Chapter 31 – Research Study Design

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ABSTRACT

Types of epidemiological studies are either observational or experimental.

The choice of study design depends on the available sample (i.e., frequencies of exposures and outcomes), the populations available for study, and the hypothesis or study question being addressed. Each study design has strengths and weaknesses and should be carefully matched to the type of data collected and the desired information. Various study designs exist, including experimental, quasi-experimental, descriptive, observational, and others that will be discussed in this chapter. The critical evaluation of published research, including the type of study design, is necessary to appropriately assign value to the conclusions of the authors of a paper.

KEY CONCEPTS

- Descriptive studies
- Analytical studies
- Case-control studies
- Cohort studies
- Experimental studies
- Community trials

BACKGROUND

Epidemiological studies are either observational or experimental. In observational studies, which may be descriptive or analytical, exposures or risk factors are not influenced by study design. In contrast, in experimental studies, certain factors or treatments that may influence the disease process or outcome are controlled as part of the study design. Both types of epidemiological studies can be used to investigate the relationship between an outcome (infection, disease progression, or death) and one or more factors (exposures or treatment).
BASIC PRINCIPLES

The choice of study design should depend on the frequencies of exposures and outcomes, the populations available for study, and the available data or participants. Each approach to study design has distinct advantages as well as limitations.1–9 (See Table 31-1.)

EPIDEMIOLOGICAL STUDIES

Descriptive Studies

The simplest observational studies describe in simple terms, such as the number of occurrences of an outcome, perhaps broken down according to time, person, and place, and can include case reports and case series as data sources. An example of an observational study is describing the characteristics and infection outcomes of 100 consecutive patients who undergo a specific procedure. Such studies provide detailed descriptions of persons with a given condition or exposure; descriptive studies do not include a control group for comparison. Descriptive studies may be useful for generating rates, identifying populations at risk, or formulating hypotheses about the cause of a given outcome. However, observational studies cannot be used to directly test hypotheses of causality.

Analytical Studies

Analytical studies, including cross-sectional, case-control, and cohort studies, compare individuals with and without an outcome by the presence of one or more hypothesized risk factors.

Cross-Sectional Studies

Cross-sectional studies take a snapshot of a sample population that may include the studied outcome and the potential risk factors. For example, a researcher interested in studying the relationship between catheters and urinary tract infections (UTIs) could assess the number of patients currently in the hospital with UTIs and determine if there are more patients with catheters than without catheters. Because outcomes (both old and new) are measured, incidence rates cannot be determined in cross-sectional studies. However, a series of cross-sectional studies can be used to estimate prevalence trends. Because risk factor and outcome data are determined simultaneously, a temporal sequence of cause and effect cannot be assessed. However, cross-sectional studies may be conducted quickly and inexpensively.
### Table 31-1. Comparisons of Epidemiological Study Designs

