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Review Article

Research protocol development: basic concepts for clinicians

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ABSTRACT

The research output from most of the teaching medical institutions of our country is dismal. Medical students and faculties can routinely contribute to the research publication by developing proper instinct and attitude. Research ideas are generated from interesting observations that one comes across during day to day clinical practice. Every research question should be assessed by FINER criteria. Methodical search of existing literature is extremely important. Research hypothesis should be written in PICOT format. Knowledge of biostatistics and collaboration with basic sciences and paraclinical specialties are keys to scientifically correct clinical research protocol development.

Keywords: FINER criteria, PICO, PICOT format, Research question, Research hypothesis

INTRODUCTION

Research is the key to scientific progress. Research in health care settings not only helps in the development of novel facts but also enhances our current understanding of healthcare practices. In the modern era of evidence based medicine, there is persistent need for rigorous assessment of old evidences and critical scrutiny of new facts before making any decision in health care. Any methodical compilation, description, analysis and interpretation of data that can be used to improve the health of people constitute the 'health research'.[1]

According to a recently published study, only 25 (4.3 per cent) medical institutions of our country have published more than 100 papers in a year while the rest 332 medical colleges have not contributed even a single publication in last decade.[2] The health ministry has expressed grave concern over the poor research output from Indian medical institutions and has initiated several measures to promote health research at the grassroots level that includes establishment of multidisciplinary research units in government medical colleges and establishment of model rural health research units in medical colleges.[3]

Lack of infrastructure for conducting research and/or lack of sensitization among the doctors in most institutes can be the probable reasons for low research output. Lack of sensitization can be addressed urgently. Most of the postgraduates and junior faculties find it difficult to write research protocol and need guidance and supervision. This article aims to enhance the knowledge of medical professions enabling them to write research proposals.

GENERATING RESEARCH IDEA

Generation of research idea is of vital importance and requires deep thought and careful considerations. Anything, which is interesting and novel can be worth sharing with rest of the world and may be a research idea. Doctors of a state medical college witnessed disproportionately large number of cases of hemorrhagic

stroke which was an interesting observation and certainly had merit to be shared with rest of the world. Thus, a study was planned to evaluate type, outcome and risk factors of stroke in that region.[4]

The ideas for a research may originate while making clinical decisions during daily rounds. One needs to be inquisitive: "Is there any other way?" "Is this the best way?" "How is it better than others?" "Is there any difference in outcome if I do it another way?"

While managing patients with preeclampsia, measuring and monitoring proteinuria is extremely important. 24 hour urinary protein measurement is Gold standard method for measuring proteinuria. However, it is very cumbersome for the pregnant females to collect urine samples for 24 hour urinary protein and most of the times errors do creep in, due to incomplete collections of urine sample. So, the question arises, "Is there any convenient way for measuring proteinuria in preeclamptic patients?" It was addressed in a research paper that compared alternative method "spot urinary albumin:creatinine ratio" among these patients with the 24 hour urinary protein measurement.[5] Similarly, another study was planned to study the association of spot urine protein:creatinine with the amount of proteinuria in preeclamptic women.[6]

A research question may be generated by giving deep thought to the problem one might be facing during everyday's clinical practice. Influenza A (H1N1) hit the headlines in early 2010. There was a state of panic. Individuals with mild symptoms of upper respiratory tract infection rushed to government hospitals for RT-PCR which was a costly test. A cheaper and reasonably accurate screening test was required to screen large number of the cases of upper respiratory tract infection. Thus, a study was planned to develop a clinical feature-based scoring system for influenza A (H1N1) and to evaluate its efficacy as a screening tool for mass screening.[7]

Detailed and through discussion during the clinical rounds is the most common source of valuable ideas for future research. After identifying a good idea, it is imperative to clearly define the problem and formulate a research question.

