Adaptive Design For Clinical Trials

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Randomization in Clinical Trials
A Comparison of Adaptive Designs in Clinical Trials
Adaptive Design of Clinical Trials with Interim Selection of Treatment Arms
Adaptive Design Methods in Clinical Trials, Second Edition
Clinical Trials in Neurology
Bayesian and Frequentist Adaptive Methods
Umbrella Trials and Basket Trials
Practical Considerations for Adaptive Trial Design and Implementation
Sequential Experimentation in Clinical Trials
Adaptive Design in Clinical Trials
Key to Unlocking Precision Medicine
Neuroscience Trials of the Future
Handbook of Adaptive Designs in Pharmaceutical and Clinical Development
Theory and Practice
Group Sequential and Confirmatory Adaptive Designs in Clinical Trials
Proceedings of a Workshop

JOHNSON SAWYER

Bayesian Adaptive Methods for Clinical Trials National Academies Press
This book covers several new areas in the growing field of analytics with some innovative applications in different business contexts, and consists of selected presentations at the 6th IIMA International Conference on Advanced Data Analysis, Business Analytics and Intelligence. The book is conceptually divided in seven parts. The first part gives expository briefs on some topics of current academic and practitioner interests, such as data streams, binary prediction and reliability shock models. In the second part, the contributions look at artificial intelligence applications with chapters related to explainable AI, personalized search and recommendation, and customer retention management. The third part deals with credit risk analytics, with chapters on optimization of credit limits and mitigation of agricultural lending risks. In its fourth part, the book explores analytics and data mining in the retail context. In the fifth part, the book presents some applications of analytics to operations management. This part has chapters related to improvement of furnace operations, forecasting food indices and analytics for improving student learning outcomes. The sixth part has contributions related to adaptive designs in clinical trials, stochastic comparisons of systems with heterogeneous components and stacking of models. The seventh and final part contains chapters related to finance and economics topics, such as role of infrastructure and taxation on economic growth of countries and connectedness of markets with heterogenous agents, The different themes ensure that the book would be of great value to practitioners, post-graduate students, research scholars and faculty teaching advanced business analytics courses.
Adaptive and Flexible Clinical Trials CRC Press
Presents a firm mathematical basis for the use of response-adaptive randomization procedures in practice The Theory of Response-Adaptive Randomization in Clinical Trials is the result of the authors' ten-year collaboration as well as their collaborations with other researchers in investigating the important questions regarding response-adaptive randomization in a rigorous mathematical framework. Response-adaptive allocation has a long history in biostatistics literature; however, largely due to the disastrous ECMO trial in the early 1980s, there is a general reluctance to use these procedures. This timely book represents a mathematically rigorous subdiscipline of experimental design involving randomization and answers fundamental questions, including: How does response-adaptive randomization affect power? Can standard inferential tests be applied following response-adaptive randomization? What is the effect of delayed response? Which procedure is most appropriate and how can "most appropriate" be quantified? How can heterogeneity of the patient population be incorporated? Can response-adaptive randomization be performed with more than two treatments or with continuous responses? The answers to these questions communicate a thorough understanding of the asymptotic properties of each procedure discussed, including asymptotic normality, consistency, and asymptotic variance of the induced allocation. Topical coverage

includes: The relationship between power and response-adaptive randomization The general result for determining asymptotically best procedures Procedures based on urn models Procedures based on sequential estimation Implications for the practice of clinical trials Useful for graduate students in mathematics, statistics, and biostatistics as well as researchers and industrial and academic biostatisticians, this book offers a rigorous treatment of the subject in order to find the optimal procedure to use in practice.

Randomised Response-Adaptive Designs in Clinical Trials CRC Press

On March 3-4, 2016, the National Academies of Sciences, Engineering, and Medicine's Forum on Neuroscience and Nervous System Disorders held a workshop in Washington, DC, bringing together key stakeholders to discuss opportunities for improving the integrity, efficiency, and validity of clinical trials for nervous system disorders. Participants in the workshop represented a range of diverse perspectives, including individuals not normally associated with traditional clinical trials. The purpose of this workshop was to generate discussion about not only what is feasible now, but what may be possible with the implementation of cutting-edge technologies in the future.

