

OVERVIEW OF STUDY DESIGNS

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ABSTRACT

Study design is the procedure under which a study is carried out. "The rules that govern the process of collecting and arranging the data for analysis are called research designs". Study designs could be either descriptive or analytical. In observational study design, the researcher observes and does not intervene, whereas in analytical study, some kind of intervention is done. Descriptive observational study designs are useful for only generating hypothesis, whereas analytical observational study designs are helpful for both generating and testing hypothesis. Each type of study design represents a different way of collecting information. Each has its own advantages and disadvantages. Depending on various factors such as the type of research question, time available for study, resources available for the study, quality of data from various sources, earlier studies, feasibility, statistical and regulatory issues, the investigator has to choose the appropriate study design which will answer his particular research question. This article gives a brief overview of the various study designs commonly used in research except experimental designs.

Keywords: Study design, Descriptive, Analytical, Case-control, Cohort

INTRODUCTION

Epidemiology is the study of the distribution and determinants of disease frequency in human populations and the application of this study to control health problems [1, 2]. The term study includes both surveillance, whose purpose is to monitor aspects of disease occurrence and spread that are pertinent to effective control [3] and epidemiologic research, whose goal is to harvest valid and precise information about the causes, preventions, and treatments for disease.

Study design is the procedure under which a study is carried out. Each type of study design simply represents a different way of obtaining information. In other words "The rules that govern the process of collecting and arranging the data for analysis are called research designs"[4].

Overall, the study design tree can be divided into two broad categories of descriptive and analytical studies [5]. An overview of these study designs is shown in Figure 1.

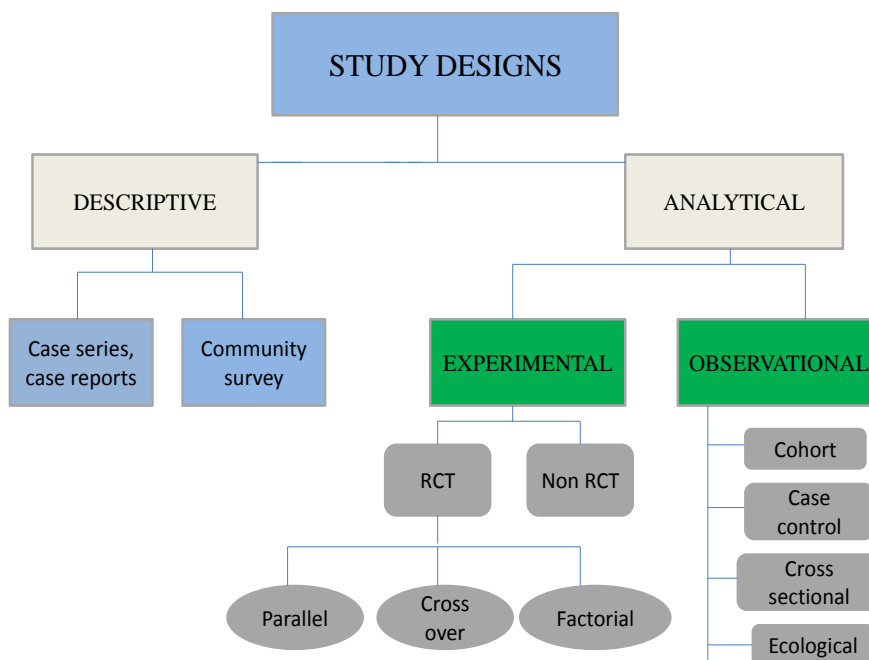


Fig. 1: Basic study designs [5].

RCT = Randomized control trials

Some investigators also include integrative studies as a type of study design which includes Meta-Analysis. Decision Analysis, cost effective analysis.

