Chapter 1: Introduction

Statistical studies may be roughly divided according to the possible scope of inference as either observational studies or controlled experiments.

Observational studies: The researcher collects data without manipulating the units. Examples:

1. Smoking and lung cancer studies involving humans are observational because the usual protocol is to observe whether a person smokes or not (or how much they smoke) and whether they develop lung cancer.

2. Recruit a set of volunteers (children) and administer the Sabin polio vaccine. The proportion of subjects that contract the disease provides suggestive information on the effectiveness of the vaccine. However, it is not possible to be confident that the results are attributable to the vaccine since there may be other factors are responsible. The 1960 Sabin polio vaccine trial in the Soviet Union used 10 million children in this manner.

Observational studies are one of two types:

1. Retrospective studies: The current condition of the subjects are known (for example diseased or not) and data are collected on the past history of the subjects. 
   Example: A 1995 study carried out in Wales examined the association between oral contraception use and heart attacks. Two samples of women were collected. The first sample consisted of women that had been treated for a heart attack, the second consisted of women that had not experienced a heart attack. The rate of contraceptive use was compared between groups.
   - The response variable values (whether or not they had experienced a heart attack) was observed at the time the data was collected. The explanatory variable (whether or not they used an oral contraceptive) reflects the past history of the women.

2. Prospective studies: The explanatory variable (but not the response variable) is observed at the beginning of the study. The subjects are observed a later time to record the value of the response variable.
   Example: In the observed control arm of the Salk vaccine trials, 221,998 second-graders received the vaccine and 503,175 first- and third-grade volunteers acted as controls (receiving nothing). Records were maintained on general health and incidence of polio-like symptoms of these volunteers from the beginning to the end of the 1954 polio

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1Polio is a seasonal disease, and the severity of the polio season depends on weather and other factors.
season. Based on these data, the odds of contracting paralytic polio are estimated to be 2.60 for an unvaccinated child compared to a vaccinated child.

**Controlled Experiments:** The researcher controls (manipulates) the value of the *explanatory variable* on each unit. Specifically, each experimental unit is randomly assigned to a group. Subjects in each group receive the same treatment (one level of the explanatory variable), and no two groups receive the same treatment.

- Before receiving the treatments, there are little or no systematic differences between groups.

- If there are systematic differences after the treatments are administered, then it can be concluded the explanatory variable was the cause of the differences. It’s possible to draw a statistically valid conclusion stating that a *cause-and-effect* relationship exists between the response and explanatory variable.

- In the experimental arm of the 1954 Salk vaccine trials, 200,745 volunteers received the Salk vaccine (without their knowledge) and 201,229 volunteers received a placebo (without their knowledge). The assignment of volunteers to groups was random. The response variable was the incidence (y/n) of paralytic polio. The experimental branch estimate of the odds of contracting paralytic polio was 3.49.

**Strength of inferences - observational studies**

- While observational studies can establish association between two variables, they cannot establish cause-and-effect because there may be other uncontrolled variables that affect the response variable. When other variables affect the response variable, then the effect of the explanatory variable is *confounded* with the other variables.

- Kenneth Brownlee, an eminent statistician that reviewed the Salk trials, called the observed control arm (involving 725,173 volunteers) as *stupid and futile* and the results as *worthless*. Why? Without random assignment of the vaccine treatment to subjects, cause-and-effect is not a valid conclusion of this branch of the Salk trials. There may be some systematic differences between first- and third-graders, and second-graders that explains differences in the rates of paralytic polio infection.

**Strength of inferences - controlled experiments**

- It is possible to establish cause-and-effect with a high degree of confidence by conducting a properly designed controlled experiment. The key is to randomly assign subjects to different treatment groups. Each treatment group receives a different level of the explanatory variable. The only systematic differences between groups are the levels (values) of the explanatory variable. The potential effect of confounding variables is minimized and if large differences in the response variable are observed, then it is valid to conclude that differences are attributable to the explanatory variable.
Random assignment of experimental units to treatment groups cannot completely eliminate the possibility of systematic differences between groups before the treatments are applied. The risk of residual systematic differences can be minimized by using large numbers of experimental units.

**Experimental design terminology**

1. The *experimental units* are the units used in the experiment. If the units are people, they are referred to as subjects or participants. The experimental units must be representative of the population, and so they ought to be selected using a simple sampling design.

2. The explanatory variable is referred to as a *factor*. A factor may be quantitative or categorical.

3. A factor has several *levels* (or values) in an experiment. Levels are chosen by the researcher. In the 1954 Salk polio vaccine trials, the factor was amount of the vaccine in the injection given to a subject. Levels were present and absent.

4. A *treatment* is a particular combination of factor levels applied to some units in the experiment. In the experimental arm of the 1954 Salk polio vaccine trials, the treatments are present and absent (since there is one factor). If there is more than one factor in the experiment, then a particular combination of levels applied to some units is a treatment.

5. An *experiment* is a study wherein the researcher *controls* the levels of the factors to create the treatments. Units are randomly assigned to treatment groups.

*Example*: To assess the effect of diet on mice lifetimes, two factors are identified:

1. Caloric intake. Levels: 100 calories/day (normal), 80 calories/day (reduced)

2. Protein intake. Levels: 5 grams/day (high), 2 grams/day (low)

The four treatments are (normal,high), (normal,low), (reduced,high), (reduced,low). The number of mice randomly assigned to the following four treatments are shown in Table 1:

<table>
<thead>
<tr>
<th>Protein level</th>
<th>Calorie level</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>high</td>
<td>normal</td>
<td>50</td>
<td>40</td>
</tr>
<tr>
<td></td>
<td>reduced</td>
<td>40</td>
<td>50</td>
</tr>
</tbody>
</table>

John Fox is concerned with the application of statistics to the social sciences wherein experimental studies are rare. He argues that an accumulation of observational studies consistently
leading towards a common conclusion provides a basis for accepting the conclusion as true. Some academics may argue that this approach is inconsistent with the philosophy of science. In fact, no single experiment is conclusive; rather, it is only through repetition (repeating the experiment and arriving at consistent results) that new ideas are adopted in science.

It is now recognized that there is often a diminishment of effects in studies. For example, Linus Pauling found that vitamin C significantly reduced the likelihood of contracting cold and the severity of contracted colds. Later trials did not support the results. It should not be concluded that Pauling, one of only two people awarded Nobel Prizes in different fields (the Chemistry and Peace prizes), falsified data, but rather, that he was unlucky.

With this mind, it seems reasonable to accept Fox’s views on observational studies and causation. Who among us would deny that smoking does not cause lung cancer, coronary heart disease, stroke and chronic obstructive lung diseases (such as chronic bronchitis and emphysema)?