Class Room

Study Design - A Pragmatic approach

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Abstract

Research, in simpler terms, refers to a quest for knowledge. It can also be defined as a search for pertinent information on any given topic, in a scientific and systematic way. Clinical research broadly falls into two categories based on the assignment of exposures by the investigator – experimental and observational. Experimental trials can be further subdivided into randomized and non-randomized trials; observational studies can be analytical or descriptive. The main feature of an analytical study is the presence of a comparison (control) group. Also, cohort studies, a part of analytical studies, are useful in following up of a study from the time of exposure to outcome. On the contrary, case control studies work in retrospect, i.e from outcome to exposure. Other studies like cross-sectional studies measure both the exposure and outcome at any given point and descriptive studies like case reports have no control group.

Key Words: Study design, Observational study, Experimental study, Case control, Cross sectional, Cohort.

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Introduction

Research can be defined as a systematic investigation of any particular question to help derive new conclusions and thereby establish new facts. It involves the discovery of new knowledge and the interpretation and revision of current knowledge. The process involves asking questions thereby collating and integrating current knowledge on the topic and then designing a method to collect information for the research question; and finally deriving new conclusions from the evidence.

In an epidemiological research, the primary step is defining the hypothesis that is to be tested. This includes a clear-cut definition of the exposure(s) and outcome(s) that are under study. The next step is to decide the appropriate study design for the particular study hypothesis. This article emphasize on the various types of study designs and its implications, in order to help the beginners have a brief knowledge before getting into research work.

Study Design

Usually, the design of a study holds more significance than the analysis derived out of it. In that, a poorly designed study may never be retrieved while a poorly analyzed study always has hope for reanalysis. Therefore, it is of vital importance to give utmost consideration to the design of the study as that will govern the analysis of the data. In most of the medical studies, there are 2 main parameters - input and output. An input is an intervention or exposure to a potentially toxic compound and an output is the measure of health that is supposed to be affected by the intervention. Studies are to be categorized with reference to the time sequence in which both the parameters are studied. Clinical research has two large kingdoms: experimental and observational research. This is based on a simple question, whether the investigator assigned the exposure (e.g., treatments) or the investigator has just observed the usual clinical practice. Hence the study design can be classified as in figure 1.

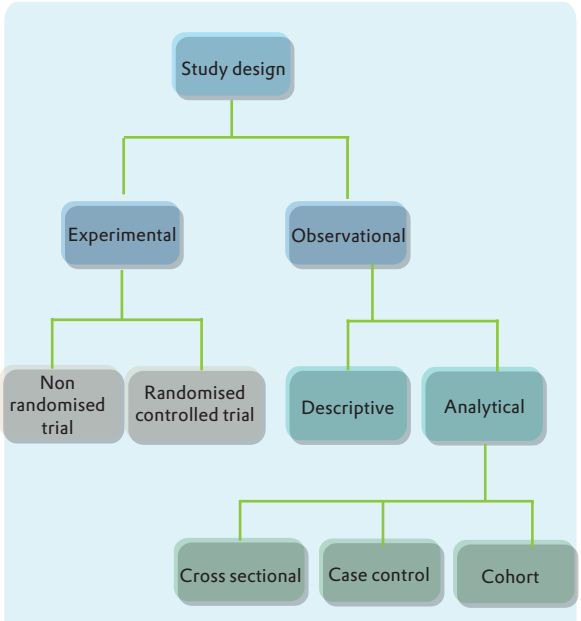

Fig 1: Classification of types of clinical Research

Experimental Study

Experimental study is the one in which an intervention is made by the investigator during the study to find the outcome of the intervention. For example, a litter of rats may be divided into two groups- intervention and control group. The rats for the intervention group are randomly selected and exposed to a supposed carcinogenic agent. After exposure, the frequency of cancer development is recorded in each group. Clinical trials of experimental nature can be further divided into randomized and non-randomized clinical trials.

Non randomized controlled trials: These are study designs in which the participants are assigned to the intervention in a non-random manner. In these trials the alternatives are defined and managed by the investigator.

Randomized controlled trial: This study design though simple, is one of the most powerful tool of research. In a randomized controlled trial the participants are randomly selected and subjected to the clinical intervention[1]. Usually, the term 'intervention' refers to treatment, but it can also be used in a broader sense so as to include any clinical management that is offered to study its effect on the health of the participants. As the name suggests, in a randomized clinical trial, the participants are subjected to the intervention in a purely random manner, or as the popular phrase goes 'by the play of chance'[2]. The likelihood of bias in determining the outcome is reduced in this type of study design. It also precludes selection bias when implemented well. A uniform diagnostic criteria is often featured in clinical trials, and further blinding of the study helps reduce the information bias. This study design is unique as it eliminates confounding bias, whether known or unknown and also is bound to be statistically efficient. Randomized controlled trials are particularly useful for examining low to moderate effects, if properly designed and implemented as they are likely to be free of bias.

