protocol should adequately describe the study so that a reviewer can clearly understand the hypothesis being tested, how the study will be carried out to test the hypothesis, and the potential benefits from conducting the study. The choice of study design is, to a large extent, influenced by the patient population in which the trial is to be conducted, the nature of the treatment (and disease) and the effect you are trying to demonstrate. Some granting agencies provide a template for the structure of the protocol in their application forms and if so, it should be followed exactly.

Objectives and Endpoints

For a trial to be confirmatory it is important that the key hypothesis follows directly from the primary objective.

Endpoints are the quantitative measurements implied or required by the objectives.

The research protocol brings all aspects of the trial together creating a complete and self-contained picture of the study.

WHY WRITE A STUDY PROTOCOL?

A protocol is a very useful document for:

- Collecting one's thoughts
- Anticipating potential difficulties
- Enlisting support of collaborators, providers of data and resources
- Ethics Committee Approval
- Grant applications
- Nucleus of paper/report/treatise. Most of these will take the same format as the protocol.

HYPOTHESIS

Research is undertaken to make observations about nature. It usually begins with a speculative contention which the investigator may seek to confirm or disprove. This contention is the hypothesis. It takes the form of a short sentence. It is a statement not a question. If you need two hypotheses you need two studies. Examples include;

- Hepatitis K is sexually transmitted
- A defined counseling program will not influence recurrence rates of herpes genitalis
- Older women have different prevalences of STDs compared with younger women
- Famciclovir therapy has similar clinical benefit to acyclovir in first episode genital herpes

Note: Hypothesis 2 and 4 are examples of a null hypothesis

RESEARCH QUESTIONS

Research questions examine particular aspects of the study hypothesis. These usually number two to five and beg a definite answer. Two types are common;

Questions begging a yes/no answer. They usually begin "Do...?", "Is.....?", "Can.....?", etc

Questions seeking association or correlation between two phenomena or groups of phenomena. These questions can be graphically shown in a table which is usually a 2 x n table of the form below.

	Study (+)	Study (-)
Outcome Factor 1		
Outcome Factor 2		

Note that the outcome factor can be a categorical variable (0 – 5, 5 – 10, etc; yes or no; male or female) or a continuous variable (a number, a %, a proportion). These questions typically begin: "How much....?", "To what extent....?", "How does X vary with Y", etc.

BACKGROUND

This includes a literature review and is the justification for the study. The review should be brief (maximum 4 pages) and contain no more than 10 references. The content should be narrowly relevant to the proposed study and should leave the reader in no doubt that the proposed study is exactly what this research field is in desperate need of. It typically ends "In order to, we plan to conduct a study.....".

METHOD

This section describes what is to be done and how. It should be described in as much detail as possible and include a discussion of trial design (see Fact Sheet 2). Not all the following sections may be relevant.

STUDY POPULATION

Who and how many?

Why this number chosen? Power calculation?

Why chosen?

How enlisted/enrolled? Randomisation?

Inclusion criteria?

Exclusions criteria?

What is the generalisability to other populations?

DATA COLLECTION

What instrument will be used, such as a data collection instrument (DCI) or case report form (CRF). This is a pro forma document designed specifically for the research being undertaken. Data may be derived from laboratory tests, measurements conducted for the study or may also include any of the following:

- Questionnaire
- Database search request
- Review of medical records
- “Already have data”

Remember to include discussion about what personnel are required to collect the data, e.g. medical staff (SMO, fellow, nurse?) and who will enter the data into a database (data entry person?). Who will monitor the data collection and process of undertaking the study (is this required?), and who will process and analyse the data.

LAB METHODS

Provide some detail of laboratory tests, even those not performed for the purpose of the study but will be included in analysis. The amount of detail will depend on the type of study and whether you are doing these tests yourself.

VARIABLES

Variables are either outcome or study (dependent and independent respectively) and should be listed under these headings (study and outcome). Provide full details on how each is to be measured including discussion of possible measurement problems and potential for bias should it exist.

