

Formulation of a research project

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India abounds in reportable clinical material of all kinds. There are a huge number of postgraduate students in clinical subjects for whom writing a thesis is obligatory. A fresh resident or researcher with no previous training in research methodology is faced with the task of formulating a research subject. This article is aimed at introducing a new doctor to research methodology in clinical research.

Research in general is a thirst or quest for knowledge through diligent search or investigation or experimentation. It is aimed at discovery and interpretation of new knowledge or at resolving debatable existing knowledge. It involves a systematic body of procedures and techniques for investigations targeted at obtaining new knowledge. It is not a casual observation but systematic and methodical research that remains valued forever.

PRINCIPLES OF RESEARCH

Before discussing the various steps in structuring a research protocol, we would like to say that "honesty" is of the utmost importance in any research. It is not very easy to check wrong data. If research is really a quest for knowledge, then there is no place for fraud. The important purpose of the research is not to prove or disprove, but to improve. This should be always kept in mind.

CONCEPTUALIZATION OF RESEARCH

Conceptualization remains the first step in research and it undoubtedly begins in the inquisitive mind. For the postgraduate student, it should start with the selection of an area of interest in dermatology without which, research will obviously become monotonous and unappealing. The subject

of research or dissertation should be decided after thorough and detailed discussion involving the student, teacher and experts in the proposed area of research.

Before starting any research, the investigator must always ask: Why am I undertaking this investigation? In other words, what is its relevance in relation to the local community, state or the country? How will the outcome of the research change the way one looks at the problem? For example, in the Indian scenario it will not be cost effective to carry out research on say, a subject like solar keratoses, which is rare in Indian skin.

RESEARCH QUESTION

Clinical research is the understanding of challenges in clinical practice. *Staphylococcus aureus* is the causative organism in furuncles. Why does everyone exposed to this organism not get furuncles? This could be accepted as a challenge, *i.e.* there could be a "point of departure" in the patient's profile. The patient's profile in the two groups may be different and this needs to be studied to try to resolve this issue. For the purpose of understanding, the patient's profile could be divided into the 'clinical profile' and the 'non clinical profile'. The clinical profile concerns the illness *e.g.* symptoms, signs, laboratory test results, etc, while the non-clinical profile is related to age, sex, etc. It also includes constitutional, environmental and behavioral characters. Research should evolve around answering the research question with the help of a scientific study design rather than a haphazard and unmethodical attempt to answer the research question.

The conceptualization and formulation of the research question should be pertinent to clinical practice, *i.e.* it should

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be applied research. Hence, the aim of clinical research is to improve the scientific basis of knowledge in practice. Such improvement is conditional on the existing base of knowledge. If earlier studies had been carried out, it involves adding to the existing type of evidence or adding a new type of evidence. In other words, its outcome is expected to confirm or modify existing practice.

Statement of the problem

This should be described clearly, precisely and concisely. This is going to be the basis of designing the project. Define the problem in such a way that a reader can at once grasp the essence of it, e.g., Impetigo contagiosa is a common skin problem in children during the months of June to September in India, which is the monsoon season. The intake of mangoes is very high during this period. It is generally believed that mangoes are responsible for impetigo. The important question here is whether the alleged association between mango intake and the incidence of impetigo is true or false.

Statement of research hypothesis

It translates the statement of the problem into a precise, unambiguous prediction of expected outcomes. In other words, it is a tentative explanation of the relationship between two or more variables. There should not be any haphazard guesses but it should reflect the depth of knowledge (gained from the review of literature), imagination and experience of the researcher. The originality and logic with which hypotheses are formulated are important in any research. A hypothesis can be as simple in form as predicting the relationship between two variables, one independent and one dependent. It could have many variables all of which must be identified. An example of a simple hypothesis is "Health education involving active participation by leprosy patients produces greater treatment compliance in patients than lectures alone". Here the independent variable is the type of health education and the dependent variable is the compliance rate.

