

Chapter 2

Planning a Study

The main focus of a research can be in any one of three areas:

- Basic research, also at times referred to as pure research,
- Applied research, also called action research or policy research
- Evaluation of programmes, also sometimes called assessment or appraisal research.

Basic research seeks the new knowledge needed to understand a phenomenon; applied research attempts to provide useful information that can be applied to a problem being studied; and evaluative research provides an evaluation of an on-going programme. Each type of research needs the help of the other varieties, even though researchers of any one type of orientation tend to feel strongly about the worth of their own kind of research.

An investigator is normally searching through many sets of data to find the most significant bits required to answer a question at hand. The greater the mastery the researcher has of basic knowledge, theory, design, and methodologies of research planning the greater are the options available. This holds true whether the research task involves defining a problem. Designing research strategy, collection and analysis of data, or final validation or rejection of hypotheses. Skill in creative research begins here. This rule applies, no matter whether the inquiry falls in the domain of basic, applied, or evaluative research.

The characteristics of these different types of research are described in table 2.1:

Table 2.1 Focus of Research design.

	Basic Research	Applied Research	Evaluative Research
Nature of the Problem	New knowledge about a phenomenon is being sought so as to establish general principles with which it can be explained.	Application of scientific knowledge to understand phenomenon and developing remedial strategies.	Assessing outcome of interventions, or the outcome of current practice.
Goal of Research	To produce new knowledge or discover relationships and the capacity to predict outcome under various conditions	To secure the information that can be immediately applicable.	To provide cost/benefit accounting of an intervention, program or policy.
Guiding Theory	Hypothesis testing to provide reinforcement for a theory under investigation	Selection of theory or intuitive hunches to explore the phenomenon	Selection of a theory to fit the problem under investigation. At times findings may be related to a new theory or an established one.
Appropriate Technique	Theory formulation, hypothesis testing, sampling, data collection, statistical treatment of data, validation or rejection of hypothesis	Experimental and non-experimental techniques for data collection, analysis of data, and drawing inferences.	Use of conventional techniques as appropriate to the problem.

Practical Considerations in Research Planning

The usual progression in scientific reasoning is as follows:

- The process begins with an awareness, intuition, or suspicion about the possible influence of a particular factor on the occurrence of a phenomenon or disease. Such an idea may arise out of the day to day run of clinical work, examination of a disease pattern, observations arising from laboratory research, or just theoretical speculation. Any one of these may lead to formulation of a specific hypothesis.
- Appropriate studies are next planned, leading to collection and analysis of data to determine whether any statistical association is demonstrable concerning the interaction between variables defined by the hypothesis.
- The validity of the observed association is then checked by excluding chance, bias, confounding and so on.
- Judgment is then made about true existence of the statistical association. This often goes far beyond the data from any single study, but takes into account the consistency of findings from several studies of different designs in different populations by other researchers, both past and present.

The planning of any research revolves around five factors:

1. The *question* to be answered (or hypothesis to be tested).
2. The *subjects* for the research; how will they be recruited for the study; the source from where they will be recruited (e.g. hospital; outpatients or the community). The same applies to the controls, if any.
3. The *type of data* to be collected, as well as the *methods* of data collection to be employed (e.g. interviews; tests; clinical examination etc.).
4. Type and methods of *data analysis*.
5. Reporting of the results.

We now take up each one of these factors in detail.

The question

This is the crucial first step, and forms the kernel of all research. It calls for creativity, innovation and an inquisitive approach. Originality is difficult to define, but a fertile mind can be cultivated through wide and critical reading of the scientific literature, through participation in scientific discussions, and through scientific discourse with colleagues. An inquiring mind is the hallmark of all scientific research. Wide reading of the literature and being knowledgeable about the growing points in one's specialty helps to judge originality and to assess the creativity element in a research proposal.

How are research questions selected?

The sources include:

- 1). Hypotheses logically derived from existing theories.
- 2.) Hypotheses suggested by clinical observations and insight.
- 3). Questions raised from previous research.
- 4). Questions raised about the effectiveness of current or new drugs or assessment methods.

