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Faculty

Revolutionary Thinker

One statistician's maverick quest for a 'unified theory of everything'

Kent Dayton/HSPH

It probably started with Einstein, the stereotype of a scientific genius always in disarray, so focused on formulas and hypotheses that he never seems to come down to earth long enough to comb his hair, tidy his papers, or make it to appointments on time.

In so many ways, Harvard School of Public Health (HSPH) epidemiologist and biostatistician James Robins fits the mold. He is widely considered one of the most original and influential statisticians of his generation, developing theorems that are transforming the way researchers work at levels as high as the Food and Drug Administration and the National Institutes of Health. And then there's the absent-minded-professor part. He is famous for his tardiness and his housekeeping. More than once he's apologized to University police summoned to check on his "ransacked" office (one officer finally solved the problem by tacking a photograph to Robins's door with a note reading, "It always looks like this").

Then there was the time a friend, the author Susanna Kaysen, volunteered to cook Robins dinner when he had surgery to repair an elbow shattered in a bicycling accident. Phoning ahead to ask when she should come by, she found he'd been discharged from the hospital the previous day.

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James Robins

"So, what did you have for dinner last night?" she asked, knowing his cupboards were often bare.

"A jar of mustard," came the reply.

"You could probably poll 50 people and not one would think you could eat a jar of mustard for dinner," says Kaysen, laughing. "But it reveals something wonderful about Jamie. He doesn't have any preconceived notions—which is why he's such a good thinker. He doesn't rule things out off the top of his head just because they don't seem right. And that can get you a great theory, or it can get you a mustard dinner."

For the most part, it has gotten Jamie Robins great theories.

ABOUT NINETY PERCENT of research in epidemiology and the social sciences is based on observational data, Robins says, adding that "It's easier to do an observational study than a randomized study." While an observational trial looks at phenomena in a population—say, heart attacks in postmenopausal women—and infers possible causes from other data collected, such as diet or medications, a randomized trial artificially assigns subjects to either a test group or a control group by the flip of a coin and then compares outcomes. Though considered the gold standard in research, randomized studies are often impractical, too costly, or even unethical: To observe the effects of second-hand smoke on children, for example, scientists would have to expose some kids intentionally.

But there's a problem with interpreting observational data, and it's known as causality.

At the most basic level, establishing causality means proving that one thing causes another, explains Gary King, the David Florence Professor of Government and director of Harvard's Institute for Quantitative Social Science, where Robins is a faculty associate. Demonstrating cause and effect is "easy to do when the signals are screamingly clear: When a bullet goes through your heart, you die. But when the signals are not strong, as in nutrition, for example, causality is a lot more difficult to define," King says.

"You read in the paper, 'Eat more fish and you'll live longer.' But what does that mean, eat more fish? If you continue with your present diet and eat more fish, you will become huge. So what will you not eat? Maybe you don't drink milk; but if you don't drink milk, you might get osteoporosis. The newspapers typically do not define precisely what they mean by the causal effect—or sometimes even what the cause is."

Jamie Robins took a meandering path on the road to his interest in causality. He majored in math and philosophy as a Harvard undergrad, but dropped out before finishing his senior year to plant fruit trees in Cuba with the Venceremos ("We shall overcome") Brigade, a coalition of Americans who showed their support for Castro's revolution by working alongside laborers. Upon Robins's return to the United States, he spent some time hitchhiking around the country and hanging out at Mama's Cosmic Consciousness Kitchen in San Francisco's Haight district before enrolling in medical school at Washington University, where both of his parents were professors. After a few more colorful detours, he opened an occupational-health clinic with a friend at Yale-New Haven Medical Center.

"We started having to testify on workers-comp cases on the issue of whether somebody's disease was caused by their exposure at work," he recalls. "I was a physician. I didn't know about statistics and epidemiology."

Robins signed up for a few statistics courses at Yale, but having taken "more abstract stuff" at Harvard, he says he found his natural bent for mathematics suddenly undermined by the "cookbook" method of teaching that then predominated. It wasn't until he read a Bayesian critique of what he was being taught that the light began to dawn. The field of Bayesian statistics, which incorporates prior knowledge and accumulated experience into probability calculations, was "the first thing that clarified all of this" for Robins. He spent the next several years teaching himself the foundational ideas and language of statistics while simultaneously working out solutions for several common problems in the field.

