Introduction to Clinical Research Methods

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Clinical research either directly involves a particular person or group of people or uses materials from humans such their behavior or samples of their tissue. It can involve epidemiological and behavioral research, health services research and patient-oriented research like drug trials or accuracies of diagnostic tests. It is a series of steps that lead from question to answer. There is an organized structure by which we formulate questions, develop methods to gather information and answer clinical problems. The purpose of organizing the structure is to allow studies to be repeated and validated by other researchers. There are several research designs, and the choice should be influenced by the main objective of the research. The methodology is the manner of collection of data that will give confidence in the results and conclusion. This requires identifying all sources of bias and uncertainty, and developing a method that can minimize them. Actual data collection can be obtained by inspecting the records, by conducting interview or physical examination or laboratory/ imaging investigations, or by a combination of these data-eliciting methods. Lastly, the final report should be concise but contain all the details in relation to the objective of the research. The format of the written report depends on the methodology and the requirement of the journal where it is intended to be published.

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Introduction

The National Institutes of Health (NIH) defined clinical research as research that either directly involves a particular person or group of people or uses materials from humans such their behavior or samples of their tissue. It can involve epidemiological and behavioral research, health services research and patient-oriented research like drug trials or accuracies of diagnostic tests.[1] There are evolving concepts in research i.e., translational and outcomes research. Translational research is translating the results of basic research, in-vitro studies and animal studies into research conducted to humans to improve health care. While outcomes research is the use of real-world data from large databases and determine effective health interventions that can be adopted by the health community.[2] The next concept is similar to translation research and involve the adoption of clinical research results into standard practices in the health community i.e., clinical practice guidelines.

The goal of clinical research is to improve health, and the purpose is to learn how systems in human body work, why we get sick, and how to get back to health and stay fit. It is a systematic process to better determine etiology, pathophysiology, diagnosis, therapy and prognosis. Research is the very foundation of improved medical care. It can also provide evidence for policies and decisions on health development.

Steps in Conducting Clinical Research

Clinical research is a series of steps that lead from question to answer (and then usually to more questions). There is an organized structure by which we formulate questions, develop methods to gather information and answer clinical problems. The purpose of organizing the structure is to allow studies to be repeated and validated by other researchers.

Step 1 – Establish the Clinical Problem

Research projects usually start out as a vague perception of some problem, either real or imagined. Research ideas come from everyday experiences, talking with colleagues, and reading books and journals. This vague notion must be converted into a concise question statement, usually only one or two sentences in length. Once you have key research questions, relate their relevance and applicability for improving health in one way or the other. A good research question is backed up by theoretical considerations and biological explanation. An important strategy to establish this is by conducting a thorough search of medical literature.[3] The objective is to identify the specific information gaps. This can be found as recommendations for further research by the authors.

After a thorough review and analysis of gaps in the literature, refine your research question.

Step 2 – Evaluate the Research Project with "FINEST"

FINEST stands for Feasibility, Interesting, Novel, Ethical, Significant and Time bound. Feasibility depends on your knowledge and skills on the topic and on the basic methods of conducting research. Feasibility also depends on available facilities, resources or funding. Interesting must be viewed from the researcher or intended reader. Novel means the research must contribute new information on the topic. This can be achieved if the research problem was developed with an adequate review of literature. Ethical means the research respects the subject's privacy, autonomy and does not put the put them at unnecessary risk. Significant research usually contributes information that may impact medical care. Time bound means that the research project should be finished within a reasonable time.

Step 3 - Formulate the Objective

The objectives must match with the perceived utility of the results. The objectives should be consistent with meaningful decisions taken in actual practice. In formulating the objectives, be guided by SMART which stands for Specific, Measurable, Attainable, Relevant and Time bound. Clearly identify the specific aspect of the observation to concentrate on. It must be measurable and attainable within a specific time period. They must be relevant to medical care and not focus on trivial issues that can be answered without research.

Step 4 - Determine the Right Study Design and Methodology

The design should be influenced by the main objective of the research. If the objective is to prove effectiveness of intervention, then an experimental design is warranted. If the main objective is to study prevalence or risk factors for development of disease, an observational study design is appropriate. The methodology is the manner of collection of data that will give confidence in the results and conclusion. This requires identifying all sources of bias and uncertainty, and developing a method that can minimize them. The researcher must consider either prospective or retrospective data collection, appropriate process of sampling, accurate measurements and collection of data, statistical analysis, etc.