There is no shortage of questions. The difficulty is in finding an important one which can be developed into a study plan.

Once a research topic looks attractive from the originality point of view, there are a few practical issues that need to be considered next:

- How big a burden of illness is the condition on which research is proposed? How important will the answer be in improving the efficiency of the service being provided?
- What is the current state of knowledge in the area?
- What characteristics are being looked for? (e.g. the prevalence of disease or exposure to risk factors for a given disease; the natural history of a given condition; the outcome in response to intervention; and so on).
- Will the study be ethical in the way it is planned?
- Is the research practical in terms of time and available resources?
- Several of these issues are included in the mnemonic FINER, wherein the letters stand for the following:

F - Feasible (e.g. adequate number of subjects; adequate resources; availability of the necessary expertise; manageable etc.)

I - Interesting

N - Novel (e.g. provides new findings; extends previous findings; confirms or refutes new findings etc.)

E - Ethical

R - Relevant (e.g. to clinical practice or to health policy; to ongoing and future research; to scientific knowledge etc.) (See Table 2.2)

Table 2.2 Problems related to the research question and possible solutions

Problem	Solutions
with the research question	
1). Vague	* Write and rewrite the research question , at an early stage sharpening and refining it each time.
.	* Be specific about: What variables are to be studied. How they would be measured How the subjects would be sampled

Table 2.2 continued

Problem	Solutions
	* Then consider

How the variables and their measurements could be more representative of the phenomenon of interest.
 What predictor variables best describe it.
 What outcome variables would precisely describe the outcome.
 How can the subjects be more representative of the target population.

2). Not practical.

Research question too broad.

- * Consider fewer variables.
- * Narrow down the question.

Not enough subjects available

- * Expand inclusion criteria.
- * Reduce exclusion criteria.
- * Consider additional sources of subjects.
- * Lengthen duration of the study.
- * Consider more efficient study designs, or variables.

Methods beyond the skills of the investigator

- * Learn skills.
- * Collaborate with colleagues who have skills.
- * Consult experts and literature for alternative skills.

Table 2.2 continued

Problem

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Too expensive.

- * Seek additional support
- * Consider less costly study designs.

3). Not relevant or sufficiently novel.

- * Modify research question.

4). Uncertain about
ethical issues.

* Modify research question.
* Consult ethical committee.

The major function of the research question is to guide research through its different stages, and identify type of data to be collected, determining what cases should be included in the study, designing and implementing the research plan, organizing data in patterns that can be interpreted, and drawing conclusions from the research. Hence a thorough and painstaking examination of the research question is an important first step.

Subjects

Research in Mother and Child Health is often in the field, but at times it can be clinical, and occasionally laboratory based. In field and clinical studies the number of subjects and the characteristics to be measured are important. What will be the source for recruiting the subjects, and how are they to be enrolled? These are important issues in study design. The initial step would be to specify the characteristics of the target population, giving special consideration to clinical and demographic variables to be measured. How accessible is the target population? What would be the most practical way of recruiting subjects for the study? Are they to be recruited from the community, in out-patients clinics, or in hospital wards? These decisions require defining the inclusion and exclusion criteria. In doing so the important consideration is to make decisions which are sensible, can be applied consistently throughout the study, and which would provide a basis for applying the conclusions to other populations and settings. In deciding the inclusion criteria it helps to pay attention also to the administrative aspects and the timing of the study, bearing in mind that in real life there is a trade-off between the scientific and the practical aspects of the study.

Exclusion criteria specify subjects who are eligible but who are likely to affect the quality of the data (e.g. by non-compliance or dropout), or its interpretation. One is trying to make the study more practical at the cost of generalizability.

Type and methods of data collection

The attributes of the subjects and measurements performed on them are referred to as variables. They are so called because they vary i.e. take on different values in different subjects. There are two main types of variables according to the scales on which they are measured - numerical and categorical.

