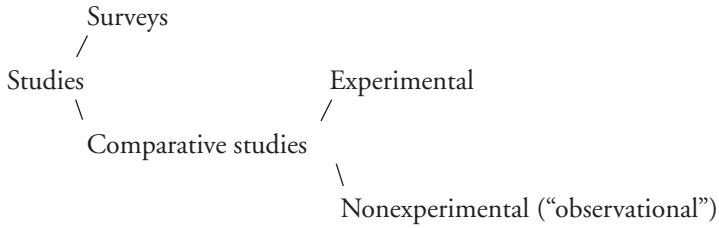
CHAPTER 2

Types of Studies

This chapter considers how data are generated for studies. Two general classes of studies are considered: **surveys** and **comparative studies**. Comparative studies come in experimental and nonexperimental forms. Therefore, our study taxonomy consists of:



The general purpose of a survey is to quantify population characteristics. Comparative studies are done to quantify relationships between variables. Because these are distinct goals, we consider surveys and comparative studies separately, starting first with surveys.

2.1 Surveys

Surveys are used to quantify population characteristics. The population consists of all entities worthy of study. A survey that attempts to collect information on all individuals in the population is a **census**. Because a true census is seldom feasible, most surveys collect data on only a portion or **sample** of the population. Data in the sample are then used to **infer** population characteristics. Sampling has many advantages. It saves time and money. It can also be more accurate,

because when fewer individuals are studied, a larger percentage of resources can be devoted to collecting high-quality information on a broad scope of variables. Sampling is the "rule" in statistics; rarely are data collected for the entire population.

Illustrative Example: *Youth Risk Behavior Surveillance (YRBS).* The Youth Risk Behavior Surveillance System monitors health behaviors in youth and young adults in the United States. Six categories of health-risk behaviors are monitored. These include: (1) behaviors that contribute to unintentional injuries and violence; (2) tobacco use; (3) alcohol and drug use; (4) sexual behaviors; (5) unhealthy dietary behaviors; and (6) physical activity levels and body weight. The 2003 report used information from 15,240 questionnaires completed at 158 schools to infer health-risk behaviors for the public and private school student populations of the United States and District of Columbia.[a] The 15,240 students who completed the questionnaires comprise the sample. This information is used to infer the characteristics of the several million public and private school students in the United States for the period in question. ■

Simple Random Samples

Samples must be collected in such a way to allow for generalizations to be made to the entire population. To accomplish this goal, the sample must entail an element of chance; a random sample must be used. The most fundamental type of random sample is a **simple random sample (SRS)**. The idea of simple random sampling is to collect data from the population so (a) each population member has the same probability of being selected into the sample and (b) the selection of any individual into the sample does not influence the likelihood of selecting any other individual. These characteristics are referred to as **sampling independence**.

Here is a more formal definition of what constitutes a simple random sample:

A simple random sample (SRS) of size *n* is selected so that all possible combinations of *n* individuals in the population are equally likely to comprise the sample.

[a]Grunbaum, J. A., Kann, L., Kinchen, S., Ross, J., Hawkins, J., Lowry, R., et al. (2004). Youth risk behavior surveillance—United States, 2003. *MMWR Surveillance Summary*, 53(2), 1–96. Available: www.cdc.gov/mmwr/preview/mmwrhtml/ss5302a1.htm.

An SRS can be achieved by placing identifiers for population members in a hat, thoroughly mixing up the identifiers, and then blindly drawing entries. In practice, a table of random digits or a software program is used to aid in the selection process.

Tables of Random Digits

Table A in the back of this book lists 2000 random digits. Each digit 0 through 9 is equally likely to occur at any position in the table. This makes selection of any sequence of digits equally likely no matter where you enter the table.

Numbers are listed in groups of five to make it easier to follow sequences along the table.[b] Here is the first line of digits in the table:

79587 19407 49825 58687 99639 82670 73457 53546 30292 75741

To select an SRS of size n from a population with N individuals:

1. Number each population member with a unique identifier number 1 through N.
2. Pick an arbitrary spot to enter Table A. Change the spot of entry each time you make a new selection.
3. Go down the rows (or columns) of the table, selecting appropriate tuples of numbers. For example, select digit-pairs if N is no more than 99, select triplets if N is no more than 999, and so on.
4. Continue selecting tuples until you have n relevant entries.