DATA ANALYSIS

In general outcome factors are analysed by study factors. The type of test will depend on the type of variable analysed (chi squared or Fisher's exact method for categorical variables; student's t-test for continuous variables; rank tests for non-parametric (non measurable) or non “normal” data. In most cases it will be useful, if not essential, to consult with a biostatistician to perform analyses to ensure the correct tests are conducted and the results are interpreted correctly. The biostatistician can also suggest wording to describe the analyses performed.

This section should include detailed descriptions of how the data will be analysed and manipulated. For example, be sure to include:

- the statistical package to be used (SPSS, SAS Minitab)
- the data base to be used (if any) (Lotus, Dbase IV)
- “all t-tests will be 2-tailed” (what tests are to be performed)
- “type 2 error set at $p = 0.05$ (0.01) level” (the level at which results are defined as significant).

ETHICAL CONSIDERATIONS

What sort of research requires ethical review? This information and more advice for investigators can be found on the NZ Health and Disability Ethics Committees web site (<http://www.ethicscommittees.health.govt.nz/>).

Health and disability research that involves human participants (whether health or disability support services consumers, healthy volunteers or members of the community at large) must be submitted for ethical review where the research:

- compares an established procedure with other procedures that are not regarded as established
- involves access to personal information for purposes other than direct consumer care or clinical audit
- seeks to further scientific or professional knowledge by means of questionnaires, interviews or other techniques of information gathering, or by means of laboratory analysis of human blood or tissue from living people, cadavers, or discarded body tissue
- is conducted by a government department, except where a statutory exclusion applies (e.g. Statistics New Zealand)
- is observational research or a physiological study
- is a clinical trial
- involves the use of radiation, organ imaging or surgical technique
- involves innovative practice
- is a new treatment or intervention which uses pain or deprivation of basic food or drink as a means to change behaviours.

In most cases, ethical approval for research involving human participants will obviously be required. However, this is not always the case. If you are in doubt as to whether your research requires ethical approval, you should either contact the National Co-ordinator of Ethics Committees or contact the Administrator of the health and disability ethics committee that would review your research if a review was necessary.

The Research Protocol should contain the following components:

- “Before commencement, this study (+/- consent) will be submitted to for ethical approval”.
- “Informed consent will be obtained after first explaining the nature, potential benefits/risks of the study to participants”.
- If ethical approval is not necessary give the reasons why.
- Confidentiality/anonymity statement.
- Description of all personnel involved and the degree of their access to patient information.

What about observational research, such as audit and other related activities? To find out if your observational study requires ethics approval refer to the guidelines on the Health and Disabilities web site. Studies involving human assisted reproduction and manipulation of human genetic material may need to be reviewed by separate committees.

SCHEDULES

The protocol should include schedules on the following:

- Timing of a project e.g. study initiation, the enrolment period, completion of data collection, analysis, and publication of results
- Details of the assessments and procedures to be conducted at each study visit.

- Events which may related and/or utilised as study results but may be collected as part of routine patient care.

RESOURCES REQUIRED

This section should outline the requirements of the study and may need to be quite detailed for funding applications. (See Fact Sheet 14).

POTENTIAL SIGNIFICANCE

A statement of the potential significance of the study is essential to demonstrate the value of the study should the hypothesis be supported by the study results or not. It classically includes statements of the form “Should (study finding) ... this may have implications for in terms of ...”. This is the most important part of the protocol (especially for applications for funding or resources) and as it is at the very end is more likely to be read.

Tips

BUDGET

In most cases a budget should be prepared to accompany the protocol as an appendix detailing the costs involved with running the study. This needs to be customised for each trial but can only be generated once the protocol is complete and final. Often the schedules provide the best guidance on what the costs will be to conduct the study. However, if you are unsure consult CCRep or use the Clinical Board Form A template as a guide.