Review of literature

A literature search should begin even before any research begins. In fact, the topic of research is selected only after the person has reviewed the literature and found some lacunae in it. At this stage of preparing a protocol, a more extensive and critical review of the existing knowledge about the research problem is essential. One must find out whether or not others have investigated the same or a similar problem. This is important because:

- a) It helps further understanding the problem proposed for the research and may lead to improving on the "statement of the problem".
- b) Study variables can be better understood and their relationship conceptualized.
- c) A research hypothesis can be formulated.
- d) It helps in finding out what others have reported on the issue. Taking this into account will help in designing the research protocol.
- e) One would become familiar with various other methods, which could be used in the research topic. The parameters to be assessed and various end points to be observed during a study can be finalized in the protocol only after one has studied the methods of previous workers in the field.

Sources of literature have improved drastically during the last decade. Computer-based literature searches have made reviews easier and faster. However, statistics obtained at the national or state levels may be needed in some epidemiological researches and these may not be available in Medline or PubMed.

METHODOLOGY OF THE RESEARCH

How should I do a study? This question is undoubtedly on the top of a researcher's mind. The study would be futile and lead to insignificant findings if conducted using incorrect methodology. Conversely, the research question can only be answered satisfactorily if proper study methodology is adopted. Structured methodology has the following components:

1. Stating aims and objectives clearly
2. Selection of proper study design
3. Sample size calculation depending upon the type of a study
4. Deciding inclusion / exclusion criteria
5. Determination of efficacy parameters (in case of interventional studies)
6. Conduct of the study
7. Analysis of the study including statistical analysis

It is of utmost importance to get feedback from seniors, experts in the area of research and a biostatistician on the methodology of the proposed research. Valuable insight and suggestions should be critically looked upon and suitable changes made. The study methodology can be only modified at this stage of conception of the study. Ethical aspects and scientific aspects of study methodology are critically

analyzed by Ethics Committee (EC) and Institutional Review Board (IRB) respectively. Hence, it is mandatory in academic centers in India to submit a study protocol of a dissertation (including study synopsis, case record forms and informed consent documents) to EC and IRB for approval of study methodology.

AIMS AND OBJECTIVES

Objectives are the goals to be achieved by a research project. Goals could be “general” or “specific”:

1. The general objective of the research relates to what is to be accomplished by the project and why? For example, a study to determine whether a new molecule (H1 antagonist) is effective in chronic idiopathic urticaria.
2. The specific objectives are the specific aims of the project in detail. They relate to the specific research questions expected to be answered through the study. For example, in evaluating a new H1 antagonist, a specific objective would be to determine the relative efficacy of the new molecule compared to conventional H1 antagonists in patients with chronic idiopathic urticaria.

SAMPLE SIZE CALCULATION

The number of subjects should be of sufficient size to allow tests of statistical significance to be applied. Otherwise one may realize at the end of a study that the results are not significant and that the research project was futile. There are different formulae to calculate the sample size for estimation of the prevalence and incidence rates, for estimation of quantitative data and for clinical trials. Hence, it is important to involve a biostatistician in the project at the time of designing a protocol. Inadequate sample size often leads to spurious results, which may not be true or ‘significant’.

SELECTION OF A PROPER STUDY DESIGN

Study design is a vehicle to achieve the desired outcomes of the proposed research. Answering your research question is only possible with the selection of proper methods of research. Study design forms the core of research methodology.

The various strategies in applied clinical research are descriptive, analytical, experimental, operational or a combination of all these.

1. Descriptive strategies are generalization of an observation hypothesis and not testing of a hypothesis. These include knowledge-attitude-practice (KAP) studies, a population

survey (e.g. leprosy survey), studies of existing data like case series or surveillance reports. It also includes an epidemiologic description of a disease by person, place and time.