Step 5 – Write the Protocol

The preceding steps lead to writing the research protocol. Different institutions have different formats. It should be detailed and serves as a set of instructions for investigators and other personnel involved in the research. The protocol is also the basis for evaluation by supervisors, review boards and funding agencies.

Step 6 – Collect the Data

Data collection tools for medical research are of two types. First is the questionnaire and data collection form that is uniformly followed throughout the investigation. Second are the measurement and investigation tools such as a laboratory test. There is always a need to pretest these tools for their performance in actual research condition. Often the tool must be revised as problems occur during pre-test. Problems can be missing data, inaccurate data, or wrong response. Similarly, a pilot study, which is a small forerunner of the actual investigation, also provides useful inputs regarding changes required in the measurements to be taken, in the interview or examination method, in the laboratory or imaging investigations, in the recording system, etc. During actual data collection which can be obtained by inspecting the records, by conducting interview or physical examination or laboratory/imaging investigations, or by a combination of these data-eliciting methods, always watch out for unanticipated problem. Anticipate such nonresponse and keep it at the minimal level to avoid bias in the results. Make all efforts to extract at least the basic information that can help in adjusting for any bias.

Step 7 – Analyze the Data

Analysis of data is an umbrella term that incorporates a number of steps. First is by tabulating the data in a manner that all the information on one subject constitutes one record i.e., spreadsheet. In an Excel format, this really means that there is only one row of data for each subject. Second is exploring the data for their pattern. Then summarize the data using descriptive statistics. The next step is grinding the data through the process of statistical analysis. Finally, you must interpret the findings and form your conclusions. Whereas statistical analysis is mostly computer-based, interpretation of the results requires critical thinking. The results must be analyzed based on the context of the research problem, and there is a plausible explanation for the results. The results may also be subjected to analysis of uncertainty and limitation.

Step 8 - Write the Report

The final report should be concise but contain all the details in relation to the objective of the research. The format of the written report depends on the methodology and the requirement of the journal where it is intended to be published. In terms of format, refer to the Consolidated Standard for Reporting Trials (CONSORT) for clinical trials or Standard for Reporting Observational Studies (STROBE) for observational studies.[4-5]

Step 9 – Disseminate the Report

There is no point in doing all the work of a study if you do not communicate and disseminate your findings to your colleagues. Dissemination to the intended audience through publication in peer-reviewed journal or presentation during conference could be the most fruitful step in a research project.

Study Designs

Case Report/Case Series

A clinical case report is a written account of the course of treatment and associated outcomes for an individual subject, client, or patient. It

has been helpful in the identification of adverse and beneficial effects, the recognition of new diseases, unusual forms of common diseases and the presentation of rare diseases. But not all cases warrant a case report. Only the interesting ones that might result to improvement in health care.[6]

Cross-sectional Study

Systematic collection of data that describe the health situation in certain population at a given point in time. It is used to study prevalence of diseases, knowledge, attitudes and practices and validation of diagnostic tests. It is also used to explore correlation and association of variables like risk factors and health outcomes prior establishing a cause-and-effect relationship with case-control or cohort study.[6]

Case-control Study

This study design establishes the cause-and-effect relation between risk factors and health outcomes. The selection of subjects in this design starts with those who have the health outcome and those without. It is retrospective if data collection will be obtained from existing records and prospective if data collection will be from actual patients with or without the health outcome.[6]

Cohort Study

This study design establishes the cause-and-effect relation between risk factors and health outcomes. The selection of subjects in this design starts with those who have the risk factor and those without. It is retrospective if data collection will be obtained from existing records and prospective if data collection will be from actual patients with the risk factor or without.[6]

Clinical Trials

Clinical trials are interventional studies that examine the effect of treatment on a particular patient. Treatment can be a drug or non-drug intervention. It can be single arm, randomized or non-randomized parallel groups.[7]

Community Trials

Community health trials are research studies conducted to evaluate the effectiveness of interventions aimed at improving health outcomes at the community level. These trials often focus on public health initiatives, preventive measures, and health promotion strategies, and they involve a collaborative approach that engages community members and local stakeholders. These trials can inform policies and practices that enhance health outcomes and reduce health disparities.