Illustrative Example: *Selecting a simple random sample.* Suppose a high school population has 600 students and you want to choose three students at random from this population. To select an SRS of $n = 3$:

1. Get a roster of the school. Assign each student a unique identifier 1 through 600.
2. Enter Table A at (say) line 15. Line 15 starts with these digits:

   76931 95289 55809 19381 56686

3. The first six triplets of numbers in this line are: 769, 319, 528, 955, 809, and 193.

continues

[b] Number groupings have no special meaning.

continues

4. The first triplet (769) is excluded because there is no individual with that number in the population. The next two triplets (319 and 528) identify the first two students to enter the sample. The next two triplets (955, 809) are not relevant. The last student to enter the sample is student 193.

The final sample is composed of students with the IDs 319, 528, and 193. ■

Software programs that generate random numbers are often used in practice.[c]

Notes

1. **Sampling fraction.** The ratio of the size of sample (n) to the population size (N) is the sampling fraction. For example, in selecting $n = 6$ individuals from a population of $N = 600$, the sampling fraction $= \frac{6}{600} = 0.01$ or 1%.[d]
2. **Sampling with replacement and sampling without replacement.** Sampling a finite population can be done with replacement or without replacement. Sampling with replacement is accomplished by "tossing" selected members back into the mix after they have been selected. In this way, any given unit can appear more than once in a sample. This may seem odd, but all N members of the population still have a $\frac{n}{N}$ chance of being selected at each draw and random sampling is still achieved. **Sampling without replacement** is done, so that once a population member has been selected, the selected unit is removed from possible future reselection. This too is a legitimate way to select a simple random sample. The distinction between sampling with replacement and without replacement is of consequence only when more complex sampling designs are used.

[c]A true random number generator is available at www.random.org. This site is owned and maintained by Mads Haahr, Distributed Systems Group, Department of Computer Science, University of Dublin, Trinity College, Ireland.

[d]If the sampling fraction is above 5%, a finite population correction factor must be incorporated into some statistical formulas. In this introductory text, we consider only sampling fractions are smaller than 5%. For addressing samples that use large sampling fractions see Cochran, W. G. (1977). *Sampling Techniques* (3 ed.). New York: Wiley.

3. **Cautions.** Samples that tend to overrepresent or underrepresent certain segments of the population can **bias**[e] the results of a survey in favor of a certain outcome. Here are examples of selection biases we wish to avoid:

   - **Undercoverage** occurs when some groups in the source population are left out of or are underrepresented on the population listing. Sampling from such a list will undermine the goal of achieving equal probabilities of selection.
   - **Volunteer bias** can occur because self-selected participants of a survey tend to be atypical of the population. For example, web surveys may produce flawed results because people who are aware of a web site or its sponsor are often interested in a particular point of view. Individuals who take the time to respond to a web survey are further self-selected.
   - **Nonresponse bias** occurs when a large percentage of individuals refuse to participate in a survey or cannot otherwise be contacted. Nonresponders often differ systematically from responders, skewing results of the survey.

4. **When random sampling is not possible.** Surveys should use random sampling techniques to collect data whenever possible. However, practical limitations often prevent this from happening. When a sample is not random, it is necessary to ask if the data in the survey can reasonably be viewed as if it were generated by a random sampling technique.

Other Types of Probability Samples[f]

A **probability sample** is a sample in which each member of the population has a known probability of being selected into the sample. Simple random sampling is the most basic type of probability sample, serving as the building block for more complex sampling designs. In practice, more complex probability samples are often required. Three such schemes are stratified random sampling, cluster sampling, and multistage sampling.

A **stratified random sample** is a sample that draws independent SRSs from within relatively homogeneous groups or "strata." For example, the population can be divided into 5-year age groups (0–4, 5–9, . . .) with simple random samples of varying sizes drawn from each age-strata. Results can then be combined based on the sampling fractions used within each stratum.

Cluster samples randomly select large units (clusters) consisting of smaller subunits. This allows for random sampling when there is no reliable list of sub-

[e]The term *bias* in statistics refers to a systematic error.
[f]Your instructor may choose to skip this section without hindering further study.

units but there is a reliable list of the clusters. For example, we may have a list of household addresses but not of individuals within the households. Households (clusters) are selected at random, and all individuals are studied within the clusters.

Large-scale surveys often use **multistage sampling** techniques in which large-scale units are selected at random. Then, subunits are sampled in successive stages. The Youth Behavior Survey (introduced earlier) used a multistage sample.