<table>
<thead>
<tr>
<th>Study Type</th>
<th>Other Names</th>
<th>Basic Design</th>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Descriptive</td>
<td>Case report</td>
<td>Description of one or small number of cases by person, place, and time</td>
<td>Quick; easy; may be useful to formulate hypotheses and identify potentially important populations</td>
<td>No controls for comparison, and risk factors cannot be estimated</td>
</tr>
<tr>
<td></td>
<td>Case series</td>
<td>Description of a defined number of cases by person, place, and time</td>
<td>As case report, except rates may be estimated</td>
<td>As case report</td>
</tr>
<tr>
<td>Analytical cross-sectional</td>
<td>Prevalence, correlational, or survey</td>
<td>Outcome and potential risk factors are assessed in a population at one point in time</td>
<td>Quick; easier, and cheaper than cohort studies; useful to describe extent of exposure or incidence; cohort or case-control studies can investigate changes in prevalence</td>
<td>Incidence cannot be determined; temporal sequence of exposure and outcome cannot be determined; risk of selection bias</td>
</tr>
<tr>
<td>Case-control</td>
<td>Case-referent, comparison</td>
<td>Population of individuals with and without the outcome are identified, then compared for exposures to one or more potential risk factors</td>
<td>Quick; easier, and cheaper than cohort study, especially if outcome is rare or has long latency period; useful in studying multiple possible risk factors for an outcome; smaller case size is needed than for a cohort study</td>
<td>Measures exposure rate, not exposure-specific incidence; risk exposure may be unavailable or difficult to assess, subject to recall bias; or inaccuracy, or biased by knowledge of outcome; selection of proper controls may be difficult</td>
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<tr>
<td>Cohort</td>
<td>Prospective, longitudinal</td>
<td>Population of individuals with and without exposure to potential risk factors are identified and followed to compare the incidence of the outcome in each group</td>
<td>Exposure-specific incidence of outcome can be measured directly; usually less bias in patient selection and determining exposure in case-control studies; useful in studying outcomes with short latency period; multiple possible outcomes from exposure to a potential risk factor; provides stronger evidence for a direct causal association than do prevalence or case-control studies</td>
<td>Longer, more expensive to conduct, especially if outcome has a long latency period following exposure; if outcome event is rare, a large study size is needed; outcome determination may be biased, and individuals may be lost to follow-up</td>
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<tr>
<td>Experimental clinical trials</td>
<td>Controlled trial, randomized clinical trial (RCT)</td>
<td>Investigator assigns interventions to an experimental (or placebo) group and to a control (or placebo or standard) group (randomized allocation is the best method); experimental and control groups should be treated similarly in all respects, except for the intervention, and are followed to compare the incidence of the outcome in each group</td>
<td>Randomization minimizes bias; double-blinding minimizes bias in determining outcomes; randomized clinical trial provides better evidence for a direct causal association than do other study designs and is the best design to use to establish efficacy of treatment or intervention</td>
<td>More expensive, difficult to conduct; artificial; only a select subgroup of individuals are included, which limits generalization to other groups; randomization does not guarantee similar comparison groups; if historical controls are used, they are subject to selection bias, and findings may be interpreted with caution</td>
</tr>
<tr>
<td>Community trials</td>
<td>Investigator assigns interventions to experimental (or at least treated) communities and to control (or placebo or standard) communities; experimental and control groups should be treated similarly in all respects, except for the intervention, and are followed to compare the incidence of the outcome in each group</td>
<td>More appropriate than clinical trial when the intervention cannot be implemented easily on an individual basis</td>
<td>Large, expensive to conduct; difficult to determine, if communities are similar in other respects.</td>
<td></td>
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</table>
Case-Control Studies

Case-control studies begin with the identification of persons who have the outcome of interest. Then a control group of individuals without the outcome is selected for comparison. For example, in a study to determine risk factors for healthcare-associated bacteremia, patients with bacteremia are identified and compared with a control group of hospitalized patients without bacteremia; medical records are reviewed to determine exposures to various factors, such as intravenous devices, invasive monitoring devices, prior infections, and immunocompetence.

Case-control studies may be undertaken in a timelier and less-expensive manner than prospective cohort studies because cases may be identified retrospectively, and at least some exposure data are often available through medical record review. Case-control studies are particularly well suited for studying relatively rare outcomes or outcomes that develop over a long time after exposure. Because determination of exposure is usually made retrospectively, bias can result from difficulty in recalling exposures or from the incompleteness and inaccuracy of medical records and other data sources. Sometimes the desired measure of exposure is unavailable, and surrogate measures must be substituted. The selection of an appropriate control group is critical in that control patients must not only have the outcome of interest but also should be similar to the cases in the potential for exposure during the period of risk being evaluated.

Cohort Studies

Cohort studies assess individuals with and without exposure to a potential risk factor who did not have the outcome of interest at study enrollment. The incidence of the outcome is determined in each group defined by exposure during follow-up observation. For example, a study is undertaken to follow a population of hospitalized patients with and without exposure to invasive devices to determine the association of device exposure and nosocomial infections.

Cohort studies are usually conducted prospectively, although if past exposure data are available for a population in whom current outcomes can be determined, a cohort study can be conducted retrospectively. Cohort studies may provide more compelling evidence for causal association than do case-control studies because the exposure occurrence is established before the outcome occurs, and exposure-specific incidence of the outcome can be measured directly. Also, prospectively designed cohort studies may be less susceptible to sources of bias in patient selection and exposure determination than retrospective cohort and case-control studies.

Compared with other analytical study designs, prospective cohort studies are better suited for assessment of outcomes with a short latency period after exposure. As the latency period increases, retention of study participants becomes more difficult. When the outcome event is rare, it may not be practical to recruit a cohort of sufficiently large study sample size. Because of the careful effort required to ensure high rates of even short-term follow-up, cohort studies tend to be more expensive to conduct than case-control studies.
Experimental Studies

Experimental studies are prospective studies designed to compare outcomes in individuals who are assigned to an experimental (intervention) or control (placebo or standard care) group. The intervention may be a procedure, drug, or other treatment, and the comparison group usually receives a placebo, the previously accepted treatment, or, if appropriate, no treatment. The two major types of experimental studies are randomized clinical and community trials. Uncontrolled trials, in which an intervention is given and patients are followed for the development of outcomes with no comparison group, are not considered clinical trials and are more appropriately classified as case series.

