The evolution of controlled trials before the middle of the 20th century

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Contrary to widely believed assertions, the concept of unbiased creation of treatment comparison groups in clinical trials was not ‘a seminal statistical idea’, but was rooted in the much older idea that fair tests of treatments involve comparing like with like. This was achieved using alternate allocation to treatment comparison groups at least 200 years ago.¹

Strict alternation deals with selection bias as effectively as strict random allocation, but alternation is more likely to result in foreknowledge of allocations among those recruiting research participants. The historical importance of the iconic MRC streptomycin trial published in 1948 is not its use of random sampling numbers to generate the allocation schedule. Rather, it is its clear description of the precautions taken to conceal the schedule, and so secure unbiased allocation.²³⁴⁵⁶⁷

Taking advantage of increasing possibilities for full text searches, several hundred reports of controlled trials published before 1948 have already been identified.¹ However, without multilingual, collaborative research

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⁴ I. Chalmers, ‘Why transition from alternation to randomisation in clinical trials was made’, BMJ, 319 (1999), 1372.
⁷ I. Chalmers, ‘Statistical theory was not the reason that randomisation was used in the British Medical Research Council’s clinical trial of streptomycin for pulmonary tuberculosis’, In: Jorland G, Opinel A, Weisz G (eds.) Body counts: medical quantification in historical and sociological perspectives (Montreal, McGill-Queens University Press, 2005), pp 309-34.
the history of the evolution of the controlled trial - a crucially important technology in medical research - will remain seriously incomplete.\textsuperscript{8}