Advances in Clinical Trial Biostatistics CRC Press

Every patient is unique, and the evolving field of precision medicine aims to ensure the delivery of the right treatment to the right patient at the right time. In an era of rapid advances in biomedicine and enhanced understanding of the genetic basis of disease, health care providers increasingly have access to advanced technologies that may identify molecular variations specific to an individual patient, which subsequently can be targeted for treatment. Known as biomarker tests for molecularly targeted therapies, these complex tests have the potential to enable the selection of the most beneficial treatment (and also to identify treatments that may be harmful or ineffective) for the molecular underpinnings of an individual patient's disease. Such tests are key to unlocking the promise of precision medicine. Biomarker tests for molecularly targeted therapies represent a crucial area of focus for developing methods that could later be applicable to other areas of precision medicine. The appropriate regulatory oversight of these tests is required to ensure that they are accurate, reliable, properly validated, and appropriately implemented in clinical practice. Moreover, common evidentiary standards for assessing the beneficial impact of biomarker-guided therapy selection on patient outcomes, as well as the effective collection and sharing of information related to those outcomes, are urgently needed to better inform clinical decision making. Biomarker Tests of Molecularly Targeted Therapies examines opportunities for and challenges to the use of biomarker tests to select optimal therapy and offers recommendations to accelerate progress in this field. This report explores regulatory issues, reimbursement issues, and clinical practice issues related to the clinical development and use of biomarker tests for targeting therapies to patients. Properly validated, appropriately implemented biomarker tests hold the potential to enhance patient care and improve outcomes, and therefore addressing the challenges facing such tests is critical.

The Theory of Response-Adaptive

Randomization in Clinical Trials CRC Press
ExpDesign Studio facilitates more efficient clinical trial design This book introduces pharmaceutical statisticians, scientists, researchers, and others to ExpDesign Studio software for classical and adaptive designs of clinical trials. It includes the Professional Version 5.0 of ExpDesign Studio software that frees pharmaceutical professionals to focus on drug development and related challenges while the software handles the essential calculations and computations. After a hands-on introduction to the software and an overview of clinical trial designs encompassing numerous variations, Classical and Adaptive Clinical Trial Designs Using ExpDesign Studio: Covers both classical and adaptive clinical trial designs, monitoring, and analyses Explains various classical and adaptive designs including groupsequential, sample-size reestimation, dropping-loser, biomarker-adaptive, and response-adaptive randomization designs Includes instructions for over 100 design methods that have been implemented in ExpDesign Studio and step-by-step demos as well as real-world examples Emphasizes applications, yet covers key mathematical formulations Introduces readers to additional toolkits in ExpDesign Studio that help in designing, monitoring, and analyzing trials, such as the adaptive monitor, graphical calculator, the probability calculator, the confidence interval calculator, and more Presents comprehensive technique notes for sample-size calculation methods, grouped by the number of arms, the trial endpoint, and the analysis basis Written with practitioners in mind, this is an ideal self-study guide for not only statisticians, but also scientists, researchers, and professionals in the pharmaceutical industry, contract research organizations (CROs), and regulatory bodies. It's also a go-to reference for biostatisticians, pharmacokinetic specialists, and principal investigators involved in clinical trials. ERRATUM Classical and Adaptive Clinical Trial Designs Using ExpDesign Studio By Mark Chang The license for the ExpDesign Studio software on the CD included with this book is good for one-year after installation of the software. Prior to the expiration of this period, the software will generate a reminder about renewal for the license. The user should contact CTriSoft International (the owners of ExpDesign Studio) at www.CTriSoft.net or by email at license@ctrisoft.net, about renewal for the license. This should have been made clear in the first printing of this book. We apologize for this error.
Classical and Adaptive Clinical Trial Designs Using ExpDesign Studio Springer
From aspects of early trials to complex modeling problems, Advances in Clinical Trial Biostatistics summarizes current methodologies used in the design and analysis of clinical trials. Its chapters, contributed by internationally renowned methodologists experienced in clinical trials, address topics that include Bayesian methods for phase I clinical trials, adaptive two-stage clinical trials, and the design and analysis of cluster randomization trials, trials with multiple endpoints, and therapeutic equivalence trials. Other discussions explore Bayesian reporting, methods incorporating compliance in treatment evaluation, and statistical issues emerging from clinical trials in HIV infection.
Adaptive Design Methods in Clinical Trials, Second Edition Chapman and

