CHAPTER
2

Healthcare Research Methods

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INTRODUCTION

Research methods and statistics are foundational concepts for evidence-based practice (EBP). This chapter was written with the expectation that you have taken courses at the undergraduate level that address both research methods and statistics. We recommend that you have books related to these topics nearby as you read this chapter. Furthermore, we recommend having references regarding statistics and research on your bookshelf throughout your career. We have found two types of books to be particularly useful with this subject matter: a dictionary of statistics/research terminology and a dictionary of epidemiology.

Different degree programs offer varying amounts of instruction on these topics. We have written this text with the assumption that you are taking a course in EBP early in your health professional degree program. If you have had multiple courses in research and statistics, you might be familiar with much of the material in this chapter.

Another piece of advice we have for you is to know people who specialize in research and statistics. It will help you in your professional program and in your career if you know people who have specialized knowledge in these fields. Just as you work with a team of healthcare providers from different disciplines, we recommend that your teams include people with these backgrounds. You might find a classmate or colleague who has worked as a research assistant. Your college, university, or hospital most likely has an office of research. There might even be tutors on your campus who can help you grapple with any concepts you encounter that are new or unfamiliar. We encourage you to identify the resources and people available to you wherever you go as a student and as a clinician.

Research and statistics tend to be areas in which practitioners and students feel hesitant. This is understandable. Each of these domains has numerous degrees and specialties. Full proficiency in these subjects requires advanced education; it would be unrealistic to ask every healthcare provider to also achieve an advanced degree in statistics and

another in research. However, avoiding these topics can place you in a dependent position.

If you avoid research and statistics, you will have to rely on the authors of information sources regarding the trustworthiness of the information they provide. One of our goals is to give you the tools to avoid such dependence. In fact, we have already mentioned one of the best tools to use—teaming up with people who have research and statistics knowledge. Furthermore, with time and experience you will become a resource to others. You will be able to share the knowledge and skills you gain from learning EBP with classmates, fellow clinicians, and with your patients.

In this chapter, we focus on the most common research concepts found in healthcare literature. Many of the concepts fall under the category of **biostatistics** (i.e., statistics applied to biological research).[1] Some authorities refer to statistics applied to medical research as **medical statistics**.[2] For the sake of simplicity, we use the term *biostatistics* to refer to medical statistics in this chapter.

By no means can we cover every concept in biostatistics in this chapter. However, as with the rest of health care, biostatistics is an area that requires lifelong learning. Just as you commit to gaining knowledge about health care throughout your career, you will need to continuously grow your knowledge about statistics and research. You will need to commit a little bit of time on a regular basis to these topics.

RESEARCH PARADIGMS

The two major research paradigms are *naturalistic*, also referred to as qualitative, and *positivistic*, which is also known as quantitative. For the purposes of this chapter, the term *qualitative* is used interchangeably with the word *naturalistic*. *Positivistic* and *quantitative* are similarly interchangeable.

The two paradigms of **qualitative** (naturalistic) and **quantitative** (positivistic) research represent different philosophical perspectives regarding knowledge, the design of research, and the types of data collected.

This interchangeability is a matter of much debate among research theorists. In addition to the terminology we have selected, the designation of two research paradigms has been debated. As Pope and Mays explain, "The differences between qualitative and quantitative research [sic] are frequently overstated, and this has helped to perpetuate the misunderstanding of qualitative methods within such fields as health services."[3(p. 5)]

However, these debates are well beyond our purposes here. Because our intended audience is beginning practitioners, we leave the fine points of research philosophy to other courses and texts that prepare you to perform research.

As an aside, we hope someday you do perform research, because there is no better way to learn about a topic than to actively engage in it.

According to the qualitative perspective, knowledge comes from the internal reality of the individual or group, whereas the quantitative perspective views knowledge as coming from an external, measurable reality. Naturalistic researchers usually view reality as fluid and ever-changing, whereas positivistic researchers tend to view reality as fixed and unchanging. Many researchers fall in between these two positions and combine qualitative and quantitative research strategies. Combining qualitative and quantitative perspectives is referred to as **mixed-method research**. **Table 2–1** compares the fundamental distinctions between naturalistic and positivistic research. Few studies fall strictly within one paradigm.

More than likely you are familiar with positivistic research, the type of research that quantifies observations and makes predictions about populations based on samples. The majority of biomedical research falls within the positivistic domain. We will briefly discuss naturalistic research and give some examples of its application in health care. However, this text focuses mainly on research in the positivist domain because of its predominant role in making health decisions. This emphasis on positivism does not diminish the importance of clinicians understanding qualitative research. Qualitative research can expose layers of meaning and significance that cannot be detected by

Table 2–1 Characteristics of Qualitative and Quantitative Research

	Naturalistic/Qualitative	**Positivistic/Quantitative**
Questions	Open-ended	Focused
Focus	Lived experiences of individuals, groups, or cultures that reveal meaning and significance of phenomena	Causal relationships or statistical differences that explain or predict phenomena, measuring effects of interventions
Sampling	Small, purposeful, and sometimes emergent selection or serial selection of participants	Large, preferably random samples blinded to the intervention
Setting	Natural, uncontrolled; studied as part of the research	Laboratory or controlled by design of research
Data	Observation, artifact, textual, visual, field notes, audio recordings, includes data from researchers as well as participants	Numerical, measurable, objective data collected from subjects only
Reasoning	Typically inductive, seeking descriptions	Typically deductive, seeking predictions
Analysis	Thematic, narrative, content-analytic procedures	Descriptive and/or inferential statistics
Role of researcher	Active engagement with participants and phenomenon; researcher is one of many data sources within the study	No or minimal engagement with participants and phenomenon; subjects and instruments are the sources of data, not researchers
Design	Emergent, guided by data as study proceeds, utilizing no intervention	Fixed, predetermined, utilizing one or more interventions

a survey or other instrument.[4] Qualitative research allows us to examine increasingly complex questions and is open to all possible answers to a question, not simply predetermined answers (which are examined in a quantitative study).

It is invaluable for you to understand qualitative research so that you have the skills to assess the quality of a naturalistic study (such as a case report). A foundation in evaluating qualitative research will, for example, give you tools for contending with the marketing tactics of companies that sell health-related products to clinicians and to patients. Perhaps of greater value is the perspective qualitative research can offer regarding the experiences of individuals and groups with health problems and with the healthcare system. Qualitative research has an advantage in this arena due to its holistic focus, which includes the individual and social context, emotions, perceptions, actions, beliefs, values, and interactions of patients with their health.

Naturalistic (Qualitative) Research

Naturalistic research emerged from the social sciences, primarily from anthropology, as researchers recognized the need to understand and describe phenomena experienced by people as well as the nature of the people being studied. Creswell offers the following definition:

> *Qualitative research is an inquiry process of understanding based on distinct methodological traditions of inquiry that explore a social or human problem. The researcher builds a complex, holistic picture, analyzes words, reports detailed views of informants, and conducts the study in a natural setting.*[5(p. 15)]

In a naturalistic study, the researcher's goal is to gain a deep understanding of the lived experiences of individuals or groups and to develop a rich, thick description of these experiences. Naturalistic researchers attempt to understand the meaning of experiences according to those who live them. Typical data collected during naturalistic studies include field notes, photographs, videos, interview recordings, artifacts, and journals.

Qualitative research can stand alone or complement quantitative research through preliminary or subsequent research. A qualitative study might independently explore a question, such as the criteria family practice physicians use to determine when to refer a patient to a specialist. A qualitative study can be used in advance of a quantitative study to establish the questions and choices used in a survey, for example. Qualitative research can follow positivistic research by helping explain phenomena observed in the quantitative study. For instance, an epidemiologic study found a significant difference in the rate of tonsillectomies across two regions, despite there being no difference in incidence or severity of illness.[3] A subsequent qualitative study found that physicians with high rates of surgical referral had a greater range of clinical signs that they defined as indications for surgery, whereas those with low surgical referral rates had a narrowly defined set of criteria.

