Biometrics 73, 1054–1061
September 2017

DOI: 10.1002/biom.12756

BOOK REVIEWS

EDITOR:
DONNA PAULER ANKERST

WILLIAM F. ROSENBERGER, JOHN M. LACHIN. **Randomization in Clinical Trials: Theory and Practice, 2nd edition**. Hoboken: John Wiley & Sons.

This second edition of the text by Rosenberger and Lachin is a comprehensive overview of the role of randomization in clinical trials, with a blend of theory and practice, and serves as both reference and text (with problems throughout).

The authors give 2 main reasons for randomization, with a nod to Jerry Cornfield:

1. To promote comparability among study groups, and
2. To provide a probabilistic basis for inference.

On the first point all (or certainly almost all) statisticians agree, both frequentists and adherents of the likelihood principle. The second reason given is quite a bit more controversial. The authors come down strongly on the point of view that randomization tests and not tests based on population models are correct, and emphasize the former to the virtual exclusion of the latter. This will be disappointing to the many statisticians who disagree, and limits the universality of this text.

The first five chapters provide an overview of issues in the design of clinical trials, and a very thorough review of the many strategies for randomization that have been studied over the years (most but I suspect not all of which have been implemented). This includes a quantification and thus comparison of accidental bias (imbalance on covariates) and selection bias (predictability of treatment assignment) for various strategies.

Chapter 6 makes the case for randomization as the correct basis for inference, and gives exact and large sample results along with newer methods based on Monte Carlo re-randomization. The authors discuss the appropriate reference set for the randomization distribution, and argue for conditioning on the sample sizes actually achieved. However, they present the issue of how to sample from the conditional randomization distribution as an open question for most of the randomization schemes presented.

Stratified randomization and stratified-adjusted analysis are presented in Chapter 7, which contains a nice discussion of whether and to what extent stratification is desirable. A series of practical examples and numerical considerations make up Chapter 8.

The remaining three chapters are somewhat heavier going, covering covariate-adaptive (Chapter 9) and response-adaptive (Chapters 10–11) randomization. Covariate-adjusted methods, which strive for marginal balance across treatment, are questioned as "cosmetic" and described as controversial. However, this technique has been

used by at least one major cancer cooperative group (SWOG) for 30 years. In contrast, response-adaptive randomization, which I would submit raises real practical and ethical issues, is described in glowing terms as the wave of the future. I was surprised to see no reference to the recent literature reflecting the debates among trialists on this topic (e.g., the series of articles in Volume 12(2) of Clinical Trials 2015).

I did enjoy finding in various places throughout some mention of the tension between unequal allocation (which would be a result of response-adaptive randomization) and equipoise, and also the limited circumstances making equal allocation optimal. For example, optimal Neyman allocation, which is unequal to the extent that 2 treatments have different variances, shows up as Problem 2.6, and the square-root rule for allocating more to the control group in the comparison of K-1 treatments to a control is presented briefly on page 58 (I remember this was a problem in the analysis of variance text by Scheffe).

Despite some qualifications I find this book a useful reference on the techniques of randomization in clinical trials. It is extremely helpful to have this vast literature summarized so ably. Many of the more theoretical properties of the randomization strategies are due to the work of the authors themselves, and they are to be commended for their scholarship and exposition.

John Crowley
Cancer Research And Biostatistics
Seattle, Washington, U.S.A.
johnc@crab.org

SHIGEYUKI MATSUI, MARC BUYSE, RICHARD SIMON, EDS. **Design and Analysis of Clinical Trials for Predictive Medicine**. Boca Raton: CRC Press.

There is growing expectation that molecular markers (such as genomic, proteomic, and others) will allow physicians to tailor treatments based on an individual's unique characteristics (Manolio et al., 2013; Lindsey et al., 2015). Towards this direction, President Obama launched the Precision Medicine Initiative in 2015 that will fund a plethora of basic and translational research projects aiming to materialize individualized patient care into a reality (Collins and Varmus, 2015). Ultimately, the highest level of evidence will come from—hopefully randomized—clinical trials (Ioannidis and Khoury, 2013), whose design and analysis pose challenges given the complex nature of the questions being asked. Statistical methods in this area have been developed for years, however, there has been a sparsity of trustworthy sources that summarize the array of available methodologies which can be applied in all steps from drug development to regulatory approval.

