Chapter 5

Experiments, Good and Bad
Example: Online Learning

In a study at Nova Southeastern University, Florida the authors claim that students taking undergraduate courses online were “equal in learning” to students taking the same course in class.

Replacing college classes with web sites saves colleges money, so this study suggests we should all move online.
Example: Pig whipworm eggs

Chron’s disease is a chronic inflammatory bowel disease. An experiment reported in a British medical journal, claimed that a drink containing thousands of pig whipworm eggs was effective in reducing abdominal pain, bleeding, and diarrhea associated with the disease.
Example: Day care for low-income children

- Should the government provide day care for low-income children?

- If day care helps these children to stay in school and hold good jobs later in life, the government would save money by paying less welfare and collecting more taxes, so even those who only count dollars might support day care programs.

- The Carolina Abecedarian Project has followed a group of children since 1972. The results show that good day care makes a big difference in later school and work.
• The study about online learning is an observational one that can’t be trusted to give good evidence about learning in online college courses.

• The experiment involving pig whipworm eggs to treat Chron’s disease in intriguing but not conclusive.

• The results of Abecedarian Project are about as convincing as evidence about the long-term effects of day care can be.

• What makes some studies, especially some experiments, convincing? Why should we ignore others?
Common Language

• **Response variable**
  – what is measured as the outcome or result of a study

• **Explanatory variable**
  – what we think explains or causes changes in the response variable
  – often determines how subjects are split into groups

• **Subjects**
  – the individuals that are participating in a study

• **Treatments**
  – specific experimental conditions (related to the explanatory variable) applied to the subjects
• College students are the subjects in the Nova Southeastern study.

• The explanatory variable is the setting for learning (in class or online).

• The response variable is a student’ score on a test at the end of the course.
Figure 5.1 Confounding in the Nova Southeastern University study. The influence of course setting (the explanatory variable) cannot be distinguished from the influence of student preparation (a lurking variable).
Confounding

• Lurking variable
  – A variable that has an important effect on the relationship among the variables in a study but not one of the explanatory variables studied.

• Confounded
  – Two variables are **confounded** when their effects on a response variable cannot be distinguished from each other. The confounded variables may be either explanatory variables or lurking variables.
Placebo effect

• Experiments that study the effectiveness of medical treatments on actual patients are called **clinical trials**.
• The clinical trial suggested that a drink made from pig whipworm eggs might be effective in relieving the symptoms of Chron’s disease had a “one-track” design:

  Impose treatment \(\rightarrow\) Measure response

  Pig whipworms \(\rightarrow\) Reduced symptoms?

• The patients did report reduced symptoms but we can’t say that the pig whipworm treatment caused the reduced symptoms. It might be just the **placebo effect**.
• A **placebo** is a dummy treatment with no active ingredients.
• Many patients respond favorably to **any** treatment, even a placebo.
• Designing an experiment to include a group of subjects who receive only a placebo. This would allow us to see whether the treatment being tested does better than a placebo and has more than the placebo effect going for it.
Randomized Experiment versus Observational Study

Both typically have the goal of detecting a relationship between the explanatory and response variables.

• Experiment
  – *create* differences in the explanatory variable and examine any resulting changes in the response variable

• Observational Study
  – *observe* differences in the explanatory variable and notice any related differences in the response variable
Randomized Comparative Experiments

- The first goal in designing an experiment is to ensure that it will show us the effect of the explanatory variable on the response variables.
- Confounding often prevents one-track experiments from doing this.
- The remedy is to compare two or more treatments.
Example: Sickle cell anemia

• Sickle cell anemia is an inherited disorder of the red blood cells that in the U.S. affects mostly blacks.

• NIH carried out a clinical trial of the drug hydroxyurea on 299 adult patients who had at least three episodes of pain from sickle cell anemia in the previous year.

• Simply giving hydroxyurea to all 299 subjects would confound the effect of the medication with the placebo effect and other lurking variables such as the effect of knowing you are the subject in an experiment.

• Instead, approximately half of the subjects received hydroxyurea, and the other half received a placebo that looked and tasted the same.

• All subjects were treated exactly the same except for the content of the medicine they took. Lurking variables therefore affected both groups equally and should not cause any differences between their average responses.
Example: Sickle cell anemia

• An SRS of 152 of the subjects formed the hydroxyurea group; the remaining 147 subjects made the placebo group.
• The experiment was stopped ahead of schedule because the hydroxyurea group had many fewer pain episodes than the placebo group. This was compelling evidence that hydroxyurea is an effective treatment for sickle cell anemia.

