dependence. Chapter 7 discusses various important and interesting aspects of frailty modeling, such as the independence assumption between the observed covariates and the frailty variable; nested frailty models; tests for heterogeneity; and time-dependent frailty models.

Overall, *Frailty Models in Survival Analysis* is extremely well-written and a useful collection of frailty-based survival models and estimation techniques that are of interest to statisticians. The book also contains practical important information regarding software implementation, pointing out for each models considered whether it can be applied in R, SAS and STATA. The book would make a good supplementary text for an applied graduate level course, although it lacks sufficient theory for more theoretical courses. While there are no exercises in the book, there are many enlightening examples comparing various models.

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Fundamentals of Clinical Trials, Fourth edition.

Lawrence M. FRIEDMAN, Curt D. FURBERG, and David L. DEMETS. New York, NY: Springer, 2010, xviii + 445, pp $69.95 (P), ISBN 978-1-441-91585-6.

The first edition of *Fundamentals of Clinical Trials* came out in 1981, with two more editions in 1995 and 1998. The fourth edition continues adding improvements to this comprehensive guide on clinical trials. Unlike reviews of previous editions in statistics journals, which were written by biostatisticians and clinical trials experts (Pocock 1982; George 1987), this reviewer has no experience in clinical trials and is not a biostatistician. My review will therefore most likely be of interest to those intending to become familiar with clinical trials, or to expand their knowledge of how statistics is used in this domain. Before getting into detail, I would like to commend the authors for creating such a readable book and to recommend it to applied and theoretical statisticians, academics and practitioners, as well as to students as an eye opener into the important field of clinical trials, which relies heavily on statistical methods.

This book offers a holistic view of how and where statistical thinking and methods are integrated into the particular scientific domain of clinical trias, from design through implementation, analysis, and reporting. In particular, the statistical approaches are presented as solutions to particular issues that arise within practical constraints, challenges and requirements. Plenty of sections are focused on nonstatistical issues such as challenges of recruitment, regulatory aspects of adverse events, and reasons for participant non-adherence. Yet understanding the contextual issues is clearly important for a statistician involved in clinical trial design and analysis. Understanding this context is also useful for researchers interested in developing new statistical methods that can effectively address practical problems in clinical trials, as well as for choosing the methodologies to teach in biostatistics courses. For example, procedures such as blinding and recruitment challenges require going beyond standard statistical sampling and randomization methods.

The authors also raise ethical questions related to sharing versus hiding information from participants, physicians, and researchers and how such dynamics should be dealt with from a statistical point. Dealing with lives, health, and humans-patients, physicians and clinical staff, investigators, their sponsors and competitors-creates environments, and dynamics that are far from classic experimental design or even survey settings. Chapter 2 on "ethical issues" is new to this edition.

The book consists of 20 chapters, and the chapter titles and ordering well reflect the process of carrying out clinical trials, from design stage to implementation, data analysis and reporting (with the exception of chapter 18 on "closeout", which should have preceded chapter 17 on "issues in data analysis"). The flavor of the book is almost completely bare of formulas or technical notation, such that the writing provides a high-level qualitative discussion. One weakness is the change to technical language in a couple of chapters (chapter 8 on "sample size" and chapter 15 on "survival analysis") and in three sections (chapter 16 section on "sequential methods" and chapter 17 section on "meta analysis" and its appendix). I found the change in writing to be confusing and disruptive of the flow. I also found that while the qualitative discussion is rich in real examples of clinical trials, the technical sections suffer from a "statistics only" view with very weak ties to clinical trials. I'd have preferred to see the technical parts described in a non-technical fashion (as in the rest of the book), or at least the technical part separated into an appendix or even posted on a companion website. With such changes, the book would be completely readable to non-statisticians as well.

Being accustomed to statistics books that are methodology-focused rather than domain-focused, I found the 400+ pages of diverse topics to be a dense reading. Chapters range between 10–30 pages, with two especially long chapters on "monitoring response variables" (Chapter 16) and "issues in data analysis" (Chapter 17). However, the authors used a few strategies to break the reading into digestible chunks and to highlight the main points. Each chapter consists of multiple short sections, which provide for good break points. Each chapter also opens with a useful "Fundamental Point" paragraph that summarizes the main takeaway. Still, as an applied statistician and an advocate of visuals, I greatly missed more figures, tables, and graphical illustrations. The first 14 chapters contained less than a handful of such.

What I found compelling in the book was the extensive use of real examples throughout the different chapters. The authors, who have extensive expertise in clinical trials, use examples from their own experience to illustrate approaches, challenges, solutions, and open questions. They are also not hesitant to point out problems and errors that are common and have caused serious erroneous decisions in the past. I appreciate their honest assessment, even though it has increased my levels of unease and uncertainty associated with the results coming out of clinical trials.

In terms of statistical methodology, I was surprised to see the extreme reliance on statistical inference and p-values. I was also surprised by the scant coverage of Bayesian methods (there is a slight mention in Chapter 1 ("introduction") and the brief "other approaches" for interim analysis section in Chapter 16).

The book is most likely intended for researchers and biostatisticians working in clinical trials. In terms of pedagogy, end-of-chapter exercises would have made for a useful addition to the book. With so many interesting clinical trial examples, it would be useful to engage the reader (students and others) in a more active fashion.

In summary, this book provides a highly-readable crash course into the mysteries of clinical trials from multiple angles: procedural, ethical, statistical and more. It would be useful for statisticians in any field to see how statistics must fit into "the big picture" rather than live in isolation. And of course, understanding more about how clinical trials are designed, run, analyzed, and reported improves our ability to better evaluate the incredible number of (often conflicting) medical advice that we are bombarded with.

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Handbook of Markov Chain Monte Carlo.

Steve BROOKS, Andrew GELMAN, Galin L. JONES, and Xiao-Li MENG (Eds). Boca Raton, FL: Chapman & Hall/CRC Press, 2011, xxv + 592 pp., $99.95 (H), ISBN: 978-1-420-07941-8.

Markov chain Monte Carlo (MCMC) has revolutionized Bayesian statistics over the last two decades. Instead of using off-the-shelf models that allow simple closed form calculation, MCMC practitioners are now using MCMC to fit realistic models that account for the complexity of the particular application under investigation. *Handbook of Markov chain Monte Carlo*, edited by S. P. Brooks, A. Gelman, G. L. Jones, and X.-L. Meng, with contributions from