

## An observation about numbers

**H**ard data: The very crispness of the words sounds solid and incontrovertible. But when it comes to crunching the complex numbers in observational medical studies, it turns out that different statistical methods can produce dramatically different results.

When DMS researchers, led by Thérèse Stukel, Ph.D., used four different analytic methods to interpret the same set of observational data, they found that only one accurately predicted the success rate of a routine invasive cardiac procedure. The study, published in the *Journal of the American Medical Association*, offers researchers—as well as patients and doctors—what Stukel calls “a word of caution.”

**Sure-fire:** In a perfect world, all medical treatments would be based on randomized controlled trials, the gold standard of medical science. Such studies are a nearly sure-fire method for getting good data but are also costly, time-intensive, and sometimes not possible because of ethical concerns. For example, randomly assigning people to smoke or not smoke to study the effects of tobacco use would be unethical because it is already known that smoking is harmful.

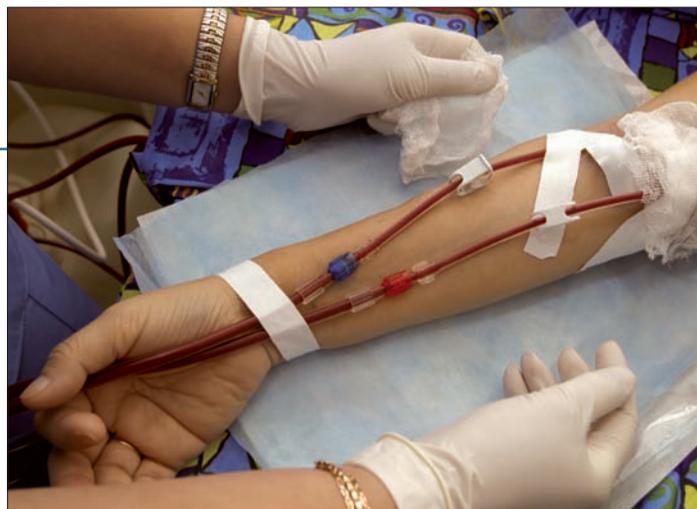
So researchers often depend on observational studies because they are less expensive to conduct and the data is easier to collect. But such data can be trickier to interpret. The subjects being compared may differ in all sorts of ways—such as age, income, education, and medications they take. And there may be hidden biases; for example, some physicians may be more likely to choose younger and healthier patients for surgery. So researchers apply statistical models designed to adjust the data and “remove” the differences.

Stukel’s team set out to compare the effectiveness of several such models. They applied three standard methods and one nonstandard method to the same set of data about long-term survival after a heart attack. The subjects were 122,124 Medicare patients hospitalized for a heart attack in 1994-95; some had received an invasive cardiac treatment, and the rest had received one of several nonsurgical therapies. The researchers looked to see if predictions based on the observational data were consistent with actual results from randomized trials.

They weren’t. The results of the randomized trials showed that surgery reduced relative mortality between 8% and 21%, while the three standard analytic methods put relative mortality at one year at 50% lower for those who got surgery, a result that Stukel termed “clinically implausible.” But the fourth method—instrumental variable analysis, a technique used in econometric research—predicted a 16% reduction in relative mortality; it was more accurate, the team concluded, because it mimicked randomization.

The study, says Stukel, should be “a teaching example to show medical researchers to use caution in certain circumstances in interpreting the results of certain observational studies.” **KELLEY MECK**

**Randomized controlled trials are both costly and time-intensive.**



BORIS KAULIN/ISTOCKPHOTO

**This patient is getting dialysis through a fistula, but that’s not always possible.**

## Aspirin shows faculty against staph

**A**spirin, the wonder drug, may have yet another use. Its pain-killing and cardiovascular effects are well known, but Dartmouth researchers only recently found that catheter-dependent dialysis patients who take aspirin daily have a much lower incidence of deadly *Staphylococcus aureus* infections. Catheters—tubes threaded into a vein—are not the safest way to have dialysis because they offer a point of entry for bacteria. “The best known way to have dialysis,” says Martin Sedlacek, M.D., a DHMC nephrologist, is through a fistula, a surgical connection between an artery and a vein. Over several months, the increased blood flow from the artery causes the vein to thicken so it can tolerate repeated sticks from dialysis needles.

**Deadly:** Yet almost a third of dialysis patients in the U.S. still rely on catheters because they either don’t want to have fistula surgery or didn’t have time for it before starting dialysis. As a result, 3% to 4% of long-term dialysis patients contract potentially deadly *S. aureus* infections each year. John Gemery, M.D., an interventional radiologist who places catheters, and Ambrose Cheung, M.D., a microbiologist, noticed this problem and wondered if aspirin, which has known anti-staphylococcal effects, might help prevent infections. So they teamed up with Sedlacek and Brian Remillard, M.D., chief of nephrology at DHMC, plus a researcher at the University of California at Los Angeles, to investigate their hypothesis.

The team looked at blood cultures from 872 DHMC patients who received dialysis through a catheter from 1995 to 2005. They divided the patients into three groups based on their daily aspirin intake. The group taking the most aspirin, 325 mg daily, had a much lower rate of *S. aureus* infection, only 13 infections per 100 patients with a catheter for one year, compared to 34 infections per 100 patient-catheter-years for those taking no aspirin.

**Bottle:** But dialysis patients using catheters shouldn’t go running for the aspirin bottle yet. “This is just one first study,” cautions Sedlacek. He and his colleagues will be looking at national data next to see if they can find a similar pattern. For now, the best thing that dialysis patients can do is get a fistula, he says. **JENNIFER DURGIN**