

(63) Niels Tygstrup, John M Lachin and Erik Juhl (eds) (1982)

The Randomized Clinical Trial and Therapeutic Decisions

Statistics Textbooks and Monographs, volume 43

New York: Dekker

Preamble

This book was the 43rd in a series of statistics textbooks and monographs edited by DB Owen (Department of Statistics, Southern Methodist University, Dallas, Texas, USA) and RG Cornell (School of Public Health, University of Michigan, Ann Arbor, Michigan, USA, for the publisher Marcel Dekker. It originated from a postgraduate course held at the Villa Monastero in Varenna, Como, Italy, 14-16 November 1977, organised by the Italian Society of Gastroenterology. The individual chapters include comments from discussants.

It is dedicated to the memory of Franz J Ingelfinger (1910-1980), one of the authors, and editor of the *New England Journal of Medicine* (1967-1976).

Aims

In the recent past randomised clinical trials have had increasing impact on clinical practice and therapeutic decisions. Previously, however, therapeutic decisions were often made without guidance from randomised clinical trials, simply because relevant trials were lacking. This is changing with the increasing number of trials being conducted. What may be more important, however, is that the randomised clinical trial is being accepted as a tool for the solution of therapeutic problems, which in turn represents an approval of the classical scientific approach to clinical practice. The general success of scientific methodology in the acquisition of new knowledge gives promise that the randomised clinical trial will have a significant impact on medical care. In principle, the randomised clinical trial resembles the manner in which clinicians have always gained skills and experience, i.e., by systematic, not random, trial and error. The difference lies in the increase in precision offered by the clinical trial. By systematic collection and analysis of relevant data, the clinical trial attempts to quantify therapeutic effects in comparative terms. The risk of reaching a wrong conclusion is not eliminated, but usually it is smaller (and always better defined) than when therapeutic evaluations are based on general impressions, anecdotal experience, or beliefs. Furthermore, the need for precision regarding criteria for selection of patients and evaluation of therapeutic effects in clinical trials serves to reveal where current diagnostic concepts and therapeutic objectives are inaccurate or irreproducible. This book is not intended to be a handbook on the conduct of clinical trials. It does not intend to give the complete recipe of how to conduct a trial, even though we hope that it will encourage more physicians to engage in such activity. The intention is to provide the consumers and prospective participants, perhaps including patients, with an understanding of the mechanism of a clinical trial and the kind of information it yields, so that they can interpret, evaluate, and apply its results critically (Preface, pages vii and viii).

Contents (xviii+296 pages)

[Sub-headings omitted]

Foreword (Francesco Orlandi)

Preface (Niels Tygstrup, John M Lachin, Erik Juhl)

Contributors

Part I: The relation between clinical medicine and the randomized clinical trial

1. How therapeutic decisions are motivated (P Riis)
2. The randomized clinical trial as a basis for therapeutic decisions (TC Chalmers)
3. Contributions of randomized clinical trials over a decade (1964-1973) to

gastroenterological therapy (E Juhl)

Part II: Clinical fundamentals of the randomized clinical trial

4. Clinical elements of the randomised clinical trial (E Juhl)
5. Principles for selection and exclusion (AL Blum)
6. Clinical evaluation of success (AL Blum)

Part III: Statistical fundamentals of the randomized clinical trial

7. Statistical elements of the randomised clinical trial (JM Lachin)
8. Why randomization is essential and how to do it (A Petrie)
9. Statistical inference in clinical trials (JM Lachin)
10. Choice of variables for evaluation of therapeutic effects: the statistical point of view (A Petrie)
11. Statistical analysis of the randomised clinical trial (JM Lachin)
12. The crossover design (A Petrie)

Part IV: Implementation of the randomised clinical trial

13. Elements of an ideal protocol (LJ Schoenfield)
14. Achieving an adequate sample size: the multicenter trial (N Tygstrup)
15. The execution of a protocol (JM Lachin)
16. Early termination of a clinical trial (TC Chalmers)

Part V: Perceptions of the randomised clinical trial

17. Randomized clinical trials and the producers (LJ Schoenfield)
18. Randomized clinical trials and the consumers (TC Chalmers)
19. Randomized clinical trials and the patients (P Riis)
20. Randomized clinical trials and the public (FJ Ingelfinger)

Part VI: Appendixes

- A. National Institutes of Health guidelines for data-safety monitoring in clinical trials
- B. Declaration of Helsinki, II

Index

Authors

The three editors are Niels Tygstrup MD (Professor of Medicine and Chairman of Medical Department A, Rigshospitalet, University of Copenhagen, Denmark); John M Lachin ScD (Associate Research Professor, Department of Statistics, and Director, Biostatistics Center, George Washington University, Washington DC, USA); and, Erik Juhl MD (Associate Professor of Medicine and Chairman, Department of Internal Medicine, Division of Hepatology, Hvidovre Hospital, University of Copenhagen, Denmark). The authors are André L Blum MD (Medical Clinic, Triemli Hospital, Zurich, Switzerland); Thomas C Chalmers MD (Mount Sinai Medical Center, Mount Sinai School of Medicine, New York, NY, USA); Franz J Ingelfinger MD (*New England Journal of Medicine*, Boston MA, USA); Aviva Petrie MSc (Department of Medical Statistics and Epidemiology, London School of Hygiene and Tropical Medicine and Department of Medical Statistics, Royal Postgraduate Medical School, London, England); Povl Riis MD (Department of Internal Medicine, Herlev Hospital, University of Copenhagen, Denmark); Leslie J Schoenfield MD (Department of Gastroenterology, Cedars-Sinai Medical Center, University of California at Los Angeles, USA); and Ralph Wright MD (Medical Unit, University of Southampton, Southampton General Hospital, Southampton, England). The foreword is by Francesco Orlandi (Department of Gastroenterology, School of Medicine and General Hospital, Ancona, Italy).