FIGURE 5.2 The design of a randomized comparative experiment to compare hydroxyurea with a placebo for treating sickle-cell anemia, for Example 4.
Example: Sickle cell anemia

FIGURE 5.2 The design of a randomized comparative experiment to compare hydroxyurea with a placebo for treating sickle-cell anemia, for Example 4.

- This figure illustrates the simplest Randomized Comparative Experiment, one that compares two treatments.
- The placebo group in this example is called a control group because comparing the treatment and control groups allow us to control the effects of lurking variables.
Why Not Always Use a Randomized Experiment?

- Sometimes it is unethical or impossible to assign people to receive a specific treatment.
- Certain explanatory variables, such as handedness or gender, are inherent traits and cannot be randomly assigned.
Confounding (Lurking) Variables

• The problem:
  – in addition to the explanatory variable of interest, there may be other variables that make the groups being studied different from each other
  – the impact of these variables cannot be separated from the impact of the explanatory variable on the response
Confounding (Lurking) Variables

• The solution:
  – **Experiment**: randomize experimental units to receive different treatments (possible confounding variables should “even out” across groups)
  – **Observational Study**: measure potential confounding variables and determine if they have an impact on the response (may then **adjust** for these variables in the statistical analysis)
The logic of experimental design

- **Randomization** produces groups of subjects that should be similar in all respects before we apply the treatments.
- **Comparative design** ensures that influences other than the experimental treatments operate equally on all groups.
- Therefore, differences in the response variable must be due to effects of the treatments.
Principles of experimental design

1. **Control** the effects of lurking variables on the response, most simply by comparing two or more treatments.

2. **Randomize**—use impersonal chance to assign subjects to treatments.

3. **Use enough subjects** in each group to reduce chance variation in the results.
Statistical Significance

• If an experiment or observational study finds a difference in two (or more) groups, is this difference really important?

• If the observed difference is larger than what would be expected just by chance, then it is labeled statistically significant.
• The difference between the average number of pain episodes for subjects in the hydroxyurea group and the average for the control group was “highly statistically significant”.

• That means that a difference of this size would almost never happen just by chance.

• We do indeed have strong evidence that hydroxyurea beats a placebo in helping sickle cell disease sufferers.
Key Concepts

• Critical evaluation of an experiment or observational study

• Common terms
  – explanatory vs. response variables
  – treatments, randomization

• Randomized experiments
  – basic principles and terminology
  – problem with confounding variables
Exercise 5.2

• Treating breast cancer. What is preferred treatment for breast cancer that is detected in early stages? The most common treatment was once removal of the breast. It is now usual to remove only the tumor and nearby lymph nodes, followed by radiation. To study whether these treatments differ in their effectiveness, a medical team examines the records of 25 large hospitals and compares the survival times after surgery of all women who have had either treatment.

a) What are the explanatory and response variables?
b) Explain carefully why this study is not an experiment.
c) Explain why confounding will prevent this study from discovering which treatment is more effective. (The current treatment was in fact recommended after a large randomized comparative experiment.)
Exercise 5.6

- Aspirin and heart attacks. Can aspirin help prevent heart attacks? The physicians’ Health Study, a large medical experiment involving 22,000 male physicians, attempted to answer this question. One group of about 11,000 physicians took an aspirin every second day, while the rest took placebo. After several years the study found that the subjects in the aspirin group had significantly fewer heart attacks than subjects in the placebo group.

a) Identify the experimental subjects, the explanatory variable and the values it can take, and the response variable.

b) Use a diagram to outline the design of the Physicians’ Health Study. (When you outline the design of an experiment be sure to indicate the size of the treatment groups and the response variable.)

c) What do you think the term “significantly” means in “significantly fewer heart attacks”?
Exercise 5.11

• Do antioxidants prevent cancer? People who eat lots of fruits and vegetables have lower rates of colon cancer than those who eat little of these foods. Fruits and vegetables are rich in “antioxidants” such as vitamins A, C, and E. Will taking antioxidants help prevent colon cancer? A clinical trial studied this question with 864 people who were at risk for colon cancer. The subjects were divided into four groups: Daily beta-carotene, daily vitamins C and E, all three vitamins every day, and daily placebo. After four years, the researchers were surprised to find no significant difference in colon cancer among the groups.

a) What are the explanatory and response variables in this experiment?
b) Outline the design of the experiment.
c) Assign labels to the 864 subjects and use Table A, starting at line 118, to choose the first 5 subjects for the beta-carotene group.
d) What does “no significant difference” mean in describing the outcome of the study?
e) Suggest some lurking variables that could explain why people who eat lots of fruits and vegetables have lower rates for colon cancer. The experiment suggests that these variables, rather than the antioxidants, may be responsible for the observed benefits of fruits and vegetables.