Anthropologists are arguably the best known for engaging in qualitative research. They go into the field and immerse themselves into the group that they are studying. They become part of the group, the proverbial fly on the wall. Early anthropologists recognized that "only if one lived with the people who are being studied, and attempted to behave and think like them, could one truly understand a different society."[6(p. 4)] This type of research has come to be known as *ethnography*. Ethnographers diligently collect detailed data on what they observe as well as their own behaviors, assumptions, biases, and reactions. Ethnographic researchers do not perform interventions. The goal of their study is to understand the phenomenon as it occurs naturally.

The amount of qualitative research performed varies by healthcare discipline. Nursing research, for instance, includes more qualitative publications than other healthcare fields. For example, a search of the Internet using the phrase, "Qualitative research in nursing" produced 849,000 hits, whereas a search for "Qualitative research in medicine" resulted in 7,330 hits. Furthermore, the results of the above search led to qualitative nursing research publications that dated back to 1986, whereas those related to medicine dated back to 1999. According to Risjord,[4] qualitative research became popular among nursing researchers in the early 1980s. Risjord explains the appeal of qualitative research in nursing as follows: "The nice fit between qualitative methodology and nursing practice promised a form of nursing theory that would be more congruent with the goals and practices of nursing."[4(p. 190)]

Styles of Naturalistic Research

There are numerous styles of naturalistic research. The most common styles include ethnography, biography, phenomenology, case study, and grounded theory. The definitions of each type are as follows:

- **Ethnography** is a description and interpretation of a cultural or social group or system. The ethnographic researcher examines the group's observable and learned patterns of behavior, customs, and ways of life. Ethnography involves prolonged observation of the group, typically through participant observation in which the researcher is immersed in the day-to-day lives of the people or through one-on-one interviews with members of the group.[5(p. 58)]
- **Biography** is the study of an individual and her or his experiences as told to the researcher or found in documents and archival material.[5(p. 75)]
- **Phenomenology** is the study of the lived experiences of several individuals centered on a single **phenomenon**.[5] A phenomenology is similar to a biography in its procedures,

differing primarily in terms of the examination of a group as opposed to an individual.

- **Case study** is an exploration of a *bounded system* (a case or multiple cases) over time through detailed, in-depth data collection involving multiple sources of information rich in context. The bounded system is bound by time and place such that the case or cases of interest may be an event, an activity, or the individuals themselves.[5]
- **Grounded theory** is the study of abstract problems and their processes.[7(p. 24)] It is a general methodology of analysis linked with data collection that uses a systematically applied set of methods to generate an inductive theory about a substantive area. The research product constitutes a theoretical formulation or integrated set of conceptual hypotheses about the substantive area under study.[(p. 16)]

In medical and nursing research, the **case report** is a commonly used qualitative research strategy. The term *case report* is simply another name for *case study*. A clinical case report explains the course of an illness and often the patient's response to treatment. The clinical case report serves two functions: sharing information and supporting learning in an area of medical or nursing care.[8] In fact, the case report serves a vital function in health research:

> *New diseases or unexpected effects of drugs or procedures may all first emerge as case reports. This is particularly true of information related to drugs. Patients selected for clinical trials do not often represent the patients who are offered treatment once the drug is launched and there are many examples where new information on the action of the drugs has emerged after the drug has been licensed for use.*[8(p. 97)]

Furthermore, throughout your career as a clinician, you will approach care from the case report perspective as you observe the course of an illness in each patient and critique the patient's response to treatment. On a nearly daily basis you will engage in discussions with colleagues from the viewpoint of a case study.

Applications of Qualitative Research in Health Care

Naturalistic research has many applications in health care, the most obvious being studies related to the impacts of illnesses and treatments. Other uses of qualitative research in health care include sales and marketing, development of classification systems, patient education, patient and provider behavior, law and policy, patient satisfaction, and healthcare ethics. Pharmaceutical sales and marketing, in particular, have immeasurable impact on selection of treatments and patient outcomes.

Marketing researchers frequently use naturalistic studies to learn what motivates consumers and how to influence them to purchase their products. This strategy is of particular interest in health care as it is used by pharmaceutical companies to sell products to healthcare providers and directly to consumers. Each sales strategy is carefully tested on consumers, including patients and healthcare providers as key consumer groups. Pharmaceutical companies conduct studies with target patient populations in order to develop effective direct-to-consumer sales techniques. They also study medical practitioners, pharmacists, and nurses to identify effective methods and channels of communication.

It is important for you to be aware of the motivational techniques employed for purposes of selling healthcare-related products in order to help you and your patients make decisions. Knowledge about motivational research has another helpful purpose. Motivational research can also be useful in helping to identify and overcome barriers to healthy behaviors. One well-documented example of research in this arena is motivational interviewing.

Patient behavior change is an increasingly important aspect of health care in the twenty-first century. The previous century saw astounding advances in curing and preventing acute illnesses and controlling the spread of infectious diseases. Today, "the majority of maladies that now cause people to consult healthcare professionals are largely preventable or remediable through health behavior change."[9(p. 3)] A process called **motivational**

interviewing (**MI**) was developed as a treatment modality that identifies and utilizes the intrinsic motivation of individuals with substance-related problems. It has been adapted to many other health areas, such as cancer treatment, smoking cessation, domestic violence, and so on. MI relies on many of the same influencing factors in human behavior as marketing and sales, however with quite different objectives. MI offers a strategy for providers to collaborate with patients to identify their health-related goals and make self-directed changes toward achieving those goals.

Limitations of Qualitative Research

We will begin this discussion of limitations by first mentioning a characteristic of qualitative research that is *not* a limitation. We begin here because some theorists argue that qualitative research is itself of little value because it is not quantitative. Qualitative research is, by nature, designed to explore phenomena in depth. As such, it does not serve the purposes of measuring **differences** or **relationships** between variables (the purview of quantitative research). We liken such declamations of qualitative research as similar to stating that an automobile is limited because it cannot float, whereas a boat is not limited because it can. The two modes of transportation differ in their methods, but each serves a highly useful and worthwhile purpose.

The limitations of qualitative research must, therefore, be judged based on its purposes and intent. Qualitative research is time consuming, for example. A 1-hour interview, including field notes, an audio/video recording, photographs, and transcripts can consume hundreds of pages. These hundreds of pages, as well as the associated audio or video files, require innumerable hours to organize and synthesize into meaningful and digestible chunks of information. The work is laborious and tedious. It must be performed to exacting standards in order to be of high quality. Furthermore, a well-designed qualitative study will include a peer-reviewing researcher as part of the team. This internal reviewer examines and critiques the data and conclusions generated by the principal investigator. This internal check adds more time and labor to a qualitative study, not to mention expense.

Another limitation of qualitative research is difficulty with sharing data. The size of audio and video files created during interviews or field observations can easily exceed the storage capacity of email attachments or DVDs, USB drives, or other modes of transportable storage. Furthermore, the original data files often include identifying information regarding subjects. Subject identity is information that needs to be carefully protected. It can be exquisitely difficult to de-identify a video recording, for example.

Similarly, anonymity can be a challenge with qualitative research. Procedures for data collection and storage must be rigorously evaluated. Subjects must be carefully informed of the potential risk of inadvertent identification. The use of human subjects in qualitative research can make the approval process more complex and time consuming; yet another reason qualitative research can be slow.

The steps for evaluation of qualitative and quantitative studies are similar and boil down to essentially one question: Is the information provided in the publication trustworthy? The characteristics of trustworthiness differ between the two styles of research, but in the final analysis the quality of the research, and its applicability to your patient, determine the role of a given study in an evidence-based clinical decision.

Positivistic (Quantitative) Research

Positivism displaced the widely accepted philosophy that reality can be known only by God or through God, a belief that held sway in Europe until the Enlightenment.[10] As a general rule, **positivistic research** is thought of as *objective* in its perspective, as opposed to the *subjective* view taken by naturalistic research. A quantitative (or positivistic) study involves the computation of numerical values that represent phenomena. The positivistic

perspective emerged from the period in European history referred to as the Enlightenment in the eighteenth century. The term *positivism* was coined by Auguste Comte (1798–1857) to give name to this philosophical perspective.[11] Positivism holds that reality is both external and objective. Reality can be measured using systematic observations of nature, which is a process we refer to today as the scientific method.