Randomized Clinical Trials

In randomized clinical trials (RCTs) the participants are randomly assigned to treatment or control groups to ensure that the allocation is unbiased. The Consolidated Standards of Reporting Trials (CONSORT) group has established standards for the conduct and reporting of RCTs. Studies that use historical controls instead of concurrent randomized controls are subject to biases in patient selection and should be interpreted cautiously.

During the follow-up period, experimental and control groups are treated the same in all other respects. On completion of follow-up observations, the groups are compared for the incidence of the outcome of interest. To avoid bias in classifying the outcome, the clinical trial ideally should also be double-blinded (i.e., neither the trial participants nor the investigators know the assigned treatment). For example, patients undergoing specific surgical procedures are assigned to receive antibiotic prophylaxis or a placebo. The identities of the antibiotic and the placebo are masked from the participants, investigators, and the persons administering the drug. Patients are followed, and infection rates are compared.

The RCT design minimizes bias and provides the best evidence for direct causal relationships between the experimental factor and the outcome. However, RCT studies are technically demanding, expensive, and usually conducted on a select subgroup of patients according to established selection or exclusion criteria. Because the study group may not represent the full spectrum of individuals for whom the intervention may be intended, care must be taken in generalizing to other broader groups.

Community Trials

Community trials use community-level or treatment facility rather than individual-level interventions. Community trials are appropriate when the impact can be anticipated at the population level. For example, treatment of bacterial sexually transmitted infections has been hypothesized to prevent transmission/acquisition of human immunodeficiency virus (HIV) infection. Community-level randomized trials have been undertaken in Rakai and Mwanza to test this hypothesis. Although community-based randomized trials are complex and expensive to conduct, they may provide the most compelling evidence for population-based efficiency of an intervention.
Evaluating Published Studies

The critical evaluation of published research is necessary to appropriately assign value to the conclusions of the authors of any given paper. Understanding the basic structure of typical published research papers is an initial step in the critical review process. Papers typically include an abstract and introduction, material and methods, results, and discussion sections, as well as tables/figures and references.

The abstract is a brief summary of the purposes of the study, methods, main findings, and conclusions. A structured approach to abstracts is now used by many journals.

The introduction presents the justification and purpose of the research in the context of the existing problem and its relationship to other current research. The research question(s) to be addressed should be clearly stated.

The materials and methods section describes the study population, including selection criteria and methods used to determine sample size as well as methods used for data analysis. Methods used for biological measures should be clearly stated.

The results section should directly address the research question(s) posed in the introduction. Data are presented in the text and summarized in tables or figures. Statistical analyses should include appropriate measures of association (p values) and relative risk or odds ratio summary measures and confidence intervals.

The discussion section includes interpretation of the major finding(s) of the study, a statement of study limitations, and suggestions for applications of the findings and future research.

Reviewing Published Studies

Many factors should be considered in critically reviewing an article in the scientific literature. Although most journals require both editorial and expert (peer) review, the quality of published articles does vary, and it is up to each healthcare professional to critically review each article based on its merits. To evaluate articles that report original research, appropriate questions should be asked about each component of the paper.

The following questions may serve as a basic guide:

Introduction: “Is the study question important, appropriate, and stated clearly?”

Materials and methods: “Is the study population appropriate and adequately described?” “Is the choice of study design applicable to the purpose of the study?” “Are selection and exclusion criteria described?” “Were outcomes of groups evaluated equally and by persons blinded to study treatment arm?” “What were the proportions lost to follow-up in each study arm described?”
Results: “Are the statistical tests appropriate for the study design?” “Is the sample size adequate?”5,19,23 “Are there factors that could have confounded results and were these taken into account?”24,25 “Do the data that are presented in the text, tables, and figures provide an answer to the stated research question(s)?”26

Discussion: “Are the conclusions that are drawn reasonable and justified?”27 “Could other explanations account for the observed results?”

CONCLUSIONS

Many study designs, observational or experimental, are available to investigators. Understanding the advantages and disadvantages of each study design should prepare the infection control professional to critically evaluate published research studies so as to appropriately assign value to the findings.
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**SUPPLEMENTAL RESOURCES**

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