Illustrative Example: *Youth Risk Behavior Survey (YRBS).* The population ("sampling frame") for the YRBS consisted of all public and private schools with students in grades 9–12 in the 50 United States plus the District of Columbia. This sampling frame was divided into 1262 primary sampling units, which consisted of counties, areas of large counties, or groups of small counties. From these 1262 primary units, 57 were selected at random with probability proportional to overall school enrollments. The next stage of sampling selected 195 schools at random with probability proportional to the school enrollment size. The third sampling stage consisted of randomly selecting one or two intact classes from each grade from within the chosen school. All students in the selected classes were then eligible to participate in the survey. Here's a schematic representation of the three stages of sampling used by the YRBS:

1262 primary sampling units (counties or other large areas)
|
Stage 1 random sample
↓
57 primary sampling units
|
Stage 2 random sample
↓
195 schools
|
Stage 3 random sample
|
Unstated number of classrooms
↓
15,240 questionnaires

■

Exercises

2.1 ***Sample and population.*** For the scenarios presented here, identify the source population and sample as specifically as possible. If information is insufficient, do your best to provide a reasonable description of the population and sample and then suggest additional "person, place, and time characteristics" that are needed to better define the population.

(a) A study that reviewed 125 discharge summaries from a large university hospital in metropolitan Detroit found that 35% of the individuals in the hospital received antibiotics during their stay.

(b) A study of eighteen 35- to 44-year-old diabetic men found a mean body mass index that was 13% above what is considered to be normal.

2.2 ***A survey of rheumatoid arthritis patients.*** A survey mailed questionnaires to 486 patients with rheumatoid arthritis. Responses were received from 334 patients, corresponding to a response rate of 69%. Nonresponders were traced and approached for a telephone interview. Two percent (2%) of the responders reported "never having pain" during the study interval, while 6% of eligible participants reported "no pain." Two percent (2%) of responders reported "no contact" with health care services during the follow-up interval, compared with 4% of eligible responders.[g] Would you trust the results of the survey based solely on the information from initial responders? Explain your response.

2.3 ***California counties.*** As a pilot investigation for a survey of California county health departments, you want to select four counties at random from the list of counties in **Table 2.1** Use the table of random digits (Table A) starting in row 33 to select your simple random sample.

2.2 Comparative Studies

The Basics

The general objective of comparative studies is to learn about the relationship between an explanatory variable and response variable. Whereas being able to infer population characteristics based on a sample was the leading concern in

[g]Rupp, I., Triemstra, M., Boshuizen, H. C., Jacobi, C. E., Dinant, H. J., & van den Bos, G. A. (2002). Selection bias due to non-response in a health survey among patients with rheumatoid arthritis. *European Journal of Public Health, 12*(2), 131–135.

Table 2.1 California counties.

01 Alameda	21 Marin	41 San Mateo
02 Alpine	22 Mariposa	42 Santa Barbara
03 Amador	23 Mendocino	43 Santa Clara
04 Butte	24 Merced	44 Santa Cruz
05 Calaveras	25 Modoc	45 Shasta
06 Colusa	26 Mono	46 Sierra
07 Contra Costa	27 Monterey	47 Siskiyou
08 Del Norte	28 Napa	48 Solano
09 El Dorado	29 Nevada	49 Sonoma
10 Fresno	30 Orange	50 Stanislaus
11 Glenn	31 Placer	51 Sutter
12 Humboldt	32 Plumas	52 Tehama
13 Imperial	33 Riverside	53 Trinity
14 Inyo	34 Sacramento	54 Tulare
15 Kern	35 San Benito	55 Tuolumne
16 Kings	36 San Bernardino	56 Ventura
17 Lake	37 San Diego	57 Yolo
18 Lassen	38 San Francisco	58 Yuba
19 Los Angeles	39 San Joaquin	
20 Madera	40 San Luis Obispo	

surveys, "comparability" is the leading concern in comparative studies; that is, when we compare groups, they should be similar in as many ways possible except for that of the explanatory factor. This is because the effects of a factor can be judged only in relation to what would happen in its absence; "like-to-like" comparisons are necessary for valid results.

In their most basic form, comparative studies compare responses from one group that is exposed to an explanatory factor to those of a group that is not exposed. There are two general ways to accomplish this; either experimentally or nonexperimentally. In **experimental studies**, the investigator assigns the exposure to one group while leaving the other nonexposed. In **nonexperimental studies**, the investigator merely classifies individuals as exposed or nonexposed without intervention. Nonexperimental studies are also called **observational studies**.[h] **Figure 2.1** depicts schematics of experimental and nonexperimental study designs.

Various types of control groups may be used in experimental studies. One type is the **placebo** control. A placebo is an inert or innocuous intervention. Even though the placebo is inert, we expect changes to occur after its adminis-

[h]"Nonexperimental study" is preferable because both experimental studies and nonexperimental studies require observation.