LITERATURE SEARCH

Initial and important step in protocol development

The primary challenge in developing an appropriate research question is determining whether the idea conceived can be studied or is worth studying? This entails a comprehensive knowledge about the subject under question. Further enhancement in familiarity with the existing literature will help one to identify the gaps in existing knowledge. Besides, this will help in the planning, implementation and the writing of the research protocol. This can be achieved by systematically searching the literature online, focus group discussion, in-depth interviews, and discussions with the experts in the field.[8-11]

Information sources

It is rather a challenging task to navigate through the jungle of current medical literature. Four information sources (4S) have been suggested by Gray et al.[9]

- Studies: Original research studies such as those retrieved from MEDLINE/ PubMed.
- Syntheses or summaries: e:g Cochrane reviews that provide systematic reviews.
- Synopses: Pre-appraised abstracts published as journals. www.ebmny.org/journal.html
- Systems: e.g. UpToDate (www.uptodate.com), Clinical Evidence (www.clinicalevidence.com) which usually integrate original researches, summaries and synopses. The three search systems which are free, comprehensive and easy to use are Sumsearch, TRIP, Google and Google scholar.

US National library of medicine (NLM) is the largest library in the world that provides information about research, health care, and education. MEDLINE is NLM's bibliographic database available for online searching. It can be accessed through NLM website http://www.nlm.nih.gov. PubMed is the most commonly searched system that provides access to not only MEDLINE but also other citations and PubMed central. PMC provides full texts of more than 100,000 articles from more than130 journals.

After exhaustive literature review of the subject, additional questions may develop. However, it is best to establish a single primary research question which would form the basis of hypothesis and study objectives.

FORMULATING THE RESEARCH QUESTION "FINER CRITERIA" AND "PICOT FORMAT"

A good research question should be feasible, interesting, novel, ethical and relevant (as suggested by Hulley) commonly known by the acronym FINER.[10] F stands for Feasible i.e. there should be adequate sample size, adequate resources available in terms of time, staff with expertise and funds, appropriate study design manageable in scope. I stands for Interesting i.e. the research question arouse excitement among the researcher, colleagues and scientific community. N-Novel i.e. the research should contribute new information which may confirm, refute or extend the previous findings. E-Ethical i.e. the research should follow ethical guidelines so that it can get approval from Institutional Review Board. R-Relevant i.e. the research should have the potential to advance scientific knowledge, help in clinical decision making, affect the health policy and invoke future research.

While the FINER criteria sketch out the important attributes of the question, the PICOT format clearly describes the components of the research question given in Table 1.[11,12]

Table 1: PICOT format.

P	**Patient/population/problem i.e. population of patients with the problem understudy**
I	Intervention of interest i.e. new treatment or new diagnostic test to be considered.
C	Control/comparison/comparator group i.e. the main alternative to the intervention.
O	Outcome of interest i.e. health consequence of the intervention.
T	Time i.e. time period over which an outcome is to be measured.

Well defined research question formulated through the PICOT approach helps in making decisions about the study design and population to be studied and setting desired outcomes.

Hence, the original research idea "Is there any faster way for measuring proteinuria in preeclamptic patients?" can be rewritten as research question as "Can spot urine protein:creatinine ratio (I) be used as an alternative to 24 hours urine protein (C) for the diagnosis and severity of preeclampsia (O) in pregnant women (P)."

GENERATING A RESEARCH HYPOTHESIS FROM RESEARCH QUESTION

After defining a sound research question, scientifically correct research hypothesis should be generated. This is essential as it will avoid any spurious positive associations through chance alone. Basically, research hypothesis is a testable statement which will be tested by various research design and biostatistical methods. The importance of hypothesis testing lies in the fact that it helps in making a correct inference about the population of interest based on the random sample taken from that population.

