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Basics of Research Methodology

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ABSTRACT

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Introduction: Research is a planned activity leading to generation of information that will help in answering a specific question. Medicine is said to be inherently experimental. Even the most widely accepted treatments need to be monitored and evaluated to determine whether they are effective for specific patients or for patients in general. This is one of the functions of medical research.[1] Even the best proven prophylactic, diagnostic, and therapeutic methods must continuously be challenged through research for their efficacy, accessibility and quality. Another function is the development of new treatments, especially new investigational drugs, medical devices and surgical techniques. In other words, the purpose of medical research involving human subjects is to improve prophylactic, diagnostic and therapeutic procedures and understanding of the etiology and pathogenesis of disease.

Discussions: The research question, framing the protocol and designing the study and writing the report are all discussed.

Conclusions: Medical research, on the whole, has been very illuminating and has brought benefit to the scientific community, individuals and the society. Considering the major emphasis on methodological aspects, it is expected that the future research would be more efficient, and the benefits would be available to a larger segment of population at lower cost. Protection of rights, safety and wellbeing of trial subjects and credibility of data are two important points to be taken care of throughout the study.

Keywords: Clinical Research, Research Question, Objective, Study Design, Literature Review, Analysis

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INTRODUCTION

Medicine is an amazing science which have many general principles which may be valid most of the time. Every patient is different in the way the disease manifests and also in the response to treatment. An effective treatment for 90% of the population may not work for the other 10%. Thus, medicine is said to be inherently experimental. Even the most widely accepted treatments need to be monitored and evaluated to determine whether they are effective for specific patients or for patients in general. This is one of the functions of medical research.1Even the best proven prophylactic, diagnostic, and therapeutic methods must continuously be challenged through research for their efficacy, accessibility and quality. Another function is the development of new treatments, especially new investigational drugs, medical devices and surgical techniques. In other words, the purpose of medical research involving human subjects is to improve prophylactic, diagnostic and therapeutic procedures and understanding of the etiology and pathogenesis of disease.[2] Almost all doctors make use of the results of medical research in their clinical practice. Even if they do not engage in research themselves, physicians must know how to interpret the results of research and apply them to their patients. Thus, a basic familiarity with research methods is essential for competent medical practice.

Research is a planned activity leading to generation of information that will help in answering a specific question. Conventional research includes descriptive studies and analytical studies. Unconventional research, which is gaining more importance nowadays, includes operational research, evaluation of health systems, economic studies (cost- benefit, cost-effectiveness, etc.), qualitative research, and research synthesis (reviews and meta-analysis).[3] This article will be dealing with basics of conventional research.

STEPS IN MEDICAL RESEARCH

1. Identify the problem

The first step in medical research is to identify a problem area that needs investigation. An alert researcher can easily find a large number of issues around in day to day practice that need investigation. The three aspects which need to be considered before confirming on the problem are:

1. Interest and expertise: the topic should be interesting

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to the investigator, funding agency, and the medical community

2. Relevance and applicability: The research should add new information to the scientific society or expected result is likely to alter clinical decisions in future;
3. Feasibility: should be feasible in terms of time, manpower and money. These three aspects should considerably narrow down the problem area. Then the problem is converted into a specific question, the research question, to which answers are looked for.[4]

2. Formulating a research question

Research question is a formal statement of the goal of the study.[5] It states clearly what the study will investigate or attempt to prove. As mentioned earlier best ideas for research can come up from everyday clinical problems. When an idea comes up, write it down to see if it is worth pursuing. Once you can describe your idea clearly and explain why it is important and how it could be done, it becomes beginnings of a research proposal.

There are several characteristics for a good research question.

1. Foremost among these is whether the question is interesting. It is important that the investigator is genuinely curious about the question being investigated, so that he or she can remain motivated till the successful completion of the study. Curiosity is also an asset in terms of stimulating questions for future studies.
2. Next is feasibility. One could have a very good idea, but it may not be practicable to actually implement. Think about how manageable the scope of the study is, and what resources are available. These include availability of participants or subjects, money and time to conduct the study, and access to technical support and expertise. It is better to ask a narrowly defined question that can be investigated with a reasonable amount of time, money, and effort.
3. The third consideration is the novelty factor, or the potential of the study to contribute something new to the knowledge base. In order to know whether the research question meets this criterion, review the existing research literature to see what work has already been done. The question could also confirm or refute previous findings.
4. Related to novelty is the relevance of the research question. It should add to existing knowledge, guide future studies, or have implications for education, clinical practice or health care policy.
5. Finally, the idea must be ethical. Studies that invade people's privacy or create possible physical or psychological risks are ethically unacceptable. Think about any potential risks that the proposed study could entail for subjects or participants, and also look for the benefits that might accrue. A good research question could thus be described by the acronym FINER: Feasible, Interesting to the investigator, Novel, Ethical and Relevant.[6] We will now consider a question, does treatment with XXX more efficacious in patients with pneumonia?