A simple definition of the **scientific method** is that it is, "the process of formulating a hypothesis, performing objective experiments, and engaging in sound reasoning supported by the collected data."[10(p. 8)] The term *scientific method* was born from the positivist philosophical paradigm, which can be traced back to some of the earliest authorities in Western civilization, such as Aristotle, Galileo, Francis Bacon, and Descartes.[11] Quantitative research relies on the scientific method as its principal procedural foundation and on positivism for its philosophical underpinning.

One of the earliest published applications of the scientific method in medicine is credited to Dr. John Snow (who is also considered the Father of Epidemiology, as well as the Father of Anesthesiology). Snow, a British physician, lived in London during the mid-nineteenth century.[12] In the 1850s, there had been a series of outbreaks of cholera, leading to significant illness and death. At the time, physicians did not know how cholera spread. There were many beliefs as to how it was spread, but no method of containment had succeeded.

Snow had an insight that the rate of disease appeared to vary with the source of drinking water.[13] Drinking water was supplied to residents by several water companies. He compared the cholera mortality rates for residents who purchased water from two of the major suppliers: Southwark and Vauxhall Water Company and Lambeth Water Company. He visited every house in which a cholera death had occurred and collected information about the family's water supply.

A pattern of illness emerged that was associated with the Southwark and Vauxhall Water Company. The cholera incidence was significantly higher among Southwark and Vauxhall customers. Snow also observed that the Southwark and Vauxhall Water Company used sewage-contaminated water from the Thames River, whereas the Lambeth Water Company obtained its water from a sewage-free source. Based on his discovery, he closed the Southwark and Vauxhall well, and cholera all but disappeared among customers who had received water from that well. This procedure confirmed his hypothesis that water carried the disease.

Through systematic observation, mathematical computations, careful data collection, and reporting of his findings, Snow demonstrated that the cholera outbreak could be traced back to the water supply. His findings also supported the hypothesis that water is the mechanism of transmission of the disease. This important finding led to segregating sewage from the drinking water supply and, thus, perhaps to the first public health intervention based on the use of the scientific method. The story of Dr. Snow exemplifies the scientific method and also represents the founding of the science of epidemiology.

A familiar example of the positivistic research paradigm is the association between cigarette smoking and lung cancer. Cigarette smoking/lung cancer research was positivistic in nature because the outcome and exposure were treated as numbers, and statistical calculations were performed using the numbers. In these studies, researchers were looking for one of two significant findings: relationships between the predictor and response variables or differences between exposure groups. Relationship testing involved counting the numbers of smokers/nonsmokers (predictor variables) and the numbers of lung cancer/non–lung cancer cases (response variables) and then testing the hypothesis that there was a correlation between smoking and lung cancer.

In the tests for differences, researchers calculated rates of lung cancer and compared the rates between groups. They hypothesized that there was a significant difference in lung cancer incidence between smokers and nonsmokers. Tests for relationships and differences are performed in many positivistic (quantitative) studies.

Styles of Quantitative Research

There are many types of quantitative research, which can be grouped into three design categories: observational, quasi-experimental, and experimental. For each type of research discussed in this section, we will describe its location on the evidence pyramid (**Figure 2–1**).

Observational Research

Observational research quantifies phenomena, but it does not involve the use of an intervention. An **intervention**, in the context of biomedical research, is an activity intended to alter an outcome, such as a risk reduction strategy, a pain management procedure, a drug therapy, or a diagnostic tool. In observational research, outcomes are measured without researchers employing any kind of intervention. Observational research can be used to identify trends and variables of interest: "Observations are not just a haphazard collection of facts: in their own way observational studies must apply the same rigor as experimental studies."[2(p.173)] Epidemiologic studies fall in the category of observational research. Case studies can also be categorized as observational. Observational research is low on the evidence pyramid.

Quasi-experimental Research

Quasi-experimental research involves studying a phenomenon in which researchers cannot randomly select subjects or randomly assign subjects to treatment and control groups; however, researchers are able to control some independent variables.[1] An **independent variable** is a **predictor variable** that can affect the **response variable** (also known as a **dependent variable**), such as sex or age being a predictor of heart disease. These studies are often conducted in the same manner as experimental research.[2] For example, in studying lung cancer researchers were unable to randomly assign patients into the treatment (smoking) and control (nonsmoking) groups due to the obvious harm that such random assignments would cause for those in the treatment group. A quasi-experimental design is needed in such situations. There are many instances with interventional research in which a quasi-experimental design is preferable, although the design is inherently limited in terms of generalizing the findings to the entire population of smokers and nonsmokers. For this reason, studies of this type tend to rank in the lower region of the evidence pyramid.

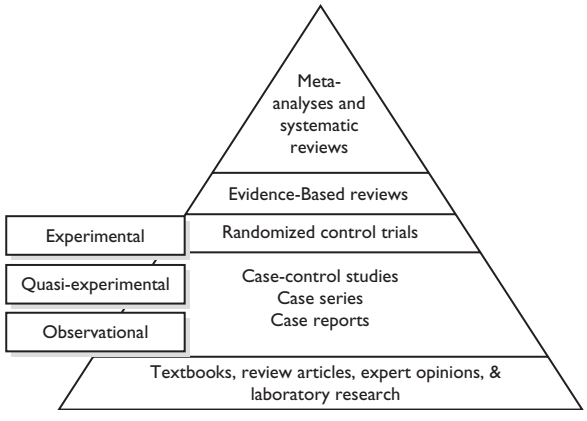

Figure 2–1 Evidence Hierarchy and Styles of Research

Experimental Research

Experimental research involves dividing patients randomly, selecting subjects from the entire population or randomly assigning participants into intervention and control groups, and measuring differences between them or associations between predictor and response variables. Researchers are able to control variables in this type of study.[1] For example, subjects in a drug trial are randomly assigned to receive the usual treatment (active control) or the experimental treatment (the new drug), and researchers control for explanatory variables such as age, gender, severity of disease, and so on.

Styles of quantitative research also can be grouped according to their time orientation (i.e., **temporal style**) into the categories of *retrospective*, *cross-sectional*, and *prospective*. Not all studies can be easily categorized into just one of these types, but the concepts are helpful in understanding the various quantitative research strategies.

Retrospective Research

Retrospective research examines an outcome or exposure that has already occurred and utilizes

numerical data to test for relationships between variables or differences between groups that can be associated with the phenomenon. This type of research is also referred to as a **case-control study**. For example, case-control studies were repeatedly performed when researchers were looking for a relationship between smoking cigarettes and lung cancer. Data were collected from patients with lung cancer, or from their charts, and exposure to cigarette smoking was calculated according to the amount and duration of exposure. This research can be categorized as both observational and retrospective. The research was retrospective because lung cancer had already occurred in the patients and the data were collected after the outcome. The research was observational because no intervention was employed.

Incidentally, cigarette smoking research was conducted because healthcare providers observed a significant difference in incidence of lung cancer among patients who smoked cigarettes compared to those who did not. The striking difference between groups sparked many studies examining the relationship between the outcome (lung cancer) and the exposure (cigarette smoking). Through the early 1960s, as many as 7,000 scientific articles had been published on the topic of smoking and lung cancer.[14] The results of these studies were disputed for decades by tobacco companies.

Clinicians are interested in retrospective research in that it helps identify risk factors associated with disease, or behaviors associated with good health, for that matter. Retrospective studies, however, are generally placed fairly low on the evidence pyramid because they can more readily fall prey to several types of bias. Selection of subjects can be especially problematic. It can be challenging to identify subjects without a given exposure or subjects who will not later develop an outcome that would place them in a different group in a study. Furthermore, patient charts, which are a common data source in retrospective research, can be fraught with errors and omissions.

