INVITED ARTICLE

Understanding Research Study Designs

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Abstract

In this article, we will look at the important features of various types of research study designs used commonly in biomedical research.

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We use a variety of research study designs in biomedical research. In this article, the main features of each of these designs are summarized.

Terms Used in Research Designs

Exposure vs Outcome

Exposure refers to any factor that may be associated with the outcome of interest. It is also called the predictor variable or independent variable or risk factor. Outcome refers to the variable that is studied to assess the impact of the exposure on the population. It is also known as the predicted variable or the dependent variable. For example, in a study looking at nerve damage after organophosphate (OPC) poisoning, the exposure would be OPC and the outcome would be nerve damage.

Longitudinal vs Transversal Studies

In longitudinal studies, participants are followed over time to determine the association between exposure and outcome (or outcome and exposure). On the other hand, in transversal studies, observations about exposure and outcome are made at a single point in time.

Forward vs Backward Directed Studies

In forward-directed studies, the direction of enquiry moves from exposure to outcome. In backward-directed studies, the line of enquiry starts with outcome and then determines exposure.

Prospective vs Retrospective Studies

In prospective studies, the outcome has not occurred at the time of initiation of the study. The researcher determines exposure and follows participants into the future to assess outcomes. In retrospective studies, the outcome of interest has already occurred when the study commences.

Classification of Study Designs

Broadly, study designs can be classified as descriptive or analytical (inferential) studies.

Descriptive Studies

Descriptive studies describe the characteristics of interest in the study population (also referred to as sample, to differentiate it from the entire population in the universe). These studies do not have a comparison group. The simplest type of descriptive study is the case report. In a case report, the researcher describes his/her experience with symptoms, signs, diagnosis, or treatment of a patient. Sometimes, a group of patients having a similar experience may be grouped to form a case series.

Case reports and case series form the lowest level of evidence in biomedical research and, as such, are considered hypothesis-generating studies. However, they are easy to write and may be a good starting point for the budding researcher. The recognition of some important associations in the field of medicine—such as that of thalidomide with phocomelia and Kaposi's sarcoma with HIV infection—resulted from case reports and case series. The reader can look up several published case reports and case series related to complications after OPC poisoning.[1,2]

Analytical (Inferential) Studies

Analytical or inferential studies try to prove a hypothesis and establish an association between an exposure and an outcome. These studies usually have a comparator group. Analytical studies are further classified as observational or interventional studies.

In observational studies, there is no intervention by the researcher. The researcher merely observes outcomes in different groups of participants who, for natural reasons, have or have not been exposed to a particular risk factor. Examples of observational studies include cross-sectional, case–control, and cohort studies.

Cross-sectional Studies

These are transversal studies where data are collected from the study population at a single point in time. Exposure and outcome are determined simultaneously. Cross-sectional studies are easy to conduct, involve no follow-up, and need limited resources. They offer useful information on prevalence of health conditions and possible associations between risk factors and outcomes. However, there are two major limitations of cross-sectional studies. First, it may not be possible to establish a clear cause–benefit relationship.

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For example, in a study of association between colon cancer and dietary fiber intake, it may be difficult to establish whether the low fiber intake preceded the symptoms of colon cancer or whether the symptoms of colon cancer resulted in a change in dietary fiber intake. Another important limitation of cross-sectional studies is survival bias. For example, in a study looking at alcohol intake vs mortality due to chronic liver disease, among the participants with the highest alcohol intake, several may have died of liver disease; this will not be picked up by the study and will give biased results. An example of a cross-sectional study is a survey on nurses' knowledge and practices of initial management of acute poisoning.[3]

