PROGRAMME OF THE SIXTY-NINETH ANNUAL DEMING CONFERENCE ON APPLIED STATISTICS

Sponsored by
AMERICAN SOCIETY FOR QUALITY
NY/NJ Metropolitan Section ~ ~ Statistics Division
AMERICAN STATISTICAL ASSOCIATION: Biopharmaceutical Section
December 9 – December 11, 2013: Three-Day Conference
Tropicana Casino and Resort, Havana Tower, Atlantic City, NJ

Short Courses: – December 12-13, 2013

1. Group Sequential and Adaptive Methods in the Design of Clinical Trials Professors Chris Jennison University of Bath and Bruce Turnbull Cornell University

2. Design and Analysis of Experiments Using Generalized Linear Mixed Models Professor Walter Stroup University of Nebraska

A $4,000 college scholarship will be awarded to an undergraduate spouse, child, stepchild, or grandchild of a registrant

ONSITE REGISTRATION WILL BE ON THE FOURTH FLOOR OF THE HAVANA TOWER.
It will start at 6:00 pm on Sunday December 8th and will be followed by a one-hour reception with cold drinks and snacks.
It will continue at 7:30 AM Monday December 9th through Wednesday December 11th and 8 AM Thursday December 12th.
ALL REGISTRANTS WILL RECEIVE A BOUND COPY OF THE AVAILABLE HANDOUTS FOR ALL SESSIONS.
Register and pay for both the conference and the Tropicana online at www.demingconference.com. This will give you an instant e-mail acknowledgement. Only if absolutely necessary, mail a check with your completed registration form on page 7 in this program. If checks are not postmarked on or before the early discounted registration date, you will be charged the next higher amount.

Walter R. Young
Chairman
16 Harrow Circle
Wayne, Pa 19087

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Meeting facilities are in the Tropicana's Havana Tower state-of-the-art complex with 502 nonsmoking rooms where attendees stay in soundproof climate controlled rooms with direct-dial phones, cable color TV, coffee makers, hairdryers, refrigerators, safe, iron and board, complimentary wireless internet and gorgeous views of the Atlantic City skyline. Use the Havana Tower parking garage (sign says "The Quarter") on Brighton Avenue. Self or valet parking is $10 per stay for hotel guests.

- There is a guest check in desk on the 3rd floor of the Havana Tower and all meeting facilities are on the 4th floor.
- It is one of the largest hotels in New Jersey, with 2,078 rooms, elegant public areas, exclusive retail shops & fine dining.
- It is on the beach with a fully equipped fitness facility (free for conference registrants) and a heated indoor pool.
- It has free wi-fi in the rooms and conference floor. The casino is in a distant, separate connected building.
- A free Trop Advantage Card can offer rewards based on your play and may offer dining and show discounts.

Jim Albert (PhD in Statistics from Purdue University) is currently Professor of Statistics at Bowling Green State University. His research interests are in Bayesian inference for categorical data, statistical computation, statistics education, and the application of statistical thinking in sports. He is currently editor of the Journal of Quantitative Analysis and has written books on Bayesian modeling, introductory statistics from Bayesian and baseball perspectives, and statistical computation using R.

Thomas E. Bradstreet, Ph.D. is Senior Principal Scientist, Experimental Medicine Statistics, Merck Research Labs. Dr. Bradstreet's current statistical areas of interest include Bayesian statistics, statistical education, & graphics. He has published numerous book chapters, papers, and book reviews as well as taught several short courses and tutorials on graphics and other areas of statistics. Dr. Bradstreet has been an associate editor for the *Journal of the American Statistical Association* (Reviews), *The American Statistician* (Reviews), and the *Biopharmaceutical Report*. He has received best paper awards for both statistics and SAS software presentations and manuscripts.

Joseph C. Cappelleri, PhD, MPH, MS earned his M.S. in Statistics from the City University of New York, Ph.D. in Psychometrics from Cornell University, and M.P.H. in epidemiology from Harvard University. In June 1996, he joined Pfizer as a Biostatistician collaborating with Outcomes Research and is a Senior Director of Statistics at Pfizer. He is also an Adjunct Professor of Medicine at Tufts Medical Center and an Adjunct Professor of Statistics at the University of Connecticut. He has delivered numerous conference presentations and has published extensively on clinical and methodological topics, including on regression-discontinuity designs, meta-analyses, and health measurement scales. He has been instrumental in developing and validating a number of patient-reported outcomes for different diseases and conditions. He is an ASA Fellow.

Ding-Geng (Din) Chen (PhD in Statistics from University of Guelph in 1995) is a professor in biostatistics at the University of Rochester Medical Center. Previously, he was the Karl E. Peace endowed eminent scholar chair in biostatistics from the Jiann-Ping Hsu College of Public Health at the Georgia Southern University. He is also a senior biostatistics consultant for biopharmaceuticals and government agencies with extensive expertise in clinical trials and bioinformatics. He has more than 80-refereed professional publications and co-authored three books with Professor Karl E. Peace.