Hall/CRC
Praise for the First Edition “All medical statisticians involved in clinical trials should read this book...” - Controlled Clinical Trials Featuring a unique combination of the applied aspects of randomization in clinical trials with a nonparametric approach to inference, Randomization in Clinical Trials: Theory and Practice, Second Edition is the go-to guide for biostatisticians and pharmaceutical industry statisticians. Randomization in Clinical Trials: Theory and Practice, Second Edition features: Discussions on current philosophies, controversies, and new developments in the increasingly important role of randomization techniques in clinical trials A new chapter on covariate-adaptive randomization, including minimization techniques and inference New developments in restricted randomization and an increased focus on computation of randomization tests as opposed to the asymptotic theory of randomization tests Plenty of problem sets, theoretical exercises, and short computer simulations using SAS® to facilitate classroom teaching, simplify the mathematics, and ease readers’ understanding Randomization in Clinical Trials: Theory and Practice, Second Edition is an excellent reference for researchers as well as applied statisticians and biostatisticians. The Second Edition is also an ideal textbook for upper-undergraduate and graduate-level courses in biostatistics and applied statistics. William F. Rosenberger, PhD, is University Professor and Chairman of the Department of Statistics at George Mason University. He is a Fellow of the American Statistical Association and the Institute of Mathematical Statistics, and author of over 80 refereed journal articles, as well as The Theory of Response-Adaptive Randomization in Clinical Trials, also published by Wiley. John M. Lachin, ScD, is Research Professor in the Department of Epidemiology and Biostatistics as well as in the Department of Statistics at The George Washington University. A Fellow of the American Statistical Association and the Society for Clinical Trials, Dr. Lachin is actively involved in coordinating center activities for clinical trials of diabetes. He is the author of Biostatistical Methods: The Assessment of Relative Risks, Second Edition, also published by Wiley.

Fundamental Concepts for New Clinical Trialists John Wiley & Sons
Translating laboratory discoveries into successful therapeutics can be difficult. Clinical Trials in Neurology aims to improve the efficiency of clinical trials and the development of interventions in order to enhance the development of new treatments for neurologic diseases. It introduces the reader to the key concepts underpinning trials in the neurosciences. This volume tackles the challenges of developing therapies for neurologic disorders from measurement of agents in the nervous system to the progression of clinical signs and symptoms through illustrating specific study designs and their applications to different therapeutic areas. Clinical Trials in Neurology covers key issues in Phase I, II and III clinical trials, as well as post-marketing safety surveillance. Topics addressed include regulatory and implementation issues, outcome measures and common problems in drug development. Written by a multidisciplinary team, this comprehensive guide is essential reading for neurologists, psychiatrists, neurosurgeons, neuroscientists, statisticians and clinical researchers in

the pharmaceutical industry.

Perspectives on Current Issues CRC Press

Statistical Challenges in Oncology Clinical Development presents an overview of statistical considerations in oncology clinical trials, including both early and late phase of development. It illustrates how the novel statistical methods can enrich the design and analysis of modern oncology trials. The book covers wide spectrum of statistical methodology with real life examples. The book covers all aspects of cancer clinical trial starting from early phase development. The early part of the book covers novel phase I dose escalation design, exposure response analysis and innovative phase II design. This includes early development strategy for cancer immunotherapy trials. The authors also emphasized the role of biomarker and modern era of precision medicine. The second part focuses on the late stage development. This includes the application of adaptive design, safety analysis and quality of life data analysis. The final part discusses current regulatory perspective and challenges. Statisticians, key opinion leaders and strategy makers involved in oncology trials will find this book useful. This book provides researchers a solid overview of available methodologies. Along with describing the necessary statistical theory, the authors illustrate the practical application of the techniques. The authors include many relevant real life examples from pharmaceutical industry and academia based on their first-hand experience. Along with relevant references, the book highlights current regulatory views. Features: It covers a wide spectrum of topics related to real life statistical challenges in oncology clinical trials. This provides a comprehensive overview of novel statistical methods to improve trial design and statistical analysis. Detailed case studies illustrate the real-life applications. Authors are eminent members from pharmaceutical industry, FDA and academia who have several years of hands in experience in clinical trial.