Numerical variables are those expressed in whole numbers, fractions or decimals. They can be discrete (e.g. body temperature, blood pressure etc.) or interval. The important characteristic of interval variables is that equal distances exist between successive intervals. Age, weight, height, blood glucose concentration, are all examples of interval variables. Number of children in a family, or adverse events recorded in a follow-up study are examples of discrete numerical variables. In general, what we measure are interval variables. What we count are discrete variables.

Categorical variables are those in which the measured value is assigned to one of two or more categories. For example, the variable sex can be one of two viz. male or female. Other examples are: immunized/not immunized; literate/illiterate; rural/urban; white/black/mixed race and so on. Categorical variables which have named categories that bear no relationship to each other are called nominal. For example, male/female. When the categories bear an ordered relationship to each other the categorical variable is called Ordinal. For example, illiterate/just able to read/primary school education/secondary school education/post secondary education. Unlike interval variables the intervals between ordinal categories are not necessarily equal.

At the analysis stage different types of variables call for different types of statistical tests. For example interval variables are analyzed using parametric statistics, whereas for nominal and ordinal variables non-parametric statistics are employed. Analysis of data is further discussed in Chapter 12. The important question to consider at the design stage is how well the variables represent the research question. Internal validity depends on this decision.

How accurately and with what precision the variables would be measured is another important consideration. Internal validity depends on this issue also. The overall degree to which the study population represents the target population and the measurements represent the true values is subject to two sources of error - sampling error and measurement error. Both of these have a random, or chance, as well as a systematic component.

Orientation in time also requires attention. For example, are the subjects to be observed prospectively? Or, are the subjects to be observed after undergoing an intervention (like immunization) or exposure (e.g. smoking) in the past? These were previously called prospective and retrospective studies, which used to cause a great deal of confusion. It is best to look on these two terms as time keepers, informing the reader about the orientation of the study in time.

Is the study primarily intended to describe a population or topic (a descriptive study), or is it intended to describe two or more populations comparing and contrasting them?

Will the subjects be observed in their normal setting without any attempt being made to change either them or their setting? Or will an attempt be made to control one or more factors involved? How much success is the investigator likely to have in assembling the study population, and a comparison group, allocating and administering the intervention, not losing any subjects or controls during the course of the study, measuring and recording all the data that need to be assembled? All these questions need to be carefully considered before deciding on the study design.

Data analysis

What type of data will be gathered to describe the study and comparison groups, and what analyses of data would be performed for testing the hypotheses? Statistics used could be both descriptive and inferential. The types of statistical tests best suited for the purpose should be considered at the outset. Often preparing dummy (or mock) tables helps to form a mental picture of the spread of the data, and the relationships between variables.

Reporting

The format for reporting the results of the study must be continually kept in the mind as it helps to give structure to the study as it progresses, and stops one from being blown off course. The basic format is as follows:

Study Objective - Describes the purpose of the study.

Study Design. - Describes the type of the study.

Setting - Whether clinical, laboratory or community based.

Subjects - How the subjects (and controls, if any) were recruited into the study.

Interventions - Describes the interventions.

Measurement - Data collected and analyses made.

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Results - What results were obtained as a result of the data analysis.

Conclusions - Conclusions with regard to how well the research question was answered.

Before designing and conducting a research project one important step is literature review. It involves the identification and critical evaluation of scientific and clinical publications relevant to a research project. The literature review provides an appropriate background and context for the investigation. It also enables the researcher to think critically about research aims and hypotheses, as well as to plan an appropriate research strategy.

Research Aims and Hypotheses

Frequently the researcher is testing a hypothesis. A hypothesis is usually concerned with: relationships between variables or differences between groups.

Some research projects state aims and objectives. In both situations, the researcher must define precisely all the significant variables and how they will be measured (e.g. coronary disease; malnutrition; street children).

Researchers are commonly seeking causal effects. They are seeking relationships to fit such propositions as : "Under conditions A, B, and C, if X were increased (or decreased) by a given magnitude, then Y can be expected to increase (or decrease) by a measurable magnitude. They attempt replication to confirm the findings.