Evidence-based medicine classifies different types of studies on the basis of research design as the criterion for hierarchical

rankings [6]. Randomized control trials (RCTs), systematic reviews and meta-analysis of RCTs are at the top of the pyramid, while anecdotal evidence is at the bottom [7] as shown in Figure 2. However, the evidence pyramid does not provide the disclaimers that all study designs are not possible to conduct to answer all research questions.

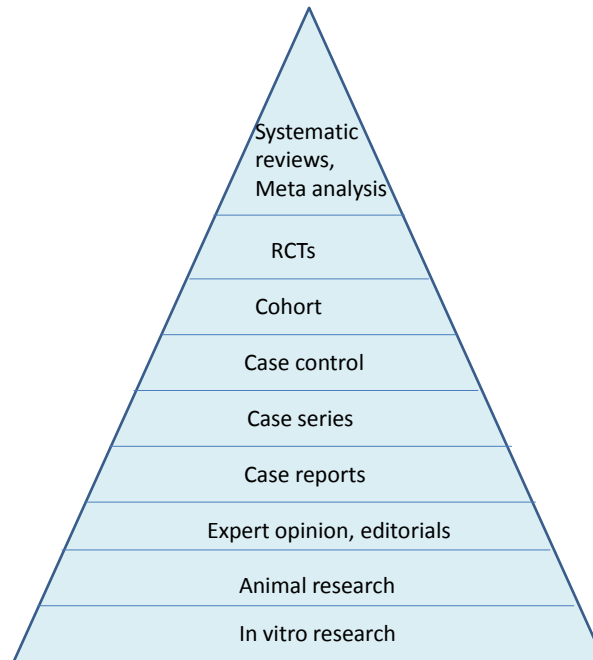


Fig. 2: Hierarchy of evidence pyramid [6].

Another way of classifying the hierarchy of strength of evidence for treatment decisions is based on level of evidence [8].

Levels of Evidence

Level I: N of 1 randomized trial (double-blinded, cross-over)

Level I (A): Systematic reviews of randomized trials

Level I (B): Single randomized trial

Level II (A): Systematic review of observational studies addressing patient-important outcome

Level II (B): Single observational study addressing important outcome

Level III: Physiologic studies

Level IV: Unsystematic clinical observations (case-reports, anecdotal)

Choosing an established design gives you a huge head start in design, analysis and eliminating bias.

Choice of a study design to depends on:

- What is the research question
- Time available for study
- Resources available for the study
- Common or rare disease
- Type of outcome of interest
- Quality of data from various sources
- Medical, statistical and regulatory issues
- Earlier studies, feasibility

Descriptive epidemiology

This is the first foray into research. These studies describe the frequency, natural history and determinants of a factor or disease. It is a study to identify patterns or trends in a situation, but not the cause and effect linkages among its different elements.

Descriptive studies examine differences in disease rates among populations in relation to age, sex, race, and differences in temporal or environmental conditions. Descriptive study designs are helpful in generating a hypothesis [9].

These studies

- Seek to measure the frequency in which diseases occur or collect descriptive data on possible causal factors
- Describe occurrence of outcome
- Used to organize and summarize data according to time, place, and person.
- Describe natural history of disease
- Extent of public health problem
- Identify populations at greatest risk
- Allocation of health care resources
- Suggest hypothesis about causation
- Often used for generating hypotheses for further research.

Generally speaking, these studies can only identify patterns or trends in disease occurrence over a period of time or in different geographical locations but cannot ascertain the causal agent or degree of exposure.

Case Reports

These studies deal with presentation of a single case or handful of cases in detail. They are most likely to be useful when the disease is uncommon.

Generally report a new or an unique finding

- e.g. previous undescribed disease
- e.g. unexpected link between diseases
- e.g. unexpected new therapeutic effect
- e.g. adverse events

Example of a case report

Initial report of five cases of pneumocystis pneumonia in previously healthy, homosexual men. MMWR 1981; 30:250-2.

Case Series

A case series is a descriptive study that occurs in a group of patients who have a similar diagnosis or who are undergoing the same treatment over a certain period of time. Generally report on new or a unique condition. An outline of case report/series is shown in Figure 3.

