22S:30/105 Statistical Methods and Computing

Designing Experiments

Lecture 8
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Experiments

- Recall: What is the critical difference between an *experiment* and an *observational study*?
- **experimental units**: individual items on which experiment is done
  - usually called **subjects** when they are human
  - we can measure a response variable individually on each experimental unit
- **treatment**: a specific experimental condition, controlled by the experimenter, and applied *to the units*

- example: agricultural field experiment
  - land available for use in the experiment is divided up into equal-sized "plots"; each plot is an experimental unit
  - same variety of corn planted in all plots
  - response variable for each plot is average number of bushels of corn harvested per acre
  - treatments are different types of fertilizers assigned to plots
- **factor**: a particular explanatory variable manipulated by the experimenter
  - a factor has one or more **levels** — different values that are assigned to different units
    - e.g., each type of fertilizer in the agricultural example is a different level of the factor "fertilizer type"

- A single experiment may involve more than one factor. In this case, each *treatment* is defined as the combination of levels of different factors.
  - example: more complex agricultural field experiment
    - factor A: fertilizer type with 3 levels
    - factor B: variety of corn, with 2 levels
    - then one of 6 possible treatments is assigned to each plot

The importance of comparison in experiments

- **Comparative experiments** are used to separate the effects of an experimental treatment from those of extraneous variables.
- important when we can't control all extraneous variables

- Example:
  - Autism is a severe emotional and developmental disorder that occurs in some children.
  - A medical case study reported that an autistic child who received a single injection of a hormone called secretin experience marked improvement in his autism.
  - We have no way of knowing what other variables might have influenced the child's autism.

- Groups of subjects in a comparative experiment
  - **experimental group(s)** receive treatment(s) the effects of which are under study
  - **control group** receives no treatment or a sham treatment
- Example:
  - study reported in *Consumer Reports*, Feb. 1976
  - a group of senior citizens was randomly divided into 2 groups
    - group 1: daily doses of vitamin C
    - group 2: no treatment
  - At end of winter, vitamin C group reported fewer colds than no-treatment group. Investigator concluded that vitamin C helps to prevent colds.

The placebo effect

- definition: A placebo is a dummy treatment
  - no direct (physical) effect on response variable
- In another study decribed in the same *Consumer Reports* article, two treatment groups
  - one group of subjects were given daily vitamin C and told it was a placebo
  - other group received a placebo and were told it was vitamin C
  - The group who *thought* they were receiving vitamin C reported fewer colds.

An aside concerning medical studies

- Note: A study of the last-mentioned type would be considered unethical today.
  - "informed consent" required for participation in clinical trials
- For testing new treatments of diseases or conditions for which a treatment already exists, the best standard treatment is given to the control group.
  - It would be considered unethical to withhold an effective known treatment

Blinding in experiments with human subjects

- refers to preventing some people involved in the experiment from knowing which subjects are receiving which treatment
- single-blind experiment: subjects do not know which treatment they are receiving, but study personnel are not blinded
- double-blind experiment: neither the subjects nor any study personnel who administer treatment or evaluate response variable know which treatment subjects are receiving

Randomization

- Another aspect of experimental design is how to determine which experimental units receive which treatment.
- randomization: assignment by chance
- **completely randomized design**: all experimental units are assigned at random among all the treatments

Example: the Lung Health Study

- clinical trial sponsored by the NIH involving 10 clinical centers in the US and Canada
- aim: to determine the effects on the decline of lung function in smokers already at risk for COPD (a lung disease) of:
  - a "stop smoking" program
  - daily use of an inhaled asthma drug
- response variable: change in FEV1 (a measure of lung function) from the time a subject entered the study until a follow-up visit 5 years later
- subjects: approximately 6000 smokers with mild impairment of lung function

- groups
  - Usual Care group (control group)
    * received neither the smoking cessation program nor any medication
  - Special Intervention Placebo group
    * received the smoking cessation program but a placebo inhaler
  - Special Intervention Active drug group
    * received the smoking cessation program and the active inhaled drug

- Was the LHS an experiment or an observational study?
- Was it comparative?
- What were the factors?
- What were the treatments?

Blinding in the LHS

- Patients and study personnel knew who was in UC group.
- Patients and study personnel knew everyone in both SI groups received smoking cessation program.
- *Double blinding* as to which SI patients were receiving placebo and which active drug.
  - Neither patients, clinic personnel, nor study directors knew this until end of study.

Randomization

- assignment of experimental units to treatments based on *chance*
- purpose: effort to make sure the experimental groups are not systematically different from one another in ways other than the treatment assignment
  - in particular, subjects are not assigned by the experimenter
- carried out by computers

Completely randomized design

- All the experimental units are allocated at random among all the treatments.
- example: if LHS had had a completely randomized design, idea would have been:
  - put 6000 envelopes in a hat, each with a slip of paper inside, 2000 saying "UC," 2000 saying "SIP" and 2000 saying "SIA"
  - each time a new patient enrolls in the study, draw an envelope at random and have the pharmacists dispense the appropriate treatment

Other systems of randomization

- matched pairs design
  - can be used only if there are only 2 treatments
  - subjects are paired up, so each pair is as similar as possible on important known factors that might affect the response variable
  - for each pair, randomly as one of the treatments to each subject

- randomized block design
  - block: a group of experimental units that are known before the experiment to be similar in some way that may affect the response variable
  - randomized block design: randomization of units to treatments is carried out separately within each block
  - in LHS, the patients enrolled by each of the 10 different clinics were a block
    - randomization to the treatments was carried out separately within each clinic's patients to make sure all treatment groups were represented within each clinic
    - Why?

Randomized comparative experiments

Logic:

- Randomization forms experimental groups that are likely to be similar in all respects *except* treatment assignment.
- Comparative design ensures that influences other than the experimental treatments operate equally on all groups.
- Consequently, differences between treatment groups in average response variable must be due to either
  - effects of treatment
  - pure chance

Replication

- Imagine that the Lung Health Study had had only 2 patients in each treatment group instead of 2000.
- Experiments need to use a large enough number of experimental units to reduce chance variation to within acceptable bounds.
  - As we study different methods of statistical analysis, we will learn how to compute "sample sizes."
- An observed effect so large that it would rarely occur by chance is called *statistically significant*.
  - We will use the laws of probability to learn how likely we would be to see treatment effects as large as those observed by pure chance.