Research hypothesis begins with an assumption that it is not true called 'null hypothesis'. At the end of the study, the null hypothesis is tested statistically using appropriate statistical tests. If the findings are not statistically significant, null hypothesis cannot be rejected. Hence, hypothesis testing confirms or refutes the statement that any observed finding did not occur by chance alone. Hence, for the research question "Can spot urine protein:creatinine ratio (I) be used as an alternative to 24 hours urine protein (C) for the diagnosis and severity of preeclampsia (O) in pregnant women (P)", the research hypothesis will be "Spot urine protein:creatinine ratio (I) can be used as an alternative to 24 hours urine protein (C) for the diagnosis and severity of preeclampsia (O) in pregnant women (P)."

DEVELOPMENT OF RESEARCH OBJECTIVE

Research objectives are the specific aims of the study. Usually it is an active statement about how the study will answer the specific research question. Outlining of research objective is imperative for development of protocol and design of study, calculation of sample size and determining the power of study. It is important to develop clear and well defined primary objectives. Secondary objectives if needed may also be mentioned.

So, for the above research hypothesis, the research objective will be

- To study whether spot urine protein creatinine ratio correlates with 24 hours urinary protein in patients of preeclampsia
- To study whether spot urine protein creatinine ratio can be used to predict the severity of preeclampsia.

METHODOLOGY FOR RESEARCH

Planning for the methodology of the research is a vital step that provides all the information about research design, research participants, sample size, any interventions, ethical issues and type of statistical analysis to be done. The methodology should be sound and feasible and should convince the research committee that it will definitely answer the research question.

In order to answer a research question, the researcher has to select the most appropriate study design. The choice of study design whether descriptive, analytical, experimental or a combination of these will ultimately depend on the study objective. A biostatistician must be consulted while planning to address various issues related to methodology in the very beginning.

Ideally the entire target population should be studied. However, it is not possible due to large numbers, cost and time. Hence only a subset of population that is representative of the population is studied and the conclusions of the study are drawn on to the target population. Inclusion criteria and exclusion criteria should be outlined. The type of sampling procedure selected to ensure the representativeness and reliability should be clearly mentioned. A correct sampling procedure increases both the internal and external validity of the research results. Furthermore, control or comparison groups must also be defined for all analytical or experimental studies to increase the validity of conclusion.

Calculation of sample size

Although sample size can be calculated easily with the help of computer statistical programs, the concept behind it is very simple. A level of probability or uncertainty is decided beforehand by the researcher. Most studies usually set the level of statistical significance at 0.05 i.e.

accepting a chance of 5% of finding an association when it is actually not there. It is also necessary to provide the statistician an estimate of the frequency of the condition under study for calculation of sample size. Other factors like attrition and loss to follow up should also be taken care of. A very large size increases the cost and duration of study while a small size may not have enough power.

Selection of statistical test

Various commercial statistical software package SPSS or SAS have made statistical work quite easy. However, the advice and help of professional biostatisticians should be taken for large studies since the beginning. The researcher should also familiarize himself with the different types of data to be analyzed and the various statistical terms in order to understand the research and correctly pursue it. The simplest statistical test is t-test for nominal data and chi square test for categorical data.

COLLABORATION WITH OTHER SPECIALITIES

Good research requires collaboration with basic sciences and paraclinical specialties. Medical biostatistics expert should be consulted right in the planning stage. Experts from physiology, pathology, microbiology and biochemistry departments may be extremely helpful in finding answer of many dilemmas of clinical practice. Medical education, Medical Humanities, skills like Communication skills, evaluation methods are some areas that have yet not been extensively explored. Good Communication skills among doctors are extremely useful for clinicians and can be studied.[13] Similarly, Medical humanities and its incorporation in medical curriculum is very relevant and can be also be studied by clinicians.[14]

CONCLUSION

The most important aspect of any successful research process is extensive planning and a systematic approach. The transformation of a clinical problem to a research question requires a thorough knowledge about the subject of interest. This not only helps to outline the research objective but also give the investigator an idea about the study design, the sample size and the methodology. The PICOT format, the most widely recommended strategy for formulation of research question may be extremely beneficial for novice investigators. Communication of the research conducted methodically to the scientific community through publications should be considered to be the final step of research process as it has the potential to empower and motivate new investigators.

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