Qualitative Studies

Qualitative research is a type of research that explores and provides deeper insights into real-world problems. Instead of collecting numerical data, it gathers the subject's experiences, perceptions, and behavior. It answers the how and why instead of how many or how much. Data gathering is usually asking open-ended questions. But it can also be mixed methods that combine qualitative and quantitative data. The strength of qualitative research is its ability to explain processes and patterns of human behavior that can be difficult to quantify. Experiences, attitudes, and behaviors can be captured quantitatively, but cannot explain how, why or what they were thinking, feeling, and experiencing.[8]

Defining the Study Population

The choice of an appropriate research design and sampling of subjects or units for observations are two links in the logical chain of the research process. When defining the population of interest and deciding how to choose a sample appropriate to the research problem, there are key points that the researcher needs to understand. First is the target population from which the cases to which research results (observations or conclusions) are intended to be applied or generalized. But the target population is not easily accessible. Only a certain number of the target population is available to the researcher. This is the accessible population which needs to be defined in terms of inclusion and exclusion criteria. From this accessible population, the researcher will get the sample or study population, from whom observation and data collection will be conducted. If a sample is representative of the population from which it is drawn, then measurements from the sample can be generalized to the target population. On the other hand, poor sampling methods can cause sample bias, and the sample will not represent the population.

The following points and recommendations apply to selecting samples for a research study. First, populations are defined by the researcher and should be clearly specified. Second, populations need not necessarily be large but enough in number for a more valid result. And third, the accessible population from which a sample is drawn should be clearly described in the inclusion and exclusion criteria, since the accessible population determines the target population. Be aware that a narrowly defined accessible population limits the ability to generalize results to a defined target population. This happens if the researcher developed so many detailed inclusion and exclusion criteria.

Data Collection

One of the most important considerations for clinical studies is the method used for data collection. There must be a plan for how and by whom the data will be collected and recorded. Test results should be entered into the record or database as soon as possible. All entries should be made and should be as legible and complete as possible and keep your records in a secure location.

Data collection can be by interview, survey or observation. A data collection form usually has demographic information of the subject and measurement for the main study variables. If interview or observation, the data collector must be trained so measurements and observation will be standardized. A questionnaire can be self-administered, or interviewer administered.

Data collection is easier on specially made forms especially when others will be collecting the data. The best way to make forms is to use a spreadsheet or database program to design a form that can be printed on paper. The spread sheet or database program can also be used for data entry. Basic computer skills may be necessary for this. At minimum, you need to know how to use word-processing and spreadsheet software and preferably, how to use statistical and database software. You need to know the basics of how to store data in files and how to make backup files. In addition, many journals are now accepting electronic submissions of abstracts and papers emphasizing the need for basic computer skills.

Another area of information technology is the use of personal digital assistants like tablets or smartphones. These little handheld computers can be used to collect data much more conveniently than paper forms. The data collected can readily be shared or uploaded to the main database computer where data analysis will be done.

Data Analysis

Statistical analysis of the numbers generated by observation and measurement is usually one of the most challenging steps in medical research. It can be simple descriptive statistics, which include frequency distributions of sex of individual or different diseases, measures of central tendency (mean, median, and mode) like age or blood pressure patients and its measures of variability (variance, standard deviation, and coefficient of variation), and various correlation coefficients. It can also be inferential statistics, which is the application of the theory of probability to descriptive data and allow us to test hypotheses. We can obtain the probability of getting the observed results by random chance and decide whether the treatment made a difference. Inferential statistics include parametric statistics (those based on specific distributions such as the normal and t-distributions) and non-parametric tests (those that do not assume the data are distributed in any particular fashion).

Writing and Publication

Any research project that is important enough to require careful thought in design, and sustained effort in data gathering, merits a written report at its conclusion. Always start with the major outline of the paper. Never just start writing off the top of your head. The International Committee of Medical Journal Editors and other journals recommend a standard manuscript that contains major parts, i.e., title, abstract, background or introduction, methods, results, discussion, conclusion and references.[9] Some may request brief sections on acknowledgement and appendices. Use these major sections as your initial general outline. Sometimes it is easier to start with the results because that is what is most fresh in your mind after data analysis. Then write an interesting and informative introduction, making sure you include the research objectives. This section should be written in relation to the results. Then write the discussion and conclusions. As you are writing these sections, keep in mind the updated references you're citing. Next fill in the methods, making sure that they correspond with the results. The methods can be converting the written research protocol into past tense. Finally, write the abstract. Share it to your co-authors, leave the manuscript alone for a week or two. Then proofread the manuscript and make corrections. Lastly, share it with your colleagues and mentors who will be better able to read it from an external perspective and ask for comments and suggestions.

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