In addition to data integrity problems in charts and subject-selection bias, there is also a problem with patient-recall bias. When patients with an outcome are asked to remember exposures or behaviors in their past, they are much more likely to respond positively than patients who do not have the outcome. Porta[2] gives the following example of recall bias: "A mother whose child died of leukemia may be more likely than the mother of a healthy living child to remember details of such past experiences as use of x-ray services when the child was in utero."(p. 208)

Cross-sectional Research

Cross-sectional research includes studies that collect data at a single fixed point in time. Studies of prevalence are perhaps the most commonly accessed cross-sectional research. **Prevalence** is the proportion of a population with a given disease at a single point in time. The Centers for Disease Control and Prevention (CDC) are best known for this type of research. Surveys are another commonly used cross-sectional strategy. Quality-of-life studies, clinically oriented questionnaires, and satisfaction with hospital stays are other common examples.[15]

Cross-sectional studies are affected by limitations similar to those of retrospective research, with risks including selection bias, recall bias, nonresponse bias, instrument bias, confounding and covarying factors, and reciprocal influences (to name a few). Due to the risk of bias, cross-sectional studies are low on the evidence pyramid. Nonetheless, cross-sectional studies can provide invaluable data about the status of disease and the risk factors or exposures associated with disease. Neither cross-sectional nor retrospective studies are used to make predictions about the outcome of a given intervention. Research of this type is *prospective* in nature, whereas retrospective and cross-sectional research is considered *observational*.

Prospective Research

Prospective research involves the formulation of a hypothesis, followed by the collection of data and subsequent analysis of findings. Data are collected over a defined period of time, of sufficient duration to draw reliable inferences based on the sample. It is possible for prospective research to be

observational, quasi-experimental, or experimental in design. The defining characteristic is its forward orientation in time. An outcome is predicted based on a predetermined set of characteristics, a specified experience, or a chosen intervention. The following are commonly used prospective biomedical research strategies.

Control Trial In research, the term *control* has several meanings. It can refer to a group or to a research procedure. In this instance, it refers to the use of a specific group in the design of a study. The **control group** serves as a basis of comparison to ascertain the magnitude of the effect of an intervention. Results in the treatment group are compared to the control group. A control group makes it possible for researchers to determine if the effect of treatment is greater or less than nontreatment. It also allows them to determine if the experimental treatment has a greater or lesser effect than the existing standard of care (which is also referred to as the *usual treatment*). It is possible for researchers to perform studies without control groups; such studies are referred to as **pre/post** designs because the outcomes are measured prior to treatment and again subsequent to treatment. Pre/post studies are greatly limited because it is difficult to determine if the effect is clinically meaningful or if the effect differs from the current standard of care.

A **control trial** (also referred to as *controlled trial*) is a study in which there is at least one treatment group and one control group. In a control trial, group allocation is not random and often cannot be concealed. For example, a study on rotator cuff injuries might compare a surgical intervention with a physical therapy intervention. In this case, it is not possible to conceal from patients and providers what type of intervention the patient receives. Also, in this study patients might be involved in the selection of their treatment modality, which is why random assignment would not be possible.

The distinguishing characteristics of this type of study are the presence of the control group and the lack of random group allocation. The control group might receive no treatment, a placebo, or the usual care given for the condition of interest. There might be more than one type of control group. Patients also might act as their own controls, or they might be crossed over from the control group to the treatment group (which is referred to as a *cross-over study*). Control trials are relatively low on the evidence pyramid.

Cohort Study **Cohort studies** are observational studies that are usually large in size and longitudinal in duration. The groups in the study are determined by a given exposure, characteristic, or risk factor. Patients are followed forward in time to monitor for the development of a given outcome. These studies can include comparisons of various levels of exposures and numerous factors that may influence the frequency of outcomes and their severity.

A well-known cohort study whose results are frequently referenced in healthcare decisions today is the Framingham Heart Study.[16] The study seeks to identify the risk factors (e.g., gender, age, smoking, family history, height/weight, etc.) that predict heart disease and stroke. In 1948, researchers recruited 5,209 men and women between the ages of 30 and 62 to enroll in the study. These patients have been followed ever since, and new cohorts have been enrolled in order to establish representative samples. Based on the findings of this study and others, a set of risk criteria has been established that can be used to help predict the likelihood of a patient having a cardiovascular event within a 10-year period. Cohort studies are relatively low on the evidence pyramid. However, as demonstrated by the Framingham Study, they can produce highly useful information for clinical care decisions and for educating patients.

Randomized Control Trial The **randomized control trial** (**RCT**) is a study in which the allocation of patients to treatment or control groups is random and concealed. At least one control group must be utilized. Preferably patients, as well as providers, are not informed (blinded) regarding which intervention patients receive. When both the patients and providers are blinded, the study is referred to as a **double-blind RCT.**

Random assignment of patients to treatment and control groups is the defining characteristic of an RCT. Although blinding is important, it is not a requirement in order for a study to be considered an RCT. Nonblinded RCTs are lower on the evidence pyramid than blinded RCTs. Similarly, a double-blind RCT is higher on the pyramid than a single-blind RCT. It is also possible for a study to have additional types of blinding, such as blinding of the data analyst (which would be referred to as a **triple-blind RCT)**. Blinding is intended to reduce bias and ensure that the treatment and control groups are representative of the population from which they are drawn.

RCTs are greatly affected by the strategy used for identifying subjects. An RCT is intended to provide data that can be applied to a larger population. Hence, the **sampling strategy** (i.e., procedures for identifying and recruiting subjects) is critical to the validity of findings in an RCT. The degree to which a sample is representative of the population determines the likelihood that the study's results will be generalizable to that population. Well-designed RCTs of sufficient sample size and duration are placed in the upper section of the evidence pyramid. Such studies are considered the gold standard in biomedical research. That is not to say that well-designed RCTs are free from error or bias. Recent research examining the frequency of studies being disproved found that even large, high-quality RCTs are controverted nearly 10% of the time.

Cross-over Trials, Systematic Reviews, Meta-analyses, and Clinical Trials

Several special types of biomedical research do not fit neatly into any of the categories we have discussed in this chapter, including the cross-over trial, the systematic review, the meta-analysis, and the clinical trial.

Cross-over Trial A **cross-over trial** is a prospective study in which patients are moved from one group to another. They are in the control group for a period of time and then are moved to one or more treatment groups. Subjects remain in each group long enough to determine the effect of the given treatment. Allocation of patients from one group to the next can be randomized. It is not always possible for group allocation to be random, depending on the research circumstances and question. Random allocation makes a cross-over trial stronger, however.

In a cross-over trial, two types of control are possible: the control group in which patients receive the placebo or usual treatment and a within-subject control. This procedure allows researchers to determine if individuals have unique responses to a treatment. A *washout period* is usually required in between the phases of the study in order to reduce the potential for carry-over effects from one treatment to the next.[2] The length of the washout timeframe needs to be of sufficient duration to eliminate the effects of the first intervention before employing the second intervention.

Although it is preferable for a cross-over trial to be performed with random assignment and blinding of treatment, it is not always possible for these studies to be done in this manner. It is important for clinicians to read the study design information carefully in order to determine the level of evidence represented by an individual study. Of course, this consideration is always important, regardless of the type of study. When a cross-over trial is randomized and blinded, it can be considered to be high on the evidence pyramid.

A study performed by Rajaram et al.[18] regarding the effects of walnuts and fatty fish on cholesterol levels is an example of a randomized cross-over trial. In the study, 25 normal to mildly hyperlipidemic (high cholesterol) adults, aged 23 to 65, were randomized into one of three groups: (1) control diet, (2) walnut diet, or (3) fatty fish (salmon) diet. Each subject spent 4 weeks on each of the three diets. Subjects had a weekend break in between diet periods. Subjects were weighed twice weekly, and fasting blood samples were drawn on two alternate days at the end of each study period. Cholesterol levels were compared to baseline levels taken at the beginning of the study and compared to the beginning of each study period.

The cross-over design allowed researchers to compare the three diets with one another and

to account for individual patient responses. This design was preferable to having a simple RCT because it helped researchers determine if one diet was particularly effective in individual patients. A criticism of the study design relates to the time of the washout period. Is a weekend enough time to eliminate the effects of one diet? This procedure allows for a smaller sample size while assuring valid results. Without the cross-over, a larger sample and a longer trial period would have been necessary.