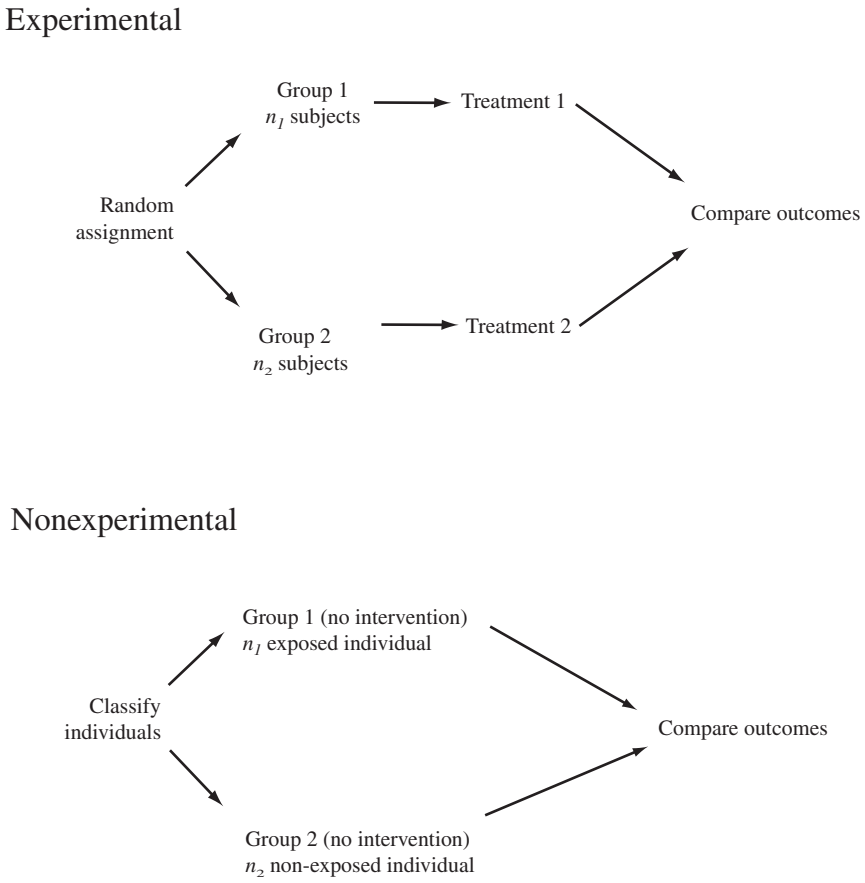


FIGURE 2.1 Experimental and nonexperimental study designs.

tration. Some of this change is random, some is due to the natural history of events, and some is due to "the placebo effect."[i] Another type of control group is the active control group. Active controls receive an alternative physiologically active treatment or intervention. In using either a placebo control or active control, the control group is handled and observed in the same manner as the treatment group. This helps sort out changes due to the treatment and those due to other factors.

[i]The placebo effect is the perceived improvement following treatment with a placebo. Why the placebo effect occurs is a bit of a mystery but may be related to the fact that subjects know they are being observed and cared for.

Illustrative Example: *Multiple Risk Factor Intervention Trail (MRFIT).* The Multiple Risk Factor Intervention Trial (MRFIT is pronounced *Mister Fit*) was conducted in the late 1970s and early 1980s to test the effectiveness of coronary disease prevention programs.[j] Study subjects were randomly assigned to either a treatment group that received special interventions intended to reduce the risk of heart disease or a control group that received their usual sources of health care. The study found that heart disease mortality declined significantly in both groups. This is because observations took place at a time when the population was learning about the benefits of low-fat diets, exercise, smoking cessation, and other cardiovascular disease-prevention strategies. Had there been no concurrent control group, the interventions would have mistakenly been viewed as effective and considerable resources might have been wasted on ineffective programs. This shows the importance of using a concurrent control group to establish the effect of a treatment. ■

Explanatory Variable and Response Variable

Comparative studies have explanatory variables and response variables. The **explanatory variable** is the treatment or exposure that explains or predicts changes in the response variable. The **response variable** is the outcome or response being investigated. In the MRFIT illustrative example, the explanatory variable is enrollment in the special intervention program. The response variable is whether a cardiovascular incident occurred during the observation period.

Exercises

2.4 ***Explanatory variable and response variable.*** Identify the explanatory variable and response variable in each of the studies described here.

(a) A study of cell phone use and primary brain cancer suggested that cell phone use was not associated with an elevated risk of brain cancer.[k]

(b) Records of more than three-quarters of a million surgical procedures conducted at 34 different hospitals were monitored for anesthetics safety. The study found a mortality rate of 3.4% for one particular

[j]Multiple Risk Factor Intervention Trial Research Group. (1982). Risk factor changes and mortality results. *JAMA*, 248(12), 1465–1477.

