



## STATISTICS

by Thomas Lumley

# Out of control

The results of some medical studies can be incredibly misleading.

**F**ifty-five years ago, an article appeared in the *New England Journal of Medicine* on an increasingly popular treatment for chest pain in heart disease. The treatment, which had featured in a *Reader's Digest* story two years earlier, involved tying off an artery in the chest to force greater blood flow to the heart muscle.

In previous research, the majority of patients had reported improvements, often sizeable, in their ability to exercise and in reduced pain. The reports seemed nearly miraculous: "Rise, take up thy bed and walk." A patient in Italy had gone from being bedridden to resuming his job as a carpenter.

Showing that medical journalism had the same faults then as now, the *Reader's Digest* story was relentlessly positive and unsceptical, concluding that the treatment "almost surely will become a surgical milestone".

Not everyone was convinced. No one had found any clear evidence of large amounts of blood being redirected to the heart, and the treatment didn't work nearly as well in experiments on dogs.

So Leonard Cobb, a doctor in Seattle, organised a study in which half the patients had the artery tied off and the other half just had an incision made in their chests. The decision of who to treat and who not to was made randomly and the patients weren't told which group they were in.

As in previous studies, the patients' condition improved dramatically after surgery. In both groups. In fact, the improvement was slightly larger in the group that just got an incision. A second study conducted independently at about the same time found the same results.

How could a sham surgical procedure provide such huge benefits? It really isn't clear, but probably through a combination of factors. The placebo effect would lead to reduced pain in the short term.

Reduced pain together with a willingness to try more exercise might reveal that patients could do more than they had thought.

And the patients might have been going through an especially bad period when they signed up for surgery and so improved anyway. It's hard to credit that these could add up to such a big improvement in health, but the evidence was clear.

**S**tudies like these are the reason medical treatments are evaluated in controlled trials – ideally randomised, blinded trials – whenever possible. It is almost literally incredible how misleading the results of uncontrolled studies can be.

In the modern world, sham surgery is used reluctantly, but occasionally. For example, a recent trial found placebo back surgery to be about as effective as real vertebroplasty.

Randomised trials can't do everything. In particular, the people willing to sign up to a randomised trial may be very unrepresentative.

That's especially true when there has been uncritical media coverage and unrestricted advertising of a new treatment.

Trials are also limited in estimating long-term benefit and harm; for example, there is a reasonable case that long-term benefits of cancer screening programmes are underestimated by randomised trials.

Cost is also an issue; randomised trials are expensive, and good ones are even more expensive. Even so, the list of surprises from randomised trials keeps growing. Recently, for instance, high-dose vitamin E and selenium supplements turned out to increase, rather than decrease, the risk of prostate cancer.

Cobb went on to found one of the first paramedic-staffed ambulance systems, in Seattle, and to lead research, including randomised trials, in resuscitation.

Thanks to this research and its implementation, if you are going to have a cardiac arrest, Seattle is one of the best places in the world to do it. ■