Adaptive Design of Clinical Trials CRC Press

A balanced treatment of the theories, methodologies, and designissues involved in clinical trials using statisticalmethods There has been enormous interest and development in Bayesianadaptive designs, especially for early phases of clinical trials.However, for phase III trials, frequentist methods still play adominant role through controlling type I and type II errors in thehypothesis testing framework. From practical perspectives, ClinicalTrial Design: Bayesian and Frequentist Adaptive Methods providescomprehensive coverage of both Bayesian and frequentist approachesto all phases of clinical trial design. Before underpinning variousadaptive methods, the book establishes an overview of thefundamentals of clinical trials as well as a comparison of Bayesianand frequentist statistics. Recognizing that clinical trial design is one of the mostimportant and useful skills in the pharmaceutical industry, thisbook provides detailed discussions on a variety of statisticaldesigns, their properties, and operating characteristics for phaseI, II, and III clinical trials as well as an introduction to phaseIV trials. Many practical issues and challenges arising in clinicaltrials are addressed. Additional topics of coverage include: Risk and benefit analysis for toxicity and

efficacytrade-offs Bayesian predictive probability trial monitoring Bayesian adaptive randomization Late onset toxicity and response Dose finding in drug combination trials Targeted therapy designs The author utilizes cutting-edge clinical trial designs andstatistical methods that have been employed at the world's leadingmedical centers as well as in the pharmaceutical industry. Thesoftware used throughout the book is freely available on the book'srelated website, equipping readers with the necessary tools fordesigning clinical trials. Clinical Trial Design is an excellent book for courses on thetopic at the graduate level. The book also serves as a valuablereference for statisticians and biostatisticians in thepharmaceutical industry as well as for researchers andpractitioners who design, conduct, and monitor clinical trials intheir everyday work.

Designs for Clinical Trials CRC Press

Expert clinical problem-solving methods and guidance—from the editors and contributors of the New England Journal of Medicine This invaluable resource from the New England Journal of Medicine expertly addresses methods and challenges in clinical diagnosis. Including the peer-reviewed content of the NEJM’s renowned “Clinical Problem Solving” feature, this powerful resource is packed with case discussions from both ambulatory and hospital practice. Each Case Presentation reveals thought-provoking clinical and laboratory clues as the diagnostic considerations begin to emerge. Subsequent clinical detail and discussion and expert analysis add to the diagnostic picture until a final clinical diagnosis is reached. New England Journal of Medicine: Clinical Problem-Solving features: Published cases drawn from the New England Journal of Medicine reflecting actual patient-management situations that physicians experience in their everyday clinical practice Two brand new, never-before-published chapters on medical decision-making skills and methods Wide-ranging coverage of the major considerations in each case, from underlying pathophysiology to signs from the physical examination to lab testing strategies More than 100 full-color illustrations, tables, and algorithms Meticulously selected references that open up avenues for further study And much more! From cover to cover, New England Journal of Medicine: Clinical Problem-Solving presents the best case analysis, diagnostic thought processes, and problem-solving-- direct from master clinicians.

When Multiple Treatments are Tested in Multiple Stages Cambridge University Press

This book covers domains of modern clinical trial design: classical, group sequential, adaptive, and Bayesian methods applicable to and used in various phases of pharmaceutical development. Written for biostatisticians, pharmacometricians, clinical developers, and statistical programmers involved in the design, analysis, and interpretation of clinical trials, as well as students in graduate and postgraduate programs in statistics or biostatistics, it covers topics including: dose-response and dose-escalation designs; sequential methods to stop trials early for overwhelming efficacy, safety, or futility; Bayesian designs incorporating historical data; adaptive sample size re-estimation and randomization to allocate subjects to effective treatments; population enrichment designs. Methods are illustrated using clinical trials from