Case–control Studies

Case–control studies are backward-directed studies. Here, the direction of enquiry begins with the outcome and then proceeds to exposure. Case–control studies are always retrospective, i.e., the outcome of interest has occurred when the study begins. The researcher identifies participants who have developed the outcome of interest (cases) and chooses matching participants who do not have the outcome (controls). Matching is done based on factors that are likely to influence the exposure or outcome (e.g., age, gender, socioeconomic status). The researcher then proceeds to determine exposure in cases and controls. If cases have a higher incidence of exposure than controls, it suggests an association between exposure and outcome. Case–control studies are relatively quick to conduct, need limited resources, and are useful when the outcome is rare. They also allow the researcher to study multiple exposures for a particular outcome. However, they have several limitations. First, matching of cases with controls may not be easy since many unknown confounders may affect exposure and outcome. Second, there may be biased in the way the history of exposure is determined in cases vs controls; one way to overcome this is to have a blinded assessor determining the exposure using a standard technique (e.g., a standardized questionnaire). However, despite this, it has been shown that cases are far more likely than controls to recall history of exposure—the "recall bias." For example, mothers of babies born with congenital anomalies may provide a more detailed history of drugs ingested during their pregnancy than those with normal babies. Also, since case-control studies do not begin with a population at risk, it is not possible to determine the true risk of outcome. Instead, one can only calculate the odds of association between exposure and outcome.

Kendrick and colleagues designed a case–control study to look at the association between domestic poison prevention practices and medically attended poisoning in children. They identified children presenting with unintentional poisoning at home (cases with the outcome), matched them with community participants (controls without the outcome), and then elicited data from parents and caregivers on home safety practices (exposure).[4]

Cohort Studies

Cohort studies resemble clinical trials except that the exposure is naturally determined instead of being decided by the investigator. Here, the direction of enquiry begins with the exposure and then proceeds to outcome. The researcher begins with a group of individuals who are free of outcome at baseline; of these, some have the exposure (study cohort) while others do not (control group). The groups are followed up over a period of time to determine occurrence of outcome. Cohort studies may be prospective (involving a period of follow-up after the start of the study) or retrospective (e.g., using medical records or registry data). Cohort studies are considered the strongest among the observational study designs. They provide proof of temporal relationship (exposure occurred before outcome), allow determination of risk, and permit multiple outcomes to be studied for a single exposure. However, they are expensive to conduct and time-consuming, there may be several losses to follow-up, and they are not suitable for studying rare outcomes. Also, there may be unknown confounders other than the exposure affecting the occurrence of the outcome.

Jayasinghe conducted a cohort study to look at the effect of acute organophosphorus poisoning on nerve function. They recruited 70 patients with OPC poisoning (exposed group) and 70 matched controls without history of pesticide exposure (unexposed controls). Participants were followed up or 6 weeks for neurophysiological assessments to determine nerve damage (outcome). Hung carried out a retrospective cohort study using a nationwide research database to look at the long-term effects of OPC poisoning on cardiovascular disease. From the database, he identified an OPC-exposed cohort and an unexposed control cohort (matched for gender and age) from several years back and then examined later records to look at the development of cardiovascular diseases in both groups.[5]

Interventional Studies

In interventional studies (also known as experimental studies or clinical trials), the researcher deliberately allots participants to receive one of several interventions; of these, some may be experimental while others may be controls (either standard of care or placebo). Allotment of participants to a particular treatment arm is carried out through the process of randomization, which ensures that every participant has a similar chance of being in any of the arms, eliminating bias in selection. There are several other aspects crucial to the validity of the results of a clinical trial such as allocation concealment, blinding, choice of control, and statistical analysis plan. These will be discussed in a separate article.

The randomized controlled clinical trial is considered the gold standard for evaluating the efficacy of a treatment. Randomization leads to equal distribution of known and unknown confounders between treatment arms; therefore, we can be reasonably certain that any difference in outcome is a treatment effect and not due to other factors. The temporal sequence of cause and effect is established. It is possible to determine risk of the outcome in each treatment arm accurately. However, randomized controlled trials have their limitations and may not be possible in every situation. For example, it is unethical to randomize participants to an intervention that is likely to cause harm —e.g., smoking. In such cases, well-designed observational studies are the only option. Also, these trials are expensive to conduct and resource-intensive.

In a randomized controlled trial, Li et al. randomly allocated patients of paraquat poisoning to receive either conventional therapy (control group) or continuous veno-venous hemofiltration (intervention). Patients were followed up to look for mortality or other adverse events (outcome).[6]

Summary

Researchers need to understand the features of different study designs, with their advantages and limitations so that the most appropriate design can be chosen for a particular research question. The Centre for Evidence Based Medicine offers an useful tool to determine the type of research design used in a particular study.[7]

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