Matsui, Buyse and Simon's "Design and Analysis of Clinical Trials for Predictive Medicin" comes to fill this gap. The book, edited by three leading experts in methodology of clinical trials, includes 18 chapters divided in six sections written by 36 statisticians and other methodologists with longstanding experience in academia, industry, funding agencies, and regulatory authorities. The book covers all aspects of clinical trial design from the early stages of assay validation to later phase I, II, and III trials. It also provides guidance on statistical methods for the analysis of data generated at the different stages. This comprehensive coverage of the"natural history" of drug and biomarker development can help researchers better understand the challenges encountered by their colleagues in previous or subsequent phases of this pipeline. Despite being an edited book, the concepts are well-integrated across the chapters and, most of the time, the transition from one topic to the other is done in a natural way for the reader. The particularly rich lists of references at the end of each chapter will be a very helpful starting point for readers who want to expand beyond what is covered in the 400 pages of the book.

The book starts (Chapter 1) with a clear distinction between "predictive" and "prognostic" biomarkers. This chapter also offers an informative introduction to the challenges of trials with predictive biomarkers, which stem from the fact that such efforts are concerned with the development of both a drug and a biomarker. Ultimately, neither every single biomarker nor every single drug from the pre-clinical stages will be translated to clinical practice (Ioannidis and Panagiotou, 2011, Tsilidis et al., 2013). The next two chapters describe the pre-trial steps related to the analytical validity of biomarkers to be studied in a trial setting; this is done from two different perspectives, the R&D team in industry (Chapter 2) and the regulatory agency (Chapter 3).

Section 2 focuses on phase I and II trials and how predictive biomarkers in such settings can determine which drugs will move forward and which will not. To achieve this in the era of personalized medicine, methods are available to ensure that safe and efficient drugs are pursued in phase III trials and resources are efficiently allocated. Towards this direction, Chapter 4 outlines methods to identify the optimum dose of targeted therapies in phase I trials. A variety of designs for phase II trials are presented with numerical examples in Chapter 5: randomized and non-randomized designs for single- or multiple-arm trials that evaluate single or multiple biomarkers and one or many experimental treatments. In Chapter 6, readers will find a suite of Bayesian methods for adaptive designs, while Chapter 7 picks up where the previous chapter left off to assess methods for outcome-adaptive randomization. Last, Chapter 8 summarizes many concepts presented throughout Section 2 and offers a nice bridge from biomarker-based designs for phase I and II trials to those utilized in phase III trials in the next part.

Section 3 is dedicated to phase III trials that aim to definitely assess the clinical utility of treatment decisions based on validated predictive biomarkers. Chapter 9 compares the three most popular study designs (enrichment designs, stratified designs, interaction designs) and shows the relative advantages of each one under different scenarios of biomarker "predictive-ness," accuracy, and prevalence. Chapter 10 focuses exclusively on the "all-comers" design where the biomarker status of each enrolled patient is evaluated and all patients are randomly assigned to one of two treatments. This design is more powerful when the predictive value of a biomarker is uncertain, which is nothing but

common for most biomarkers. A particular type of predictive and prognostic biomarker is discussed in Chapter 11, which covers issues related to the identification and validation of gene signatures (such as MamaPrint® and OncotypeDx®); this is a timely and clinically important topic as for some gene signatures their validity has been documented while their clinical utility is also becoming more evident (Cardoso et al., 2016).

Genomic signatures and other high-dimensional molecular data are covered in detail in the four chapters of Section 4. Chapter 12 deals with the statistical challenges related to the clinical development and validation of predictive genomic signatures. Along these lines, one clinically interesting application is the evaluation of the added predictive value of genomic (and eventually other -omics) markers in addition to well established and easily obtainable clinical prognostic factors; such analyses are becoming increasingly common as electronic medical records and -omics data are integrated in healthcare systems. From a more methodological perspective, a whole chapter (i.e., Chapter 13) is dedicated to the problem of multiple comparisons. With all types of high-dimensional data, there is a small fraction of signal that needs to be dissected from large quantities of noise in the data, and therefore multiplicity of comparisons becomes a main concern. However, when the aim is the identification of predictive biomarkers (which is what the book focuses on), both estimation and selection are simultaneously of interest, and hence the problem of multiple comparisons has its own particularities which are discussed here along with methods (e.g., false-discovery rate, empirical Bayes, receiver operating characteristics curve analysis, and others) to overcome them. The section concludes with two chapters on machine-learning techniques (such as support vector machine, boosting, kernel methods, lasso, and others) for classification (Chapter 14) and risk prediction in the survival setting in the presence of competing risks (Chapter 15) using high-dimensional genomic and other molecular markers.