Fang Chen (PhD in Statistics from Carnegie Mellon University in 2004) is Senior Manager of Bayesian Statistical Modeling in Advanced Analytics Division at SAS Institute Inc. Among his responsibilities are development of Bayesian analysis software and the MCMC procedures. He has written about Bayesian modeling using the MCMC procedure and taught courses and tutorials on practical Bayesian computation.

Valerii Fedorov (PhD in Mathematics and Physics from the Moscow State University and a D.Sc. in Statistics from the Russian Academy of Sciences) is the VP and the Head of the Predictive Analytics, Innovation, Quintiles, NC. Previously he was the head of the Research Statistics Unit at GSK. He authored more than 200 publications including several books in various areas of statistics and biostatistics, such as design of clinical trials, bioequivalence, random effects models, regression analysis, numerical methods in design of experiments, theory of optimal design of experiments, model oriented adaptive design of experiments, and Bayesian methods in experimental design. He is an ASA fellow, Honorary Professor of Cardiff University, UK, and an adjunct Scholar of University of Pennsylvania.

H. M. James Hung, PhD, is Director of Division of Biometrics I, CDER, FDA. This division provides services for 3 medical divisions of drug products (cardiovascular- renal, neurology, psychiatry). In his FDA tenure, he reviewed many large mortality/morbidity trials in cardiovascular-renal areas. He published in Biometrics, Statistics in Medicine, Biometrical Journal, etc. His research covers factorial trials, utility of p-value distribution, adaptive design/analysis, non-inferiority trials and multi-regional trials. He received two FDA/CDER level Scientific Achievement Awards and was recently awarded an FDA level Scientific Achievement Award in recognition of his sustained excellent achievements to regulatory science in areas of clinical trial methodology. He is a Fellow of the ASA and an elected member of the International Statistical Institute

Mohammad. Huque (PhD in Statistics from the University of Missouri in 1973) is Division Director for the Division of Biometrics IV at the Office of Biostatistics under the Office of the Translational Sciences (OTS), Center for Drug Evaluation and Research (CDER), FDA since 1997. He directs the statistical review and research programs for therapeutic areas under the Office of Antimicrobial Products. He also supports the statistical review program of consumer behavior studies intended for non-prescription drugs. He is an ASA Fellow. He won the FDA Scientific Achievement Award in 1998 for his efforts in FDA decision-making in critical areas of multiple endpoints and multiple comparisons of clinical trials. He is a member of the FDA committee that is currently drafting FDA guidance on multiple endpoints.

Yuan Ji (PhD in Statistics from the University of Wisconsin at Madison in 2003) is Director of Cancer Informatics, NorthShore University HealthSystem, as well as an Associate Professor of Biostatistics at The University of Chicago. Previously he was an Associate Professor at the M. D. Anderson Cancer Center. He is a past president of the ASA's Houston Area Chapter. He is the principal investigator of an NIH R01 grant and has 60+ peer-reviewed publications in a variety of scientific journals, including JASA, Biometrics, JCO, Lancet Oncology, Bioinformatics, etc.

Sergei Leonov (PhD in Mathematical Statistics from the Institute for Systems Analysis, Russian Academy of Sciences, Moscow) is Senior Principal Scientist at AstraZeneca, Wilmington, DE. Previously he was with Vertex Pharmaceuticals, Modeling and Simulation (Cambridge, MA) and GSK, Research Statistics Unit (Collegeville, PA, 12 years). He has worked, among other projects, on adaptive designs for nonlinear models, dose-response modeling and optimization of sampling times for population PK/PD studies. Prior to joining the pharma industry, Sergei worked in academia (Institute for Systems Analysis, Moscow, and University of Southern California, LA). His research interests include stochastic approximation, nonparametric statistical estimation and smoothing, optimal experimental design for nonlinear models and statistical computing.

Robert T. O'Neill is the Senior Statistical Advisor to CDER in the Office of Translational Sciences in the Center for Drug Evaluation and Research (CDER), FDA. Up until June 2011, Dr. O'Neill was the Director of the Office of Biostatistics that provides biostatistical and scientific computational leadership and support to all programs of CDER. Prior to October 1998 he was Director of the Office of Epidemiology and Biostatistics, responsible also for the post-market safety surveillance of new drugs. He is a fellow of the ASA, member of several professional societies, a past Member of the Board of Directors of the Society for Clinical Trials, the 2002 recipient of the Marvin Zelen Leadership Award in Statistical Science, and the 2004 Lowell Reed Lecture Awardee from the American Public Health Association.