While the FINER criteria outline the important aspects of the question in general, a useful format to use in the development of a specific research question is the PICO format — consider the population (P) of interest, the intervention (I) being studied, the comparison (C) group (the intervention being compared) and the outcome of interest (O). Often timing (T) is added to PICO, indicating the time frame in which the study will be completed.[7] So the question could be modified as "In patients with pneumonia (P) whether treatment with XXX (I) compared to YYY (C) reduces the number of days of hospital stay (O)".

3. Refining the research question: Literature review

Once the problem or question is specified, the next step is to collect as much related information as possible. Literature review will help to determine to what extent the issue or research question has been previously researched, to identify the past relevant studies as well as methods used, to refine the research question and also to put the project and methodology into a relevant context.[8] This will also add valuable background to the study and would suggest areas requiring further investigation.[9] Conventional sources of literature include text books, subject reviews including monographs and clinics series, print version of journals, yearbooks, Indexes, doctoral dissertations and WHO/Government publications. Discussion with a colleague or an expert can also bring in more information. Various medical databases are now available like Medline (Pub Med), Medical Matrix, MD consult, Cochrane library, NICE guidelines, HINARI etc.

4. Formulate hypotheses and research objectives

The research hypothesis is developed from the research question. For example, in the research studycomparing treatment XXX versus treatment YYY in patients with pneumonia, the experimental group would be treatment XXX and the control/ conventional group would be

treatment YYY. The investigative team would first state a research hypothesis. This could be expressed as a single outcome, e.g., treatment XXX leads to improved functional outcome.

However, when formally testing statistical significance, the hypothesis should be stated as a "null" hypothesis.[10] The null hypothesis is that there is no difference in mean functional outcome between the treatment XXX and treatment YYY. After forming the null hypothesis, there can be an "alternate" hypothesis. The alternate hypothesis would be that there is a difference in mean functional outcome between these two treatments. At the end of the study, the null hypothesis is then tested statistically. If the findings of the study are not statistically significant (i.e., there is no difference in functional outcome between the groups in a statistical sense), we cannot reject the null hypothesis. If the findings were significant, we can reject the null hypothesis and accept the alternate hypothesis (i.e., there is a difference in mean functional outcome between the study groups). In other words, hypothesis testing confirms or refutes the statement that the observed findings did not occur by chance alone but because of a true difference in outcomes between these treatments.[11]

The primary objective should be coupled with the hypothesis of the study. Study objectives define the specific aims of the study and should be clearly stated in the introduction of the research protocol. Ensure that the research question and objectives are answerable, feasible and clinically relevant.[12] There could be secondary objectives also. For intervention studies the objectives could be to find out efficacy, safety, acceptability etc. Here in our example the primary objective could be to find out the Efficacy of treatment XXX in patients with pneumonia, admitted to the hospital.

5. Decide the study population and setting

The definition of the subject of study and the target population should be clearly spelt out. The inclusion and exclusion criteria should be decided in the beginning itself. Sample size is also very important. The smaller the sample, the more will be the uncertainty. Sample size should be chosen in such a way that the finding in the study accurately reflects what is going on in the population.[13] To decide on the appropriate sample size the help of the statistician should be sought for at the beginning itself.

6. Decide on the study design & methodology

To get valid and reliable answer to the questions, appropriate research design and method is a prerequisite. Study design is the frame work in which investigation is planned and carried out. Selection of design is necessarily based on type of research question.[14]

