Experimental Design

Controlled Experiments and Observational Studies
Does a “treatment” have an “effect?”

• Does vitamin C help to prevent colds?
• Does the use of cell phones while driving increase the probability of an accident?
• Does coffee consumption increase the risk of coronary disease?
• Does second-hand smoke cause cancer?
• Is moderate alcohol consumption beneficial?
• Does decreased dietary cholesterol lead to higher suicide rates?
• Are breast-fed babies smarter?
• Can prayer heal illness?
How do we find out?

The basic idea is to compare two groups:

• An unexposed “control” group
• An exposed “treatment” group

How is the composition of these two groups to be determined?

• In a *controlled* experiment, membership is determined by the investigator.

• In an *observational study* the subjects select their own memberships

A controlled experiment has very substantial advantages.
Observational Studies and the Problem of Confounding

Is the use of cell phones while driving dangerous?
People with cellular phones in their cars run a 34 percent higher risk of having accidents, researchers said yesterday.

And, according to the study, the danger mounts when drivers use the phone a lot or while doing something else, such as lighting a cigarette or drinking coffee.

Most often, it seems, motorists engrossed in a phone conversation run red lights and get into collisions at busy intersections. But even on the open highway, a car-phone can take people’s minds off their driving.

“They kind of forget about the rest of the world,” said John Violanti, a criminal justice Professor at the Rochester Institute of Technology who helped conduct the study. “They're not intentionally cutting somebody off, (they're) just not seeing them.”

The study, believed to be the first of its kind appears in the March issue of Accident Analysis and Prevention, a British journal.

The Cellular Telecommunications Industry Association in Washington, D.C., dismissed the study as limited and flawed. “It has glaring research shortcomings,” said spokeswoman Pam Small.

The researchers, who plan a larger survey, countered that their findings, even though preliminary, should not be ignored at a time when cellular-phone sales are booming.

Violanti and James Marshal, a professor of social and preventive medicine at the State University of New York at Buffalo, randomly selected 100 New York motorists who had been in an accident and 100 who had not. Of those in accidents, 13.7 percent owned cellular phones, and 10.6 percent of the accident free drivers had a phone in the car.

Through surveys and phone records, the researchers determined that the motorists who used car phones more often than average--50 minutes per month--were five times more likely to have accidents than those who either talked less or did not own a car phone.
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Comparison groups

Greater than average use while driving  vs  Less than average use while driving

5 times more likely to have an accident

Are these two groups comparable? Might they differ in ways other than the amount of cell phone usage?
Confounding

These are examples of *confounding*: a difference between the treatment and control groups which affects the responses being studied.

**Confounders:**
- The amount a person drives
- Where that person drives
- When a person drives

There is always a possibility of confounding in observational studies.

What could be done about the first confounder above?
Another Study of Cell Phones and Accidents

First proof: driving while talking on phone is a hazard.


Gina Kolata

The good news is that cellular phones do not cause brain cancer. The bad news? They are unfortunately a cause of car accidents. In fact, according to research by Drs. Donald A. Redelmeier and Robert J. Tibshirani, driving with the use of a cell phone can be likened to driving with a blood alcohol level of about 0.10 per cent. The chances of getting into an car accident while using a cellular phone is nearly equal to the chances of having an accident while slightly drunk.

Another factor in the chance of having an accident is the topic and content of conversation: A person who is not talking on the phone cannot become distracted by a shouting match with a boss or a significant other." Thus, the risk gets even greater if the person is discussing something important or especially is in the middle of an argument.

The researchers, a professor of medicine at the University of Toronto and a statistician at the same school, ran a study of 699 drivers who had cellular phones and who had also been involved in an accident. They analyzed 26,798 phone calls on cellular phones and determined that the risk of having an accident quadrupled when drivers spoke on the phone. With heated discussions, this rate is even higher.
The Design

Screened accidents for those involving drivers who owned cell phones. Determined from phone records that

• 25% were talking at time of accident

• 5% were talking on the phone at the same time on the previous day

This is the basic idea, but the details are more complicated. See Redelmeier and Tibshirani, *Chance*, vol 10, no. 2 1997: “Is using a car phone like driving drunk?”
Some details:

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Sex and Death

Study Suggests Sex May Help Men Live Longer

But researchers, critics agree more data needed

New York Times, December 1988

Men who have more sex seem to live longer, a statistical study of Welsh villagers in The British Medical Journal has found.