Deepayan Sarkar (PhD in Statistics from the University of Wisconsin at Madison in 2006) won the 2004 John M. Chambers Statistical Software Award for writing lattice while he was a graduate student in Statistics at the University of Wisconsin-Madison. He then worked as a postdoctoral fellow in Computational Biology at the Fred Hutchinson Cancer Research Center in Seattle before his current position as Assistant Professor at the Indian Statistical Institute, Delhi. He has been a user and developer of R for several years and is the primary developer of the lattice package for statistical graphics.

Sue-Jane Wang, PhD is Associate Office Director for Pharmacogenomics and Adaptive Design, Office of Biostatistics, Office of Translational Sciences, CDER, FDA. She is an author of over 90 papers and book chapters in statistical, clinical, genetic, bioinformatics, and pharmacogenomics literature. She received two FDA Outstanding Intercenter Scientific Collaboration Awards and was recently awarded the FDA level Scientific Achievement individual Awards in recognition of her sustained record of published regulatory research in statistical design and methodology advancing complex and emerging clinical trial designs and analysis that support regulatory guidance, policies and review in 2010. She is an ASA Fellow and an elected member of the International Statistical Institute.

Monday December 9, 2013 8:30 – 11:30 AM

Session A 🕮
Bayesian Computation with R
Prof. Jim Albert, Bowling Green State University
Moderator: Alfred Balch

There has been a dramatic growth in the development and application of Bayesian inferential methods. Some of this growth is due to the availability of powerful simulation-based algorithms to summarize posterior distributions. There has been also a growing interest in the use of the system R for statistical analyses. R's open source nature, free availability, and large number of contributor packages have made R the software of choice for many statisticians in education and industry. This tutorial describes the use of the statistical system R in simulation experiments and Bayesian computation. R tools are described for generating random variables, computing criteria of statistical procedures, and replicating the procedure to compute quantities such as mean squared error and probability of coverage. The use of R in Bayesian computation is described, including the programming of the posterior distribution and the use of different R tools to summarize the posterior. Special focus will be on the application of Markov chain Monte Carlo algorithms & diagnostic methods. The use of general-purpose R packages to implement MCMC algorithms is described.

Session B 🕮
Patient-Reported Outcomes: Measurement, Implementation and Interpretation
Dr. Joseph C. Cappelleri , Pfizer Inc
Moderator: Xiaoming Li

This tutorial provides an exposition on health measurement scales – specifically, on patient-reported outcomes. Some key elements in the development of a patient-reported outcome (PRO) instrument are noted. Highlighted here is the importance of the conceptual framework used to depict the relationship between items in a PRO instrument and the concepts measured by it. The core topics of validity and reliability are discussed. Validity, which is assessed in several ways, provides the evidence and extent that the PRO taps into the concept that it is purported to measure in a particular setting. Reliability of a PRO instrument involves its consistency or reproducibility as assessed by internal consistency and test-retest reliability. Exploratory factor analysis & confirmatory factor analysis are described as techniques to understand the underlying structure of a PRO measure with multiple items.

While most of the presentation centers on psychometrics from a classical test theory perspective, attention is also given to item response theory as an approach to scale development and evaluation. Cross-sectional analysis and longitudinal analysis of PRO scores are covered. Also covered is the topic of mediation modeling as a way to identify and explain the mechanism that underlies an observed relationship between an independent variable and a dependent variable via the inclusion of a third explanatory variable, known as a mediator variable. Variations of missing data for PRO measures are highlighted, as is the topic of multiple testing. Finally, approaches to interpret PRO results are elucidated in order to make these results useful and meaningful. Illustrations are provided

Monday Lunch (On Your Own) 11:30 AM - 1:00 PM

1:00 - 4:00 PM

Session C
Practical Bayesian Computation Using SAS
Fang Chen, SAS Institute Inc.
Moderator: Wenjin Wang

This tutorial reviews the basic concepts of Bayesian inference and focuses on the practical use of Bayesian computational methods. The objectives are to familiarize statistical programmers and practitioners with the essentials of Bayesian computing, and to equip them with computational tools through a series of worked-out examples that demonstrate sound practices for a variety of statistical models and Bayesian concepts.

The first part of the tutorial provides an introduction to Bayesian inference, covers the fundamentals of prior distributions and concepts in estimation. The course will also cover MCMC methods and related simulation techniques, emphasizing the interpretation of convergence diagnostics in practice.

The second part of this tutorial discusses applications using Bayesian capabilities in SAS/STAT software in the GENMOD, LIFEREG, and PHREG, and FMM procedures. Examples will include methods such as linear regression, generalized linear models, survival analysis, and finite mixture models.

The final part of this tutorial takes a topic-driven approach to cover broad Bayesian topics, such as random-effects models, sensitivity analysis, prediction, model assessment, and missing data problems. The examples will be done using PROC MCMC, a general-purpose simulation procedure in SAS/STAT software.

