Collecting Data

The article from the L.A. Times discusses claims to anyone who has read a fitness or health magazine. These claims bounce all over the media and our social conversations, but what data really support them. Here are some health related claims that have been floating around recently:

Claim: Switch from carbohydrates to protein to lose weight.

Claim: Limit your diet to less than 30% fat to prolong your life.

Claim: Lower your cholesterol level to lower risk of heart disease

Claim: Moderate alcohol consumption will lower heart disease risk.

Claim: The childhood mumps vaccine causes autism.

Each of these was based on data, and hence statistics were used. But they may not all be true. Confusingly, sometimes a claim is proclaimed true, and later false. (Have you seen the Woody Allen movie "Sleeper"?) Whom should you believe?

While data are necessary for making informed decisions, they depend on well designed studies. Particularly if the claim is very subtle and complex, as are all of these claims, the study has to be flawless. For most interesting situations, it takes a large number of studies before scientists feel confident (or should feel confident) in the outcome. And of course you should learn to make a distinction between what the media says scientists say and what scientists actually say. Often complex arguments between scientists get distilled into the media as a "consensus" with a few lone, renegade (and therefore wrong) dissenters.

The latest issue of Science (March 30, 2001) has an article you might enjoy called "The Soft Science of Dietary Fat." In it, the author says "It's a story [that dietary fat is deadly] of what can happen when the demands of public health policy -- and the demands of the public for simple advice -- run up against the confusing ambiguity of real science."

Most of these claims are *causal*. This means that they claim that doing A will cause B to happen. (Or prevent B from happening.) As we shall see, causal claims are particularly difficult to determine. (Causality has a long history; the early Greek philosophers, for example, spent time understanding how to conclude that A has caused B. And of course this is what most of our legal system tries to determine as well.)

Types of Studies

There is a basic structure to the studies we'll consider. There is a Treatment variable (also called a covariate or a predictor variable). Subjects are assigned to a Treatment group determined by the value of the treatment variable. For example, the Treatment variable might be high fat vs. low fat diets, and subjects are assigned to one of these groups. The response variable is the outcome we are interested in. For example, it might be weight change or life-span.

There are two main types of studies. The book uses slightly non-conventional terminology, but here's my terminology.

**Controlled Study**: (also called an experiment). Subjects are assigned to treatment groups by the experimenters. When done well, controlled studies are the ONLY studies which allow researchers to make causal conclusions.

**Observational Study**: subjects are assigned to treatment groups by natural circumstances or by their own decisions. Observational studies can be "controlled" in part. We'll talk about this.

An Illustrative Example

Polio is a disease that afflicts children. It causes paralysis and death. The first polio epidemic hit the US in 1916, and by the 1950s there were several promising vaccines. The Salk vaccine seemed the most promising.

How would you test that the vaccine worked?

Note that the treatment variable here has two basic values: Vaccine or No Vaccine. The response is whether or not a person gets polio.

Sample Size Matters

As a first step, you should see that it is not sufficient to test the vaccine with just two people. If the vaccinated one does not get polio and the other does, it might just be due to the fact that for whatever reason, the vaccinated child managed to avoid exposure, or that his or her natural immune defenses were adequate to fight off the infection.

So we need to test this with a large number of children. In that case, what we are really interested in using as a response variable is the polio rate: what percent of children get polio in each case.

If the vaccine is 100% effective, then none of the children would get polio. But probably this is not the case. So we would hope that at least the rate would be lower in the vaccinated children than the unvaccinated children.

To Measure the Effectiveness of a Treatment, you must have a control group

Suppose we decide to give all children the vaccine. And suppose the polio rate decreases the next year. Can we conclude the vaccine was responsible?

No, because polio rates vary from year to year. Quite possibly we just got lucky.

For this reason we need another group, called a Control group, to compare to.

To Compare Treatment effects, the two groups must differ only in their treatment.

Giving a vaccine to a child, particularly an experimental vaccine, requires parental consent. One experimental test of the Salk vaccine proceeded as follows:

1st and 3rd graders in public schools would be used as controls. They would get no treatment of any kind.

2nd graders would be asked for consent. If their parents consented, they would get the vaccine. If not, they would be used as controls.

Here were the results:

| Treatment | Size | Polio Rate (per 100,000) |
|---|---|---|
| Grade 2 (vaccine) | 225,00 | 25 |
| Grade 2 (no consent) | 125,000 | 44 |
| Grades 1 & 3 (Control) | 725,000 | 54 |

What does this tell us? First note that the "effect" of the vaccine, comparing the vaccine group to the control group, is large. The polio rate goes from 54 to 25. Good news. Can we conclude that the vaccine caused this?

But also note that the Grade 2 children suffered less polio than the grades 1 and 3 children. What are we to conclude? It is best to have the vaccine but it is also good to refuse the vaccine?

Note that this is, according to the definition I gave you, an observational study. The children were assigned to a treatment group based on their ages and on their parents decision. This leads to two possible explanations for the observed responses.

1) SES: Polio can be thought of as a disease of hygeine. The poor tend to have less control over their surroundings and often live in dirter circumstances than, say, the rich. For this reason, poor children were more likely to be exposed to the polio virus. These children either died before the $2^{nd}$ grade or built up a resistance to the virus. Thus, poor children in the $2^{nd}$ grade were more likely to have an immune defense against polio.

Now who is most likely to refuse consent, a poor parent or a middle class? A tough call, but in this study it turned out that the middleclass parents were much LESS likely to refuse consent, and so most of the no consent $2^{nd}$ grade students were from the lower SES and had (in theory) a greater defense against polio. Which is why this group has a lower polio rate even though no one got the vaccine.

