

What is *Statistics*?

The science of collecting, summarizing and analyzing data.

In particular, Statistics is concerned with drawing inferences from a sample about the population from which the sample was drawn.

Statistics = Data Science

(*) Collection of data — Experiments and Observational studies.

(*) Summarizing data — Descriptive statistics.

(*) Analyzing data — Inferential statistics.

Data Collection: Controlled Experiments

(*) Treatment group vs. Control group (no treatment).

(*) Second meaning of the word 'control': In a *controlled* experiment, the researchers *control* who goes into each group.

(*) There are different ways to do this ...

... but the goal is that the treatment and control groups should differ only in the treatment, vaccine vs. no vaccine in this case.

(*) *Randomized controls* – subjects are assigned to each group randomly.

(*) *Blind* – subjects do not know which group they are in.

(*) *Double-blind* – researchers do not know which group each subject is in during the experiment

Example 1: *Salk polio vaccine trials.*

(a)

The NFIP study

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

(b)

*The randomized controlled
double-blind experiment*

	<i>Size</i>	<i>Rate</i>
Treatment	200,000	28
Control	200,000	71
No consent	350,000	46

(*) Consent is a *confounding variable* — the parents of children from poorer backgrounds were less likely to give consent, and polio was more likely to affect children from more affluent backgrounds.

Example 2: 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.)

	<i>Randomized</i>	<i>Not randomized</i>
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.

Table 2. A study of 51 studies on the portacaval shunt. The well-designed studies show the surgery to have little or no value. The poorly-designed studies exaggerate the value of the surgery.

<i>Design</i>	<i>Degree of enthusiasm</i>		
	<i>Marked</i>	<i>Moderate</i>	<i>None</i>
No controls	24	7	1
Controls, but not randomized	10	3	2
Randomized controlled	0	1	3

Source: N. D. Grace, H. Muench, and T. C. Chalmers, "The present status of shunts for portal hypertension in cirrhosis," *Gastroenterology* vol. 50 (1966) pp. 684–91.

Example 3: Historical controls.

Table 4. A study of studies. Four therapies were evaluated both by randomized controlled trials and by trials using historical controls. Conclusions of trials were summarized as positive (+) about the value of the therapy, or negative (−).

<i>Therapy</i>	<i>Randomized controlled</i>		<i>Historically controlled</i>	
	+	−	+	−
Coronary bypass surgery	1	7	16	5
5-FU	0	5	2	0
BCG	2	2	4	0
DES	0	3	5	0

Note: 5-FU is used in chemotherapy for colon cancer; BCG is used to treat melanoma; DES, to prevent miscarriage.

Source: H. Sacks, T. C. Chalmers, and H. Smith, “Randomized versus historical controls for clinical trials,” *American Journal of Medicine* vol. 72 (1982) pp. 233–40.

(*) Different experiments conducted to test the same therapy can lead to opposite conclusions depending on the design.

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 are placed in the treatment or control groups based on their own 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.

⇒ *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 4: 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.

	<i>Clofibrate</i>		<i>Placebo</i>	
	<i>Number</i>	<i>Deaths</i>	<i>Number</i>	<i>Deaths</i>
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.

<i>Major</i>	<i>Men</i>		<i>Women</i>	
	<i>Number of applicants</i>	<i>Percent admitted</i>	<i>Number of applicants</i>	<i>Percent admitted</i>
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.

Coffee consumption and pancreatic cancer.

A statistical link between the drinking of coffee and cancer of the pancreas, the fourth most common cause of cancer deaths among Americans, was reported yesterday by scientists of the Harvard School of Public Health. The discovery was unexpected, and its significance is not yet clear.

“If it reflects a causal relation between coffee drinking and pancreatic cancer,” the report said, “coffee use might account for a substantial proportion of the cases of this disease in the United States.”

The findings need to be pursued with further research, said the report in today’s issue of the New England Journal of Medicine. ...

From the New York Times, March 12, 1981.

(*) At the time, coffee drinking was strongly associated with smoking. Once smoking was controlled for, the association between coffee drinking and pancreatic cancer disappeared.

(*) More recent, large-scale studies indicate that drinking coffee appears to *reduce* the risk of pancreatic cancer.