The next two chapters (i.e., Chapters 16–17 of Section 5) cover several study designs that allow for the co-development of a new treatment and a validated biomarker to predict sensitive subgroups, while there is separate mention to the development of genomic scores as continuous predictors. Some concepts here, such as the adaptive design, are familiar from earlier chapters dealing with phase I trials but now the focus is on larger, phase III trials where the aim is the evaluation of both a treatment effect and the predictive-ness of a biomarker. The concluding chapter of the book (i.e., Chapter 18 in Section 6) focuses on the use of biomarkers as surrogate endpoints. Here, the book offers a thoughtful discussion on the use of surrogate endpoints in single and multiple trials instead of costly or difficult to obtain clinical endpoints. With the advent of high throughput technologies, it is anticipated that there will be an increase in the number of drugs developed based on the alteration of laboratory values. It yet remains to be seen the extent to which these high-dimensional biomarkers constitute valid surrogates of clinical outcomes in phase III trials.

Throughout the book, of particular value from a reader's standpoint are the examples that are drawn from real studies as well as from the authors' experience. Unavoidably, most of the methods described in the book are heavily motivated from and focused on clinical problems in the field of oncology and cancer research. This is not surprising given the toxicity of cancer treatments and the biological characteristics of tumors—both of which motivate the development of targeted treatments. However, with the advent of genome-wide association studies, there is interest in using genomic information to predict response to treatments other than oncological ones, such as pharmacological interventions for smoking cessation (David et al., 2015) or physical activity for weight loss (Livingstone et al., 2016). Similarly, proteomic biomarkers have been shown to be predictive of cardiovascular outcomes (Ganz et al., 2016) and it is natural that future investigations in this area will focus on treatment effects. Nevertheless, readers working in research areas other than cancer should not feel discouraged that the methods described in the book are not applicable to other lines of work. Experienced statisticians and methodologists should be able to identify how and to what extent this book can be used to guide the design and analysis of predictive trials for other clinical questions.

In conclusion, I found the book a very informative introduction to a new kind of clinical trials that will become more common in the future years as the community intensifies the pursuit of "individualized treatments." Current initiatives, such the Cancer Moonshot and others that will craft the way we conduct clinical and translational research over the next years make this book extremely timely. Researchers involved in the design and analysis of trials with predictive biomarkers will benefit from using this book as a quick reference guide, as well as statisticians who design and analyze these trials, translational scientists who work on assay development and biomarker validation, clinician scientists who conduct these trials and interpret the findings, and scientists who oversee and regulate trials.

References

Cardoso, F., van't Veer, L. J., Bogaerts, J., Slaets, L., Viale, G., Delaloge, S., et al. (2016). 70-gene signature as an aid to treatment decisions in early-stage breast cancer. *The New England Journal of Medicine* **375**, 717–7129.

Collins, F. S. and Varmus H. (2015). A new initiative on precision medicine. *The New England Journal of Medicine* **372**, 793–795.

David, S. P., Bergen, A. W., Munafò, M. R., Schuit, E., Bennett, D. A., and Panagiotou, O. A. (2015). Genomic analysis to guide choice of treatment for smoking cessation. *Cochrane Database of Systematic Reviews*, Issue 8. Art. No.: CD011823. https://doi.org/10.1002/14651858.

Ganz, P., Heidecker, B., Hveem, K., Jonasson, C., Kato, S., Segal, M. R., et al. (2016). Development and validation of a protein-based risk score for cardiovascular outcomes among patients with stable coronary heart disease. *JAMA* **315**, 2532–2541.

Ioannidis, J. P. and Khoury M. J. (2013). Are randomized trials obsolete or more important than ever in the genomic era? *Genome Medicine* **5**, 32.

Ioannidis, J. P. and Panagiotou O. A. (2011). Comparison of effect sizes associated with biomarkers reported in highly cited

individual articles and in subsequent meta-analyses. *JAMA* **305**, 2200–2210.

Lindsey, M. L., Mayr, M., Gomes, A. V., Delles, C., Arrell, D. K., Murphy, A. M., et al. (2015). Transformative Impact of Proteomics on Cardiovascular Health and Disease: A Scientific Statement From the American Heart Association. *Circulation* **132**, 852–872.

Livingstone, K. M., Celis-Morales, C., Papandonatos, G. D., Erar, B., Florez, J. C., Jablonski, K. A., et al. (2016). FTO genotype and weight loss: Systematic review and meta-analysis of 9563 individual participant data from eight randomised controlled trials. *British Medical Journal* **354**, i4707.