Session D 🕮
Applied Meta Analysis Using R
Professor Din Chen, University of Rochester
Moderator: Walter R. Young

This tutorial provides a most up-to-date development and a thorough presentation of meta-analysis models for clinical trial and biomedical applications with detailed step-by-step illustrations and implementation using R. The examples are compiled from real medical and clinical trial literatures and the analyses are illustrated by a step-by-step fashion using the most appropriate R packages and functions which should enable attendees to follow the logic and gain an understanding of the meta-analysis methods and R implementation so that they may use R to analyze their own data. Specifically, I will start with some basic review on meta-analysis using fixed-effects and random-effects models as well as the meta-regression illustrated with R packages. Advanced methods, such as using individual-level patient data, meta-analysis method with rare-events in clinical trials, combining p-values in meta-analysis, multivariate meta-analysis will be discussed as below.

- **Brief introduction to R**
- **Overview to meta-analysis for both fixed-effects and random-effects models in meta-analysis. Real datasets in clinical trials are introduced along with two commonly used R packages of "meta" and "rmeta"**
- **Meta-analysis models for binary data, such as for risk-ratio, risk difference and odds-ratio**
- **Meta-analysis models for continuous data, such as for mean difference and standardized mean difference**
- **Methods to quantify heterogeneity and test the significance of heterogeneity among studies in a meta-analysis and then introduce meta-regression with R package of "metafor".**
- **Meta-analysis methods for individual-patient data (IPD) analysis and meta-analysis (MA)**
- **Meta-analysis methods for rare-events that is timely for clinical trials of adverse-events.**
- **Multivariate meta-analysis and other relevant topics in meta-analysis.**

7 PM Speaker's Dinner (Optional Added Fee Event)

Tuesday December 10, 2013 8:30 – 11:30 AM

Session E
Effective Communication Using Graphics
Dr. Thomas Bradstreet, Merck
Moderator: Kalyan Ghosh

Effective communication using graphics is a prerequisite skill for any working professional or student, either statistician or non-statistician, practicing in industry, government, or academia who is involved either with data analysis, the visual display of data, or is a consumer of this information. Formal training in these skills is often overlooked by many disciplines including statistics. Consider the price to be paid due to poorly designed and ineffectively constructed graphs which can perpetuate poor scientific, business, and public policy decisions, especially among quantitatively naive individuals. Participants will gain an awareness of, and exposure to, the principles of visual perception, design, and construction of graphic displays of both quantitative and qualitative information. Participants will be able to design and construct their own graphics, and critically review published graphics, based upon a set of guidelines that are general and flexible enough to be applied in most data analysis and final presentation situations. The guidelines will be demonstrated with specific examples of what-to-do and what-not-to-do, based upon graphs of real data sets, graphs from peer reviewed journals and reference books, and an in-house course that was designed for both non-statisticians & statisticians. This tutorial is meant to be interactive with lots of collaborative discussions.

Session F
Some Recent Practical Bayesian Adaptive Designs for Early-Phase Clinical Trials in Oncology
Dr. Yuan Ji, NorthShore University Health System / The University of Chicago
Moderator: Naitee Ting

Two topics will be covered: 1) A new Phase I design, named the modified toxicity probability method (mTPI), that is superior in all aspects than the 3+3 design, and much easier to implement than most current adaptive designs (e.g., CRM) in practice. The new Phase I design is based on posterior probability interval estimates to evaluate the toxicity of each dose, thereby automatically accounting for the variability in observed data that are typically noisy. This is a critical and novel feature of the mTPI method. It will be demonstrated through freely available software the key features of the new design, with thorough comparisons with 3+3 and CRM. 2) A novel Phase I-II design that dynamically and seamlessly link Phase I and Phase II trials into a single study that investigates the toxicity and efficacy of different doses. Significant savings in time, cost, and efficiency with the new design will be shown, comparing to the traditional sequential strategy in the drug development by performing Phase I dose finding and Phase II proof of concept trials separately. The key feature of the new design is to allow doses that deemed promising in Phase I to graduate to a companion Phase II design for immediate investigation, which essentially eliminates the gap between Phase I and Phase II studies. Again, software will be provided and demonstrated using the new design.

Tuesday Lunch (On Your Own) 11:30 AM - 1:00 PM

1:00 - 4:00 PM

Session G 🕮
Trellis (Lattice) Graphics
Prof. Deepayan Sarkar, Indian Statistical Institute
Moderator: Alfred Balch

R is rapidly growing in popularity as the environment of choice for data analysis and graphics both in academia and industry. Lattice brings the proven design of Trellis graphics (originally developed for S by William S. Cleveland and colleagues at Bell Labs) to R, considerably expanding its capabilities in the process. The lattice an add-on package implements Trellis graphics (originally developed for S and S-PLUS) in R. Lattice is a powerful and elegant high level data visualization system that is sufficient for most everyday graphics needs, yet flexible enough to be easily extended to handle demands of cutting edge research. It is a powerful and elegant high-level data visualization system with an emphasis on multivariate data. In this tutorial, we will cover basic usage of lattice and give pointers to further documentation that describes how to customize lattice plots. We will also describe some tricks that make some common types of customization easier. Many of the examples presented will emphasize principles of good graphical design; almost all will use real data sets that are available in various R packages. All code and figures in the book are also available online, along with supplementary material covering more advanced topics.

