### (55) Lawrence M Friedman, Curt D Furberg and David L DeMets (1981) *Fundamentals of Clinical Trials* Boston: John Wright

### Preamble

This is the first text on clinical trials to include a chapter on survival analysis. A second edition of the book was published in 1985; a third in 2008; fourth in 2010; and a fifth in 2015.

## Aims

The clinical trial is the most definitive tool for evaluation of the applicability of clinical research. It represents a key research activity with the potential to improve the quality of health care and control costs through careful comparison of alternative treatments. While many reported clinical trials are of high quality, a careful reviewer of the medical literature will notice that a large number have deficiencies in design, conduct, analysis, or presentation of results. In this book we hope to assist investigators in improving the quality of clinical trials by discussing fundamental concepts with examples from our experience and the literature. This book is intended primarily for investigators with some clinical trial experience as well as for those who plan to conduct a trial for the first time. It may also assist members of the scientific and medical community who wish to evaluate and interpret published reports of trials (Preface, page vii).

## Contents (ix+225 pages)

[Sub-sub-headings omitted]
Preface
Acknowledgments

Introduction to clinical trials
Fundamental point
What is a clinical trial?
Why are clinical trials needed?
Problems in the timing of a trial
Study protocol
Appendix: Protocol outline
References

1 What is the question?

Fundamental point

Selection of the questions Response variables Adverse effects Natural history Ancillary questions General comments References

# 2 Study population

- Fundamental point Definition of study population Generalization Recruitment References
- 3 Basic study design Fundamental point

Randomized control studies Non-randomized concurrent control studies Historical controls Cross-over designs References 4 The randomization process Fundamental point Fixed allocation randomisation Adaptive randomisation procedures Mechanics of randomisation Recommendations Appendix: Adaptive randomisation algorithm References 5 Blindness Fundamental point Types of trials Special problems in double-blind studies References 6 Sample size Fundamental point Statistical concepts Sample size calculation for dichotomous response variables Adjusting sample size to compensate for noncompliance to intervention Sample size for continuous response variables Sample size when the rate of change is the response variable Sample size for testing "equivalency" of interventions Multiple response variables References 7 Baseline assessment Fundamental point Uses of baseline data What is a true baseline measurement? Balance and imbalance References 8 Recruitment of study subjects Fundamental point Planning stage Conduct of recruitment General techniques Recruitment problems Recycling of potential subjects References 9 Data collection and quality control Fundamental point Problems in data collection Minimizing poor quality data Quality control monitoring References 10 Subject compliance Fundamental point

Considerations before subject enrollment Maintaining good subject compliance Compliance monitoring References 11 Monitoring response variables Fundamental point Data monitoring committee Repeated testing for significance Decisions for early termination Decision to extend a trial Statistical methods used in monitoring References 12 Issues in data analysis Fundamental point Which subjects should be analysed? Covariate adjustment Comparison of multiple variables Data exploration Appendix: Mantel-Haenszel statistic References 13 Survival analysis Fundamental point Estimation of the survival curve Comparison of two survival curves References 14 Closeout Fundamental point Termination procedures Post-study follow-up Data clean-up and verification Storage of study material Dissemination of results References 15 Reporting and interpretation of results Fundamental point Did the trial work as planned? How do the findings compare with results from other studies? What is the clinical impact of the findings? References 16 Multicenter trials Fundamental point Reasons for multicenter trials Conduct of multicenter trials General comments References Index

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