Blinding, randomisation and authority within clinical trials

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As we are increasingly called on to demonstrate the evidentiary basis of health research, policy and clinical practice, it is important to consider how methodological rigour can impact on the nature and quality of clinical care. 'Blinding' is one of the cornerstones of modern clinical research and along with randomising patients within a clinical trial, represents the most fundamental points at which researchers can ensure the scientific objectivity of their work. Yet it is a practice which was born out of a specific historical context and which significantly affects the exercise of power between clinical practitioners and patients.

The birth of the randomised clinical trial

The evaluation of streptomycin for the treatment of tuberculosis is widely cited as marking the beginning of the modern era of randomised trials.[1] When streptomycin became available shortly after World War II both clinicians and pharmaceutical manufacturers wanted prompt evaluation to justify the cost of its production and use. Multi-centre trials were undertaken by the Veterans Administration in the United States, and the Public Health Service in the United Kingdom.

The American trials did not use any form of control group but, due to post-war shortages, the supply of streptomycin in the UK was limited. By randomly allocating patients to either a control group or an active treatment group British researchers were able to creatively incorporate the shortage of drugs into their trial design. Their study was confined to a subgroup of soldiers who were severely ill with tuberculosis. Green writes:

'The shortage of streptomycin in Britain at the time (which was so distressing from the humanitarian point of view) here proved scientifically advantageous, for it allowed [those overseeing the trial] to arrange, with a clear conscience, a rigidly controlled trial of the value of bed rest with streptomycin, as compared with bed rest alone, in young adults with rapidly advancing bilateral pulmonary tuberculosis...' [2]

The features of this trial which have marked it out as historically significant were the random allocation of patients to either control or experimental group and the blinding of radiographers to the treatment each patient was receiving. Yet these were features that were ethically acceptable only because of the shortage of streptomycin. It was the contingency of the material availability of the drug during the immediate post-war reconstruction which determined this aspect of the design of the trial. The 'scientific benefits' of using controls would probably have been bypassed had the material conditions been more favourable as they were in the US streptomycin trials which are now only remembered because of the way they contrast methodologically with the UK trial.

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The methodological benefits for clinicians of blinding and randomisation

Modern medicine is marked by a tension between the importance of the craft-skills of the clinical practitioner, and the scientific foundation of the discipline. For the purposes of research, blinding and randomisation seek to limit the clinical authority of practitioners in favour of their authority as scientists.[3]

Blinding is the process whereby people who are involved with research interventions are prevented from knowing which of the therapeutic agents trial participants are being given. Blinding is said to be important for maintaining neutrality and impartiality, because if clinicians and researchers know which treatment patients are being given they may lose their professional objectivity and be tempted to interpret observations and outcomes in a manner that favours their preferred outcomes. The more blinding, the better, is generally taken to be

the rule: it is desirable to extend blinding to all those handling materials deriving from the trial (for example radiologists or pathologists).

Likewise, randomisation limits the subjective input of clinicians. When randomisation is effective the allocation of treatment options occurs in a totally unpredictable manner, eliminating the possibility that clinicians' personal interests can affect the composition of treatment groups.[4] Relinquishing personal and professional responsibility for a patient's treatment within a clinical trial is acceptable only because clinicians have faith that randomisation is a scientifically reliable process which overcomes the fallibility of individual judgement. A consequence of randomisation which is less widely publicised is that it reduces the ability of individual clinicians to stray from an agreed research plan.[5]

There are two reasons why it is also important that the trial participants are blinded to which treatment they are receiving: firstly, debate continues as to whether patients who know they are being given an experimental agent may well actually do better simply because of that knowledge.[6] Secondly, and more significantly for the requirements of randomised trials, if patients know which treatment they are being exposed to and if it is not their treatment of choice, they may withdraw from a trial and seek alternative treatment, or corrupt the trial by seeking additional treatment 'on the side'.

These actions undermine clinical research. Every withdrawal must be considered when calculating final results and may require the withdrawal of another subject from the opposing arm of the trial thereby weakening the statistical power attributable to outcomes. Seeking additional treatments may affect the actions of experimental therapies and confound outcomes in ways that researchers cannot account for.

Discussion

Blinding and randomisation present a paradox in the operation and ideology of medicine. By constraining clinical judgement, blinding and randomisation serve to maintain and further establish the scientific authority of researchers while assuming and formalising a fundamental lack of authority or expertise among trial participants. By attempting to maintain the neutrality and disinterestedness of the clinician, blinding and randomisation seek to reinforce their cognitive and professional authority.

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Blinding within patient groups, on the other hand, is directed at stopping patients making decisions about treatment during a trial and in so doing threatening the scientific validity of the enterprise. Blinding thus affects the exercise of power very differently for clinicians and patients. It reinforces the scientific status of the clinical researcher while undermining trial participants who would disrupt the research process. General practitioners who engage in clinical research should be aware of this dynamic and be prepared to discuss it with their patients, should the need arise.

Key points

- Blinding significantly affects the exercise of power between clinical practitioners and patients.
- For the purposes of research, blinding and randomisation seek to limit the clinical authority of practitioners in favour of their authority as scientists.
- By constraining clinical judgement, blinding and randomisation serve to maintain and further establish the scientific authority of researchers while assuming and formalising a fundamental lack of authority or expertise among trial participants.

References

1. For example see, Marks HM (1997). The progress of experiment: Science and therapeutic reform in the United States, 1900-1990, Cambridge, Cambridge University Press, Chapter 2. Feinstein AR. (1985), Clinical Epidemiology: The architecture of clinical research, London, WB Saunders Company, 687.
2. Green FKH. (1954) The clinical evaluation of remedies, Lancet, 267:1089.
3. Armstrong D. (1977) Clinical sense and clinical science. Social Science and Medicine, 11:599–601.
4. Feinstein A. (1989) Epidemiologic analysis of causation: The unlearned scientific lessons of randomized trials. Journal of Clinical Epidemiology, 42, 6:481–89.
5. Marks HM. (1988) Notes from the underground: The social organization of therapeutic research, in Maulitz RC and Long DE (eds.). Ground Rounds: One hundred years of internal medicine, Philadelphia, University of Pennsylvania Press, 319-329.
6. Vickers AJ, de Craen AJ. (2000) Why use placebos in clinical trials? A narrative review of the methodological literature. Journal of Clinical Epidemiology, 53, 2:157–61.