Session H
Statistical Approaches to Multiplicity Issues in Modern Clinical Trials
Dr. Mohammad Huque, Office of Biostatistics, OTS, CDER, FDA
Moderator: Xiaoming Li

Modern clinical trials for evaluating efficacy and safety of new treatments typically involve multiple objectives which are generally classified into primary and secondary types, the former for establishing treatment effect, and the later for provide supporting evidence. For some trials these objectives may be simple and few, and easy to handle statistically, but modern trials are now designed with more than a few objectives that are often complex and mulitimensional in structure. For example, one dimension may relate to the effects of the treatment on multiple endpoints, the other to the effects of multiple doses of the treatment, and yet another to the type of tests (e.g., non-inferiority and superiority tests). Additionally, there may be interests in assessing treatment effects for targeted subgroups. Addressing such intricate problems for controlling the Type I error probability requires the use of advanced statistical methods. The FDA on recognizing the importance of this topic has written draft guidance. The purpose of this presentation is to share concepts, issues and methods addressed in this draft guidance.

4 – 5 PM: Student Scholar and Attendee Poster Session Moderator: Nandita Biswas

Adjusting Object-Level Agreement in the Presence of Nested-Level Agreement by Mat D. Davis, J. Richard Landis, Warren Bilker; University of Pennsylvania, School of Medicine

Frequentist Model Averaging: A General Framework and Theories by Priyam Mitra and Min-ge Xie; Rutgers University

Wednesday December 11, 2013 8:30 – 11:30 AM

Session I

Monitoring Clinical Trial Outcomes with Delayed Response: Incorporating "Pipeline" Data with Group Sequential Designs and With Adaptive Designs

Professors Chris Jennison University of Bath & Bruce Turnbull, Cornell University

Moderator: Ivan Chan

In many clinical trials, the primary endpoint is measured some time after the start of treatment. Thus, when group sequential monitoring is applied, there are subjects at interim analyses who have been treated but are yet to respond. These "pipeline" subjects pose problems for standard group sequential methods that expect a trial either to stop with a firm decision at an interim analysis or to continue recruiting further patients. We shall describe the work of Hampson and Jennison (J. Royal Statistical Society, B, 2013), which proposes a new framework for designing and implementing group sequential tests in the presence of a delayed response. Studying optimal versions of these designs reveals how the benefits of lower expected sample size normally achieved by a group sequential test are reduced when there is a delay in response. This loss can be ameliorated by modeling data on a correlated short-term endpoint that is available for patients with partial follow-up.

Adaptive designs, such as the "promising zone" approach of Mehta and Pocock (Statist. Med 2011), have been proposed that can also accommodate delayed observations. Two-stage designs with adaptive sample size modification can deal with "pipeline subjects" by including their number in the minimum sample size for the second group. We shall show how to improve such adaptive designs with respect to their expected sample size, and that this leads to designs very similar to the two-stage case of Hampson and Jennison's delayed response group sequential tests.

Session J

FDA and The Discipline Of Regulatory Science: A Perspective on an Academic Discipline of Regulatory Statistics In Medical Products

Dr. Robert T. O'Neill, CDER, FDA

Moderator: Naitee Ting

This lecture is about the emerging area of regulatory science with a specific focus on regulatory statistics and its impact on all aspects of the evaluation of medical products from pre marketing to post marketing and life cycle evaluation. Several topics will be covered in the lecture starting with a discussion of how the field of regulatory statistics emerged, what constitutes the body of topics, the case studies that help define the evaluation of evidence of efficacy and safety, and the resources available to develop course modules that might be incorporated into academic programs. In particular, the lecture will cover some of the events that forged the current approach to medical product evaluation beginning with the evaluation of evidence for the effectiveness of new drugs, continuing with the emerging area of quantitative safety assessment, post approval monitoring of product safety through the Sentinel system, and finally suggestions for case studies and available resources to develop course content.

Wednesday Lunch (On Your Own) 11:30 AM - 1:00 PM

1:00 - 4:00 PM

Session K 🕮

Model-Based Optimal Experimental Design In Early Phases of Drug Development

Drs. Sergei Leonov, AstraZeneca & Valerii Fedorov, Quintiles

Moderator: Kalyan Ghosh

The course focuses on optimal experimental design and its applications in drug development. We introduce the key concepts via linear regression and least squares estimators, and then proceed with nonlinear models and maximum likelihood estimators. Once a reasonable estimator is constructed, it is natural to discuss design of experiments and to introduce criteria for design comparison. Most of the criteria are defined by the variance-covariance matrix of parameter estimators, are related to confidence regions and admit transparent geometrical and statistical interpretation.