The judgment about a cause and effect relationship is always made in the context of all available evidence. The judgment is revised each time there is new evidence. This is considered further in Chapter 11. If there is a causal association then any change in the frequency or quality of an exposure must result in a corresponding change in the frequency of the disease or outcome. In making a judgment about a cause one ought to consider two major questions:

1. Is the observed association valid? There is a need therefore, to rule out other possible explanations like chance, bias, confounding and reverse causality.

2. causality? There is a need therefore, to look beyond the results of one single study.

Research Strategies

Broadly speaking a study has one of two objectives: description or analysis.

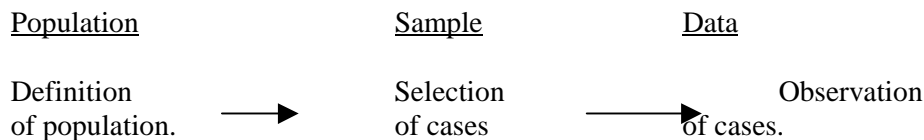
In a *descriptive study* data are assembled and summarized in the form of rate, mean, distribution etc. regarding one or more attributes in a group of subjects. No associations are sought, and no causes are inferred. The focus is on describing a *target population* which has certain geographic, socio-demographic and clinical attributes of interest. Since the entire target population cannot be studied, the investigator must select a sample. The more representative the study sample is of the target population, the more valid will be the sample estimate of the population. The larger the sample size the more reproducible the sample estimate.

In an *analytic study*, one or more groups of subjects are studied for the purpose of drawing inferences about the association between two or more variables, with a view to cause-and-effect association. A sample must usually be selected from the relevant target population. And the more representative the study sample is of the target population, the more valid will be the estimate of the association. The larger the sample the more reproducible the estimate.

There is usually a great deal of overlap between descriptive and analytic studies. A primarily descriptive study may compare and contrast variables between one or more subgroups within the study, and examine association between belonging to the subgroup and variables of interest. Inferences may be drawn about the association in the target population. A primarily analytic study may well begin with a description of the sample population. The important consideration in both descriptive and analytic research is that the research objectives must be clear. These should be stated before the project is designed and data collected. The target population as well as the variables of interest should be defined. Analytical studies are further subdivided into non-experimental (or observational), and experimental.

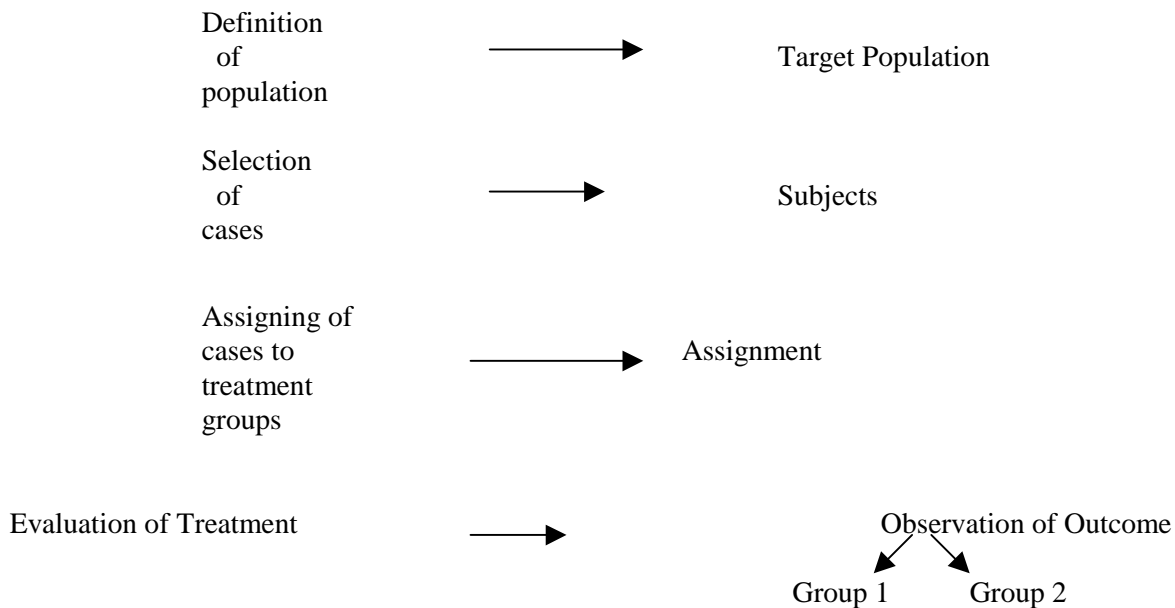
Non-experimental studies.