Systematic Review and Meta-analysis A **systematic review** is a research procedure in which all prior studies on a given topic are brought together and analyzed collectively. There is a rigorous protocol for performing a systematic review. Systematic reviews are typically deemed to be at the top of the evidence pyramid. An area in which systematic reviews are especially valuable is in comparative research. It is costly and time consuming for researchers to perform all available interventions related to the same problem. For example, dozens of interventions have been examined for reducing cholesterol, including psychotherapy, exercise, nutrition, drugs, and even surgery.

Each type of intervention has any number of subtypes. Exercise, for instance, can include various types of activities (walking/jogging, weightlifting, swimming, dancing, etc.) for various amounts of time at various levels of intensity. Researchers generally select a handful of related interventions and compare them to one another. In fact, many studies compare just one intervention with a control. Systematic reviews offer a means for gathering all of the various studies and comparing outcomes across them.

It is critical for readers to carefully ascertain that a publication is in fact a systematic review as opposed to being merely a literature review article. A literature review article is not research, but rather a summary of publications on a given topic. Occasionally, the term *systematic review* is used in the title of a published article that is not in fact a systematic review. This error has occurred less frequently with time as journals have become more careful in the use of the term.

One way to recognize if a publication is a genuine systematic review is the source of the article. The **Cochrane Collaboration** is considered the leading organization in the world for this type of research, and it sets the standards for design and quality of systematic reviews and meta-analyses. The organization explains systematic reviews as studies that "collate all evidence that fits pre-specified eligibility criteria in order to address a specific research question" and "minimize bias by using explicit, systematic methods."[19]

In a systematic review, a research team formulates a question, follows a specified literature search strategy (locating published and unpublished studies), sets strict selection criteria for inclusion of studies in the systematic review, critiques the designs of the studies, summarizes the findings, characterizes the validity of the findings, and provides recommendations about the application of the research to patient care decisions. Systematic review team members perform searches and analyses independently. A separate team member, or group, then evaluates the similarity (homogeneity) of studies identified and the findings reported by the independent reviewers.

A **meta-analysis** is an added step to a systematic review in which a statistical analysis is performed to quantify the findings of the review. Porta describes the meta-analytic process as, "a statistical analysis of results from separate studies, and leading to a quantitative summary of the results if the results are judged sufficiently similar to support such synthesis."[2(p. 154)] A meta-analysis can also include aggregation of pooled data from the original studies, if the data are available. The research question is then retested with the aggregated data and results compared to the original separate studies. A systematic review with a meta-analysis is considered the highest level of evidence on the pyramid.

Systematic reviews and meta-analyses might be composed of lower levels of evidence, such as

cohort studies, nonrandomized trials, and small RCTs. This does not alter the ranking of systematic reviews and meta-analyses as top-tier evidence, however. They retain their strength because the findings, even when inconclusive, are more reliable than an individual study, even if the individual study is a large RCT. We caution you, however, to look for newer evidence when reading a systematic review or meta-analysis. Even these studies are occasionally found to be incorrect, and new research can refute their findings. Furthermore, new research can fill in missing information or add new information. The Cochrane Collaboration often publishes updates to its studies as new research emerges.

Clinical Trial Another type of study that is difficult to categorize according to the groups discussed in this chapter is the clinical trial. **Clinical trials** take various forms and can combine styles, including case series, surveys, control trials, cohort studies, and RCTs. Clinical trials either directly involve a particular group of people or use materials from humans. Researchers observe subjects and/or collect data to answer a health-related question about the safety or efficacy of an intervention. The National Institutes of Health (NIH) website ClinicalTrials.gov is a repository of federally and privately funded clinical trials conducted in the United States. The NIH divides clinical trials into five types of research questions (treatment, prevention, diagnosis, screening, and quality of life) and into four phases. The phases are defined as follows:[20]

- In **Phase I trials**, researchers test an experimental drug or treatment in a small group of people (20 to 80) for the first time to evaluate its safety, determine a safe dosage range, and identify side effects.
- In **Phase II trials**, the experimental study drug or treatment is given to a larger group of people (100 to 300) to see if it is effective and to further evaluate its safety.
- In **Phase III trials**, the experimental study drug or treatment is given to large groups of people (1,000 to 3,000) to confirm its effectiveness, monitor side effects, compare it to commonly used treatments, and collect information that will allow the experimental drug or treatment to be used safely.
- In **Phase IV trials**, postmarketing studies delineate additional information, including the drug's risks, benefits, and optimal use.

Table 2–2 organizes the various types of quantitative research we have discussed into categories

Table 2–2 Quantitative Styles of Biomedical Research

Style of Research	**Temporal Characteristic**		
	Retrospective	**Cross-sectional**	**Prospective**
Observational	Case studies Case-control studies	Prevalence studies Surveys	Case studies Control trials Phase IV clinical trials
Quasi-experimental	N/A	Longitudinal cross-sectional studies	Cohort studies Nonblinded RCTs Phase I, II, and III clinical trials
Experimental	N/A	Proof-of-concept experiments*	Blinded RCTs Phase I, II, and III clinical trials

*A **proof-of-concept experiment** is a single-group study in which the plausibility of an underlying principle is tested.

according to the most common style of research and the typical temporal characteristics of the studies. This is not a definitive listing of all types of biomedical research, nor are these categorizations set in stone. This table is merely a tool to visually support the discussion in this chapter. It will always be necessary for you to read the authors' descriptions of their studies to determine the style of research and its temporal characteristics.

Applications of Quantitative Research in Health Care

Quantitative research is predominant in health care. It could even be described as ubiquitous. Observational, quasi-experimental, and experimental studies are utilized to determine the following:

- The prevalence or incidence of disease and associated risk factors
- Survival longevity (with and without treatment)
- Accuracy, harms, or side effects of screening tools and diagnostic procedures
- Effectiveness and complications of treatment modalities
- Interactions between interventions
- Quality of life
- Cost of care
- Patient satisfaction

You will often turn to quantitative research for information to facilitate patient care decisions, but quantitative research has many other applications. For example, quantitative research is used to assess health professional workforce issues such as provider-to-patient ratios, reimbursement levels, salaries, and availability of jobs. Quantitative research is utilized by policymakers, organizational administrators, journalists, patients, and just about everyone else. When hospitals or other organizations decide on the standards of care they will follow, they turn to the quantitative research literature for guidance. You might be involved in a decision of this kind at some point in your career. When laws are being written with regard to health insurance coverage, quantitative research is referenced. When malpractice lawsuits are filed, quantitative research is brought forth as evidence. You might be called as an expert witness or even (hopefully not) as the respondent in a malpractice lawsuit. A command of quantitative research could even protect your career.

Limitations of Quantitative Research

Time and cost are the two greatest limiting factors for all types of research (qualitative and quantitative). Quantitative studies can be limited in a number of different ways. One important limitation of quantitative research lies in the philosophical perspective on which positivism is based. The fundamental assumption of quantitative research is that an inferencex can be drawn from a sample of patients that will hold true with the population represented by the sample. This concept is referred to as **generalizability**. In order to perform a quantitative study, researchers must formulate a **hypothesis**, a belief about what is true. This hypothesis is tested with rigorous means. However, the formation of a hypothesis limits the potential outcomes to those answers that were imagined by the researcher in advance. Consider the following example.

A team of researchers is interested in the best treatment for high cholesterol. They set out to conduct a comparative systematic review of all of the treatments that have been published. This includes exercise, nutrition, drugs, and other treatments. They select the treatments that have been previously researched, which immediately limits the answer to the question. Even though this type of study would be deemed as high-level evidence, it would not even consider many other potential answers or alternate perspectives.

