

The non-significant difference to which Ziliak alludes<sup>4</sup> does not overturn this result and nor does Fisher's approach to significance testing suggest that it should. The real controversy is otherwise. Did the significant difference compared with naproxen established by 2000 logically imply that rofecoxib was inferior to placebo? It can be argued that it did not. Did it make any practical difference in choosing between the two as to whether naproxen was cardio-protective or rofecoxib was cardiotoxic? Again it can be argued that it did not. None of this confusion can be laid at Fisher's door.

As for Ziliak's attack on randomisation, I suggest that any readers in doubt as to its value look no further than the TARGET study.<sup>5</sup> Patients were allocated not at random to one of two substudies, either lumiracoxib versus naproxen or lumiracoxib versus ibuprofen. They were, however, randomised *between* groups *within* studies. Between substudies there is substantial imbalance in prognostic factors. Within substudies there is not.

Fisher was not infallible, but he was a scientist of the very first calibre whose work deserves to be taken seriously.

I consult for the pharmaceutical industry, including Merck and Novartis, and have consulted for Roche. I own shares in Novartis. I am secretary of the Fisher Memorial Trust.

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- 1 Ziliak ST. The *Validus Medicus* and a new gold standard. *Lancet* 2010; **376**: 324–25.
- 2 Fisher RA. Statistical methods and scientific inference. In: Bennet JH, ed. *Statistical methods, experimental design and scientific inference*. Oxford: Oxford University, 1990.
- 3 Bombardier C, Laine L, Reicin A, et al. Comparison of upper gastrointestinal toxicity of rofecoxib and naproxen in patients with rheumatoid arthritis. *N Engl J Med* 2000; **343**: 1520–28.
- 4 Lisse JR, Perlman M, Johansson G, et al. Gastrointestinal tolerability and effectiveness of rofecoxib versus naproxen in the treatment of osteoarthritis: a randomized, controlled trial. *Ann Intern Med* 2003; **139**: 539–46.
- 5 Farkouh ME, Kirshner H, Harrington RA, et al. Comparison of lumiracoxib with naproxen and ibuprofen in the Therapeutic Arthritis Research and Gastrointestinal Event Trial (TARGET), cardiovascular outcomes: randomised controlled trial. *Lancet* 2004; **364**: 675–84.

### Author's reply

In my Art of Medicine essay, I said that “[t]here are few scientists who would not rejoice at the breaking of our gold fetters”. By “gold fetters” I mean the illogical system of rewards that is currently spoiling medicine and other sciences—through research based on “artificial randomisation”, “statistical significance”, and “validity” descended from Ronald Fisher.<sup>1,2</sup>

Stephen Senn is apoplectic but the cause is not scientific. His remarks do not pass the tests of history and basic human values. “Student's” priority over Fisher—and the demonstrated value of his economic, balanced, and repeated small sample approach to the design and evaluation of experiments—is undoubted.<sup>3</sup> Yet Student is not mentioned by Senn. On the Student-Fisher debates on design, testing, and estimation—and on the gross distortion of Student's methods by the younger Fisher<sup>4</sup>—Senn is mute.

Nietzsche said that the twilight of the idols will be denied by some. Some will try to impede the inevitable decline and new dawn of science. Senn does not seek merely to save randomisation and significance; he employs several Aristotelian fallacies to try to place them and Fisher higher up in the annals. He applauds when Fisher says that “[a] test of significance contains no criterion for ‘accepting’ a hypothesis”. But the pregnant phrase here is “no criterion”; in Fisher's method there is no criterion for assessing medical and other knowledge—the exact opposite of what Senn claims and human beings need most.

“Finally”, Fisher emphasised, “in inductive inference we introduce no cost functions for faulty judgments.” Some help. “In fact”, in his view, “scientific research is not geared to maximize the profits of any particular organization... We make no attempt to evaluate these consequences, and do not assume that they are capable of evaluation in any currency”.<sup>5</sup>

Student and his students have a better gold standard. We value

balanced designs; prior knowledge; variable—including extreme—odds; inputs of personal probability; shows of minimum real error; cost functions; and explicit demonstrations of power to detect large and real treatment differences across independent and repeated trials. Fisher's waning faithful do not.

I declare that I have no conflicts of interest.

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- 1 Altman DG, Schulz KF, Moher D, et al. The revised CONSORT statement for reporting randomized trials: explanation and elaboration. *Ann Intern Med* 2001; **134**: 663–94.
- 2 Bruhn M, McKenzie D. In pursuit of balance: randomization in practice in development economics. *Am Econ J Appl Econ* 2009; **1**: 200–32.
- 3 Ziliak ST. Guinnessometrics: the economic foundation of ‘Student’s’ t. *J Econ Persp* 2008; **22**: 199–216.
- 4 Ziliak ST, McCloskey DN. The cult of statistical significance: how the standard error costs us jobs, justice, and lives. Ann Arbor: University of Michigan Press, 2008.
- 5 Fisher RA. Statistical methods and scientific induction. *J R Stat Soc* 1955; **17**: 69–78.

### Web-surfers beware: know thy source

As the managing editor at theheart.org, one of the cardiology websites cited by Christopher Cannon (Aug 14, p 505),<sup>1</sup> I was delighted to read Cannon's belief that “cardiology's move online... will hopefully improve health care.” I would, however, point to some potential pitfalls.

As Cannon notes, physicians now have countless websites to turn to for information, and ever-increasing formats—news, scientific papers, blogs, tweets, webcasts, podcasts—in which to get it. Indeed, I believe the rise of independent medical websites probably spurred meeting organisers, journal editors, and now textbook publishers not only to diversify the content they offer online, but also to offer it more quickly: simultaneous presentation and publication of new research being a case in point. Add to this the rise of “sharing” via social



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