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J Guy Scadding and the move from alternation to randomisation

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Dr Guy Scadding was a member of the committee that planned, supervised and reported the Medical Research Council's randomised trial of streptomycin in pulmonary tuberculosis. Following the meeting in October 1998 to mark the 50th anniversary of the *BMJ* report of that study, Dr Scadding published a letter in the *BMJ* entitled 'Memories of why allocation by random sampling numbers was used'. In his letter, Dr Scadding wrote of his recollection that

> the committee was aware of the difficulty of avoiding allocation bias in allocation to test and control groups in a trial in which blinding was impossible. Because of this (they) readily accepted the procedure of allocation by random sampling numbers advocated by Bradford Hill and hoped that it would prove practicable.[1]

He went on to describe how he was 'familiar with Bradford Hill's work on the design of clinical trials, both from a course of lectures that he gave in the late 1930s and from reading his book published in 1937', and he drew attention to the fact that, in 1944, during war service in Egypt, he had 'designed and carried out a double blind placebo controlled study of the effects of sulphonamides in bacillary dysentery'. He wrote that, in that trial, 'allocation bias had been eliminated by the formulation of test and control medications as indistinguishable suspensions, identified by letters'. However, he noted that 'The streptomycin trial could not be blind, either to observers or to patients, and the more complicated method of allocation by random sampling numbers seemed to offer the most promising way of minimising bias'.

We were intrigued by Dr Scadding's recollections and delighted when he agreed to let us visit him to clarify further some issues about the control of bias, which he had raised in his *BMJ* letter. He and his wife Mabel welcomed us to their home in Beaconsfield on the afternoon of Thursday 10 June 1999. Over tea and Mrs Scadding's delicious apricot flapjacks, our conversation with Dr Scadding was very informative.

Dr Scadding's[2] *Lancet* report (which had originally been submitted by the army authorities to the *Journal of the Royal Army Medical Corps*, and rejected!) had used strict alternation to allocate patients to the comparison groups, a technique he had also used in a study reported in the *Lancet* the previous year.[3] We asked Dr Scadding what had led him to design a controlled experiment using alternation and blinding. He said he wanted to learn how to treat his patients effectively and that it simply seemed sensible to do this in a controlled way.[4] He supposed that he must have based the design of his studies in the Egyptian desert on what he had learned from his exposure to Bradford Hill's lectures, articles and book in the late 1930s, in Southern England. At that time, Bradford Hill advocated alternation (rather than randomisation) for abolishing allocation bias when assembling treatment comparison groups, and the use of placebos for minimising observer biases. He felt that 'the concepts of 'randomisation' and 'random sampling numbers' are slightly odd to the layman, or, for that matter, to the lay doctor, when it comes to statistics'.[5]

We asked Dr Scadding what advantage he felt randomisation offered over alternation. He said that, because of its unpredictability, it could provide better protection against allocation bias than alternation, particularly in trials in which people could not be blinded to the identity of the comparison groups. As far as he could recall, this was the main motivation for using randomisation in the streptomycin trial. He had no recollection that statistical theory had been invoked at all as a reason, and could not remember being aware of Fisher's ideas. Indeed, as a

chest physician who first communicated the results of Doll and Bradford Hill's study showing the links between smoking and lung cancer to the British public in the 'Matters of Medicine' series presented by Charles Fletcher (broadcast from Alexandra Palace on 13 January 1953), Dr Scadding knew Fisher mainly as a consultant paid by the tobacco industry to challenge the (correct) inferences drawn from this study about the carcinogenic potential of tobacco.

Dr Scadding's response to our question accords exactly with the response to the same question that Bradford Hill gave to one of us (IC) and William Silverman in a conversation in 1986.[6] Statistical theory appears to have had little or no role in the adoption of randomisation for the early controlled trials in the UK. Indeed, there is no statistical advantage of randomisation over strict alternation. The key issue is that whichever of the two methods is used to generate the allocation schedule, care must be taken to minimise the risk that the schedule can be identified (and thus ignored) in advance of patient recruitment. It was the use of a technique to ensure successful concealment of the allocation schedule in the streptomycin trial that made the study a landmark, not the process of randomisation *per se*.

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References

1. Scadding JG. Memories of why allocation by random sampling numbers was used. *BMJ* 1999; 318: 1352.
2. Scadding JG. Sulphonamides in bacillary dysentery. *Lancet* 1945; 2: 549–553.
3. Scadding JG. Comparative effects of sulphonamide drugs in mild bacillary dysentery. *Lancet* 1944; 1: 784.
4. Fletcher RG and Scadding JG. Observations on the MI room treatment of ''acute simple diarrhoea with sulphaguanadine''. Unpublished manuscript, 1945.
5. Hill AB. Memories of the British streptomycin trial in tuberculosis. *Control Clin Trials* 1990; 11: 77–79.
6. Silverman WA and Chalmers I. Sir Austin Bradford Hill: an appreciation. *Control Clin Trials* 1991; 13: 100–105.