Because of his still-nascent statistical communication skills and the unconventional nature of his views, "None of us understood his work initially," remembers Jim Ware, dean of academic affairs at HSPH, the Frederick Mosteller Professor of Biostatistics, and a member of the search committee that hired Robins in 1982. "But we had an intuition it was important."

That intuition paid off. Over the next two decades, Robins came up with formulas that more accurately assess margin of error; that correctly account for missing data, such as "don't know" and "other" survey responses; that more precisely consider confounding data, such as occur when doctors independently adjust the medication doses of individual patients during the course of a study; that analyze the effects of a particular treatment over time, rather than at a particular moment; and more.

The upshot of Robins's labors was to cast new light on epidemiologists' old bugaboo: the question of causality. Suppose chemical A is found in the blood of thousands of workers with disease B.

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Does that mean A causes B? Or might chemical A be just an innocent bystander, linked in some way to as-yet-unknown cause C ... or even, perhaps, causes C, D, and E? Robins's novel statistical methods can help researchers sort spurious associations from true causes and effects by accounting for confounding factors and intermediate variables clouding the pathway from cause to effect.

Moreover, Robins's statistical wizardry can explain why observational and randomized studies of the same health problem sometimes appear at first glance to yield conflicting results. For example, while results from a number of large observational studies in post-menopausal women have indicated that hormone replacement therapy (HRT) involving estrogen and progesterone can prevent heart attacks, results from the Women's Health Initiative's randomized trial found that HRT appears to cause heart attacks.

Similarly, a number of observational analyses of HIV-infected study subjects showed that highly active retroviral therapy (HAART) slowed the rate of their progression to AIDS or death only marginally. A randomized trial, however, revealed a much larger drop in the disease progression rate.

Such disparities have led some scientists to question the reliability and utility of observational trials. Explains Robins: "Usually it's assumed that observational studies are biased, because they may not account for important, and possibly also unknown, common causal factors." In the case of both HRT and HAART, however, reanalyzing the observational trials using Robin's methods has yielded results consistent with the randomized trials.

Given that so much of research is observational, colleagues say Robins's statistical methods could steer biomedical research down a very different road, influencing not only the precision of their findings but ultimately also health practices and policies. HSPH Dean Barry R. Bloom foresees nothing short of a revolution in the way observational studies are analyzed, predicting that causal inferences derived from observational studies using Robins's methods "will come to be regarded as a new standard, second only to the gold standard of randomized trials."

"THE POTENTIAL FOR JAMIE'S WORK is huge," says Miguel Hernan, a former student of Robins's who is now an associate professor of epidemiology at HSPH. "Every time the doctor tells you to take a certain drug, every time you hear a nutritional recommendation, every time a new policy is implemented, it is because someone conducted a study and analyzed the data using a statistical method. Jamie is changing the way data are collected and analyzed, and in the past five years or so we've begun to see the practical impact of these new methods. The only problem with his work is, it's 20 years ahead of its time."

Though Robins's insights are "respected at the very highest level of statistical science," says Jim Ware, they have not yet caught on universally.
"There's no controversy over whether Jamie is correct," says Mark van der Laan, a biostatistician at the University of California at Berkeley who has worked with Robins. "His theories are revolutionary. But his methods are truly challenging to learn. There's a certain element of, 'What I'm doing is working fine for me. I don't need the more complicated stuff.'"
"I'm not a particularly energetic salesman," Robins admits. The work "has to spread to enough people who are good at selling new ideas, if it ever will." As his theories of causality slowly wend their way through the scientific community, Robins—whose professorship was endowed in 2001 by longtime admirers Mitchell L. Dong and his wife, Robin LaFoley Dong—has moved on to a project he expects will take up his remaining years: a unified theory of statistics.

"The field of statistics is currently divided into parametric, nonparametric, and semiparametric schools of thought," he says, launching into an explanation that quickly moves beyond the average listener's grasp. "I just have a feeling that there should be one unified story for everything. I think it will allow for more accurate estimates of uncertainty. But I don't know if it will be useful yet; that's part of the research."

Asked to comment on Robins's chances of succeeding at this latest self-imposed challenge, Jim Ware smiles. "In physics, Einstein spent the latter part of his life trying to develop a unified theory," he says. "Einstein didn't actually succeed. But I'm not prepared to say Jamie won't."

Elizabeth Gehrman writes about science, medicine, and public health

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