STAT 500

Unit 1 - Randomized Experiments

Basic Terminologies of Experiments

- **Experiment**: an investigation in which the investigator applies (assigns) some treatments to experimental units and then observes the effect of the treatments on the experimental units by measuring one or more response variables.

- **Treatment**: a condition or set of conditions applied to experimental units in an experiment.

- The assignment rule, or, the **experimental design**, specifies which experimental units are to be observed under which treatments.

Basic Terminologies of Experiments

- **Experimental Unit**: the physical entity to which a treatment is randomly assigned and independently applied.
  - the smallest division of experimental material (e.g. land, plant, animal, etc) that may receive different treatments
- **Response Variable**: a characteristic of an experimental unit that is measured after treatment and analyzed to assess the effects of treatments on experimental units. (e.g. yield, gene expression level, etc.)
- **Observational Unit**: the unit on which a response variable is measured. There is often a one-to-one correspondence between experimental units and observational units, but that is not always true.

Basic Principles in Design of Randomized Experiments

- **Replication**
  - Applying a treatment independently to two or more experimental units
  - Level of variability can be estimated for units that are treated alike.
- **Randomization**
  - Random assignment of treatments to experimental units
  - Reduce or eliminate sources of bias (treatment groups are equivalent, *on average*, except for the assigned treatment)
  - Cause and effect relationships can be demonstrated
  - Create a probability distribution for a test statistic under the null hypothesis of no treatment effects

Basic Principles in Design of Randomized Experiments

- **Blocking / matching**
  - Group similar experimental units into blocks
  - Apply each treatment to (the same number of) experimental units within each block (balance)
  - Separate random assignment of units to treatments is done within each block (randomization)

- **Blinding**
  - Subjects do not know which treatment they received
  - Researchers making measurements do not know the treatment assignments

Basic Principles in Design of Randomized Experiments

- **Control of extraneous variation**
  - Control non-intervention factors
  - Use homogeneous experimental units
  - Accurate measurement of outcomes (responses)
  - Tradeoff between accuracy and generalizability

- Comparison with a **control group**
  - Untreated (placebo) group
  - Gold standard (best available treatment)

Basic Principles in Design of Randomized Experiments

- Inferences are restricted to only those units used in the experiment

- Extending inferences beyond the units in the experiment
  - Were the units used in the experiment obtained from **a representative random sample** from some larger population?
    * Yes $\Rightarrow$ can make inferences about the population
    * No $\Rightarrow$ cannot make inferences about the population

Study Ethics

- Does the potential gain from performing (or continuing) the study outweigh the risks to the subjects?
  - Some experiments are unethical
  - Human and animal safety committees
  - Data Safety Monitoring Boards
- Informed consent
  - Subjects must be informed of objectives and risks
  - Subjects must agree to participate
  - Subjects must be free to withdraw at any time (need to deal with incomplete sets of responses)

Planning and Execution of Randomized Experiments

- Idealized story
  - Clearly define objectives
  - Identify population of interest
  - Obtain a random sample of units for the study
  - Random assignment of units to treatment groups
  - Apply treatments to units and record responses
  - Analyze the data
  - Report inferences about the population
- Volunteers (samples of convenience)
  - Subjects seeking treatment at a medical clinic
  - Limits the type of inferences that can be made

Example: Low Birthweight Babies

- Objective:

  Determine if a specific program of assistance to families of low birthweight babies can increase weight gain during the first 12 months after release from the hospital?

- Preliminary planning
  - Gather expert information
    - Identify factors that could affect weight gain
    - Which factors can be controlled?
    - What outcomes will be measured ?
  - Identify source of subjects (low birthweight babies)

Example: Low Birthweight Babies

- Develop a plan (or protocol)
  - Carefully describe the treatments
  - Identify restrictions on recruitment
  - Use of blocking
  - Use of randomization
  - Use of blinding
  - Describe how and when responses will be measured
  - Specify methods of analysis
  - Determine sample sizes and budget
  - Obtain ethical approval
- Secure adequate resources

Example: Low Birthweight Babies

- Perform the experiment
- Analyze the data
- Interpret results
- Report conclusions and recommendations

Example: Low Birthweight Babies

- Two treatments (two levels of one factor)
  - Printed information only
  - Printed information and scheduled visits by a nurse

- Experimental units:
  low birthweight babies born in a set of participating hospitals (and their families)

- Blocking factor: Three weight classes

Example: Low Birthweight Babies

- Replication:
  30 babies in each weight class

- Randomization:
  random assignment of 15 babies to each treatment within each weight class

- Control of extraneous variation:
  Babies with certain birth defects and illnesses were excluded

- Measured weight gain during the first year after entering study

Example: 1954 Salk Polio Vaccine Study

- Design 1: National Foundation for Infantile Paralysis (NFIP) ("observed control", not randomized)
  - grades 1 and 3 $\Rightarrow$ control,
    grade 2 with consent $\Rightarrow$ vaccine,
    grade 2 without consent $\Rightarrow$ control
  - Problems with NFIP
    *

Example: 1954 Salk Polio Vaccine Study

- Design 1: National Foundation for Infantile Paralysis (NFIP) ("observed control", not randomized)
  - grades 1 and 3 $\Rightarrow$ control,
    grade 2 with consent $\Rightarrow$ vaccine,
    grade 2 without consent $\Rightarrow$ control
  - Problems with NFIP
    * Are grades 1 and 3 valid controls?

    * No consent group from grade 2 is not a valid control (different types of children)

1954 Salk Polio Vaccine Study

- Design 2: Randomized clinical trial
  - Ask parents of second grade children for consent to enroll their child in the study
    - randomly assign 1/2 to vaccine
    - randomly assign 1/2 to placebo
  - No consent $\Rightarrow$ excluded from study
  - Double blind study
    - Doctors did not know assignment
    - Children and parents did not know assignment

1954 Salk Polio Vaccine Study

Group	Randomized Trial sample size	cases per 100,000
Vaccine	200K	28
Control	200K	71
No consent	350K	46

Group	NFIP study sample size	cases per 100,000
Grade 2 (vaccine)	225K	25
Grade 1,3 (control)	725K	54
Grade 2 (no consent)	125K	44

Comparing the two tables:

- lines 1 and 3 are similar, but line 2's are different

1954 Salk Polio Vaccine Study

- Randomization as a basis for inference
  - In the randomized trial:

    56 children in the treatment group developed polio

    142 children in the control group developed polio
  - If the vaccine had no effect, then a child would experience the same outcome in either group (198 children would develop polio)
  - Of those 198 cases, 142 occurred in the control group

1954 Salk Polio Vaccine Study

- Randomization as a basis for inference:
  - Because we randomized, we can compute the probability that at least 142 of the 198 cases would occur by chance in the control group if the vaccine had no effect (1 in 2 billion)
  - "proves" vaccine is effective