The three essential steps are : defining the population, selecting the cases to be studied, carrying out the observations and generating the data.



Experimental studies.

These involve defining a population, selecting a sample, assigning individuals to treatment (or non-treatment), carrying out observations, and gathering data.



Ethical considerations.

In all research ethical considerations are paramount. The ethics of research with mothers and children are further discussed in Chapter . At this stage some of the issues to be thought of are the following:

- Who is to benefit from the research?
- Informed Consent.
- Minimizing chances of long term deterioration
- Minimizing pain.

Economic considerations.

The economic considerations relate to recruitment of subjects; availability of equipment; availability of technical expertise; and time. The question of funding research through grants is further discussed in Chapter 18.

Bias in Research Designs

The key word for understanding the concept of bias is "different". The method of selection may turn out to be different for cases and controls. The manner in which information is obtained from different groups could be different, or differently reported, and interpreted. Based on such differences the following forms of bias can occur: selection (also called sample distortion) bias; information bias; confounding bias; and reverse causality bias.

Selection bias occurs when the study sample is unrepresentative of the target population with respect to exposure and/or outcome. Study sample can become distorted either when the subjects are selected or during follow-up. This will introduce error in the resulting estimation of the degree of the association between exposure and outcome in the target population.

Depending on the type of study sample selection can occur by exposure, by outcome or other criteria. Whatever the selection criteria, the sample subjects should be representative of those in the target population. Often this is not easy, because the investigator does not have access to the entire target population.

Studies of different designs are prone to specific types of bias. In case-control studies(case-control studies compare a group of cases who have a condition of interest with controls who do not have the condition, see Chapter 6), bias may be anticipated in the estimation of exposure-outcome association if those in the sample are either more or less likely to be exposed compared to those in the target population.

In cohort studies (cohort studies are follow-up studies in which a defined group is seen at regular intervals and health events are recorded, see Chapter 7), sample distortion can occur because of geographical maldistribution; referral patterns; selective identification of the subjects for the sample; selective response; death, withdrawal or other causes leading to loss in follow-up. If such drop-outs are different with regard to the exposure-outcome relationships compared to those who remain in the study, bias is likely. Since case-control and cross-sectional studies do not have follow-ups, it means that drop-outs due to death, withdrawal, and moving away have already occurred by the time sample is selected. Outcome status is also already determined by the time the study is begun. Any bias has already occurred.

Once the study is completed there is little that can be done to rectify the situation. The only remedy is to estimate the magnitude of the bias, and adjust the inference accordingly. The way to avoid bias is to go for random (or representative) sampling when subjects are being assembled. In cohort studies the best approach is to avoid drop-outs.

Information bias occurs as a result of error in the measurement of exposure or outcome leading to an erroneous estimate of exposure-outcome association.

Each time a measurement is performed on an individual two sources of variation can influence the result. These are biological variation and measurement error. Biological variation is a reflection on the dynamic nature of most biological characteristics, and is the basis of differences between individuals of different age, sex, race or disease condition. In the same individual variation can occur over time e.g. blood urea levels. Such changes over time are due to changes in the body physiology with age. But there are also diurnal variations e.g.

levels of growth hormone in blood. In the latter case the investigator can reduce variability by taking blood samples at a specific time each day.

Measurement error, on the other hand, is the type of error to which every measurement is subject. Measurement errors arise from either the observer or the measuring instrument. Different observers using the same instrument or method can come up with different values. This is called *interobserver variability*. Variations can also occur if different methods or instruments are used. Such errors are called *intermethod variability*. The same observer using the same method or instrument can still come up with varying values when repeated measurements are made. This is called *intramethod or intraobserver variability*.