Manolio, T. A., Chisholm, R. L., Ozenberger, B., Roden, D. M., Williams, M. S., Wilson, R., et al. (2013). Implementing genomic medicine in the clinic: The future is here. *Genetics in Medicine* **15**, 258–267.

Tsilidis, K. K., Panagiotou, O. A., Sena, E. S., Aretouli, E., Evangelou, E., Howells, D. W., et al. (2013). Evaluation of excess significance bias in animal studies of neurological diseases. *PLoS Biol* **11**, e1001609.

Orestis A. Panagiotou
Department of Health Services Policy & Practice
Brown University School of Public Health
orestis_panagiotou@brown.edu

DIPAK K. DEY, JUN YAN, EDS. **Extreme Value Modeling and Risk Analysis: Methods and Applications**. Boca Raton: CRC Press.

In order to understand and quantify risk, extreme value methods aim to describe the tail of a distribution and typically analyze a small subset of data deemed extreme while discarding the bulk of the data. The field of extremes is founded on asymptotic results, which lead to families of distributions for modeling either block maxima or threshold exceedances in univariate, multivariate, temporal, and spatial settings. Although basic extremes theory is well developed, extremes is a relatively young branch of statistics, and there is much need for methodological work in order to quantify risk of extreme events which may arise from combinations of multiple events. This edited book has leading researchers present both cutting-edge extremes methodology and realistic extremes applications, often involving complex risk scenarios.

Although the book does not intend to focus on well-developed extremes methods, it begins as it should by presenting the foundational results of extremes in Chapters 1 and 2. Focusing on the univariate case, Chapter 1 presents the generalized extreme value (GEV) distribution and generalized Pareto distribution (GPD) and explains how these arise from asymptotic arguments for the limiting distribution of renormalized sample maxima. Rather than developing these asymptotic arguments (which can be found elsewhere if needed), Chapter 1 quickly moves to important notions for the practitioner, such as the implications of the three tail types. Unlike most other introductions to univariate extremes, Chapter 1 presents simulation results designed to assess the fit of these asymptotically justified distribution models. Unfamiliar readers might be unnerved by some results presented in Chapter 1's tables which seem to question the GEV's fit to block maximum data or the model's ability to estimate the underlying tail index parameter. However, I have found via simulation that extreme value models do a very good job of estimating high quantiles (including those beyond the range of the data) and providing confidence intervals with reasonable coverage. This paradox is perhaps best explained by the argument of penultimate approximation (briefly discussed in Chapter 21) which says that the fitted GEV's parameter estimates naturally adjust to account for the fact that one's data are maxima of finite-sized blocks. Chapter 2 presents the basics of multivariate extremes by introducing the multivariate extreme value distributions, presenting metrics by which tail dependence is summarized, and, most importantly, showing the reader that extremal dependence must be described using constructs quite different from the familiar ones from standard statistics.

Having sketched the foundational results upon which extremes is built, Chapters 3–18 present current methods for extremes and are organized by topic. Chapters 3, 4, and 5 deal with the issue of threshold selection and modeling. Despite being fundamental to exceedance modeling, a practitioner must choose a threshold based on diagnostics and methods which often provide inconclusive results. Chapter 4 provides a comprehensive overview of threshold selection, while chapter 3 illustrates alternative approaches which model the entire distribution by fitting flexible models to the bulk so as not to contaminate extremes-based tail inference.

Chapters 7 and 8 discuss time series for extremes, and Chapters 9–12 focus on spatial extremes. These chapters primarily focus on max-stable process models for either time or space. Chapters 10 and 11 discuss simulation of max-stable processes, which is much more difficult than for Gaussian or other process models since max-stable processes are achieved as the index-wise maximum of an infinite number of process realizations. Chapter 12 discusses composite-likelihood fitting, which is currently the most feasible method for fitting max-stable processes due to the intractability of the full likelihoods.

Although Bayesian methods have been used in spatial extremes studies, Bayesian analysis for extremes has not been widely applied, and I am glad to see two chapters dedicated to Bayesian methods for extremes. Chapter 13 gives an extensive overview and chapter 14 presents approximate Bayesian computation, useful since full likelihoods for extremes models may be unattainable or impractical. Because inference for extremes is based on a small subset of extreme data, an analysis could potentially benefit greatly from employing external prior information. However caution is advised, since Bayesian inference for extremes is likely to be more sensitive to prior information than non-extremes studies.

In many ways, modeling dependence for multivariate extremes has proven to be even more challenging than in the temporal or spatial case where dependence can be modeled via temporal or spatial distance. Chapters 16, 17, and 18 focus on multivariate extremes respectively presenting parametric models, nonparametric models, and hypothesis tests for extremal dependence. These chapters do a good job of representing the state-of-the-art, and they also clearly illustrate the need for more work in understanding and describing extremal dependence, particularly in high-dimensional settings.