Observational Study

The objective of this study is to illustrate the cause-and-effect relationships wherein controlled experimentation cannot be performed[3]. Observational study can also be referred to as natural experiments or quasi experiments. Though different terminologies are used, the theme shared among them is common wherein the strengths of an experiment are reproduced as much as possible, in the earlier stages of designing itself. Based on the presence or absence of a comparison group an observational study can be sub-classified into analytical and descriptive studies.

Descriptive Study

Descriptive studies form the bottom of the research hierarchy, and do not involve a comparison group. This study essentially describes the frequency, natural history and possible determinants of a disease[4-6]. The results of such a study explain the frequency of people developing the disease over time along with the characteristics of the disease and the people affected by it and finally, hypotheses are generated to determine the cause. More rigorous research can then be conducted on these hypotheses through analytical studies and randomized controlled trials. An example of descriptive studies is case report/series.

Analytical studies are those in which a comparison or control group is involved. In such a study, it is imperative to identify the temporal direction of the trial, which can be any one of the following :-

- If both the exposure and outcome are determined at any one point, it is a cross-sectional study.
- If the study begins with an exposure followed by observation for a few years to determine the outcome it becomes a cohort study.
- If the study begins with an outcome and the exposure is identified in retrospect, it is a case-control study.

Cross sectional Study

This study is done in order to examine the presence or absence of a disease and an exposure at a particular time, thereby focusing on prevalence and not incidence. A drawback of this study is that the temporal relation between the outcome and exposure might be unclear as both are ascertained at the same time. A cross-sectional study is also called a frequency survey or a prevalence study[7].

Cohort Study

Cohort studies begin from exposure and proceed to outcome and are therefore easier to understand than case-control studies. Here, two groups are identified- one with an exposure of interest and another without. These groups are then followed up in time to determine the outcome. If a higher incidence of outcome is developed by the exposed group than the unexposed then it would be inferred that increased risk of outcome is due to exposure. The advantage of a cohort study is that it is possible to calculate true incidence rates, the relative risks as well as associated attributable risks[2]. However, this research design may not be suitable for study of rare event(s) that take years to develop, as the yield of results will be slow and therefore highly expensive.

Case control Study

As mentioned earlier, case control studies work retrospectively, starting with outcome and then identifying the exposures that could have resulted in the outcome. As this tangent of thought is not intuitive for all clinicians, it is widely misunderstood. This study too involves two groups – outcome group and control group. Through means of chart reviews and interviews, the prevalence(or amount) of exposure to a risk factor is assessed. If the prevalence is higher among the outcome group than the control, then exposure is associated with an increased risk of outcome. Unlike cohort studies, a case control study is especially suitable for rare outcomes or diseases that take a longer time to develop like cardiovascular disease and cancer. Also, they require lesser time and effort and not as expensive

as cohort studies[2]. However before beginning the study it is imperative to keep in mind that the criteria or characteristics of both the groups(outcome & control) are similar except for the outcome in question. Many studies have been ruined due to inappropriate control groups. Additionally, if the studies rely on memory, then recall bias (better recollection of exposures among the cases than among the controls) would be high. A major drawback a case control study is that incidence rates, relative risks or attributable risks cannot be calculated as the study lacks denominators[2].

Conclusion

The core importance of a research work is to know what type of study design needs to be implemented, along with the practical feasibility, required information, estimated duration of the study and the total cost. Each study design has its own limitations and strengths. Choosing a proper study design to carry out legitimate research work is a critical step and is a paramount of importance. A good study design will acknowledge all parameters that spell the success of the study without any bias.

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Rhythm and diet to keep the bowel quiet

Circadian rhythm coded by circadian clock genes imposes a 24 hour cycle (including sleep) in all animals. This rhythm gets disrupted in various professionals (doctors, nurses, other shift workers etc.) and travellers (jet lag). Do such disruptions affect health? In a new controlled experimental study published in PLOS ONE (Circadian Disorganization Alters Intestinal Microbiota. PLoS ONE, 2014; 9 (5): e97500 DOI:10.1371/journal.pone.0097500), the investigators disrupted the circadian rhythm in a group of mice and fed them with a diet rich in fat and sugars. This resulted in altered intestinal microbiota with a significant increase in pro-inflammatory organisms. Disruption of circadian rhythm alone was insufficient. It required the assistance of a second environmental insult (in this case, high fat/sugar diet) to produce the effect. This may play a role in the pathogenesis of inflammatory bowel disease and colonic cancer. Including prebiotics or probiotics in the diet and maintaining a fairly good schedule might help to avert these diseases.

- Dr. K. Ramesh Rao