By formulating the hypothesis that specific treatments for high cholesterol are better than others, the researchers have excluded any number of other informative views. It might be that an environmental variable is contributing to rising cholesterol levels and that any treatment is inhibited by this variable. It might be that there is a genetic

mutation at work. Additionally, it might be that, regardless of the form of treatment, ultimately patients' quality of life and longevity is only minimally affected by any treatment. All of the cost of research and treatment might be wasteful in comparison to other things that might be of greater value to us. Perhaps we would benefit more from having better schools than having 10 points lower cholesterol. We are not saying this is true; we are just using the idea to make a point.

The preliminary formulation of possible answers to a research question, which is essential for quantitative research, by nature precludes a universe of other possible answers and ideas. It becomes necessary, therefore, to research every other possible answer and idea, which then adds time and cost, making the entire endeavor ludicrous. In saying this, we do not by any means discount quantitative research; quantitative research is the best tool for most biomedical questions. Studies that fall within this paradigm are invaluable to healthcare providers and to everyone who receives health care. We criticize it precisely because of the important role it plays in health care and the significant potential for harm.

The research design strategies employed in quantitative studies are intended to overcome their limitations. Quantitative research methods are meant to reduce the potential for errors through sufficient sample sizes, representative samples, adequate duration, and objective analysis. However, mistakes are made. The regularity of drugs being recalled by the FDA evinces the problem (if you are interested visit http://www.fda.gov/drugs/drugsafety/DrugRecalls/default.htm).

Optimally, we would follow patients throughout their lives to determine if a given intervention has had a positive or negative *outcome that matters*. Optimally, we would include samples that represent every subgroup in a population, including those with and without a given disease of both sexes, at every age, from every race and ethnicity, at every income level, with every possible complicating illness. These optimal designs are not possible for practical reasons, not to mention the cost.

As a consumer of research literature, your awareness of the underlying assumptions and limitations of the quantitative research paradigm will help you discern limitations of the studies you encounter. In addition, it could lead you to envisioning the universe of answers and ideas yet to be addressed by researchers, pointing to areas you might choose to investigate yourself. After all, healthcare studies are often inspired by the astute observations of clinicians in their daily practice.

Beyond the general limitations of quantitative research, you should look for several types of limitations in the studies you read as a clinician. In this context, the term **limitations** means aspects of a study that reduce its generalizability. In well-written articles, the authors will describe study limitations. When researchers identify the weaknesses of a study, it indicates two things: first, the conclusions they draw are more likely to be reasonable and, second, there might be further research to be done that can overcome the limitations. This identification helps you as the reader determine if the researchers were rigorous in their methods, and it offers you guidance in your ongoing use of evidence related to the clinical question of interest.

Limitations can lead to **bias** in the outcomes of a study. There are hundreds of types of bias, a full discussion of which is beyond the scope of this chapter. We will describe the most common forms of bias here in order to introduce the concept. All types of bias involve something other than the predictor variable influencing the response variable. It is nearly impossible for studies to completely eliminate bias. For consumers of research information, the key to detecting bias is consideration of all of the possible causes of an outcome reported in a study.

Bias can be divided into three major groups: sampling, measurement, and other sources. *Sampling* is the process of selecting a subset of a population and recruiting members of the subset to participate in the study. *Measurement* includes any procedure used for quantifying information (e.g., counting the number of fall incidents in a hospital ward, weighing patients, and measuring cholesterol levels). Other sources of bias include things that motivate a study to be performed or to be published (or not published, as the case may be). We will finish this

chapter with explanations of the more common limitations within each area.

Common sources of **sampling bias** include the sample size, the representativeness of the sample, and selection bias. In order for a statistical test to be accurate, the size of the sample (i.e., the number of subjects) must be adequate in terms of the type of data collected, the nature of the research question, and the desired level of effect. Erroneous conclusions can be drawn from studies that have samples that are too small or too large. We will not go into the complexities of all of the factors involved in determining the correct sample size. However, you can take one simple step as a reader to determine if the sample size in a study is appropriate. Examine the article for a statement regarding a sample size calculation.

A **sample size calculation** is a step researchers take prior to performing the study. In simple terms, a sample size calculation tells researchers how many subjects they need in order to be able to answer their question. This procedure is often included in a section of an article prior to the results. Well-written articles will include a section specifically describing the methods for identifying and enrolling subjects in the study.

If the authors do not mention the results of a sample size calculation, then you cannot be sure if the sample size was appropriate. However, if they did perform a sample size calculation, then the sample size might be considered a strength of the study; that is, if the number of subjects who begin (and complete) the study are greater than the required sample size. If you imagine as you read an article a set of hash marks for strengths of a study and a set for weaknesses of a study, an adequate sample size would mean drawing a hash mark on the strengths side. Also, the number of subjects should not be too much higher than the calculated sample size, because this can also increase the potential for error.

The **representativeness** of a sample is the degree to which subjects in the sample match the population they represent. This aspect of the research is typically described fairly early in an article, usually in the same section as the description of the sampling strategy. The sample should match the population in terms of characteristics such as the distribution of people by sex, age, race/ethnicity, severity of disease, and so on. The characteristics included in an analysis of representativeness are based on the nature of the study itself. Researchers employ **probability** (**random**) **sampling** in order to attain a representative sample. This means that all individuals in the population have an equal chance of being selected for a study. When combined with a sample size calculation, the use of probability sampling makes it likely that the sample will be representative of the population.

It is often difficult, however, for researchers to perform a simple random sample (i.e., to include every individual in a population as a member of the pool of subjects from which a sample is drawn). Many factors involved in sampling need to be considered in determining representativeness. In terms of your critique of a publication, you need to decide if you think the subjects in the study are representative of the population the authors intended and if the subjects represent your patient. You will base this decision on the description of the sample and the purpose of the study.

A concept closely related to representativeness is **selection bias**. Selection bias occurs when there is a systematic procedural error in the selection of subjects or when a nonrandom (nonprobability) sample is utilized. It is important to note that random sampling is often not possible or even advisable, depending on the amount of time available for the study as well as financial and labor resources. The population might be spread out geographically such that a true random sample could mean having to conduct the study in thousands of communities.

Nonrandom sampling can be acceptable for certain types of studies, such as proof-of-concept studies. A proof-of-concept study can involve verifying the presence of a condition in a population or it can be used to determine a study's protocol. Several types of nonrandom sampling procedures are possible. The key point for healthcare providers is to recognize when a nonrandom sample has been used. Well-written studies will include a detailed explanation of the sampling procedure and a justification for

the use of a nonrandom sample. The authors should avoid making generalizations about the population of interest based on a nonrandom sample.

The second major group of research bias comes from **measurement bias**. Measurement bias can include inaccurate measurement tools, calculation errors, mistakes in recording measurements, participant bias, recall bias, and more. When inaccuracy in measurement occurs, it often leads to incorrect conclusions. There are countless types of measurement errors. Although we cannot describe every type of measurement error, you will have the ability to look for them in the studies you read by considering if there are any ways in which the data collected in the study were inaccurate.

For example, many studies measure BMI (body mass index). BMI is a formula that includes a patient's height and weight. An accurate calculation of BMI requires correct measurement of both variables. Errors in measurement of height can take the form of incorrect positioning of the patient, use of an inconsistent method of measurement, time of day the measurement is taken (patients tend to be taller when they get up in the morning), and so on. It is not unusual for studies to involve patients who are unable to stand, such as those in an ICU or in wheelchairs. For these patients, an estimate of height must be used, rather than a direct measure. Estimates have even greater potential for error than direct measures.

A patient's weight is even more prone to measurement error than height. Factors such as clothing and calibration of the scale can impact the accuracy of a weight measurement. If a consistent and careful protocol is not followed, then errors will occur. Patient weights can vary by several pounds from one standing scale to the next. Thus, the same type of scale must be used every time, in addition to calibrating the scale with every use. Furthermore, the person recording the weight can make mistakes reading the scale or in writing the number into the chart. In many studies, data from the chart are retyped into a computer, which introduces another moment when error can occur. The combination of errors in measurement of height and weight then produces even greater error in the resulting BMI calculation.