Having covered a wide range of extremes methods, the book shifts focus to applications in Chapters 19–23, illustrating methods for assessing risk in finance, insurance, weather and climate, clinical trials, and survival analysis. Chapter 24 presents an interesting analysis to assess whether there is a significant difference in baseball's top batting average in different eras, nicely illustrating that extremes methods are not solely dedicated to assessing risk. The book concludes with a chapter that provides a current overview of software packages for analyzing extremes.

The strength of the book is its wide range, and it gives the reader a good idea of extremes' current vanguard. Appropriately, much of the work in the book focuses on dependence in extremes, whether it be in the multivariate, temporal, or spatial setting. The book does not try to be comprehensive, because, although young, the extremes discipline is mature enough that it cannot be covered comprehensively in one volume. Rather, this book can be viewed as a good starting point for practitioners in need of extremes tools to solve complex problems. A practitioner can use this book to get a good introduction to the current state-of-the-art for their type of problem, and use the relevant chapters and references as a launchpoint for their own study.

Dan Cooley
Department of Statistics
Colorado State University
Fort Collins, Colorado, U.S.A.
cooleyd@stat.colostate.edu

LISA CHASAN-TABER. **Writing Dissertation and Grant Proposals: Epidemiology, Preventive Medicine and Biostatistics**. Boca Raton: CRC Press.

NIH grant funding has become increasingly difficult and essential for academic success, and the process of preparing a proposal can feel daunting to a young investigator. This book takes this complex and challenging process and breaks it down into tangible and guided steps, providing a comprehensive summary of how to write a clear and engaging proposal. The focus is on a dissertation proposal or an NIH grant, but many of the concepts are more general, focusing on organization and style. Thus, while it could be very useful for a doctoral student or young investigator submitting a first NIH grant, many of the ideas would be useful to even the most seasoned academic writer.

The book is broken into sections. The first focuses on preparing a proposal (including development of the hypotheses, literature search and scientific writing tips), with a focus of both the dissertation and the grant application. The second section delves into preparing each section of an NIH grant proposal (including a useful discussion on the requirements for preliminary studies). The third section focuses on grantsmanship including where to apply and what to do if the grant needs resubmission. The book contains a helpful section about how to compose and communicate aims and significance of a research project so that the reviewers can lift wording from the proposal to respond to the questions they need to answer about the impact and significance of the project. The contents are very structured and provide an easily referenced step-by-step approach to completing a submission. With a very detailed table of contents, the book is a good reference. Each section includes real examples, as well as the suggestions for improvement for each example.

The author of the book has many years of successful grant funding as well as teaching and mentoring experience. She has a doctoral training in epidemiology and this comes through in that the examples and content of the book align with this field. Thus, the examples throughout the book involve projects that analyze observational datasets with hypotheses about association of an exposure and outcome. A biostatistician could derive much from the discussions of style and content in this book. However, a purely biostatistical grant would likely differ with regard to the methods section which would focus more on the theoretical and computing aspects, and the background and preliminary studies which would be aligned with this content. Similarly, a purely statistical dissertation would likely be in a subfield of statistics; the impact this has is that not all suggestions can be directly applied. For example, the book suggests identifying a dissertation topic and then finding an advisor, but in statistics this could be challenging and instead a student may choose to select the advisor and topic simultaneously.

However, there are many aspects of this book that would be useful to a statistician. The study design section describes the sample size and design considerations of epidemiology studies as well as potential limitations (biases) to be considered. Also, the description of confounder/mediation analyses as well as reproducibility/generalizability are discussed clearly and are not given as much discussion in many statistical texts on clinical study design. These topics would be very useful for a statistician collaborating with a physician or epidemiologist on a medical or public health grant.

In general, this is a useful book as many of the ideas could improve a proposal. Further, they are generalizable to other types of technical communication such as manuscript preparation and submission. Thus this is a unique reference book, and would serve well in the library of academic programs as well as academic health center libraries.

Dianne Finkelstein
Biostatistics Unit
Massachusetts General Hospital
Boston, Massachusetts, U.S.A.
dfinkelstein@partners.org

PETER BUEHLMANN, PETROS DRINEAS, MICHAEL KANE, MARK VAN DER LAAN. **Handbook of Big Data**. Boca Raton: CRC Press.