After discussing properties of optimal designs and their numerical construction, we present examples of locally optimal, Bayesian and composite designs for various applications. These include binary models for dose-response studies, continuous logistic models that are essential for bioassays and pharmacodynamic studies, multiresponse models for correlated endpoints in dose-finding and population pharmacokinetic (mixed effects) models. Cost-based and penalized designs are introduced that enable practitioners to conduct studies within budget/ethical constraints while obtaining reliable estimators. Finally, adaptive designs are described that overcome the dependence of locally optimal designs on unknown parameters.

The course requires a modest background in matrix algebra and statistics (basics of least squares & maximum likelihood estimation). While the major results are presented at a conceptual level, the examples provide details that are key in clinical trials applications.

Session L

Some Challenging Clinical Trial Designs in Regulatory Applications

Drs. H.M. James Hung & Sue-Jane Wang, FDA

Moderator: Ivan Chan

Many trial designs in clinical research are employed for drug development and in regulatory applications, though there may be differences in the methodology for statistical inference. Depending on the characteristics of diseases and the pharmacological properties of a test drug product, a specific clinical trial design may be good for use in one type of applications but may not in other types of applications. In addition, the complexity of trial objectives and study endpoints may further advance trial designs to achieve multiple study objectives. In regulatory applications, the applicability of certain trial designs may also depend on the roles of individual trials in the drug development program. Is a trial conducted simply for learning or for providing supportive evidence for the purpose of marketing the test drug? Is a particular trial a pivotal trial from the standpoint of confirmatory evidence? This tutorial will aim at some of the challenging trial designs seen in clinical development programs and lessons learned.

1. Factorial design and crossover design
2. Sequential parallel comparison design
3. Multiple-stage design
4. Pharmacogenomics study design

TWO SIMULTANEOUS SHORT COURSES THURSDAY AND FRIDAY, DECEMBER 12-13, 2013

Registration includes (1) a hot breakfast and two refreshment breaks each day; (2) handouts and; (3) text(s). No registrations will be accepted without payment in full. We will refund full tuition if courses are canceled due to insufficient registration.

8:30–10:00 Lecture 10:00–10:20 Break 10:20–11:50 Lecture 11:50–1:10 Lunch 1:10–2:40 Lecture 2:40–3:00 Break 3:00–4:30 Lecture

Friday schedule will be a half hour earlier to facilitate students' transportation home

Design and Analysis of Experiments using Generalized Linear Mixed Models 🕮

Professor Walter Stroup, University of Nebraska

Moderator: Alfred Balch

Text: Generalized Linear Mixed Models: Modern Concepts, Methods and Applications

This course surveys generalized linear mixed model (GLMM) concepts and methods for the design and analysis of experiments, focusing on experiments with "mixed model issues" – e.g. various forms of clustering, including repeated measures, split-plot and multi-location studies – in conjunction with "generalized model" issues, i.e. non-Gaussian response variables. On Day One, GLMMs will be introduced as an encompassing family, making the connection among linear models, generalized linear models, linear mixed models, and generalized linear mixed models in terms of model formulation, distributional properties, and approaches to estimation and inference. Differences and similarities among members of the GLMM family will be presented. We discuss overarching issues that confront analysts who work with correlated, non-normal data, such as overdispersion, marginal and conditional models, and model diagnostics. We present GLMMs for common non-normal response variables – count, binomial and multinomial (categorical), time-to-event and continuous proportion – in conjunction with common design formats – block designs, split-plots and repeated measures. Examples are used throughout the day to support the discussion and development.

On Day Two, we focus primarily on GLMM applications and on issues associated with these applications. Additional supporting theory will be introduced as needed. Because different types of non-normal data present particular design challenges, we will present GLMM-based methods that address these issues to improve planning. Focus areas include comparison of pseudo-likelihood/penalized quasi-likelihood, integral approximation and transformation methods, the computation of power and sample size, model selection, and inferential tasks with and without adjustments. Computations are based on the mixed model tools in SAS/STAT, primarily the GLIMMIX procedure. No R examples will be presented, but R packages analogous to SAS GLMM procedures will be noted where relevant. The principles should be applicable to any GLMM-capable software. Attendees should have background in design and analysis of experiments.