Many measurements, like BMI, run the risk of multiple types of measurement errors, including instrumentation error, calculation errors, and data observation errors. When reading studies, consider the ways in which a measurement can be inaccurate and look for careful descriptions from the authors about the procedures they followed. This issue is especially important for the response variable in a study. If BMI were the primary response variable, for instance, then the accuracy of measuring height and weight as well as the calculation of BMI is of great importance. The authors must describe the steps taken to reduce errors in order to demonstrate that their findings are valid. Studies that include this type of detail and demonstrate the validity of their measurement procedures get another hash mark under the strengths heading.

Another type of measurement bias comes from the behavior of the subjects in the study. Patients might alter their behavior for a number of reasons, such as self-consciousness or a desire to please the researchers. For example, a patient might exercise more after enrolling in a study related to nutrition. Or, the patient can simply report a greater level of physical activity than is true. Patients might not be completely honest on a survey, or they might have wildly different perceptions, which can skew the results. On a pain scale, for example, one patient might rate a paper cut as 1 out of 10, whereas another patient might rate it as 5 out of 10. This type of measurement error is referred to as **self-reporting bias**.

A related type of measurement bias caused by the subjects in a study is **recall bias**. Patients might not remember completely or accurately the history of their symptoms, exposures, or behaviors. Furthermore, patients without a disease are less likely to recall prior exposures or behaviors compared to patients with a disease. In fact, recall bias is considered by some experts to be pervasive in case-control studies and to some degree in most observational studies.[21] Even randomized control trials can be limited by recall bias if one of the variables includes information provided by patients. As the user of healthcare literature, your task is to examine each study you read for data sources that might be affected by recall bias.

In addition to the two major categories of bias, there are many other types of bias, such as publication bias, funding bias, extraneous variables, lack of clinical value, and more. **Publication bias** occurs when the determination of whether to publish a study is based on factors other than the quality of the research and the relevance of its findings. Sometimes studies are not published because no statistical significance was found in the research. In other words, if the authors of a study find one medication is not significantly better than another, the study is less likely to get published, even though this information might be of great utility to healthcare providers. Easterbrook et al. found that studies with a statistically significant finding were 2.3 times more likely to be published.[22]

Publication bias also can occur because the editors of a journal disapprove of the research, because the research is considered controversial, or simply because of a journal's tendency to publish the articles written by people who are associated with the journal (a sort of insider's group). Sometimes the authors themselves avoid publishing a study because the findings were contradictory to their expected outcomes.

Funding bias is similar to publication bias in that it can lead to a study not being published for reasons other than the quality and relevance of the research. This type of bias can simply mean the organization funding the study has control over whether the study results are published. If the findings are not a benefit to the funding organization, the study is not released. Furthermore, the researchers themselves might financially benefit from the study by working for the funding organization or by receiving rewards such as travel money or stipends for giving lectures.

Another type of bias is a *lack of clinical or practical significance*. A numerical finding of significance does not indicate that a difference between groups was clinically meaningful. For example, a study comparing cholesterol drugs did find a significant difference in cholesterol levels between two drugs, but this difference might not be related to an outcome that matters (e.g., longer life, fewer heart attacks, or better quality of life). Furthermore, differences between groups might not be meaningful in light of the overall prevalence of the disorder.

For example, in a study comparing medications for insomnia, the researchers found that those who received one of the studied drugs had a higher *incidence* (new cases) of depression than those who received placebo.[23] Two percent of those receiving one of the insomnia medications experienced a new onset of depression, as compared with 0.9% of those who received the placebo. However, according to the CDC, the *prevalence* (rate of existing cases) of depression in the population is 9%. The article did not indicate the prevalence of depression among the research subjects. Nor did the authors account for risk factors, which include geographic location, age, sex, marital status, race/ethnicity, employment status, health insurance status, and other health conditions.[24] The study on depression and insomnia drugs compiled results of other studies that were not designed to measure depression as a primary outcome. Hence, the finding of a difference in depression rates, although statistically significant, might not be associated with the true clinical significance.

Many lists have been created to identify, categorize, and define the types of bias in research. Sackett, for example, developed a list that included 35 types of bias.[25] Other authors offer groupings of three or four categories of bias.[26] Regardless of the labels used, all types of bias have one characteristic in common: Something is influencing the outcome other than the predictor variables. These influences can come in the form of sampling errors, measurement errors, or other kinds of errors, such as publication bias or a lack of clinical significance. The key for healthcare providers is their ability to envision the ways that a study might be influenced by extraneous variables and to look for explanations related to them.

Well-designed articles will include sections related to bias, explaining carefully the sampling strategy, the measurement procedures, sources of funding, the authors' relationships with the funding agency, and limitations of the study. For example, in the study on depression and insomnia medications the authors discussed the limitations of the study as follows:[23]

This is a post-hoc analysis of trials which were not designed primarily to examine depression. The compilation had many limitations which have caused some observers to doubt that causality has been demonstrated. Information limitations included trial details, the length of exposure of many participants (correcting for dropouts), and inadequate specification of the nature and severity of incident depressions. The quality of ascertainment of depression occurring as an adverse event was quite uncertain. It is not evident that a major depressive disorder was always diagnosed by an expert when depression was listed as an adverse event. There are potential statistical pitfalls in compiling results of numerous trials of different design and duration using 4 different hypnotics. Because the FDA online files are a limited source, other methods of ascertainment might have uncovered more trials of these drugs, especially post-marketing trials. The data utilized did not lend themselves to the techniques of formal meta-analysis. Many limitations of this compilation could not be overcome unless new trials with thousands of participants are done, so some uncertainty as to the present conclusions is unavoidable.[p. 2]

Although this excerpt demonstrates several sources of bias in the study, it also exhibits one of the strengths of the study, a clear explanation of the study's limitations. This explanation helps readers determine how to apply the findings of the study to patient care. Although a difference was reported in incidence of depression, it is not clear that providers should avoid treating insomnia with the drugs included in the study. It might indicate that treatment for depression is appropriate, if the insomnia patient has depression.

When you have a patient who receives one of these drugs, because of a study like this one you will be aware to watch for development of depression and to consider withdrawing the insomnia medication if depression occurs. Or, if you are treating a patient who already has depression as well as insomnia, you might monitor the patient carefully (if you decide to prescribe an insomnia medication). It is possible that insomnia is a contributing factor to depression or a complication of it. Hence, you might choose to treat insomnia as part of a depression treatment regimen. We are most assuredly not recommending any specific treatment here, but rather putting the treatment decision into a larger context. Clearly your decision about treatment of insomnia or depression will be based on the specifics of each patient situation and not on the example given here.

CASE STUDY: MR. MARTINEZ HAS INSOMNIA

Mr. Martinez is a 45-year-old adult male of Hispanic descent with high cholesterol and high blood pressure. He is overweight and smokes cigarettes. He works at a construction company. When Mr. Martinez presented to the clinic, he said he was worried about his risk of having a heart attack and dying young like his father.

When taking Mr. Martinez's history, you learn that he suffers from insomnia. You take a general health, sleep, and medication history. You also perform a mental status exam. Based on his history, your examination of him, and his negative history of sedative medications, you decide to explore his insomnia further. You give him a sleep diary to track how long it takes him to fall asleep, how often he wakes, and how long he is awake. Mr. Martinez returns in a month with several nights of his sleep diary completed. He also provides you with information about his sleep hygiene (sleep habits and environment). The data he provides indicate possible chronic insomnia. It is unclear if his apparent insomnia is caused by a separate health condition (secondary insomnia) or if it is its own disorder (primary insomnia).

Following the clinical guideline for the evaluation and management of chronic insomnia in adults,[27] you suggest an overnight sleep assessment (nocturnal polysomnography). You will consider the results of the overnight sleep test in light of his overweight, cigarette smoking, and possible anxiety. It is also possible that he has sleep apnea, which is defined as abnormal pauses in breathing or shallow breathing while sleeping. In some cases, sleep apnea causes insomnia. The overnight sleep assessment will include testing to evaluate him for sleep apnea. Mr. Martinez agrees with the plan and he is comfortable with the expense.