[k]Muscat, J. E., Malkin, M. G., Thompson, S., Shore, R. E., Stellman, S. D., McRee, D., et al. (2000). Handheld cellular telephone use and risk of brain cancer. *JAMA*, *284*(23), 3001–3007.

anesthetic. No other major anesthetics was associated with mortality greater than 1.9%.[l]

(c) In a landmark study involving more than three-quarters of a million individuals in the United States, Canada, and Finland, subjects were randomly given either the Salk polio vaccine or a saline (placebo) injection. The vaccinated group experienced a polio rate of 28 per 100,000 while the placebo group had a rate of 69 per 100,000. A third group that refused to participate had a polio rate of 46 per 100,000.[m]

2.5 ***Experimental or nonexperimental?*** Determine whether each of the studies described in Exercises 2.4 are experimental or nonexperimental. Explain your reasoning in each instance.

Confounding

Studies (a) and (b) in Exercise 2.4 are nonexperimental because the explanatory factors (cell phone use and anesthetic type, respectively) were *not* interferred with by the study protocol. Instead, study subjects were merely classified into exposed

Illustrative Example: *WHI postmenopausal hormone use trial.* Until 2002, postmenopausal hormone use in women was routine in the United States. Nonexperimental studies had suggested estrogen use reduced heart attack risk by about 50%. Because other risks associated with postmenopausal hormone use were small by comparison, there was a general consensus that postmenopausal hormones had an overall health benefit.

Things changed following publication of an experimental trial done as part of an NIH-sponsored *Women's Health Initiative* (WHI) investigation. Results from the WHI trial revealed that hormone use did *not* reduce the risk of heart attacks. In fact, overall cardiovascular disease mortality was significantly increased in the women who were assigned hormones.[n] How can we explain the fact that the experimental studies contradicted the non-experimental studies and the then-current state of knowledge? ■

[l]Moses, L. E., & Mosteller, F. (1972). Safety of anesthetics. In J. M. Tanur, F. Mosteller, W. Kruskal, R. F. Link, P. R. S. & G. R. Rising (Eds.). *Statistics: A guide to the unknown* (pp. 14–22). San Francisco: Holden-Day.

[m]Francis, T. (1957). Symposium on controlled vaccine field trials: Poliomyelitis. *American Journal of Public Health*, *47*, 283–287.

[n]Writing Group for the Women's Health Initiative Investigators. (2002). Risks and benefits of estrogen plus progestin in healthy postmenopausal women: Principal results from the Women's Health Initiative randomized controlled trial. *JAMA*, *288*(3), 321–333.

and nonexposed groups based on what had already occurred. Because of this, nonexperimental studies like these present special challenges in interpretation.

It turns out that discrepancies in experimental and nonexperimental study results are not uncommon. In the example just mentioned, the nonexperimental studies did not interfer with hormones use in subjects, so exposure was self-selected. It was later determined that hormone users and nonusers differed in ways other than hormone use. Hormone users were generally healthier, wealthier, and better educated than nonusers. These **lurking variables** got mixed up with the effects of hormone use, **confounding** the results of the nonexperimental studies.

Confounding is a distortion in an association between an explanatory variable and response variable brought about by the influence of extraneous factors.

Confounding occurs when the effects of the explanatory variable get mixed up with those of extraneous variables. The lower risk of coronary disease in the hormone users in the nonexperimental studies of postmenopausal hormone use reflected the effect of these extraneous variables, not of hormone use. Because the experimental WHI study assigned hormone use according to the "toss of a coin," differences at the end of the study would have to be attributable to either the hormone treatment or to chance differences in the groups. It is for this reason that experimental studies provide an important point of reference for nonexperimental studies.[o] Therefore, we will initially focus on experimental studies, later applying some of these principles to nonexperimental studies.

Factors and Treatments

The term **subject** refers to an individual who participates in a study. Explanatory variables in experiments will be referred to as **factors**. A **treatment** is a specific set of factors applied to subjects.

Figure 2.2 displays the WHI study design in schematic form. Schematics such as this will be used to depict the number of study subjects, randomization scheme, and study outcome.

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[o]Miettinen, O. S. (1989). The clinical trial as a paradigm for epidemiologic research. *Journal of Clinical Epidemiology*, *42*(6), 491–496.

