Outline

Study Designs

- Randomized Trials
- Double-blind Randomized Controlled Trials
- Observational Studies
- iClicker Questions
The diet comparison example “Comparison of the Atkins, Zone, Ornish, and LEARN Diets for Change in Weight and Related Risk Factors Among Overweight Premenopausal Women The A TO Z Weight Loss Study: A Randomized Trial” by C.D. Gardner, et al. (JAMA, Vol. 297, pp. 969–977, March 2007) is a good example of randomized trials.

An important characteristic of the experiment is that the comparison groups are similar to each other in all aspects, except for the treatment (see Table 9.1 on page 81). Hence such experiment offers fair comparison of the treatment among the four diet groups.
Randomization and Randomized Trials

In a randomized trial, subjects entering the trial in a randomized fashion (using virtual roll of a die) into one of several treatment groups. This process is called:

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the best way to safeguard against potential confounders so that the comparison groups are similar in all factors except for the treatment itself.
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Randomized Controlled Experiment (or Trial)

is a randomized experiment in which one of the comparison groups is a control group or placebo group.
Double-blind Randomized Controlled Trial

is a randomized controlled trial in which neither doctor (the experimenter) nor patient (experimental subject) knows what treatment the patient receives.

- done by giving the patient a pill that looks/smells/... like the treatment pill, but is actually an inert pill or placebo.
- Blinding achieves additional protection against bias.
- All groups have the same frame of mind (as opposed to knowing you are not really getting the new drug)
- The experimenter has the same frame of mind evaluating patients from each group.
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Law Fracture Example

In many cases, randomization cannot be achieved in that the treatments being compared cannot be assigned, e.g., the study involving women and leg fractures. When a new subject enters the study (by having a car accident), we observe what gender they belong to, instead of randomly assigning it. This is an example of observational studies.
Typical Reasons for Observational Studies

1. Assigning treatment is impossible
   E.g. to compare fracture rates between men and women, we cannot randomize subjects into the comparison groups.

2. Assigning treatment is unethical
   E.g. to compare cancer rates of smokers and nonsmokers, we do not want to randomize subjects into smoker-nonsmoker comparison groups.

3. Assigning treatment is impractical
   E.g. the outcome is a rare event like cancer or stroke, and a randomized trial would need too many subjects and too much time.

In cases like these, a case-control study is generally the way to go.
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Case-control Study

starts with the outcome and then work back to the type of treatment. For instance in the diet comparison trial, a case-control study would look for people in the population who lost weight, and then ask them what diet they used.

Case-control studies, compared to randomized controlled experiments,

- are frequently used because they are cheaper and easier to conduct;
- are less time-consuming to conduct;
- are able to conclude a link or ‘association,’ but are not able to prove ‘causation;’
- provide initial evidence that can generate resources for more rigorous studies like double-blind randomized controlled trials.
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Successful Story of a Case-control Study

The first study formally linking lung cancer to smoking was a 1950 case-control study “Smoking and Carcinoma of the Lung” by Richard Doll and A. Bradford Hill (British Medical Journal, 1950 September 30; 2(4682): page 739–748). This study led to numerous studies, and consequently, it is now accepted by the scientific community that smoking causes lung cancer.
Case-crossover Study

allows subjects in the treatment group “cross over’ to the control group an vice versa. That is, each subject can be their own control.

According to “Cumulative Use of Strong Anticholinergics and Incident Dementia” (JAMA, March 2015), from 10 years of tracking older adults and their use of anticholinergic drugs (meant to reduce symptoms of allergies, inability to sleep, anxiety, depression and bladder over-activity), the risk of Alzheimer’s was 63 percent higher. What type of study is this?

A. randomized controlled experiment
B. case-control study
C. none of the previous
Which of the following is false about a case-control study when it is compared to a randomized controlled trial?

A. case-control study is less time-consuming to conduct
B. case-control study is cheaper to conduct
C. case-control study can be used to determine causation
D. case-control study is easier to conduct
A clinical trial was conducted in which 120 patients with similar clinical features were randomly divided into a control group and a treatment group, each consisting of 60 patients. What type of study this is?

A. randomized controlled trial
B. case-control study
C. none of the previous