If measurements have poor reproducibility the results will underestimate the extent of the cause-effect association. If the measurement error occurs not across the whole spectrum but only at certain levels (for example, at the higher or lower ranges of values) the results can lead to a falsely low or a falsely high estimate.

Validity of a measurement is the extent to which it corresponds to the "true" value. Validity is enhanced by minimizing measurement error, and requires both a valid method or instrument and a careful observer. Reproducibility of a measurement is the degree to which the same results are obtained when the measurement is repeated.

Information bias can be minimized by quality control of instruments and techniques, and through training of the observers so that validity and reproducibility of the measurements are maximized. Double-blind techniques (i.e. subjects and observers are unaware of the research hypothesis) also help.

There are three curious phenomena worth bearing in mind with regard to observation and measurement. When a group of individuals with an initial abnormal value of a measurement e.g. blood pressure are measured again the average value usually shows a tendency of reverting to the normal. This is known as *Regression to the Mean*. The second phenomenon is called the *Hawthorne Effect*, and is about individual behavior. Any activity e.g. productivity of factory workers who are being observed tends to show improvement. The third is *Rosenthal Effect*. It also relates to behavior which changes towards what is expected. For example, teachers who have positive expectations of their pupils tend to have classes who do well academically.

Confounding bias. The estimate of the exposure-outcome association is biased because of one or more variables influencing exposure and/or outcome. Confounding leads to deciding that a difference exists when in reality there isn't any, or vice versa.

Confounding can arise in a number of ways as follows:

1. The susceptibility for the outcome may be different in different subjects e.g. fair skin and exposure to sun for development of skin cancer.
2. Study subjects are selective of their exposure, and the motive for selection is related to the outcome.
3. The exposure is associated with other inputs that can influence outcome e.g. greater medical or nursing attention to people receiving a new treatment.

Confounding can be dealt with either by appropriate research design or by controlling for the factor during data analysis. Stratification is the common procedure resorted to during analysis, but multivariate

statistical techniques restriction and matching can all be used. The latter two e.g. restricting the analysis only to subjects with certain attributes or matching of subjects can lead to "waste" of data and carry penalties.

Reverse causality A valid inference about causality requires that exposure preceded the outcome. In cross-sectional studies this is difficult. Cohort studies can protect themselves by ensuring that the subjects were free of the outcome at the time exposure began. Cross-sectional studies can use incident outcome and specifically inquire about prior exposure.

The basic characteristic of a confounder as the above examples illustrate is that it must be associated with the exposure, and independently of the exposure, be a risk factor for the outcome.

Chance, bias and confounding dog every footstep of the researcher. They are considered further in various chapters as each relates to a particular study design. They are also discussed together in Chapter 13. These concepts have been introduced at this early stage to make the reader aware of the main pitfalls of research.

Errors in study designs.

Errors may arise in designing a study, or in the way the actual study takes place. The *research question* may be ambiguous or not correct for the phenomenon of interest. The *operational variables* defined may not be appropriate for the research question; the *measurements* may not be correct for the for the operational variables. The *sample subjects* may be different from the target population, or the subjects who finally get enrolled into the study may be different. All these influence the results (see figure.2.1).