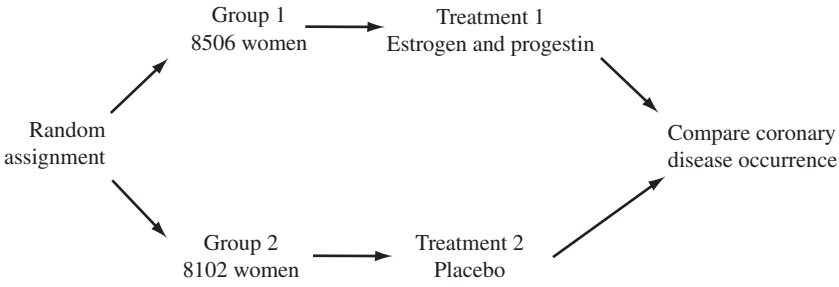

FIGURE 2.2 Study design outline, WHI illustrative example.

Illustrative Example: *WHI postmenopausal hormone use trial.* In the WHI trial, the primary study *factor* was postmenopausal hormone use. The study was initially designed to address three treatments: unopposed estrogen, estrogen plus progestin, and an inert placebo. It was later discovered that unopposed estrogen was contraindicated in postmenopausal women with intact uteri, so the protocol was altered to include only two treatments: estrogen with progestin and a placebo. Treatments were then randomized to subjects in approximately equal proportions. ■

Exercise

2.6 ***MRFIT.*** The MRFIT study discussed in an earlier illustrative example studied 12,866 high-risk men between 35 and 57 years of age. Approximately half the study subjects were randomly assigned to a special care group; the other half received their usual source of care. Death from coronary disease was monitored over the next seven or so years. Outline this study's design in schematic form.

2.7 ***Five-City Project.*** The Stanford Five-City Project is a comprehensive community health education study of five moderately sized Northern California towns. Multiple-risk factor intervention strategies were randomly applied to two of the communities. The other three cities served as controls.[P] Outline the design of this study in schematic form.

By applying factors in combination, experiments can study more than one factor at a time.

[P]Fortmann, S. P. & Varady, A. N. (2000). Effects of a community-wide health-education program on cardiovascular disease morbidity and mortality: The Stanford Five-City Project. *American Journal of Epidemiology*, *152*(4), 316–323.

Illustrative Example: *Hypertension trial.* A trial looked at two explanatory factors in the treatment of hypertension. Factor A was a health-education program aimed at increasing physical activity, improving diet, and lowering body weight. This factor had two levels: active treatment or passive treatment. Factor B was pharmaceutical treatments at three levels: Medication A, Mediation B, and placebo. Because there were two levels of the health-education variable and three levels of pharmacological variable, the experiment evaluated six treatments, as shown in **Table 2.2**.

The response variable was "change in systolic blood pressure" after six months. One-hundred-twenty subjects were studied in total, with equal numbers assigned to each group. **Figure 2.3** is a schematic of the study design.

Table 2.2 Hypertension treatment trial with two factors and six treatments.

		Factor B		
		Medication A	Medication B	Placebo
Factor A Health Education	Active	1	2	3
	Passive	4	5	6

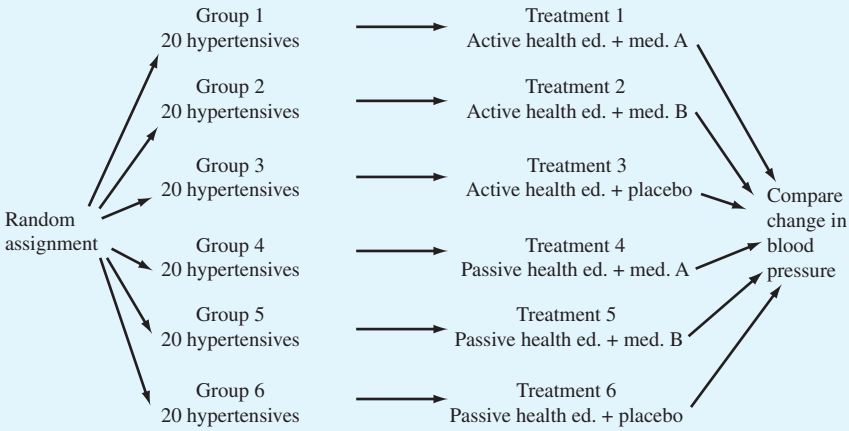

FIGURE 2.3 Study design outline, hypertensive treatment trial illustrative example. ■

Studies with multiple factors allow us to learn about the individual and combined effects of factors. For example, in the hypertension trial illustration, one of the medications might be particularly effective when combined with a lifestyle change. When two factors produce an effect that would otherwise not be predicted by studying them separately, an **interaction** is said to be present.

An interaction occurs when factors in combination produce an effect that could not be predicted by looking at the effect of each factor separately.