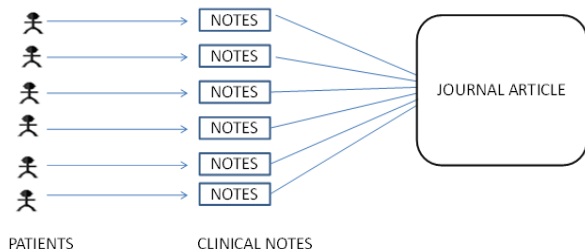


Fig. 3: Outline of a case report/series [10].

Advantages of a case report/series

- Provides first sign to identify a new disease or adverse effect
- Useful for hypothesis generation
- Characterizes averages for disorder
- Provides information for very rare disease with few established risk factors

Disadvantages

- Cannot study the relationship between cause and effect
- Cannot assess disease frequency
- Minor relevance to public health
- Usually small sample size

Example of a case series

Creech JL, Jr, Johnson MN. Angiosarcoma of liver in the manufacture of polyvinyl chloride. J Occup Med. 1974 Mar;16(3):150-151

Community survey (Surveillance or descriptive cross sectional study)

Descriptive cross-sectional (survey based) are conducted to estimate the frequency and distribution of a disease. In this study, information is collected on several individuals at one point in time about their health status, behavior, or other risk factors. Surveillance can be either active or passive.

Passive surveillance relies on data generally gathered through traditional channels, such as death certificates. By contrast, active surveillance searches for cases. Epidemiological surveillance has made important contributions to health, but none more impressive than smallpox eradication. Surveillance and containment were responsible for the elimination of smallpox from the world, an extraordinary public-health achievement [11].

Analytic epidemiology

These studies attempt to specify in more detail the causes of a particular disease.

They

- describe association between exposure and outcome and causation
- Provides a control group (baseline)
- Test hypotheses about determinants

Analytical studies are classified into two main categories of observational and experimental designs.

In experimental studies, researchers make a decision on the assignment of exposure or intervention, while in observational studies exposure is not assigned by the researcher [12].

In observational studies, a specific population is observed versus assigned and the information is collected on outcomes according to exposure. That is, unlike experimental study designs, the investigator does not control the assignment of exposure and is only involved passively in collecting data on exposure followed by outcomes assessments.

Cross-sectional studies

A cross-sectional study "examines the relationship between diseases (or other health-related characteristics) and other variables of interest as they exist in a defined population at one particular time"[13]. Cross-Sectional Studies measure existing disease and current exposure levels. They provide some indication of the relationship between the disease and exposure or non-exposure. Cross-sectional studies are fairly common in occupational settings using data from pre employment physical examinations and company health insurance plans [14]. A diagrammatic representation is depicted in Figure 4.

Examples of Cross-sectional studies

1) Hedley AA, Ogden CL, Johnson CL, Carroll MD, Curtin LR, Flegal KM. Prevalence of overweight and obesity among US children, adolescents, and adults, 1999-2002. JAMA 2004;291:2847-50.

2) Prevalence of renovascular disease in the elderly. J Vasc Surg 2002;36:443-451.

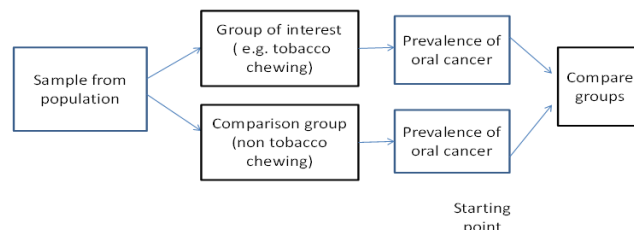


Fig. 4: Outline of cross sectional study [15].

Advantages

- Good design for hypothesis generation
- Estimation overall and specific disease prevalence can be done
- Can estimate exposure proportions in the population
- Good design to study multiple exposures or multiple outcomes or diseases
- Easy, quick and inexpensive
- No ethical issues
- Usually used as first step for new study issue.