The term "Big Data" frequently makes the headlines, even in tabloids. Thus, the layman might expect that professionals in the field agree upon what they are talking about. The "Handbook of Big Data" makes it clear that this is not the case and that many facets of this new paradigm remain to be discussed and sharpened. First, there is the purely techni-

cal perspective. Using clever mathematical and computational tricks, one tweaks algorithms for the estimation of classical models, for example logistic regression, in a way that makes them applicable in "big n" (many observations) or "big p" (many variables) situations. The result, however, is still a relatively simple model with little benefit from "Big Data," except for perhaps lower variance in the "big n" world. Some chapters, such as "Big-n versus Big-p in Big Data" and a chapter on penalized estimation, adopt this perspective.

Second, one may ask "What can be done in a big data world that is impossible in a small data world?". We are, of course, interested in estimating (or "learning") more complex models in the presence of more information. The handbook devotes several chapters, for example, one on structured distributions and a series of chapters on targeted learning, to this perspective. From a methodological point of view, it is very interesting to study more complex models, as we might hope to describe the phenomena we are interested in more precisely than it was possible with low-dimensional parametric models.

The third aspect is of more philosophical nature, yet with important implications for science in general. The editors devote the prime spot in their handbook, the introductory chapter, to this topic and Richard Starmans takes the reader on a tour-de-force through epistemology and its connections to statistics. Most statisticians will probably agree that data are a footprint, left to be seen for us by the true model. Like the paleontologist, who reconstructs features of dinosaurs from their footprints and other traces, our job is, essentially, to reconstruct this hidden truth from the data. It must be feared that this makes us dinosaurs as well, because in the big data world the data are the truth. Rendering models, and therefore theories, useless has the potential to radically change the way science will be performed in the future, as Starmans explains. But maybe things are all different. The biases naturally inherent in unsystematically collected big data might spoil the party and random samples of small data are the past, present, and future of statistics, or, as John Tukey told Alfred Kinsey, the lead author of the famous "Kinsey Report": "I would trade all your 18,000 case histories for 400 in a probability sample." Even so, the "Handbook of Big Data" is the first compilation on this emerging subject in our field and is therefore highly recommended to all statisticians and computer scientists.

Torsten Hothorn
Epidemiology, Biostatistics and Prevention Institute
University of Zurich
Zurich, Switzerland
Torsten.Hothorn@uzh.ch

TRIVELLORE RAGHUNATHAN. **Missing Data Analysis in Practice**. Boca Raton: CRC Press.

Trivellore Raghunathan, the author of this accessible and insightful addition to the missing-data literature, completed his Ph.D. studies in the Harvard Department of Statistics in the fall of 1986. On the pathway to full disclosure, I started my Ph.D. studies at Harvard in the fall of 1986, and in the spring of 1987, I served as a teaching assistant for the class Raghu (as he is known, including by himself on page xix of the book) taught that semester. And having looked up to Raghu as a role model ever since I met him, among the most satisfying professional tributes I have ever received are having my testimonial for *Missing Data Analysis in Practice* printed on the book's back cover and having been mentioned alongside many heroes of mine in the book's preface.

To locate this book in the broader literature, it occurred to me to refer to the syllabus of the "Statistical Analysis of Incomplete Data" course I taught this past year in the UCLA Department of Biostatistics to a mix of doctoral and masters students. Little and Rubin (2002) was a required text, and I listed *Missing Data Analysis in Practice* along with Rubin (1987), Schafer (1997), and Carpenter and Kenward (2013) as recommended texts. Establishing a "cut point" for a book to be recommended is a perilous task in this context, and with apologies to other worthy contenders, in hindsight I wish I had also listed Daniels and Hogan (2008), van Buuren (2012), and Molenberghs, et al. (2015). Purchasing all of these books would cost several hundred dollars, but missing data is a big topic in modern statistics, and I think the investment would be worth it for students seeking to develop expertise in the field.

One way to summarize the strengths of *Missing Data Analysis in Practice* is to quote from my own testimonial: "Applied researchers will appreciate the book's guidance on pragmatic issues like selecting the number of imputations, using transformations, and including the outcome when imputing missing covariates. Attention to finite-population estimation makes the book a valuable bridge between design-based and model-based perspectives. And with extensions to areas like longitudinal analysis, survival analysis, and disclosure avoidance, statisticians will find that the book complements the classic text by Little and Rubin."

