IJE vol.32 no.6 © International Epidemiological Association 2003; all rights reserved. *International Journal of Epidemiology* 2003;**32**:922–924
DOI: 10.1093/ije/dyg295

SYMPOSIUM

Fisher and Bradford Hill: theory and pragmatism?

Iain Chalmers

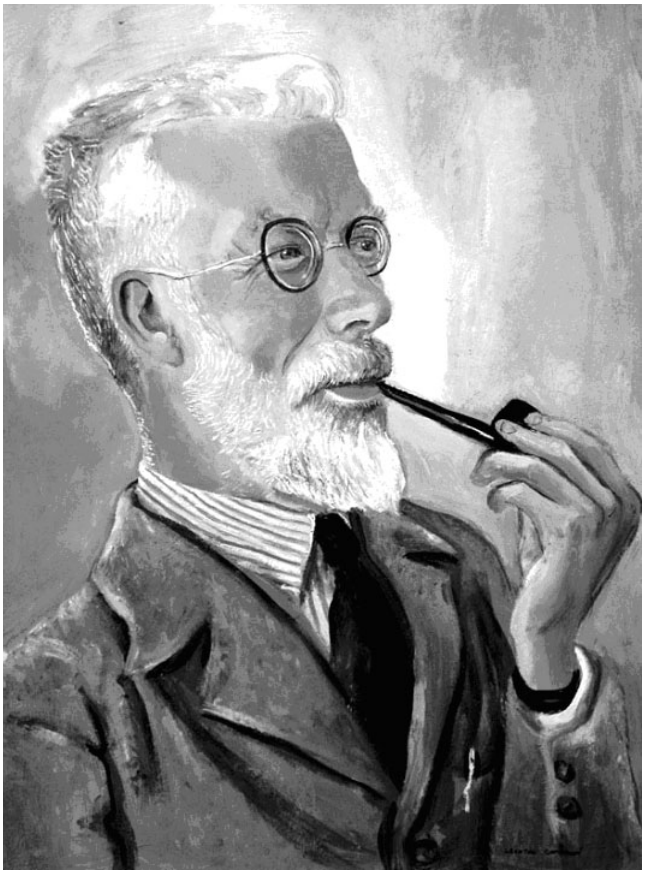
Accepted 9 July 2003

During the 1930s, RA Fisher showed how randomization provided the theoretical underpinning for tests of statistical significance.[1] Because of this, it is often assumed that Fisher must have played a key role in the evolution of randomized trials in medicine during the 1930s and 1940s. Randomization was adopted by Austin Bradford Hill for Medical Research Council (MRC) trials for a more pragmatic reason, however. Bradford Hill was aware that an alternate allocation scheme had not been strictly observed in a MRC trial done in the early 1930s[2] and that selection bias had thus probably undermined the validity of the comparisons made in the study. In designing MRC trials a decade later, he therefore used allocation schedules based on random numbers. If properly concealed, these made it more difficult for those recruiting participants to know which allocations were next in line, and, thus less likely to introduce bias in assembling therapeutic comparison groups.[3]

The papers in this issue of the *International Journal of Epidemiology*—by Peter Armitage and Richard Doll (formerly colleagues of Bradford Hill), Walter Bodmer (formerly a student of Fisher), and Harry Marks (author of a history of clinical trials[4])—were commissioned to reflect on this characterization of 'Fisher the theoretician' and 'Bradford Hill the pragmatist'. This is obviously a simplification—Fisher was interested in practical problems, and Bradford Hill was aware of statistical theory—but it does help to emphasize the very different contributions made by the two men.

Fisher left a wealth of personal papers, which have been archived very helpfully at the University of Adelaide, in Australia, and an excellent biography exists.[5] By contrast, very few of Bradford Hill's personal papers have survived (his daughter has told me that he 'threw everything away') and no one has yet taken up the challenge of writing a biography.

I obtained copies of correspondence between Bradford Hill and Fisher from the Fisher Archive, and the authors of the four papers that follow were able to draw on this. However, none of them has used any material from an unpublished hand-written 'memoir' that Bradford Hill prepared in 1988 for the Librarian at the London School of Hygiene and Tropical Medicine.[6] I want to take this opportunity to bring some of this material to a wider readership.



Fisher

Supplied and reprinted with kind permission of the North Carolina State University Institute of Statistics.