Disadvantages

- Not a useful for establishing causal relationships
- Hard to decide when disease was actually acquired
- Weakest observational design, (it measures prevalence, not incidence of disease).
- The temporal sequence of exposure and effect may be difficult or impossible to determine
- Rare and Quickly emerging diseases a problem, Confounding is difficult to control
- Susceptible to selection bias (e.g. selective survival) and misclassification (e.g. recall)

Case-control studies

Case-control study is a method of sampling a population in which researchers identify and enroll cases of disease and a sample of the source population that gave rise to the cases. Case-Control Studies identify existing disease/s and look back in previous years to identify previous exposures to causal factors [16].

- Cases are those who have a disease.
- Controls are those without a disease.

In a retrospective case-control study, the assessment of the exposure or risk factor occurs after subjects are classified as cases or controls. In a prospective case-control study, all measurements of the exposure or risk factor variables are recorded before subjects are classified as cases or controls. A diagrammatic representation of a case control study is shown in Figure 5.

Examples:

1) Case-control studies of aspirin and Reye's syndrome

2) Herbst AL, Ulfelder H, Poskaner DC. Adenocarcinoma of the vagina: Association of maternal stilbesterol therapy with tumor appearance in young women. N Engl J Med 1974;284:878-881.

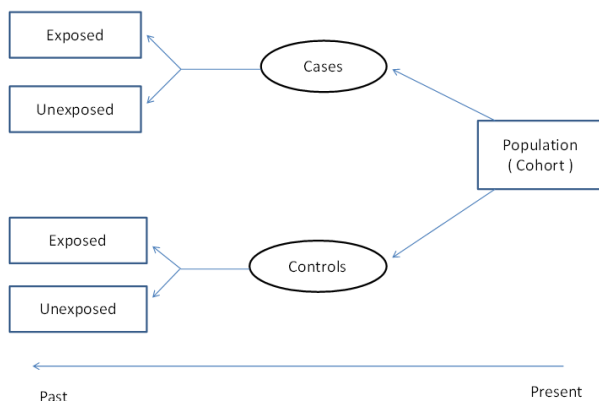


Fig. 5: Case control study [15].

Advantages

- Best design for rare diseases
- Can be completed quickly since events of interest have already occurred
- Various potential exposures can be studied at the same time
- Best suited for hospital-based studies and outbreaks
- Less expensive and time consuming
- Small sample size
- If assumptions are met, valid estimates of relative risk

Disadvantages

- Problems with temporal sequence of data
- May miss diseases which are in latent period
- Can't calculate incidence, population relative risk or attributable risk
- Can only study one outcome and have a high potential to bias
- Disease status can influence selection of subjects

Cohort Studies

A cohort is defined as a group of people with a common characteristic or experience.

In a prospective cohort study, subjects are grouped on the basis of past or current exposure and are followed up for a fixed period of

time or till the disease occurs. When the study commences, the outcomes have not yet developed and the investigator must wait for them to occur. In a retrospective cohort study, both the exposures and outcomes have already occurred when the study begins. Because high rates of follow-up are critical to the success of a cohort study, investigators have developed many methods to maximize retention and trace study participants [17].

For prospective cohort studies, strategies include collection of information (such as name and date of birth) that helps locate participants as the study progresses. In addition, regular contact is recommended for participants in prospective studies. These contacts might involve requests for up-to-date outcome information or newsletters describing the study's progress and findings [18]. A schematic diagram of prospective cohort study and retrospective cohort study is shown in Figure 6 and 7 respectively.