diverse therapeutic areas, including dermatology, endocrinology, infectious disease, neurology, oncology and rheumatology. --
Small Clinical Trials CRC Press
"This is truly an outstanding book. [It] brings together all of the latest research in clinical trials methodology and how it can be applied to drug development.... Chang et al provide applications to industry-supported trials. This will allow statisticians in the industry community to take these methods seriously." Jay Herson, Johns Hopkins University The pharmaceutical industry's approach to drug discovery and development has rapidly transformed in the last decade from the more traditional Research and Development (R & D) approach to a more innovative approach in which strategies are employed to compress and optimize the clinical development plan and associated timelines. However, these strategies are generally being considered on an individual trial basis and not as part of a fully integrated overall development program. Such optimization at the trial level is somewhat near-sighted and does not ensure cost, time, or development efficiency of the overall program. This book seeks to address this imbalance by establishing a statistical framework for overall/global clinical development optimization and providing tactics and techniques to support such optimization, including clinical trial simulations. Provides a statistical framework for achieve global optimization in each phase of the drug development process. Describes specific techniques to support optimization including adaptive designs, precision medicine, survival-endpoints, dose finding and multiple testing. Gives practical approaches to handling missing data in clinical trials using SAS. Looks at key controversial issues from both a clinical and statistical perspective. Presents a generous number of case studies from multiple therapeutic areas that help motivate and illustrate the statistical methods introduced in the book. Puts great emphasis on software implementation of the statistical methods with multiple examples of software code (both SAS and R). It is important for statisticians to possess a deep knowledge of the drug development process beyond statistical considerations. For these reasons, this book incorporates both statistical and "clinical/medical" perspectives.
Fundamentals of Clinical Trials Springer Nature
ExpDesign Studio facilitates more efficient clinical trial design This book introduces pharmaceutical statisticians, scientists, researchers, and others to ExpDesign Studio software for classical and adaptive designs of clinical trials. It includes the Professional Version 5.0 of ExpDesign Studio software that frees pharmaceutical professionals to focus on drug development and related challenges while the software handles the essential calculations and computations. After a hands-on introduction to the software and an overview of clinical trial designs encompassing numerous variations, Classical and Adaptive Clinical Trial Designs Using ExpDesign Studio: Covers both classical and adaptive clinical trial designs, monitoring, and analyses Explains various classical and adaptive designs including groupsequential, sample-size reestimation, dropping-loser, biomarker-adaptive, and response-adaptive randomization designs Includes instructions for over 100 design methods that have been implemented in ExpDesign Studio and step-by-step

demos as well as real-world examples Emphasizes applications, yet covers key mathematical formulations Introduces readers to additional toolkits in ExpDesign Studio that help in designing, monitoring, and analyzing trials, such as the adaptive monitor, graphical calculator, the probability calculator, the confidence interval calculator, and more Presents comprehensive technique notes for sample-size calculation methods, grouped by the number of arms, the trial endpoint, and the analysis basis Written with practitioners in mind, this is an ideal self-study guide for not only statisticians, but also scientists, researchers, and professionals in the pharmaceutical industry, contract research organizations (CROs), and regulatory bodies. It's also a go-to reference for biostatisticians, pharmacokinetic specialists, and principal investigators involved in clinical trials. ERRATUM Classical and Adaptive Clinical Trial Designs Using ExpDesign Studio By Mark Chang The license for the ExpDesign Studio software on the CD included with this book is good for one-year after installation of the software. Prior to the expiration of this period, the software will generate a reminder about renewal for the license. The user should contact CTriSoft International (the owners of ExpDesign Studio) at www.CTriSoft.net or by email at license@ctrisoft.net, about renewal for the license. This should have been made clear in the first printing of this book. We apologize for this error.

Covariates in Adaptive Designs for Clinical Trials CRC Press

Is adaptive randomization always better than traditional fixed-schedule randomization? Which procedures should be used and under which circumstances? What special considerations are required for adaptive randomized trials? What kind of statistical inference should be used to achieve valid and unbiased treatment comparisons following adaptive random

