AGAINST ALL ODDS
EPISODE 15 – "DESIGNING EXPERIMENTS"
TRANSCRIPT

FUNDER CREDITS

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INTRO

Pardis Sabeti
Hi, I'm Pardis Sabeti and this is *Against All Odds*, where we make statistics count.

Statistics is one way to figure out the story hidden in a mound of data. We can describe distributions, search for patterns, or tease out relationships. But just where all that analyzed data comes from is our next topic.

One method for producing data is called an observational study. Let's follow a team of marine scientists to the remote Line Islands in the middle of the Pacific Ocean. Their expedition's goal was to learn more about how human populations affect coral reef ecosystems – and they conducted an observational study to do so.

> **Stuart Sandin**
> Coral reefs are one of the most fragile ecosystems on the planet, even though they've survived for millions of years. Today, they're suffering quite a bit from the rapid changes that are being caused by human activities.

Pardis Sabeti
The Northern Line Islands are an archipelago containing four atolls that are a perfect lab for this research team because each island has a different history of human habitation. Starting in the north, Kingman Reef has never had a human population. Next comes Palmyra, home to a military base during World War II, but now basically empty again. Then Tabuaeran, with a growing population of 2,500 people. And finally, Christmas Island with a population of over 5,000.

> **Stuart Sandin**
> On both Tabuaeran and Christmas, the people actively fish for food and dump their sewage raw into the ocean…. So what the Line Islands affords us is the opportunity to look back in time, from the inhabited islands, where we see what reefs look like today, with local human impacts, moving back to lower and lower human population densities to what reefs looked like before human activities hit the region.

Pardis Sabeti
The research team recorded the size and quantity of predator fish at all four locations. They bottled up samples from each ecosystem to check for water quality, and carefully photographed how much algae was living on each island's coral.

Jennifer Smith
I was expecting to see some evidence of human disturbance on the reefs, but I would have to say I wasn't really expecting it to be as clear as it was; the fewer humans there were, the more live coral there was, the more reef-building organisms there were.

Pardis Sabeti
The fewer humans, the more big fish there were too. These Line Islands studies helped describe how reef conditions nosedive as human impacts increase. Scientists didn't try to influence reef health – the studies were purely observational. The advantage of an observational study is that you don't disturb whatever you're examining, in this case the underwater ecosystems. But observational studies can't prove anything about cause and effect. They don't tell you why you see what you see.

For help figuring out causal relationships, researchers rely on experiments. Unlike an observational study, which doesn't interfere with what's already happening in a particular setting, an experiment actually manipulates its subjects in some way to see how they respond. Here's how one team designed an experiment to see how certain dietary supplements affected the pain of osteoarthritis, a degenerative joint disease.

Domenic Reda
Despite the fact that large numbers of patients were taking these dietary supplements, it really wasn't clear whether they were effective. It wouldn't make sense if the treatment was not effective to spend money on something that's not going to work. In addition to that, if it turns out that it does have the potential to cause harm, people should be aware of that possibility.

Daniel Clegg
What we did as a study team was develop, the way to assess the question: "Do the dietary supplements help osteoarthritis pain?" And we did that by defining the population of patients that we wanted to study, i.e., patients with painful osteoarthritis of the knee, in a way that would make the patients as homogeneous as we could, and then added an outcomes measure—whether or not pain is improving.

Pardis Sabeti
The doctors started recruiting osteoarthritis patients for a randomized comparative experiment. The explanatory variable, or factor, in this case would be the type of medication patients received. The experimental treatments are the different levels or categories of the factor administered to subjects.

Domenic Reda
In an observational study, for example, you would just study patients who were, say, already taking each of the supplements and trying to do a comparison. There's problems with that approach because the types of patients taking one type of supplement may be different from those taking another type.

Pardis Sabeti
In this study, treatment groups were assigned to receive Glucosamine, or Chondroitin, or a combination of both. There was also an active control group that got a prescription arthritis medication already on the market. And a control group received just a dummy pill, or placebo. That way everyone took a pill every day so any improvement the patients had just due to being in a doctor's care would be uniform across all the groups.

Daniel Clegg
The experiment was a double-blind experiment, which means that neither the investigator nor the patient knew what agent or placebo they were being exposed to. And, I think that's important because just as patients want to do better, I think physicians want to help their patients, and so if the patient or the physician know what they're taking, then that enters an element of bias.

Pardis Sabeti
The response variable is how much the subjects reported their knee pain to decrease – if at all. When researchers calculated the mean reduction in pain after 6 months for each treatment group, it turned out that they all had fairly similar outcomes… so the dietary supplements were no worse or better than the prescription medication, or even the placebo. The quest continues for additional effective treatments for osteoarthritis.

This was a well-designed experiment – researchers randomly assigned their subjects, the treatments included control groups, and the number of subjects was large. To see exactly how not to conduct an experiment, now we can visit the lab of Dr. Confound.

Dr. Confound
Well, hello there.

I'm so glad you both came to help me test this new mood-altering medication. I'll call you research subject Number 7 and you, Number 8. Now, to begin the experiment, I'm going to ask you each to assess your mood: Very Bad, Bad, Fair, Good, or Very Good. Alright, Number 7, you first.

Very Bad? Oh, even worse than Very Bad? Oh, that's a shame, I'm sorry to hear that.

Oh, okay. And you Number 8? Very Good. Okay!

Well, why don't you each take a seat? Oh, I'm sorry, there's only one chair. Oh, Number 7, you're not feeling well. Why don't you take it? You don't mind standing for a while, do you, Number 8? Okay.

Now, I'm going to give you each a pill, and see how you feel in 1 hour. Number 7, here's your pill. There you go.

Oh, Number 8, yeah…let's see. Umm…here's something…yeah! Here, something for you.

All right, your time is up. How are you feeling, Number 7? You're looking better! Nowhere to go but up, right?

What's that you said? Between Bad and Fair. Well, let's say Fair, since you're definitely feeling better!

And you, Number 8? You're feeling worse than you did before? You're feeling Very Bad now. So sorry to hear it.

Well, thank you so much for stopping by Number 7…and Number 8. I'm happy to say, you're my final two subjects. I can't wait to publish these exciting new results. Helping mankind can be so…rewarding!

Pardis Sabeti
Well that example is a little extreme, but the point is that knowing what makes a bad experiment bad helps you appreciate a good design. Let's recap the qualities of a well-designed experiment, like the osteoarthritis study.

The subjects were randomly assigned to the treatment groups taking supplements or placebo.

The groups were as similar as chance could make them.

Equivalent groups were compared. All were treated exactly alike, except for what type of pill they received.

Neither the researchers nor the subjects knew who received supplements or medication or placebo.

And researchers had enough subjects to observe a reliable difference in the pain measurements of the groups, if it had occurred.

Unfortunately, no group stood out with drastic reduction in knee pain. But that's an important result to know about, just as important as if one group had their knee pain completely evaporate. Science can be a long, ongoing process!

For *Against All Odds*, I'm Pardis Sabeti. Tune in next time!

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