"Foundations of Clinical Research: Applications to Practice"


Review by Norman M. Goldfarb

"Foundations of Clinical Research" provides a comprehensive, practical guide to the design, analysis and communication of clinical research studies. Statisticians should love this book. Civilians will find the concepts very informative and the explanations and clinical examples mostly straightforward. Any non-statistician who has to deal with statisticians should consider this book an essential weapon in his/her armament.

If you think clinical research is all about double-blinded, randomized clinical trials, this book will set you straight. There are randomized block designs, nested designs, one-way repeated measure designs, crossover designs, Latin square designs, time-series designs; don't get me started. If you are curious about the differences between Armitage and Bross plans for sequential designs, this book is the place to get the real low-down. Statisticians did not create these designs to make trouble; each design has its use in generating the best data at the least cost in particular circumstances.

If you think the design of a valid study is about randomizing a passel of subjects to two or more treatment arms, see Table 9.2, which sets forth 25 different threats to design validity, and that's before the problems with study conduct even begin. It's no wonder that NDAs often arrive at the FDA with inadequate justification for approval.

The book includes 31 chapters in five areas:

- Foundations of Clinical Research
- Concepts of Measurement
- Design
- Analysis
- Communication

The bulk of the book is devoted to a detailed description of the use of statistics in clinical research. Topics include A-B-A design, accidental sampling, adjusted odds ratio, alternate forms reliability, and area probability sample. That's just a small selection from the "A" section of the glossary.

In case you were curious, accidental sampling is a synonym for convenience sampling, which is a nonprobability sampling procedure involving selection of the most available subjects for a study. Most randomized clinical trials employ convenience sampling. There is a problem with this approach: self-selected volunteers may not be representative of the entire population. For example, minorities will typically be under-represented. People with transportation problems, i.e., the elderly, will not be able to volunteer. If a study of back pain starts recruiting in the spring, people who overdo the snow shoveling may be excluded. (A similar problem occurs with investigator selection: inexperienced investigators who automatically sign the clinical trial agreement are enlisted first, while more sophisticated sites get left out of the study.)

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Speaking of snow, snowball sampling is a nonprobability sampling method in which subjects are successively recruited by referrals from previous subjects. We praise this strategy as “word-of-mouth”, but the results may not be what the statistician ordered. This reviewer, for example, saw a huge number of Filipinos recruited into the “Asian” cohort of a study because his site’s first subject just happened to be from the Philippines.

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