1. What evidence-based practice questions does this case study bring to mind for you in terms of epidemiology and diagnosis? Write a focused clinical question that includes a specific condition or outcome, patient demographics, and patient risk factors.
2. Locate one resource that addresses your focused clinical question.
3. Identify the following information about the resource:
   a. What type of resource is it (review article, qualitative research, randomized-control trial, etc.)?
   b. Identify where the resource would be placed on the evidence pyramid.
4. Share your question and your resource with a partner. Discuss your answers to 3a and 3b with one another. Help one another determine if you have made the correct assessment. Also, discuss the following:
   a. Does the resource apply to the patient?
   b. What are the implications of the resource regarding the question you set out to answer?
   c. What further information would you need, if any, in order to answer your question.

Case Study Summary

A number of different questions might have come to mind regarding Mr. Martinez's possible insomnia. For example:

- What is the incidence of insomnia among adult Hispanic males?
- What are the risk factors for sleep apnea (which is a possible cause of insomnia)?
- How accurate is the overnight sleep assessment for diagnosis of chronic insomnia?

For the sake of this activity, we chose to explore the second question on our list, "What are the risk factors for sleep apnea?" We performed a brief search and found a website provided by the Mayo Clinic.[28] The website describes three types of sleep apnea: obstructive, central, and complex. The most common form is obstructive sleep apnea, which occurs when throat muscles relax. Central sleep apnea occurs when the brain fails to send the proper signals to the muscles to keep breathing. Complex sleep apnea is a combination of both.

The website included a list of risk factors for each type of sleep apnea. For obstructive sleep apnea, the website listed excess weight; neck circumference greater than 17 inches; high blood pressure; a narrow airway; male sex; age older than 65 years; family history of sleep apnea; use of alcohol, sedatives, or tranquillizers; smoking; and prolonged sitting.[28] We already know that Mr. Martinez has several of these risk factors, including being overweight, having high blood pressure, being male, and being a smoker. We have ruled out several other risk factors, including being older than 65 years of age and using sedatives or tranquillizers.

Other risk factors require additional information, such as his family history, his neck circumference, if he drinks alcohol, or if he has a narrow airway. We might also need to ask him about prolonged sitting. His work at a construction company might indicate a certain amount of physical activity, but the only way to be sure is to ask. One implication already evident from the Mayo Clinic's website is our need for additional history from the patient.

Let's return to the questions we gave you to consider for this exercise. Before we go through the questions, you might want to see if you can locate the resource yourself. When we performed this activity the website address was www.mayoclinic.com/health/sleep-apnea/DS00148/DSECTION=risk-factors. Of course it is possible, even likely, that the website address has changed. But if you can locate the Mayo Clinic website, the resource might still be there.

3a. *What type of resource did we use?* The resource is a website provided by the Mayo Clinic. It included a list of medical research references. This resource is an expert review, also known as *opinion*.

3b. *Where would the source be placed on the evidence pyramid?* It would be low on the pyramid because it is opinion. Even though the source has a strong reputation, the evidence itself is still low on the pyramid.
4a. *Does the resource apply to the patient?* Yes, mostly. The resource addresses his age, smoking history, weight, and other risk factors. However, it does not provide information on his race/ethnicity.
4b. *What are the implications for Mr. Martinez's care?* It is more likely that he could have obstructive sleep apnea than the other two types. However, more information is needed to rule out the other forms.
4c. *What further information do we need?* We would like to know if his race/ethnicity might be a risk factor for sleep apnea. Also, how are the other types of sleep apnea ruled out? How accurate is nocturnal polysomnography? What other diseases or disorders cause insomnia? How are they ruled out?

As demonstrated here, many questions can arise as a result of just one focused clinical question. Perhaps more questions come up than there are hours in the day to answer them. However, if we find information we believe to be credible and it fits with our medical knowledge as well as our experience, then we might decide to act on that information even if we have questions as yet unanswered. One of the keys to EBP is the ability to make decisions and choose a course of action. This decision should not be premature, however. It is advisable to work collaboratively with your healthcare team and seek guidance and input. In this case, the expertise of an ear, nose, and throat (ENT) physician might be helpful.

One final consideration is the risk to the patient. This risk can take the form of not getting the insomnia diagnosed and treated, an incorrect diagnosis, and/or the cost of care. In this case, the risks might be less immediate and costly than with other health problems, such as if Mr. Martinez had chest pain. But there are always risks. Your command of the research evidence will help you and your patient, reduce the chances of a bad outcome, and lead to improved quality of life for your patient.

CHAPTER SUMMARY

An understanding of research methods is necessary for healthcare providers as consumers of medical research literature. Your understanding of the foundational concepts of research and statistics will enable you to critically evaluate the studies you read, the information patients bring to you, and the brochures provided by pharmaceutical representatives. The greater your understanding of research design and statistics, the less you will be dependent on information providers about the quality of their information. The scope of topics within research design and statistics is well beyond this text, or any individual text for that matter. As such, practitioners need an arsenal of resources, including books and experts, as well as a practice of engaging in lifelong learning related to research and statistics.

The two major paradigms of research—qualitative and quantitative—offer different perspectives and types of information about health and health care. Each type of research needs to be evaluated on the merits of its design and intent. Qualitative (naturalistic) research focuses on describing experiences with health-related phenomena, but does not focus on making predictions or drawing cause-and-effect conclusions. Quantitative (positivistic) research, in contrast, seeks to predict an outcome in a population based on numerical **data** collected from a representative sample of that population. Quantitative research is more widely published and referenced in healthcare literature. However, qualitative research is growing in importance. Also, it is becoming more common for studies to combine procedures from both paradigms, producing mixed-methods research.

Various styles of research fall under each paradigm. Each style of research has distinct procedures that need to be followed in order to produce trustworthy or valid results. The three major types

of quantitative research are observational, quasi-experimental, and experimental. Qualitative research is divided into five types: ethnography, biography, phenomenology, case study, and grounded theory.

When reading studies, one way you can evaluate them is to compare the procedures used in them to the recommended procedures for the given style of research. This is true regardless of the type of research performed. As you deepen your understanding of the styles of research, you will enhance your ability to critically appraise each study you read. For example, in a grounded theory study data from multiple sources need to be triangulated with one another, a **constant comparative** analytical procedure must be used (comparing each datum with every other), and researchers should have **prolonged engagement** in the field with the respondents and with the phenomenon of interest. Researchers need to carefully describe the various procedures used in the study to establish the trustworthiness of their conclusions.

In a randomized control trial, the sample must be randomly selected and representative of the population of interest. Accurate methods of measurement must be used, and the article must carefully describe not only sampling procedures and methods of measurement but also the limitations and risks of bias in the study as well as author affiliations and study funding. The validity of the study must be demonstrated through internal procedures as well as comparison with external information.

Another way to evaluate research is to consider where a study is placed on the evidence pyramid. The pyramid recognizes quantitative research as of greater strength than qualitative research. Observational research is lower on the evidence pyramid than quasi-experimental research, which is, in turn, lower than experimental research. Qualitative studies are by definition observational and could be placed on the lower region of the pyramid if they are rigorous in design and analysis.

Similarly, retrospective and cross-sectional research (which are quantitative styles) are below prospective studies (such as cohort studies and cross-over trials) on the evidence pyramid. Nearer to the top of the pyramid are prospective randomized studies, namely those that use multiple types of blinding. Located at the top of the pyramid are studies that analyze multiple well-designed, blinded, randomized control trials. These top-level studies include systematic reviews and meta-analyses.

The location of a study on the evidence pyramid is just one factor to consider when evaluating the quality of the evidence. As mentioned earlier, the purpose of the study and quality of its design in light of that purpose are essential considerations. Research has many purposes in health care. The most common objectives of health-related research include:

- Determining the prevalence or incidence of disease and associated risk factors
- Survival longevity (with and without treatment)
- Accuracy, harms, or side effects of screening tools and diagnostic procedures
- Effectiveness and complications of treatment modalities
- Interactions between interventions
- Quality of life
- Cost of care
- Patient satisfaction

The most important consideration when evaluating an article is the applicability of the information in the study to the individual patient or population.

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