The presentation in *Missing Data Analysis in Practice* has the feel of well-honed lecture material, consistent with its having grown out of short courses that Raghu taught with Rod Little. It should be understood that a text that barely clears 200 pages is not going to cover the entirety of what specialists need to know to become expert on the topic. But as an overview of the field, it is strong, and it includes many enlightening perspectives that can be expected to appeal to all readers. For example, in introducing missing-data mechanisms, the book analogizes the concept to "response propensity" in an experimental-design context, offering a bridge to a wide array of other advanced statistical methods, including weighting adjustments in surveys (Section 2.3) and inverse-probability weighting more broadly as a statistical adjustment method (Section 2.9). And for the sake of illuminating distinctions relevant to ignorable and nonignorable missingness, I regard the book's "response propensity" analogy as a key addition to such helpfully distilled and pedagogically valuable material as the discussion in Rubin, Stern and Vehovar (1995), the "Ignorability is relative" section in Schafer (1997, p. 23), and problems 6.17 and 6.18 in Little and Rubin (2002, p. 131).

As might be expected given Raghu's leading role in developing "sequential regression multiple imputation" (SRMI), both through related scientific contributions (e.g., Raghunathan

et al., 2001) and software contributions (with IVEWare remaining a leading approach for implementing SRMI along with the MICE routine in R and the MI routine in Stata), the book makes extensive use of SRMI in its many examples. The work of Su et al. (2011) describing the flexible and diagnostic-friendly "mi" routine in R is an unfortunate omission. For specialists, the book's review of nonignorable modeling is limited and does not substitute for material in Little and Rubin (2002, Chapter 15) or Daniels and Hogan (2008) illustrating the sensitivity of inferences to assumptions about missing-data mechanisms.

Underscoring the book being both readable and relevant, I think Section 1.8 ("A Chuckle or Two") deserves comment, particularly to make sure its important message is not obscured by its lighthearted heading. The section's narrative, describing a survey respondent who interrupts a face-to-face interview to take a call from his former girlfriend and then breaks off the interview to make up with her, is used to emphasize that statistical analyses can never be expected to reflect the full complexity of human response behavior. The text then pivots to the companion message that practitioners are always well-advised to consider sensitivity to underlying assumptions, which especially resonates. Although the context was a bit different, relating as it did to measurement errors in surveys, I was reminded of an experience I had accompanying a follow-up interviewer as part of the Census Bureau's 1990 post-enumeration survey. After skillfully completing many other interviews, and after skillfully connecting with an African-American woman in her 40's who seemed reluctant to participate, the interviewer faltered: instead of asking the more nuanced question of whether her 19-year-old son lived at that address in April 1990, the interviewer only asked whether the son existed, which to me left the central question of whether the census record was a correct or an erroneous enumeration unresolved. The respondent's understandable eagerness to end the interview—after all, why was the government asking yet again about her son?—further sensitized me to the potential for flawed assumptions in the incomplete-data models I was developing at the Census Bureau that year. *Missing Data Analysis in Practice* provides many such nuanced and thoughtful insights that are crucial to successfully addressing the scientific challenges posed by incomplete data—I highly recommend it.

References

Carpenter, J. R. and Kenward, M. G. (2013). *Multiple Imputation and Its Application*. New York: John Wiley & Sons.

Daniels, M. J. and Hogan, J. W. (2008). *Missing Data in Longitudinal Studies: Strategies for Bayesian Modeling and Sensitivity Analysis*. New York: Chapman & Hall/CRC Press.

Little, R. J. A. and Rubin, D. B. (2002). *Statistical Analysis with Missing Data, Second Edition*. New York: John Wiley & Sons.

Molenberghs, G., Fitzmaurice, G., Kenward, M. G., Tsiatis, A., and Verbeke, G. (2015). *Handbook of Missing Data Methodology*. Boca Raton: Chapman & Hall/CRC Press.

Raghunathan, T. E., Lepkowski, J. M., van Hoewyk, J., and Solenberger, P. W. (2001). A multivariate technique for multiply imputing missing values using a sequence of regression models, *Survey Methodology* **27**, 85–95.

Rubin, D. B. (1987). *Multiple Imputation for Nonresponse in Surveys*. New York: John Wiley & Sons.

Rubin, D. B., Stern, H., and Vehovar, V. (1995). Handling 'Don't Know' survey responses: The case of the Slovenian plebiscite. *Journal of the American Statistical Association* **90**, 822–828.

Schafer, J. L. (1997). *Analysis of Incomplete Multivariate Data*. New York: Chapman & Hall/CRC Press.

Su, Y. S., Gelman, A., Hill, J., and Yajima, M. (2011). Multiple imputation with diagnostics (mi) in R: Opening windows into the black box. *Journal of Statistical Software* **45**, 2.

van Buuren, S. (2012). *Flexible Imputation of Missing Data*. New York: Chapman & Hall/CRC Press.