2. Analytical observational studies: These are tests of hypotheses. These include a prospective study (cohort study); retrospective study (case-control study); a historical (or reconstructed) cohort study, when adequate previous records are available; an analytical cross-sectional study and follow-up study. The last one could be either a longitudinal study or a repeated cross-sectional study.
3. Experimental strategies include clinical trials (both therapeutic and prophylactic), field trials and intervention studies.

Operational studies are like a time-motion study. Among the many study designs, most of us are interested in two types of studies:

1. **Observational study:** This is a type of epidemiological research, which depends on the systemic collection of observations on the phenomenon of interest to the researcher in defined populations. Case control studies and cross-sectional studies are predominantly observational studies. These studies are devoid of active intervention and thus of any benefits or risks associated with the intervention. The main idea of conducting such studies is to get clinical or investigational profiles of the patients. In India, such studies have been commonly conducted at institutions since many years. However, such studies are susceptible to various biases and lack precision, but may add useful information to the existing literature.
2. **Interventional study:** The most popular interventional studies amongst researchers are randomized controlled trials (RCT). This forms the largest chunk of research done by the clinical scientist and is currently the “gold standard” study design. These are important as casual observations lead to erroneous conclusions. Chocolate had been incriminated as an exacerbating factor in acne for almost half a century. Clinicians had taken the dietary history of a large number of patients with acne and found that chocolate and fried foods were a common factor in almost all of them. It was very naive to attribute the causation of acne on the basis of observation. They forgot to study a similar group of population (controls) who had no acne, in which case they would have found that young people of the same age without acne also consume a comparable amount of these foods. The wrong inference of an observation has deprived young people of such tasty foods for such a long time.

Apart from study design, the variables to be used in the study

must be identified, properly defined and characterized during the planning stage. Their method of measurement should be clearly indicated.

Also called intervening variables, confounding variables are important as they may influence or “confound” the effect of independent variables on the dependent variable. For example, in a study on the effect of systemic corticosteroids (independent variable) on the vitiligo cure rate (dependent variable), the nutritional status of the patient may play a role (confounding variable).

RANDOMIZATION AND SELECTION OF CONTROLS

Sampling is a process of selecting a sample of representative and manageable size for study. Sampling consists of selection of cases and controls. Random sampling is the standard method of sampling as it offers the following advantages: (1) it eliminates selection bias on the parts of investigators and participants; (2) it tends to create groups that are comparable in all factors that could influence the results, whether these be known or unknown; and (3) it gives validity to statistical analysis of the data.

Selection of controls

We use comparison groups, which increase the validity of one's conclusions. They are drawn from the same population of people or patients, but differ in some respects like exposure to risk factors or use of a therapeutic or prophylactic measure. In experimental studies, the test and the control group should be selected and allocated randomly to each group as far as possible. The following methods may be used in selecting controls and allocating individuals of the study population into study and control groups:

- *Alternation*: This is not commonly used in clinical trials because it is susceptible to bias. Here the patients are assigned to each group by alternation e.g. one to the study group and next to the control group.
- *Before and after controls*: In this, the same individuals are used as their own controls. Some measurement or assessment is made before and after they are subjected to some event such as treatment of H1 antagonist in cases of urticaria.
- *Paired comparison methods*: In studies on topical agents, the best control is the contralateral side, which is similarly affected.

Accurate and matching controls increase the value of the study and can withstand statistical tests more easily than those without controls.

Knowledge of study methodology is central to conducting quality research. A poorly designed study can never be salvaged even after application of a panel of statistical tests. Contrary to this, a study conducted with proper study designs and methodology can always derive some valid inferences leading to ‘fruitful’ research.

If all above mentioned steps are followed systematically, it will be easier for a researcher to formulate a research project. Once the study methodology is clear in the mind of a researcher, it is very easy to conduct the actual research. This will also make research enjoyable and interesting. Again the principle that “Purpose of research is not to prove or disprove, but to improve” should be kept in mind. Ultimately, the fact that observations will be applicable to our patients, directly or indirectly, should never be forgotten.

FURTHER READINGS

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