

(67) Stanley H Shapiro and Thomas A Louis (eds) (1983)

Clinical Trials: Issues and Approaches

Statistics textbooks and monographs, volume 46

New York: Marcel Dekker

Preamble

This book was the 46th 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.

Aims

Advances in clinical research methodology during the past few decades have been extensive in both scope and volume, contributions have appeared in the medical, statistical, epidemiological, social science, and other related literatures, and continue to do so. As a result, becoming well informed can at times seem a Herculean (or even Sisyphean) task. It is thus reasonable to ask why we are adding to this already voluminous literature. Simply put, we feel that this book, rather than compounding the problem, contributes to its solution. Despite increasing efforts to improve communications, the pathways between disciplines can often appear tortuous and discouraging. Although some of the difficulty is substantive, much is attributable to the use of discipline-specific jargon or shorthand. Accordingly, in planning this work we sought a level of presentation that would be useful both to clinicians with varying degrees of methodological expertise (from medical students to seasoned investigators) and to methodologists with differing levels of clinical experience (from theoretical statisticians with an interest in medical applications to applied biostatisticians). This volume is designed to encourage critical thinking about the design and execution of a randomised clinical trial, the strategy generally regarded as the most powerful for the evaluation of medical interventions. By providing a careful examination of fundamental design, conduct, analysis, and reporting issues, this book should improve communication between producers and consumers of clinical trial results, advance both the conduct and understanding of these ethically and scientifically challenging endeavors, and ultimately help promote the development and utilization of effective therapeutic interventions (Preface, pages v and vi).

Contents (x + 209 pages)

[Sub-sub headings omitted]

Preface (Stanley H Shapiro, Thomas A Louis)

Contributors

Introduction (JC Bailar III)

1. Controversies in design and analysis of clinical trials (F Mosteller, JP Gilbert, B

McPeck)

The nature of biomedical trials

How controversy arises

How frequently do innovations succeed?

Designs

Sample sizes

Further special designs

Placebo

Problems arising from multiple comparisons and selection effects

Scoring clinical trials

Issues and needs

Do trials cost too much?

Concluding remarks

References

2. On some prerequisites for a successful clinical trial (DL Sackett)

The first prerequisite: the trial needs to be

The second prerequisite: the trial question is both appropriate and unambiguous

The third prerequisite: the trial architecture is valid

The fourth prerequisite: the inclusion/exclusion criteria strike a balance between efficiency and generalizability

The fifth prerequisite: the trial protocol is feasible

The sixth prerequisite: the trial administration is effective

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3. Ethical aspects of clinical trials (K Lebacqz)

The role of the IRB

Basic ethical principles

Informed consent

Special populations

Privacy and confidentiality

Selection of subjects

Compensation for injury

Risk-benefit calculus

Choice of controls

Summary and conclusions

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4. Exclusions, losses to follow-up, and withdrawals in clinical trials (P Armitage)

Criteria for eligibility

The patient log

Protocol deviations

Conclusion

References

5. The control of bias in clinical trials (TC Chalmers)

Bias in clinical trials

Identification of authors and sources of support

Description of patients accepted and rejected

The process of randomisation

Blinding of the patient

Blinding of the physician-investigator

Blinding of results

Measurement of blinding

Potential contribution of bias to withdrawal

Summary

References

6. Practical considerations in the coordination of clinical trials (PT Lavin)

General responsibilities

Organizational structure

Resource concepts

Problem identification and resolution

Summary

References

7. Statistical analysis of clinical trials (P Meier)

- Aims of analysis
- Simple analyses
- Complex analyses
- Problems of multiplicity
- Endpoints
- Summary
- References

8. Reporting the results of a clinical trial (ER Greenberg, T Colton, JA Baron)

- General concerns
- Data presentation
- Format
- Specific content
- Knowing when to stop
- References

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