1. From Linear to Generalized Linear Mixed Models

A. A General Setting for Statistical Modeling
B. Linear Models and Linear Mixed Models (LM, LMM)
C. Generalized Linear Models (GLM); D. Generalized Linear Mixed Models (GLMM)
E. Other Classes of Models with Random Effects

2. Marginal or Conditional Models

A. Defining a Model from Design Properties; B. Overdispersion and Other Design-Induced Issues
C. G-side (Conditional) and R-side (Marginal) Random Effect Solutions to Issues
D. GEE versus GLMM; E. Distributional Implications

3. Estimation and Inference

A. (Restricted) Maximum Likelihood; B. Quasi-Likelihood/GEE
C. Pseudo-Likelihood; D. Laplace and Quadrature Approximations
E. Estimable and Predictable Functions
F. Inference on Best Linear Unbiased Estimates vs. Best Linear Unbiased Predictors
G. Model-Based and Empirical ("Sandwich") Covariance Estimators

4. Modeling Rates and Proportions

A. Distributions; B. Binomial Proportions; C. Binary Data; D. Multinomial; E. β - Continuous Proportions

5. Modeling Counts

A. Distributions B. Poisson or Negative Binomial C. Modeling with Offsets E. Models for Zero-inflated Data

6. Within-Subject Correlation

A. Repeated Measures/Longitudinal Data Background
B. Review of Repeated Measures Methods for Normally-Distributed Data
C. Extension to Non-Normal Data – Similarities and Differences; D. Model Selection E. Spatial Variation

7. Power, Precision and Sample Size

A. Essential Background B. GLMM vs. Conventional Approaches to Power
B. Power and Sample Size for Continuous, Count, and Binomial Data
C. Comparing Competing Designs using GLMM tools
D. Power & Design Planning for Longitudinal & Spatial Data

Walt Stroup PhD, is Professor and Chair, Statistics Department; University of Nebraska. He has conducted numerous short courses worldwide on mixed and generalized linear models for industry and professional organizations. He is an ASA Fellow and was honored with Product Quality Research Institute's 2009 Excellence in Research award.

Group Sequential and Adaptive Methods in the Design of Clinical Trials 🕮

Professors Chris Jennison, University of Bath & Bruce Turnbull, Cornell University

Moderator: Ivan Chan

Text: Group Sequential Methods with Applications to Clinical Trials

This course will comprise of two halves: In the first we shall review the methods and application of (now) standard group sequential designs. In addition, we shall discuss some of the more recent controversies and developments including: controlling bias when reporting results of a trial with early stopping; reporting of results on co-primary endpoints; and accommodating delayed observations ("pipeline" data) at interim analyses. The second half of the course will discuss adaptive designs and various applications including sample size re-estimation, enrichment designs and Phase II/III seamless designs.

Formal data monitoring procedures are now a standard feature of the design and conduct of long-term clinical trials. A unified formulation of group sequential procedures allows a simple, powerful approach to their implementation with different types of stopping rule and a great variety of endpoints. We shall survey the main ideas of group sequential procedures including: superiority, non-inferiority and equivalence testing; normal, binary, survival, regression and longitudinal endpoints; inference on termination; nuisance parameters; trials with multiple arms or multiple endpoints. More recently, methods have been proposed to allow modification of a trial in mid-course while still protecting the type I error. Possible modifications include enlarging the sample size to increase power, changing the study population (for example, enrichment), modifying the treatment, or reducing the number of treatment arms. These adaptations may follow rigid rules, pre-specified in the protocol; more flexible approaches permit unplanned changes at unplanned interim analyses. We shall describe these procedures in detail and discuss their benefits and limitations. Statistical software will be used to illustrate the methods and examples.

Prerequisites: This course is aimed at Masters level statisticians who have some familiarity with clinical trials but not necessarily with the aspects of sequential monitoring or adaptive trial design.

- Principles of group sequential methods; underpinning theory and computation; the general framework, including normal, binary and survival endpoints.
- Boundaries: efficacy, futility (binding and non-binding); error spending designs; the "pipeline" problem when there is a delayed response.
- Information monitoring and nuisance parameters; estimation and confidence intervals after a sequential trial; stochastic curtailment.
- Multiple endpoints
- From group sequential to adaptive designs: sample size modification to improve power.
- Methodology for adaptive designs: combination tests and testing multiple hypotheses.
- Adaptive enrichment designs: changing the target population.
- Trials with multiple treatments: seamless Phase II/III transition.
- Case studies and discussion: participants will be invited to discuss their experiences in implementing adaptive designs, interacting with regulators or serving on Data and Safety Monitoring Boards.

By the end of the course, participants should be able to

- Assess whether a group sequential or adaptive design is appropriate for a clinical trial.
- Develop a group sequential design with a suitable number of interim analyses and maximum sample size, achieving the desired type I error rate and power.
- Implement a trial using error spending and information monitoring to cope with initially unknown parameters such as response variance or baseline hazard rate.
- Apply combination tests and multiple hypothesis tests as part of an adaptive trial in which observed responses are used to make choices on sample size modification, selecting one of several treatment arms, or focusing on a sub-population.
- Understand the potential benefits of adaptive clinical trials and how to assess these.