2) Age. Polio is contagious. If a kid in your classroom got it, you are more likely to get it. If no one gets it, you are less likely to get it. Therefore, once a third grader gets polio, we expect more third graders to get it. So perhaps next year, were we to do the study, the polio rate for $1^{st}$ and $3^{rd}$ graders might be much less. And the supposed benefits of the vaccine would seem insubstantial.

Age and SES are examples of *confounding variables*. To be a confounding variable, a variable must affect **both** the value of the Treatment variable and the response variable. SES qualifies because your SES was related to whether or not you gave consent (which determined your treatment) and also (unknown to the researchers) affected your immunity to polio. Age was a confounder because it directly determined which group a child was placed in and, because children were kept together by age, would affect whether the polio rate was higher or lower in that group.

The basic problem is that the groups were not sufficiently alike. They not only differed in their treatments, but also the age and their immunity. Of course, we can't expect them to be the same on any conceivable variable, (or can we?) but we hope that they are the same on all variables that

matter.

One way around the age problem would be to ask for the consent of 1st, 2nd, AND 3rd graders. Then at least age is not a problem. But the SES confounding variable might still be a problem. The solution to this is to assign the consenting kids to two groups: vaccine or no vaccine. So there are three groups: consenting with vaccine, consenting without (control), not consenting.

How do you decide how to assign a treatment? Remember, you want the groups to be as alike as possible. So you can't pay attention to age, or SES, or anything else that might matter. But how do you know what might matter?

The only way to ensure that none of the researchers' biases play a role in assignment is to do random assignment. A coin is flipped, and this determines whether the child gets a vaccine or the control. In this way, the two groups can be assumed to be alike in every way except their treatment.

Studies that randomize subjects to treatments are called **randomized studies**.

But a subtle problem arises. A doctor must make a decision as to whether a child has polio or not. If she knows the child received the vaccine, she might be reluctant to call it polio and might seek another explanation of the symptoms. Or, if she knows the child did not get the vaccine, she might be too quick to diagnose polio.

To prevent this from being a problem, a "blind" is imposed so that the researchers and treating physicians do not know whether or not a child received the vaccine. A record is kept, and at the end of the study the blind is "broken" so that the data can be sorted. Note that the problem here is, once again, the two groups are no longer the same. One group is being treated differently by the physician's knowledge of their treatment. Hence the need for a blind.

But what if the patient knows? The patient might tell the doctor, but even if not, the patient or subject might change his behavior. If he thinks he's immune, he might over-expose himself to the virus. Or if he thinks he is not, he might take extra precautions to prevent exposure. If this happens, the two groups are not comparable because they might behave differently, and then it might be their behavior, and not the vaccine, that's responsible for any observed differences. For this reason, the patient/subject is also kept "blind".

When both subject and researcher are blind, it is called a **double blind** study.

As you might guess, it is rather difficult to keep a patient "blind." A child who sees his friend get a shot and then doesn't get a shot can probably guess that she is in the control group. For this reason, a **placebo** is used. A placebo is a "null" treatment. Sometimes it does nothing (sugar water") sometimes it is a treatment for something completely unrelated. For example, a recent test of a vaccine for infants against whooping cough compared it to a placebo of hepatitis A vaccine.

Placebos also guard against the placebo effect. This is what happens when patients respond to the idea of treatment, rather than the actual treatment. Recent research has reinforced the theory that

the placebo effect is very real and is physiological, not only psychological. But at the same time, placebos continue to be controversial. (How can you give a placebo to a dying patient if you know there is some small chance the alternative treatment will work? What if the "treatment" is surgical? Is it ethical to give "fake" surgery to someone?)

Thus we have the "perfect" study: controlled, randomized, double-blind with a placebo.

Such a study was done with the Salk vaccine. Here are the results:

| **Treatment** | **Size** | **Rate** |
|---|---|---|
| Vaccine | 200,000 | 28 |
| Placebo | 200,000 | 71 |
| No consent | 350,000 | 46 |

Once again, not consenting seems to protect you from polio. But here the effect of the vaccine is even more dramatic. And here we can be relatively certain that it was the vaccine since there is no other way that the two groups differed other than the treatment.

WARNING about causality and observational studies

You can never make a conclusion that the treatment "caused" the response in an observational study because you can never be certain that a confounding variable wasn't accounted for.

'Controls' can be imposed within an observational study. This allows researchers to eliminate at least one possible cause for the observed changes, but still does not allow them to conclude that the treatment was responsible.

For example, studies comparing the heart disease rate between France and the US conclude, because the alcohol consumption is higher in France and heart disease is lower, than the alcohol might help prevent heart disease.

But obviously, other things, such as diet, might also provide an explanation.

So a solution is to compare drinkers of different amounts within the U.S. But even so, because you can't enforce a drinking regimen, there would be room for doubt. For example, some studies have shown that moderate drinkers are healthier than abstainers. But many people, when sick, quick drinking. So we would expect non-drinkers to be less healthy.

Example: Samaritans and suicide. (From FPP, p. 17)

Over the period 1964 to 19870, the suicide rate in England fell by about 1/3. During this period, a volunteer welfare organizaiton called "The Samaritans" was expanding rapidly. One investigator though the Samaritans were responsible for the decline. His study was based on 15 pairs of towns. The pairs were matched on variables he considred important, and one town in each pair had a branch of the Samaritans, the other did not. One the whole, the towns with the

Samaritans had lower suicide rates. Did the Samaritans prevent the suicides?

What type of study is this? What other explanations are possible?

In fact, a later study concluded that the cause for the decline was a switch from coal gas to natural gas for heating and cooking in the mid 60's.. Natural gas is less toxic. (About 1/3 of suicides in the early 1960s were from coal gas.) Also, studies showed that only suicide-by-gas rates changed. Other suicide rates remained the same.