Passages in this memoir make clear that Bradford Hill recognized his limitations as a mathematical statistician, declaring that, 'having no mathematical knowledge' he needed first class statisticians to work with him (ref. 6, p. 5). This acknowledgement did not prevent him criticizing statisticians who were out of touch with practical realities, however. Commenting on some American statisticians who had criticized a

James Lind Library, James Lind Initiative, Summertown Pavilion, Middle Way, Oxford OX2 7LG, UK. E-mail: ichalmers@jameslindlibrary.org

US trial establishing the efficacy of Salk's polio vaccine, Bradford Hill wrote:

> (They) knew all about statistical methods and mathematical formulae and nothing about medicine and the problems involved in making trials in human populations. They were ignorant of the fact that one often had to be content with far from perfect evidence and draw on the most likely explanation. (ref. 6, p. 30)

Hill was also intolerant of statisticians who were unprepared to make the effort to try to communicate effectively with non-statisticians. In 1960, the director of an Australian institution asked Hill about the success of his approach to teaching statistics to non-statisticians. A doctor at the Australian institution had been teaching statistics and 'blinding (his students) with algebra'. Bradford Hill agreed to the director's proposal that a young Australian statistician should spend some time at the London School of Hygiene to learn how to use simple teaching methods.

> He showed me a paper he had written. 'Where do you want to publish it?', I asked him. He named some medical journal. Then I said 'you must rewrite it more simply. I can't understand it and your proposed readers certainly won't'. He was a prima donna, stormed about, said I could teach him nothing and he would 'go to RA Fisher the leading statistician of the day' at Rothamstead. 'The sooner you go the better' I said, 'get out of my department and don't come back'. Of course in that situation (and I was then a friend of Fisher) Fisher would not take him.' (ref. 6, p. 19)

By contrast with his intolerance of some statisticians, Bradford Hill was very indulgent of people who had difficulty understanding statistics. Indeed, he had a policy of never failing a candidate who was 'hopeless on medical statistics'.

> When I got on to the subject of statistical tests of significance I started by stating that these were based on the laws of probability over which statisticians quarrelled violently. I was entirely ignorant of them but I knew more than the lady who congratulated her friend on the birth of triplets. 'It is remarkable' said the mother 'it happens only one in 8000 times'. 'Good gracious' said her friend. 'However did you find time for the housework?' (ref. 6, p. 12)

His light-hearted lectures were very carefully planned.

> I firstly replaced 'You can prove anything by statistics' by 'you can prove nothing by statistics'. You can 'prove' anything by the misuse of statistics, and politicians, advertisers do just that, and unless you know something about them you will be misled. In the strict sense of the word proven you can 'prove' nothing, but you can make one interpretation of the data more probable than any other (e.g. smoking and cancer of the lung). My lectures may have appeared spontaneous. They were anything but that. I put long hours of thought into them and wrote them with care. (ref. 6, p. 11)

In addition to his substantial contributions to the design and interpretation of controlled trials and epidemiological studies,

Bradford Hill

Reproduced by kind permission of the Editor, Journal of the Royal Statistical Society.

Bradford Hill deserves to be remembered for his skills as a communicator—in his writings as well as his lectures. Indeed, his talents as a communicator may go some way to explaining why the MRC's randomized trial of streptomycin appears to have been so influential in the adoption of new methodological standards for therapeutic evaluation. One manifestation of Bradford Hill's concern to communicate successfully with clinicians was his diligence in informing himself about clinical matters: during a lecture tour of the US in 1951 he had to explain to his audiences that he was not medically qualified, which 'came as a surprise to many' (ref. 6, p. 18).

After rereading Bradford Hill's 1950s papers on 'the clinical trial'[7,8] when I was drafting the methodology chapter for a book in which I was involved,[9] I sent him a postcard reiterating just how much pleasure his writings always gave me—and how frustrated I felt that I was having such difficulty in producing clear, readable prose myself. He responded in a typically modest style:

> I am glad that you enjoyed re-reading my papers on CTs of the 1950s. I believe I wrote clearly because I had a simple mind and had to try hard to make things clear to myself. And of course I must have gained by all the reading I did when I was bed-bound thro' 1917/18—pretty well all the world's classics in fiction—in English and in translations—and I deliberately studied the art of writing (Quiller Couch, Ernest

> Gowers, Fowler & so on). And I always enjoyed writing—some nice white sheets of paper & a fountain pen & away one can wander.[10]

The following year, when I felt that I had produced a reasonable draft of my chapter, I asked him if he would look over it.