Random Assignment of Treatments

Experiments involving human subjects are called **trials**. Trials with one or more control groups are **controlled trials**. When the assignment of the treatment is based on chance, this is a **randomized controlled trial**. As noted earlier, randomization helps us sort out the effects of the treatment from those of lurking variables.

Illustrative Example: *Poliomyelitis trial*. In the 1954 poliomyelitis field trial mentioned in Exercise 2.4(c), subjects were randomly assigned to either the Salk polio vaccine group or a saline placebo group. When the trial was initially proposed, there was a suggestion that everyone who agreed to participate in the study be given the vaccine while those who refused to participate serve as the control group. Fortunately, this did not occur and a placebo control group was included in the study. It was later revealed that "refusers" had atypically low polio rates. Had the refusers been used as the control group, the benefits of the vaccine would have been greatly underestimated.[9] ■

To randomly assign a treatment:

- Label each subject who will be participating in the study with numbers 1 through N.
- Let n_1 represent the number of individuals you will have in the first treatment group.
- Enter Table A at an arbitrary location. Change the location each time you use the table.

[9]Francis, T., Jr., Napier, J. A., Voight, R. B., Hemphill, F. M., Wenner, H. A., Korns, R. F., et al. (1957). *Evaluation of the 1954 Field Trial of Poliomyelitis Vaccine*. Ann Arbor: University of Michigan.

Illustrative Example: *HCV trial.* Chronic infection with the hepatitis C virus (HCV) can lead to liver cirrhosis, hepatocellular cancer, and the need for liver transplantation. More than four million people in the United States are infected with the hepatitis C virus.[r] Suppose a pharmaceutical firm develops a new treatment for HCV infection and wants to test it in 24 individuals. The new treatment will be assigned at random to half the available subjects. The other subjects will receive the current standard treatment. Decreases in viral titer will be measured after three months on both treatments. **Figure 2.4** shows a schematic of this study's design.

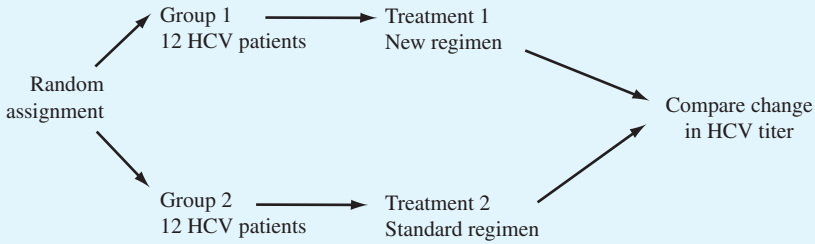

FIGURE 2.4 Study design outline, HCV treatment trial illustration.

To randomize the treatment:

- Label subjects 1 through 24.
- Twelve individuals will be assigned to each group.
- Let us enter Table A at row 34. Here are the digits in line 34 and 35 of Table A:

  34 **06**|**16**|**2** **4**|**02**|56 69|68|8 9|89|**04** 82|39|**1**
  8|29|**20**| **13**|**21**|4 2|57|43 31|80|5 8|**24**|**01**
  35 63|71|6 6|43|**11** etc.

- The first 12 pairs of digits between 01 and 24 are 06, 16, 24, 02, 04, 18, 20, 13, 21, 24, 01, and 11 (**highlighted**). Individuals with these identification numbers are assigned to the treatment group. The remaining subjects are assigned to the control group. ■

[r]CDC. (2005). *Viral hepatitis* (*NHANES Data Brief*). Available: www.cdc.gov/nchs/data/nhanes/databriefs/viralhep.pdf.

- Read across (or down) lines of the random number table to identify the first n_1 random numbers between 1 and N. Assign these individuals to treatment group 1.
- If there are two groups, the remaining n_2 study subjects are assigned to the control group. If there are more than two treatment groups, continue to select numbers from Table A to identify subjects for the next treatment group until only one group remains.

Exercises

2.8 ***MRFIT.*** The MRFIT field trial discussed as an illustrative example studied 12,866 high-risk men between 35 and 57 years of age. Use Table A starting in row 03 to identify the first two members of the treatment group.

2.9 ***Five-City Project.*** The Stanford Five-City Project (Exercise 2.7) randomized cities to either a treatment or control group. Number the cities 1 through 5. Use Table A starting in line 17 to randomly select the two treatment cities.