Thomas R. Belin
Department of Biostatistics
University of California Los Angeles
Los Angeles, California, U.S.A.
tbelin@mednet.ucla.edu

ALAN AGRESTI. **Foundations of Linear and Generalized Linear Models**. Hoboken: Wiley

In reading a text book like Alan Agresti's Foundations of Linear and Generalized Linear Models as someone who is quite familiar with its topic and material, one has a dedicated focus and asks themselves two things. First, is this a textbook I could use in my own classes? And secondly, do I learn/read things in the book that I have not known before? Let me answer these two questions ahead of my subsequent review with a clear "yes." Concerning the use of the book as textbook, I must say it is great to see the multiple technical issues of linear and generalized linear models written down in such a concise, mathematically precise and up-to-date way, which is very understandable and motivating at the same time. With regard to the second question, yes, I did learn new things, and I stress that I appreciate and admire Alan Agresti's historical knowledge and views. For instance, I did not know that Gaussian least squares has been a topic of dispute with Legendre, nor did I know that what is known under the Bonferroni adjustment traces back to a paper by George Boole from 1854. There are many more historical notes that make the material quite interesting, even for experts in the field. In fact, Alan Agresti generously shares historical quotes so that each chapter is closed by so called *Chapter Notes* which provide insight and historical views. This historical view is often overlooked in today's times of rapid new developments, warranting appreciation to Alan Agresti for composing these notes.

But let us start from the beginning. The aim of this book is best described in its preface, where Alan Agresti writes: "*My book is intended to present an overview of the key ideas and foundational results of linear and generalized linear models.*" Then he gets more specific by clarifying: "*my book has more emphasis on the theoretical foundations (. . .) and providing extensive references for historical developments and*

new methodology." Finally he states: "*my book has less emphasis than some other books on practical issues of data analysis*." These three sentences alone could serve as a very suitable book review, and in my opinion Alan Agresti describes his book with these three sentences in an excellent and extremely suitable manner. Hence, what could I add to that?

The book starts with an introduction to linear and generalized linear models as the first chapter. However, to me, this first chapter does not read like an introduction, at least not like a gentle one. It jumps directly into the subject, without motivating the topic with examples as other books on the topic typically do. For someone who has never heard of generalized linear models before, this introduction may be intimidating, leading the reader to believe that the book proceeds in this speedy fashion. However, this is not the case and the first chapter just provides the general framework of generalized linear models. The subsequent chapters discuss the various models and special properties with a lot of motivation. Insofar, one must ask the unskilled reader not to get frustrated when reading through the first chapter, as all details are discussed in depth later in the book. After this *quick* start, Alan Agresti focuses on one relevant issue in linear and generalized linear models after the other in a concentrated progression. In Chapter 2 he discusses least squares principles, primarily from a projection and matrix point of view. In Chapter 3 he follows the same route, adding the assumption of normality for the residuals in the regression model. Chapter 4 follows with a more gentle introduction to generalized linear models, which are then discussed particularly for binary data (Chapter 5), multinomial data (Chapter 6) and count data (Chapter 7). The book continues with quasi-likelihood (Chapter 8), correlated responses (Chapter 9) and Bayesian approaches for generalized linear models (Chapter 10). Extensions of the model, such as the lasso, are shown in Chapter 11.

It was hard for me to find anything relevant from the field of generalized linear models missing in the book. The only thing I could possibly venture would be deeper discussion of generalized additive models or, more generally, generalized linear models with smooth components. Wood (2017) just recently published up-to-date material in this direction.

An extremely helpful contribution of Agresti's book is the vast collection of exercises at the conclusion of every chapter, which are helpful both to the inexperienced reader and the lecturer in need of providing exercises to students. Thanks to Alan Agresti, there is no need to dig further for such materials. His book contains all the exercises one could need and use in class. And thus, in the same way as the book is a very comprehensive introduction to the field of generalized linear models, its collection of exercises fulfills the same purpose on the training side.

All in all I enjoyed reading the book, and I will certainly make use of it in my classes. Moreover, out of curiosity, I will also look into the many historical papers and documents mentioned. And most certainly I will share these historical notes and anecdotes with my students in my future lectures on linear and generalized linear models.

References

Wood, S. (2017). *Generalized Additive Models (2nd edition)*. CRC Press.

Goeran Kauermann
Institute for Statistics
Ludwig-Maximilians-Universität München
Munich, Germany
Goeran.kauermann@stat.uni-muenchen.de