Research designs Broadly research studies can be categorized as observational and experimental. In observational studies the subject is observed without any intervention, whereas in experimental studies the effect of an intervention, for example a new treatment, is observed.[15]

a). Observational: Studies in which subjects are observed- include

- Case study/case series
- Case-Control
- Cross Sectional
- Cohort/Longitudinal

b). Experimental: Studies in which the effect of an intervention is observed

- Controlled trials
- Diagnostic Test

a) Observational studies

Case study / Case series: They describe interesting and unusual cases, single case or a series of cases. Landmark discoveries have been made based on case series. Between October 1980 and May 1981, 5 cases of Pneumocystis carinii pneumonia were reported among previously healthy, homosexual men in Los Ángeles. This pneumonia had previously occurred only in older cancer patients with immune suppression. In early 1981, an unprecedented number of cases of Kaposi's sarcoma were diagnosed in young homosexual men. This malignancy had been seen almost exclusively in the elderly. This suggested that these individuals were actually suffering from previously unknown disease. As a result of these case series the CDC immediately initiated a surveillance program and developed diagnostic criteria for what appeared to be a new disease (AIDS). This program quickly identified that homosexual men were at high risk of developing this disease.

Case control studies: are concerned with what causes disease. Patients with a particular disease are matched with control (patients without disease) and data on past exposure to causative agents are collected by searching the medical records or interviewing subjects. For example to look for association between smoking and lung cancer, patients with lung cancer are enrolled to form the case group, and people without lung cancer are identified as controls. Researchers then look back

in time to ascertain each person's exposure status (smoking history). Investigators compare the frequency of smoking exposure in the case group with that in the control group, and calculate a measure of association. It is essentially a retrospective design.

Cross sectional survey: is one of the common study designs used to measure frequency of disease or risk factor in a defined population at a given time. It could be prospective or retrospective. In longitudinal survey a group of subjects are kept under surveillance over a period of time to measure new cases occurring over that specified duration. In theretrospective study the records of all patients attending the hospital could be reviewed to determine the number of patients for example, with heart failure.

Cohort studies: are observational studies of subjects with specific disease or characteristics who are followed up for a period of time (usually for years) to look for new events or complications. The group may be compared with a control. It is essentially a prospective study lasting for many years. A famous cohort study is the Framingham study of cardiovascular disease: started in 1948, 6000 citizens participated, followed up for 20 years.

b) Experimental studies

Controlled trials: Experimental drug or procedure is compared with another drug or procedure, sometimes a placebo or previously accepted treatment. This could be randomized or not randomized (open). Randomized control trials (RCT), are the best method to assess whether the intervention is effective. They are gold standard of clinical trials. This design is useful to determine efficacy of treatment, evaluation of diagnostic test and to determine cost effectiveness also.

Appropriate research design should be selected according to the research question. The table below illustrates this.[16]

7. Writing the protocol All the efforts put into preceding steps culminates into the draft of the research protocol that incorporates all the information regarding the research in a concise manner. The protocol should contain background information on the study, objectives, ethical aspects, study design, study procedures, method of assessment, statistics and evaluation, administrative issues and references.[17]

Table 1. Selection of research designs

Type of Question	Appropriate Study Design
Burden of illness	
Prevalence	Cross sectional Survey
Incidence	Longitudinal survey
Causation, risk & prognosis	Case control, cohort
Treatment efficacy	Randomized controlled study
Diagnostic test evaluation	Randomized controlled study
Cost effectiveness	Randomized controlled study

Once the protocol is ready, approval from the Ethics committee should be obtained before the start of the study. Along with the protocol, the informed consent form and other documents required by the Ethics committee should also be submitted to Ethics committee for approval. During the conduct of research, if any amendments are made in the protocol or informed consent form that also should be submitted to ethics committee and approval obtained.[18] Details of ethical aspect of research will be dealt with in the second part of this article.

8. Collecting the data Once the protocol is finalized, the data should be collected. The data forms should be legibly filled, and they should be fully completed. Ethical issues must be taken care of from the beginning to the end of study. In drug trials care must be taken to document the details of adverse events if any. Proper documentation through out the study is important to ensure credibility of data.[17]

9. Analyze the data and apply statistical significance The data should be scrutinized for internal consistency and external validity. Data should be analysed using the already decided data management plan.

1**0. Write the report** The report should be sufficiently detailed that can remove any doubt a reader might have about any aspect of the results. It should be properly worded, should be adequately illustrated by charts or diagrams or tables which enhance the clarity. All the limitations need to be described openly.

CONCLUSIONS

Medical research, on the whole, has been very illuminating and has brought benefit to the scientific community, individuals and the society. Considering the major emphasis on methodological aspects, it is expected that the future research would be more efficient, and the benefits would be available to a larger segment of population at lower cost. Protection of rights, safety and wellbeing of trial subjects and credibility of data are two important points to be taken care of throughout the study.[17]

END NOTE

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