> You told me that I should overlook the style and point out 'bad logic or other errors'. You ask the impossible. I have spent a life's time on MSS—my own, my staff's or as editor of this or that—seeking a short word in place of a long one, cutting the length of sentences, deleting adjectives and double negatives … I was floundering out of my depth immediately in your introduction—what in God's name is a 'conceptual framework'—just one, let alone a variety! And the sentence spans close on 50 words. I made an attempt to shorten and simplify but it can't be done. I beg you Iain, rewrite that introduction. There is so much to come that is clear and good—you may at the outset scare away the reader (simple-minded ones like me).[11]

Fisher's seminal contribution to the design of experiments is uncontestable. The nature of Bradford Hill's distinctive contribution to the history of randomized clinical trials as a communicator as well as a scientist is less well recognized. Twenty years after the report of the MRC streptomycin trial, Professor John Crofton was introducing Bradford Hill for an honorary Doctorate in Medicine at the University of Edinburgh. Unsurprisingly, Crofton had a good deal to say about Bradford Hill's role in the evolution of controlled trials. A passage in Bradford Hill's unpublished memoir is revealing:

> 'John', I said, 'you know I did not invent the controlled trial. It goes back at least to Lind who tried lime juice in scurvy compared with the usual nauseating mixtures of the day'. 'I know that', Crofton replied, 'but you persuaded an extremely conservative profession which regarded change with suspicion, to accept and use them'. That was, and is, I think a fair judgement. (ref. 6, p. 29)

In the year that sees the 250th anniversary of the publication of Lind's *Treatise of the Scurvy* (www.jameslindlibrary.org), Austin Bradford Hill's concurrence with Crofton's judgement helps to clarify one of the several reasons that he has a special place in the history of controlled trials.

Acknowledgements

The papers on Fisher and Bradford Hill published in this issue of the *International Journal of Epidemiology* are based on presentations commissioned for a session at a conference entitled 'Beating biases in therapeutic research: historical perspectives' held in Oxford in September 2002 (programme and abstracts available at http://www.wuhmo.ox.ac.uk/docs/bbabstracts.htm). The conference was organized jointly by the Wellcome Unit for the History of Medicine, Green College, and the UK Cochrane Centre. The UK Cochrane Centre and the Wellcome Trust provided financial support. I am grateful to the librarian and archivist at the London School of Hygiene and Tropical Medicine, Brian Furner and Victoria Killick, for help and permission to quote from Bradford Hill's memoir; and to Susan Woodburn, Special Collections Librarian at the Barr Smith Library, University of Adelaide, for providing copies of Fisher's correspondence with Bradford Hill.

References

[1] Fisher RA. *The Design of Experiments*. Edinburgh: Oliver and Boyd, 1935.

[2] Chalmers I. MRC Therapeutic Trials Committee's report on serum treatment of lobar pneumonia, BMJ 1934. In: Chalmers I, Milne I, Tröhler U, Vandenbroucke J (eds). The James Lind Library (www.jameslindlibrary.org). Accessed Tuesday 7 January 2003.

[3] Chalmers I. Comparing like with like: some historical milestones in the evolution of methods to create unbiased comparison groups in therapeutic experiments. *Int J Epidemiol* 2001;**30:**1170–78.

[4] Marks HM. *The Progress of Experiment: Science and Therapeutic Reform in the United States, 1900–1990*. Cambridge: Cambridge University Press, 2000.

[5] Fisher-Box J. *RA Fisher: The Life of a Scientist*. New York, Chichester, Brisbane, Toronto: John Wiley & Sons, 1978.

[6] Bradford Hill A. Some memories of A.B.H. Manuscript dated January 1988, held in the Archive at the London School of Hygiene and Tropical Medicine.

[7] Bradford Hill A. The clinical trial. *Brit Med Bull* 1951;**7:**278–82.

[8] Bradford Hill A. The clinical trial. *N Engl J Med* 1952;**247:**113–19.

[9] Chalmers I. Evaluating the effects of care during pregnancy and childbirth. In: Chalmers I, Enkin M, Keirse MJNC (eds). *Effective Care in Pregnancy and Childbirth*. Oxford: Oxford University Press, 1989, pp. 3–38.

[10] Bradford Hill A. Letter to Iain Chalmers, 7 June 1987.

[11] Bradford Hill A. Letter to Iain Chalmers, 15 June 1988.