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Textbooks and other publications on controlled clinical trials, 1948 to 1983

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Introduction

The evolution of controlled clinical trials to assess the effects of medical interventions began in the 1720s, progressed slowly through the 19th century and gathered speed during the first half of the 20th century.[1] Controlled clinical trials had increased particularly rapidly during the 1930s and 1940s, but it was a report of the Medical Research Council's trial of streptomycin for pulmonary tuberculosis published in 1948 which attracted international attention, particularly for the clear description of what had been done and found. Contrary to widespread belief, the Medical Research Council streptomycin trial was not the earliest example of the use of random allocation to generate treatment comparison groups, but it does appear to be the earliest example of a randomised clinical trial, in which steps had been taken to prevent foreknowledge of allocations, and so reduce the risk of biased tampering with the treatment allocation schedule.[2]

The streptomycin trial ushered in a golden age of Medical Research Council clinical trials during the 1950s and 1960s,[3] and this was reflected in articles and books referring to this research design, written by some of the scientists involved. One of the best known of these was *Principles of Medical Statistics*, a book based on a series of articles published in the *Lancet* in 1937 and which became a classic.[4] The author of the book was Austin Bradford Hill, a member of the team responsible for the streptomycin trial. Although controlled trials were mentioned briefly in the first edition of Hill's book, it was not until the sixth edition, published in 1955, that a chapter specifically about clinical trials was introduced.

The earliest whole book focusing specifically on controlled trials I have been able to identify was also published in 1955. The author, Gustav Herdan (1897–1968), was an interesting polymath, with degrees from the German University in Prague for studies in law and sinology (East Asian languages) and English philology, and, after moving to England in 1938, a degree in mathematics and statistics. This mixture of talents led him to be a founder of quantitative linguistics. He became a lecturer in statistics at the Bristol University in 1948, and it was while in that post that his book *Statistics of Therapeutic Trials* was published by Elsevier.[5]

Between 1955 and 1960, seven further documents appeared – two published in 1958 were reports of symposia in London (online Appendix, nos. 2 and 3); the third was an American book entitled *The clinical evaluation of new drugs* (online Appendix, no. 4) and the fifth, sixth and seventh were books by British authors. The last of these was based on a meeting in Vienna organised by Bradford Hill under the aegis of UNESCO and was published in French as well as English.[6]

In the following years, further books arrived thick and fast. I have assembled all those I have found between Herdan's 1955 book and that by Stuart Pocock published in 1983. The latter became both a major teaching text and an important source of reference for statisticians and doctors, to the extent that although it was never revised after the first edition, it remains popular today.

What of the intervening years between 1960 and 1983? This was a period when the pharmaceutical industry was becoming interested in the new trial methodology, wanted to understand it and to exploit it in their drug development programmes. At the same time, academic institutions, funding agencies and research organisations were also becoming interested and wanted to apply the methodology and extend it into programmes beyond drug evaluation, such as psychotherapy. There may be an impression that outside of scientific papers, comparatively little on clinical trials was published during this early period when in fact the converse is true. I have provided details of publications from 1948 to 1983, including their contents, with extracts from prefaces or forewords to convey their aims and scope. I have also added information about editors and authors, with their qualifications and locations, to provide

some idea of their background in the field of clinical trials. In addition, I have made brief comments in a preamble to some of the texts. This detailed information can be consulted in the Appendix in this article on the James Lind Library.

How did I decide which books to include in the bibliography?

An initial list of texts was developed many years ago from a selection of booklets and texts belonging to Dr Ian Sutherland, Director of the Medical Research Council Statistical Research and Services Unit in London (from 1969 to 1980) and of the Medical Research Council Biostatistics Unit in Cambridge (from 1980 to 1986). Ian Sutherland joined the Medical Research Council from the Institute of Social Science in Oxford in 1952, and he attended some of the meetings from which these early publications arose.

Decisions about inclusion and exclusion of specific publications were not easy. Basically, I have endeavoured to include those whose content extends beyond clinical pharmacology and basic experimental design to clinical assessment of drugs and other treatment modalities, and where consideration of clinical trials extends to more than a single chapter or paper. I have excluded papers in journals unless they appear as an issue devoted to a working party report, symposium or conference. However, it is worth noting that during the period of interest, the first journals devoted specifically to clinical trials were published. The first, *Clinical Trials Journal*, appeared in November 1964 and was published by Stuart Phillips Publications based in Sutton, Surrey, England, with Editor-in-Chief, Dr Kenneth Maclean MA, MD, FRCP; its aim was to record and provide reference to correctly conducted, ethical clinical trials. It continued until 1990 (volume 27) and then re-emerged as *Clinical Trials and Meta-analysis* (published by Elsevier) from 1992 to 1994 (volumes 28 and 29). From 1995, it was integrated into the second journal, *Controlled Clinical Trials: Design, Methods, and Analysis*, which started in 1980 with Editor, Dr Curtis Meinert PhD. It was published by Elsevier and became the designated journal of the Society for Clinical Trials, which was founded in USA in 1978. Coincidentally, in the same year, the International Society for Clinical Biostatistics was founded in Europe.

