Ch. 1: Controlled Experiments

Suppose we have a new drug. How do we test whether or not it helps people in the way we wish?

We must do a _____ of the new treatment to nothing or the current treatment.

We give the new drug to subjects in the _____.

We also have a _____ that does *not* receive the new drug.

We should assign subjects to the two groups at _____

We should do this _____, so that neither the subjects nor their doctors know which group each is in.

Ex: The Salk Polio Vaccine

In 1954, the Public Health Service organized an experiment to test the Salk polio vaccine on children in grades 1–3.

- 2 million children involved
- about 1/2 million received the vaccine
- about 1 million were left unvaccinated as part of the experiment
- the remaining 1/2 million were left unvaccinated because their parents refused to consent that they be included in the study

- Why could they get away with different size groups?

- Why not give all children the vaccine?

- Why not compare to the previous year?

- Why not give the vaccine to all children whose parents allowed them to participate, and leave the non-consenting children unvaccinated?

If differences *other* than the treatment exist between the treatment and control groups, the effects of the treatment can be _____ with effects of those other factors.

The result is known as a _____ (which might be in favor of or against the treatment).

Ex: The National Foundation for Infantile Paralysis (NFIP) proposed vaccinating all second-graders whose parents consented, leaving grades 1 and 3 as control groups. The results, in cases per 100,000 were as follows:

	Size	Rate
Grade 2 (vaccine)	225,000	25
Grades 1 and 3 (control)	725,000	54
Grade 2 (no consent)	125,000	44

What were some problems with this study?

How to assign the children to the two groups? Should the experimenters have tried to balance the two groups with respect to variables such as family income, child's health, etc.?

It is better to select the subjects randomly. With enough subjects, things will be balanced better than humans can. This is called a

_____.

ment, rather than the treatment itself.

- To remove this effect, control subjects were given a _____ (in this case, an injection of saltwater).

- No subject was told which group he or she was in.

- To eliminate bias in diagnosis, the children's doctors were also not told which group each child was in.

- Since both the subjects and their diagnosticians were *blind* to which group each child was in, this is called a _____ experiment.

- A randomized controlled double-blind experiment is the best kind of experiment that can be conducted.

The randomized controlled double-blind experiment found the following rates of polio (per 100,000):

	Size	Rate
Treatment	200,000	28
Control	200,000	71
No Consent	350,000	46

Was the vaccine effective in reducing the incidence of polio?

Compare this result with the result from the NFIP study – what can we conclude?

A randomized controlled double-blind experiment minimizes bias, and can make calculations about the experiment easier.

Historical Controls

Some doctors use *historical controls*, in which the treatment group is compared to past patients treated the old way. But the groups may be non-comparable.

For example, coronary bypass surgery studies had the following three-year survival rates:

	Historical	Randomized
Surgery	90.9%	87.6%
Control	71.1%	83.2%

Can you indicate any possible bias of the historical studies?

Would you recommend coronary bypass surgery?

In a _____, the investigators decide who goes in the treatment and control groups (preferably randomly).

In an _____, subjects assign themselves to groups and the investigators can only watch.

Ex: Smoking studies are not controlled experiments because the experimenter cannot influence whether the subject smokes or does not smoke.

Does smoking cause lung cancer? Although there is a strong _____ between smoking and lung cancer, this does not necessarily imply _____.

There could be a _____ related to both smoking and rate of lung cancer.

A partial solution is to *control for* possible confounding factors by comparing similar subgroups of the treatment (smoker) group and control (non-smoker) groups.

Clearly, this is not perfect, but showing an effect remains even after controlling for all likely confounding factors greatly increases the weight of the evidence that the treatment is linked to the effect.

Ex: The Coronary Drug Project was a randomized controlled double-blind experiment conducted in the mid-to-late 1960's to test whether or not drugs may reduce the risk of heart attacks.

Here are the results for a drug called "clofibrate":

Clofibrate Deaths	Placebo Deaths
20%	21%

What can we conclude?

Maybe many in the clofibrate group didn't take their medicine. The investiagtors divided the clofibrate group into "adherers" (those who took at least 80% of their prescription) and "nonadherers" (those who took less than 80%).

	Clofibrate	Deaths	Placebo	Deaths
Adherers	708	15%	1813	15%
Non-adherers	357	25%	882	28%
Total	1103	20%	2789	21%

Note, that although this was originally a controlled experiment, the adherers/nonadherers were self-selected. Therefore this investigation is observational.

What conclusions can we draw from this study?

Ex: It has been observed throughout the year that in weeks where little ice cream has been sold, a large number of flu cases has been observed. On the other hand, in weeks where a lot of ice cream has been sold, only a few flu cases have been observed. Can we conclude that ice cream prevents flu?

Association does not imply causation!

Ex: In 1973, U.C. Berkeley looked at sex bias in their graduate programs. Out of 8,442 male applicants, 44% were admitted. Of the 4,321 female applicants, only 35% were admitted.

This looks like strong evidence of discrimination, until the individual majors are investigated. For the six largest majors, the data looks like this:

	Men		Women	
Major	Number of applicants	Percent admitted	Number of applicants	Percent admitted
A	825	62	108	82
B	560	63	25	68
C	325	37	593	34
D	417	33	375	35
E	191	28	393	24
F	373	6	341	7
Total	2,691	44	1,835	30

Now is there strong evidence of sexual discrimination?

Warning:

When evaluating studies, ask:

Have they controlled for all (reasonable) confounding factors?

Who says so?

Some Examples:

A smoking study financed by the American Cancer Society is likely to be more reliable than one financed by the Tobacco Institute.

A recent study indicating that bald men are more likely to suffer heart attacks is suspicious, simply because it was financed by the Upjohn Co., manufacturer of Rogaine.