Platform Trial Designs in Drug Development Wiley-Interscience

Sequential Experimentation in Clinical Trials: Design and Analysis is developed from decades of work in research groups, statistical pedagogy, and workshop participation. Different parts of the book can be used for short courses on clinical trials, translational medical research, and sequential experimentation. The authors have successfully used the book to teach innovative clinical trial designs and statistical methods for Statistics Ph.D. students at Stanford University. There are additional online supplements for the book that include chapter-specific exercises and information. Sequential Experimentation in Clinical Trials: Design and Analysis covers the much broader subject of sequential experimentation that includes group sequential and adaptive designs of Phase II and III clinical trials, which have attracted much attention in the past three decades. In particular, the broad scope of design and analysis problems in sequential experimentation clearly requires a wide range of statistical methods and models from nonlinear regression analysis, experimental design, dynamic programming, survival analysis, resampling, and likelihood and Bayesian inference. The background material in these building blocks is summarized in Chapter 2 and Chapter 3 and certain sections in Chapter 6 and Chapter 7. Besides group sequential tests and adaptive designs, the book also introduces sequential change-point detection methods in Chapter 5 in connection with pharmacovigilance and

public health surveillance. Together with dynamic programming and approximate dynamic programming in Chapter 3, the book therefore covers all basic topics for a graduate course in sequential analysis designs.

Statistical and Practical Aspects CRC Press

With new statistical and scientific issues arising in adaptive clinical trial design, including the U.S. FDA's recent draft guidance, a new edition of one of the first books on the topic is needed. Adaptive Design Methods in Clinical Trials, Second Edition reflects recent developments and regulatory positions on the use of adaptive designs in clinical trials. It unifies the vast and continuously growing literature and research activities on regulatory requirements, scientific and practical issues, and statistical methodology. New to the Second Edition Along with revisions throughout the text, this edition significantly updates the chapters on protocol amendment and clinical trial simulation to incorporate the latest changes. It also includes five entirely new chapters on two-stage adaptive design, biomarker adaptive trials, target clinical trials, sample size and power estimation, and regulatory perspectives. Following in the tradition of its acclaimed predecessor, this second edition continues to offer an up-to-date resource for clinical scientists and researchers in academia, regulatory agencies, and the pharmaceutical industry. Written in an intuitive style at a basic mathematical and statistical level, the book maintains its practical approach with an emphasis on concepts via numerous examples and illustrations.

Group Sequential Methods with Applications to Clinical Trials CRC Press

Adaptive Design Methods in Clinical Trials, Second EditionCRC Press

Bayesian Adaptive Methods for Clinical Trials John Wiley & Sons

Randomised Response-Adaptive Designs in Clinical Trials presents methods for the randomised allocation of treatments to patients in sequential clinical trials. Emphasizing the practical application of clinical trial designs, the book is designed for medical and applied statisticians, clinicians, and statisticians in training. After introducing clinical trials in drug development, the authors assess a simple adaptive design for binary responses without covariates. They discuss randomisation and covariate balance in normally distributed responses and cover many important response-adaptive designs for binary responses. The book then develops response-adaptive designs for continuous and longitudinal responses, optimum designs with covariates, and response-adaptive designs with covariates. It also covers response-adaptive designs that are derived by optimising an objective function subject to constraints on the variance of estimated parametric functions. The concluding chapter explores future directions in the development of adaptive designs.

Modern Approaches to Clinical Trials Using SAS: Classical, Adaptive, and Bayesian Methods National Academies Press

This book provides an up-to-date review of the general principles of and techniques for confirmatory adaptive designs. Confirmatory adaptive designs are a generalization of group sequential designs. With these designs, interim analyses are performed in order to stop the trial prematurely under control of the Type I error rate. In adaptive designs, it is also permissible to perform a data-driven change of relevant aspects of the

study design at interim stages. This includes, for example, a sample-size reassessment, a treatment-arm selection or a selection of a pre-specified sub-population. Essentially, this adaptive methodology was introduced in the 1990s. Since then, it has become popular and the object of intense discussion and still represents a rapidly growing field of statistical research. This book describes adaptive design methodology at an elementary level, while also considering designing and planning issues as well as methods for analyzing an adaptively planned trial. This includes estimation methods and methods for the determination of an overall p-value. Part I of the book provides the group sequential methods that are necessary for understanding and applying the adaptive design methodology supplied in Parts II and III of the book. The book contains many examples that illustrate use of the methods for practical application. The book is primarily written for applied statisticians from academia and industry who are interested in confirmatory adaptive designs. It is assumed that readers are familiar with the basic principles of descriptive statistics, parameter estimation and statistical testing. This book will also be suitable for an advanced statistical course for applied statisticians or clinicians with a sound statistical background.