Altogether I have listed 69 publications that appeared over the 36-year period from 1948 (the year the Medical Research Council streptomycin trial was published) to 1983 (the year Pocock's book was published. Dividing this period of 36 years into five sextennial intervals shows no publications (1948–1953), 5 (1954–1959), 7 (1960 to 1965), 12 (1966 to 1971), 15 (1972 to 1977) and 30 (1978 to 1983), respectively – a curvilinear increase with mode eight, unsurprisingly, towards the end of the period in 1981. Although I have included some publications in French and German in the series, it is inevitable that I will have either missed or have not been able to trace some relevant publications, particularly those in languages other than English. I wish to be informed of potentially eligible candidates.

Over the period from 1948 to 1983, the concept of the randomised clinical trial was fully developed and underpinned by essential understanding of design, conduct, data collection, analysis and reporting, and the overarching principles of ethics and management; some or all of these appear within the individual texts presented. However, there are several fundamental topics that were not covered by individual texts specifically within the context of clinical trials until after 1983; these are cross-over trials (first covered by B Jones and MG Kenward[7] in *Design and Analysis of Cross-Over-Trials*); group (cluster) randomised trials (DM Murray's[8] *Design and Analysis of Group Randomized Trials*); meta-analysis (AJ Sutton et al.[9] in *Methods for Meta-Analysis in Medical Research* and D Stangl and DA Berry[10] in *Meta-Analysis in Medicine and Health Policy*) and sample size determination (D Machin and MJ Campbell[11] in *Statistical Tables for the Design of Clinical Trials*).

Presentation

I have numbered the publications in chronological order (and by alphabetical order of authorship within each year). For each entry, I have provided the following details in the online Appendix published in the James Lind Library:

1. Authorship and year of publication, with title and publisher;
2. A preamble for some publications to provide cross-references to other relevant publications in the list below, as well as reference to other editions either within the list or published after 1983. For some reports from specific organizations, such as the World Health Organisation (WHO), there are references to other reports from the same or other organisations that have some bearing on drug testing but are not included in the list. Finally, there are comments on specific texts that may be regarded as milestones in the evolution of clinical trials.
3. Aims of each publication as stated in Forewords and Prefaces. These are intended to provide an

Table 1. Some notable milestones in texts of clinical trials (1948 to 1983).

Appendix Article No.	Year	Milestone
1	1955	The first published textbook on clinical trials.
2	1958	First medical text setting out the rationale for random allocation.
3	1959	A text including a chapter on sequential analysis.
5	1959	The first (multi-author) *textbook* to include '*Clinical Trials*' in the title;
6	1960	First single-author comprehensive textbook on clinical trials written by a medical statistician; first text on sequential trials; and first book to include sample size Tables and confidence intervals.
7	1960	First text on clinical trials published in a language other than English.
10	1962	Austin Bradford Hill's only comprehensive textbook on clinical trials.
11	1963	First comprehensive text to cover legal, ethical and moral aspects of controlled clinical trials in humans.
13	1966	First of many WHO monographs and technical reports on clinical trials.
14	1967	First text devoted to trials in a sub-specialty of medicine; and first text to include a section on crossover trials.
17	1968	Possibly the first text with a section on protocols for clinical trials.
21	1970	First text with appendices of Tables for sample size calculations; and the first co-authored by both a physician and a statistician.
23	1970	First textbook to distinguish between explanatory and pragmatic trials.
25	1972	An early attempt to teach clinical trials using computer simulation.
43	1979	First text devoted to multi-centre clinical trials.
54	1981	First text devoted to applied statistics in the pharmaceutical industry.
55	1983	First text on clinical trials to include a chapter on survival analysis.

overview of each publication and are extracts, not necessarily contiguous text.

4. Contents (and total number of pages) comprising part, chapter, section and sub-section headings, but not sub-subsection headings unless the volume of text is substantial (omission of headings is noted for each publication where relevant);
5. Details of authors including titles and qualifications with place of work when available. For publications under the umbrella of an Editor or Committee, the names of contributors appear with chapter titles. These details provide some idea of the expertise of those contributing to the publications, the balance between industry, academia and regulators and enable tracking of individuals who made multiple contributions (I have not included lists of participants at meetings; these can sometimes be found in the original publications).

An initial analysis

I hope that the resource I have created will be used by others interested in the history of controlled clinical trials. As an example of the kind of analysis I have in mind, I have indicated in Table 1 the notable publications that were milestones in the series drawing attention to methodological insights or developments. Other milestones could have been chosen. I believe that most of these milestones are the first

examples of books which illustrate or include particular methodological features. However, earlier examples may exist and I would be happy to have these drawn to my attention.

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Provenance: Invited article from the James Lind Library.

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