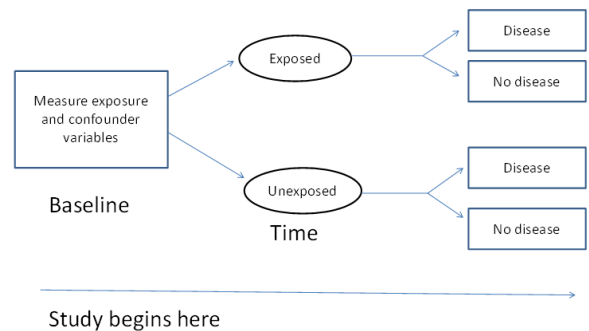


Fig. 6: Prospective Cohort study [15].

Examples of prospective cohort study:

1) Framingham Heart Study

2) Doll R, Hill AB. The mortality of doctors in relation to their smoking habits: A preliminary report. Br Med J 1954;228:1451-1455.

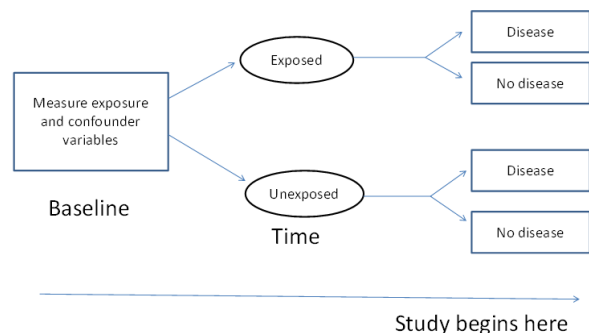


Fig. 7: Retrospective Cohort study [15].

Examples of retrospective cohort study:

1) Predictors of hospitalization and death among pre-dialysis patients. Nephrol Dial Transplant (2000) 15:650-658

2) Liddell FDK. The development of cohort studies in epidemiology: a review. J Clin Epidemiol 1988; 41(12):1217-1237.

Advantages of Cohort Studies

- Can be the best assessment of exposure and study of rare exposures
- One of the best design if exposure needs to be measured directly
- Only way to get prospective information for fatal diseases
- Describes the natural history of disease
- Can examine multiple outcomes linked to exposure
- Can estimate both overall and specific disease rates

- No recall and selection bias, more conclusive results than case-control studies

Disadvantages of Cohort Studies

- Impractical for rare diseases
- May not be statistically significant
- Larger sample size than case-control, very expensive
- Long time commitment for follow-up

Ecologic Studies (Co relational studies)

A classical ecologic study examines the rates of disease in relation to a factor described on a population level. Thus, "the units of analysis are populations or groups of people rather than individuals"[19].

Ecologic studies that identify groups by time often compare disease rates over time in geographically defined populations. For example, investigators conducted an ecologic study to compare HIV seroprevalence changes over time among injecting drug users in cities with and without needle-exchange programs [20]. The geographical information system (GIS) is a very useful new tool that improves the ability of ecologic studies to be able to determine a link between health data and a source of environmental exposure.

For example, if we study the frequency of a characteristic (e.g. cigarette smoking) and some outcome of interest (e.g. lung cancer) occurring in the same geographic location (e.g. a city, state or a country). These studies can be used for generating hypotheses but not to draw causal conclusions because we do not have information as to whether people who smoke cigarettes are the same people who developed lung cancer. Advantages include low cost, wide range of exposure levels, and the ability to examine contextual effects on health. Limitation is lack of information on important variables.

SUMMARY

In this paper, we primarily focus on the descriptive and analytical studies excluding experimental designs. Epidemiologists use both experimental and observational study designs to answer research questions. While RCTs provide most accurate answers to questions related to efficacy of competing interventions, they are not suited to answer research questions related to prognosis or diagnostic accuracy issues. Therefore, investigators are encouraged to choose an appropriate study design to match the research question. For this a thorough understanding of the research question is necessary in order to select the best study design. Choosing an appropriate study design to address a research question is the first important and a very critical step to obtain valid results. For hypothesis generation, observational, descriptive studies are generally used whereas for generation as well as hypothesis testing, analytic studies like case-control, cohort studies are commonly employed.

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