Controlled experiments

- Subjects are assigned to control and treatment groups ***by the investigators***.

$\Rightarrow$ The experiment is *controlled*, because the investigators *control* which subject goes into which group.

- ***Randomized controls***: Subjects are assigned to treatment or control groups using a coin-toss-like procedure.

$\Rightarrow$ The goal is to have the treatment and control groups be *similar in every way* ***except for the treatment***. Randomized controls tend to achieve this goal efficiently (and more accurately).

- *If the treatment and control groups differ significantly in aspects other than the treatment itself, then it is more difficult to assess the effect of the treatment.*

Example: Randomized controls *vs* nonrandomized controls in portacaval shunt studies.

Table 3. Randomized controlled experiments vs. controlled experiments that are not randomized. Three-year survival rates in studies of the portacaval shunt. (Percentages are rounded.)

	Randomized	*Not randomized*
Surgery	60%	60%
Controls	60%	45%

- When the treatment is not the only significant difference between the control and treatment groups, the other variables in which they differ may ***confound*** the conclusions of the study.
- In the poorly-controlled portacaval shunt studies, the *confounding variable* was the *health* of the subjects. The patients in the non-randomized control groups tended to be in poorer health than the patients in the treatment group.

Observational studies

- In a ***controlled experiment***, the researchers decide which subjects are in the treatment group and which subjects are in the control group. Here, *control* also refers to the fact that the researchers are controlling this aspect of the experiment.
- In an ***observational study***, the subjects of the study place themselves in the treatment or control groups based on their behavior and the choices they make. Because of this, it is frequently the case that besides exposure to the 'treatment', the two groups differ in other important ways.
- The existence of ***confounding variables*** is one of the main difficulties in assessing the conclusions of observational studies.

- To mitigate the effect of *confounding variables* in observational studies, researchers will try to ***control for*** as many of these variables as possible.

$\Rightarrow$ *The treatment and control groups are* ***divided into smaller, more homogeneous subgroups*** *based on the variables that the researchers consider to be possible confounders.*

Example: In studies of the effects of cigarette smoking on cardiac health, researchers will compare male smokers to male non-smokers and female smokers to female non-smokers. This controls for the confounding effect of *gender* on cardiac health.

They will also (likely) divide the men and women in the study into even smaller groups of similar age ranges to control for the effect of *age* on cardiac health.

Example: The Clofibrate trial (Clofibrate is a cholesterol-reducing drug).

- A double-blind, randomized controlled experiment was run to test the drug Clofibrate on middle-aged men.
- Subjects were followed for five years.
- After five years 20% of the men in the Clofibrate group and 21% of the men in the placebo group had died.
- Possible reason for the ineffectiveness of the drug – failure to adhere to the drug protocol.

  Adherence means taking at least 80% of the prescribed dosage.
- Evidence: In the treatment group, 25% of non-adherers died as compared to 15% of adherers.

Caution: The study of adherers vs. non-adherers is an *observational study.*

Table 1. The clofibrate trial. Numbers of subjects, and percentages who died during 5 years of followup. Adherers take 80% or more of prescription.

	Clofibrate		*Placebo*	
	Number	*Deaths*	*Number*	*Deaths*
Adherers	708	15%	1,813	15%
Non-adherers	357	25%	882	28%
Total group	1,103	20%	2,789	21%

Note: Data on adherence missing for 38 subjects in the clofibrate group and 94 in the placebo group. Deaths from all causes.
Source: The Coronary Drug Project Research Group, "Influence of adherence to treatment and response of cholesterol on mortality in the Coronary Drug Project," *New England Journal of Medicine* vol. 303 (1980) pp. 1038–41.

Analysis:

- The death rates for adherers was the same in both the treatment and control groups.
- Conclusions: Adherence was not the cause of the lower death rate among the adherers in the treatment group. Adherers differ from non-adherers in other ways that kept them healthier.

DEMAND AN EXPERIENCED SURGEON

The more experienced a doctor is, the better. As obvious as that sounds, there are still too many people out there who never ask their surgeons for a history of their work. The importance of knowing is illustrated by this study

Peter Starek, a surgeon at the University of North Carolina, reviewed 460 heart valve replacement operations and found that only 4 percent of the patients of the three most senior surgeons died. But one junior surgeon lost almost a third of his patients. Since that surgeon was technically the best in the group, says Starek, something was obviously lacking—perhaps the kind of good judgement that grows out of experience...

From the column of Dr. Dean Edell in the San Francisco Chronicle, 8/1/90.

(*) What's missing?

(*) Confounding variable – Pre-operation health of the patients upon which each surgeon performed the surgery. Younger, technically better surgeon took the more difficult cases.

Cervical cancer and circumcision. Cervical cancer used to be one of the most common cancers in women, but it was found to be quite rare in Jewish women and also unusual among Muslim women.

(*) *Possible explanation:* Studies in the 1950s suggested that circumcision of men helped prevent cervical cancer in their sexual partners.

(*) *Digging deeper:* Cervical cancer is now believed to be caused by certain strains of HPV. Sexual activity was the confounding variable, especially the number of sexual partners earlier in life – the more sexual partners a woman had in the 1930s and 1940s, the more likely she was to be exposed to HPV.

Gender bias in graduate school admissions. A study was done at UC Berkeley. During the study period, 8442 men and 4321 women applied to grad school there. and roughly 44% of the men and 35% of the women were admitted.

(*) *Possible explanation:* Assuming that on the whole, the male and female applicants were equally qualified, it appears that some form of gender bias was at work.

(*) *Digging deeper:*

Table 2. Admissions data for the graduate programs in the six largest majors at University of California, Berkeley.

	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

Note: University policy does not allow these majors to be identified by name.
Source: The Graduate Division, University of California, Berkeley.

Women tended to apply to majors that were more demanding/selective.