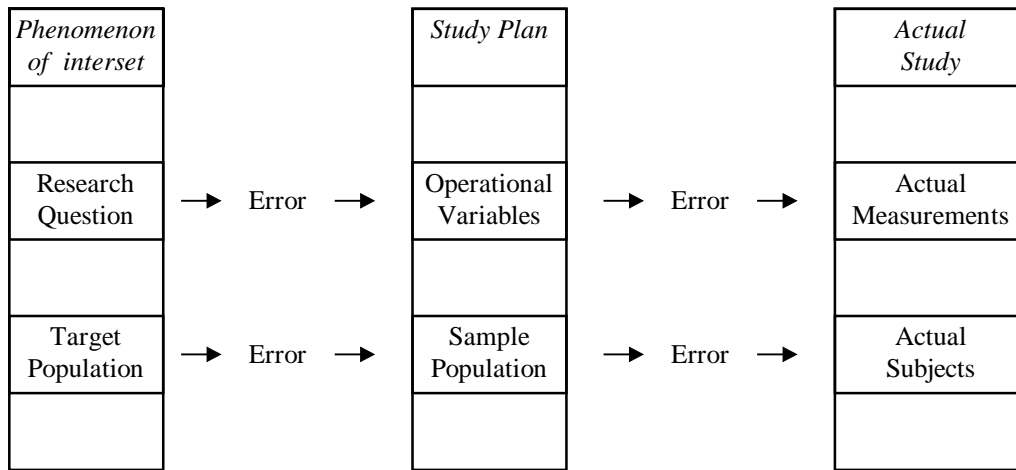


Figure 2.1: Sources of Errors in the Design and Conduct of Studies.

Appendix 2.1

STEPS IN RESEARCH PLANNING

1. Identification of the research problem.

2. Retrieval and critical evaluation of relevant literature for justifying and giving the context of the research problem.

3. Formulation of precise research aims or hypotheses in the light of:
 - the relevant variables selected for study.
 - the appropriate research strategies.
 - the time frame.
 - the ethical restraints necessary to protect subjects.
 - the projected cost

4. In addition research planning takes into account
 - how the sample is to be selected.
 - the design of the investigation
 - how the data is to be collected
 - how the data is to be analyzed.

The above points are written up in the form of a *research protocol*.

Appendix 2.2

A Checklist of issues requiring consideration in planning studies

A. REASONS FOR THE STUDY

This is the most important aspect of study design. The following need attention:

- 1). What are the questions the study is designed to answer?
 Formulation of:
 - long term aims
 - immediate objectives
 - specific hypotheses.

- 2). What is known already.
 - literature review.
 - consult colleagues doing similar research.

- 3). How will the study add to existing knowledge?

- 4). What action might be taken as a result of the study?

B. GENERAL PLAN.

- 1). Detailed definition of aims, objectives and hypotheses. (The more specifically the objectives are stated the easier it becomes to plan the study.)

- 2). Type of study design. (Cross-sectional, case-control, cohort, intervention etc.)
 Discuss suitability of the chosen design with colleagues.

3). Information required.

What items will be measured?

Essential minimum - tolerable maximum.

Variable list, and scales to be used (continuous, categorical, etc.)

How measured? What quality control?

Accuracy, practicability, variations expected, errors.

4). Sample size.

What is the minimum difference to be detected?

What precision is required?

Significance level?

Power required?

5). Data collection

Any "blinding" needed?

Define criteria for "case" and "control", inclusion and exclusion.

6). Data analysis.

What arrangements for inputting, checking and analysis?

What tests would be employed?

C. DETAILED DESIGN.

1). Target Population.

Appropriateness for the study.

Accessibility.

Cooperation.

Stability - especially for follow-up.

2). Sampling

Methods - random/ stratified/cluster. Randomization procedure.

Source - hospital, clinic, community.

Method of selection of cases and controls.

Size

Action in case of refusal or drop-out.

3.) Data Collection.

Design of questionnaire

Instruction to those who would fill questionnaire.

Specification of methods of measurement.

Equipment.

Sources of error and variation (e.g. between interviewers).

Recording of data - forms, charts etc.

How many per day?

Daily collecting and checking of data.

Monitoring of unexpected events (e.g. side effects of drugs in intervention studies).

D. SOURCE OF BIAS.

Selection of participants.

Information variation (non-response; interviewer variation).

Measurement error.

Non- "blind" assessment.

E. HANDLING OF SPECIMENS

When, where, how collected.

Labeling and recording.

Storage and transport.

Processing. - "blind" analysis.

- batch analysis.

F. ANALYSIS.

Data entry, checking and "cleaning".

Analysis.

Format of tables. Mock tables.

G. REPORTING.

What analysis and tables to be included.?

What graphics?