Blinding

Blinding is an experimental technique in which individuals involved in the study are kept unaware of treatment assignments. In a **single blinded study**, the subjects are kept in the dark about the specific type of treatment they are receiving. In a **double blinded study**, the study subjects and the investigators making

Illustrative Example: ***Ginkgo and memory enhancement.*** Ginkgo biloba is a commonly used herb that claims to improve memory and cognitive function. A randomized, double blind study in an elderly population was conducted to evaluate whether this claim is true. The treatment group consisted of subjects who took the active product according to the manufacturer's recommendation. The control group received lactose gelatin capsules that looked and tasted like the ginkgo pill. The study was *double blinded*, with subjects and evaluators administering cognitive tests unaware of whether subjects were receiving the ginkgo or placebo. Analysis revealed no difference in any of the cognitive functions that were measured.[5] ■

[5]Solomon, P. R., Adams, F., Silver, A., Zimmer, J., & DeVeaux, R. (2002). Ginkgo for memory enhancement: a randomized controlled trial. *JAMA*, *288*(7), 835-840.

measurements are kept in the dark. In **triple blind** studies, the study subjects, investigators, and statistician analyzing the data are kept in the dark.

Double blinding helps avoid biases associated with the reporting and recording study outcomes. When errors in measurement do occur, they are likely to occur equally in the groups being compared, mitagating more serious forms of bias.

Exercise

2.10 ***Controlled-release morphine in patients with chronic cancer pain.*** Warfield reviewed 10 studies comparing the effectiveness of controlled-release and immediate-release morphine in cancer patients with chronic pain.[t] The studies that were reviewed were double blinded. How would you double blind such studies?

Ethics

Because experiments require that the explanatory variable be assigned by the study protocol and not by subjects or their agents, they present special ethical concerns. In general, an experiment can neither withhold an effective treatment nor assign a potentially harmful one. Therefore, a genuine void in knowledge must exist before beginning a trial. Doubt about benefits and risk must be in perfect balance before the trial is begun. Balanced doubt of this type is called **equipoise**.

Of course there are other ethical concerns when conducting studies in human subjects. These include respect for individuals, informed consent (subjects must comprehend the consequences of participating in the study and have freely given consent to participate), beneficence (direct and indirect physical, psychological, and socioeconomic risks and benefits of doing the study have been assessed and are on balance beneficial), and justice (selection of study subjects is equitable).[u] **Institutional review boards (IRBs)** independently review study protocols and results to oversee that ethical guidelines are met.

Vocabulary

Bias
Blinding
Census
Cluster samples
Comparative study
Confounding

[t]Warfield, C. A. (1998). Controlled-release morphine tablets in patients with chronic cancer pain. *Cancer*, *82*(12), 2299–2306.
[u]Belmont Report. (1979). *Ethical principles and guidelines for the protection of human subjects of research.* from: http://ohrp.osophs.dhhs.gov/humansubjects/guidance/belmont.htm.

Controlled trial
Double blinded
Equipoise
Experimental studies
Explanatory variable
Factors
Infer
Interaction
Lurking variables
Multistage sampling
Nonexperimental studies
Nonresponse bias
Placebo
Population
Probability sample
Randomized-controlled trial
Sample
Sampling frame
Sampling independence
Simple random sample (SRS)
Single-blinded
Stratified random sample
Subjects
Survey
Treatment
Trials
Triple blinded
Undercoverage
Volunteer bias

Exercises

2.11 ***Campus survey.*** A researcher conducts a survey to learn about the sexual behavior of college students on a particular campus. A list of the undergraduates at the university is used to select participants. The investigator sends out 500 surveys but only 136 are returned.

(a) Consider how the low response rate could bias the results of this study.

(b) Speculate on potential limitations in the quality of information the researcher will receive on questionnaires that are returned.

2.12 ***Sampling nurses.*** You want to survey nurses who work at a particular hospital. Of the 90 nurses who work at this hospital, 40 work in the maternity ward, 20 work in oncology, and 30 work in the surgical ward. You decide to study 10% of the nurse population so you choose nine nurses as follows: four nurses are chosen at random from the 40 maternity nurses, two are chosen at random from the 20 oncology nurses, and three surgical nurses are chosen at random from the surgical nurses. Is this a simple random sample? Explain your response.

2.13 ***Telephone book sampling frame.*** Telephone surveys may use a telephone directory to identify individuals for study. Speculate on the type of household that would be undercovered by using this sampling frame.

2.14 ***Random digit dialing.*** Random-digit dialing is often used to select telephone survey samples. This technique randomly selects the last four

digits of a telephone number from a telephone exchange. (An exchange is the first three telephone numbers after the area code.) This type of sample gets around the problem of using a telephone book as a sampling frame, however, other types of problems may still be encountered. What types of selection biases may ensue from this method?

2.15 ***Four-naughts.*** Could the number "0000" appear in a table of random digits? If so, how likely is this?

2.16 ***Class survey.*** A simple random sample of students is selected from students attending class. Identify a problem with this sampling method.