It is one of the rare studies of sex and death, and the authors lightheartedly suggested in the Journal article that the findings might result in new kinds of promotional campaigns for healthy living.

But before then, further studies of both sexes are needed to confirm their findings, the authors said. Two other scientists commenting in the same issue cautioned that because of its design, the study might not have identified factors that could have inadvertently influenced the findings—that ill people may be less likely to have sex, for example.

Having regular sex reduces the risk of death by about half, according to the analysis, part of a longterm study of chronic disease in the Welsh town of Caerphilly.

"Sexual activity seems to have a protective effect on men's health," Dr. George Davey-Smith's team concluded after analyzing death rates of nearly 1,000 men from ages 45 to 59 in Caerphilly.

Davey-Smith's team assessed the existence of heart disease in the men when they entered the study from 1979 to 1983. They asked the men about the frequency of sexual activity, and answers were put into categories ranging from "never" to "daily."

The authors said they tried to adjust the study to account for a factor that might explain the findings—that healthier men with healthier lifestyles engaged in more sex. Even so, they could not explain the differences in risk. Hormonal effects on the body resulting from frequent sex could be one possible explanation, Davey-Smith said.
The Design
(for more details see the web site)

918 men aged 45-59 in Caerphilly interviewed
(25% declined to answer question)

• Grouped into low, medium, and high frequency of orgasm

• Attempted to “stastically adjust” for age, height, body mass, blood pressure, cholesterol, social class, existing coronary disease, smoking

• 150 dead after 10 years

• (Adjusted) death rate for high frequency guys less than half that of low frequency guys
Confounders?  
Other Problems?
Controlled Experiments

In a controlled experiment, membership is assigned by the experimenter.

An example is an experiment to determine the effectiveness of mammary artery ligation.

To force more blood to flow into the heart of people with coronary artery disease, the mammary arteries were ligated. Popularized in a 1957 *Reader’s Digest* article.
Patient entered surgery

Preliminary incision made

Random decision whether to tie off artery

Later examination by physician
Randomized, Double Blind Study

- Treatment was assigned at *random*
- *Neither* the patient nor the physician knew whether surgery was actually performed.

Study showed no essentially no difference between treatment and control, with some suggestion that control fared better.
Randomization:

• Eliminates possible human bias in assignment to treatment or control.
• Laws of chance guarantee that with enough subjects, the treatment and control groups will resemble each other with respect to other important variables.

Double Blind

• Acts as a placebo for the patient.
• Prevents unconscious bias in measuring the outcome.

Scientifically, these are the most effective designs, but they are often practically or ethically impossible.
HIV Placebo Study Poses Ethical Dilemma for U.S.

The United States is paying for experiments in poor countries in which many babies may die of AIDS because their HIV-infected mothers are given placebos instead of a protective drug, the patient advocacy group Public Citizen said yesterday.

The government says the studies are ethical because they are the only way to find new HIV protections that poor countries can afford. Pregnant women in developing countries today do not get the AZT therapy that American AIDS patients use to protect their unborn children.

But in a letter signed by prominent bioethicists and Dr. Wilbert Jordan, head of the Black Los Angeles AIDS Consortium, Public Citizen compared the U.S.-funded foreign research to the infamous "Tuskegee experiment" in Alabama, in which the government withheld syphilis treatment from poor African American patients.

Also, federal law forbids U.S. doctors from conducting experiments abroad that would not be tolerated in the United States, a letter from the critics to Health and Human Services Secretary Donna Shalala said. The letter urged a federal investigation.

Shalala did not immediately respond, but the National Institutes of Health and Centers for Disease Control and Prevention vigorously defended the studies.

"In the absence of identifying some regimen that is affordable, hundreds of thousands of kids are going to die," said the CDC's Dr. Phillip Nieburg.

Studies have indicated that taking the drug AZT during pregnancy and labor and giving it to infants for six weeks after birth cuts by two-thirds babies' chances of contracting HIV from mothers.

But that treatment costs about $800 per person, too expensive for mothers in developing countries, so doctors are studying potential alternatives such as shorter courses of AZT or giving malnourished pregnant women vitamin A.

Nine U.S.-funded studies in Africa, Thailand and the Dominican Republic compare the possible new therapies with dummy pills, instead of giving the comparison women the U.S style AZT treatment. The government says a placebo comparison is the only way to prove potential new therapies are better than no treatment.