Christopher Jennison PhD is Professor of Statistics and former Dean of the Faculty of Science at the University of Bath. His research into the sequential analysis of clinical trials started with his PhD work at Cornell University and he has continued to publish widely on group sequential methods and adaptive designs. His research is informed by applied collaborations and consultancy.

Bruce Turnbull PhD, PStat is Professor and former Chair of Statistical Science at Cornell University. He has extensive publications and over 30 years statistical consulting and collaborative experience in academic, government and industry research. He is on the Data and Safety Monitoring Committees for a number of major national and international clinical trials in the areas of cancer, heart disease, pulmonary disease and AIDS. He is an ASA Fellow.

Please register online as early as possible. Do not mail this form unless absolutely necessary. Payment must accompany this form either by an included check or by a credit card number. Make checks payable to "ASQ NY/NJ Metropolitan Section" and mail to Manoj Patel; 114 Doric Court; Cary, NC 27519. The American Society for Quality (ASQ) is a tax-exempt organization. Federal Tax ID #39-09-12502. RECEIPTS and a CERTIFICATE OF ATTENDANCE will be distributed at the conference.

Surname	First Mr. ❑ Ms. ❑ Mrs. ❑ Dr. ❑ Prof. ❑	
Organization	Address	
City	State	Zip
Phone	FAX	E-mail

Please Indicate Which Tutorial Sessions You Plan to Attend **A ❑ B ❑ C ❑ D ❑ E ❑ F ❑ G ❑ H ❑ I ❑ J ❑ K ❑ L ❑**

Conference Registration	Payment Must Be Made On or Before October 1st	 November 1st	 Later or Onsite	Amount
Three Day Conference	$550	$670	$800	_____
One Day Registration, Monday, Tuesday, or Wednesday (circle 1)	$275	$325	$380	_____
Student (Proof of full time college status needed) or Retiree	$225	$275	$325	_____
One-Hour Registrant Reception with cold drinks and snacks Sunday 6:30 PM	**Free**		**Check box**	❑
Speaker Dinner, Monday 7:00 PM	45	$50	60	_____
Course ❑ Design&Analysis of Experiments Linear Mixed Models	$740	$850	$970	_____
❑ Group Sequential & Adaptive Methods Clinical Trials	$740	$850	$970	_____

Onsite short course registration requires advance e-mail or telephone notification so we can guarantee sufficient space and materials.

Havana Tower Rate: ($65 + 14% Tax + $10 Resort Fee) $84.10 Per Room Per Night

Tropicana Cancellation Policy: 2 Days Prior to Arrival **Lower rates at other websites are for older towers, not the Havana**

Arrival December: _____ Departure December: _____ King? ❑ or 2 Queen Beds? ❑

Rooms Must Be Reserved With this Form or on our Web Site on or Before November 29th to Get the Conference Rate

The 🕮 On The Tutorials And Short Course Titles Indicate That They Are Based On The Below Books

Book Author(s) and Title Onsite availability of books cannot be guaranteed unless you place an order in advance.	# Page	Year	ISBN 13 978-	Price ($) List	 Our	# of Copy	Total ($)
Taylor and Francis							
Cappelleri; Zou; Bushmakin; Alvir; Alemayehu; & Symonds; Patient-Reported Outcomes: Measurement, Implementation and Interpretation	320	2014	1-439-87367-0	100	63		
Chen, Din and Peace, Karl; Clinical Trial Data Analysis Using R	387	2010	1-439-84020-7	90	57		
Chen, Din; Sun, Jianguo; and Peace, Karl; Interval-Censored Time-to-Event Data: Methods & Applications	421	2012	1-466-50425-7	100	63		
Chen, Din and Peace, Karl; Applied Meta-Analysis with R	342	2013	1-46-650599-5	90	57		
Fedorov, Valerii and Leonov, Sergei; Optimal Design for Nonlinear Response Models	404	2013	1-43-982151-0	90	57		
Jennison, Christopher and Turnbull Bruce; Group Sequential Methods with Applications to Clinical Trials	416	1999	0-84-930316-6	120	75		
Stroup, Walter; Generalized Linear Mixed Models: Modern Concepts, Methods and Applications	555	2012	1-43-981512-0	100	63		
Springer							
Albert, Jim; Bayesian Computation with R, Second Edition	299	2009	0-387-92298-0	60	39		
Albert, Jim and Rizzo, Maria; R by Example	359	2012	1-4614-1365-3	65	42		
Sarkar, Deepayan; Lattice	265	2008	0-387-75969-2	80	51		

Total Book Order (Books will be distributed during conference and short course registration) _____

Grand Total of Registration and Book Order _____

E-Mail Cancellations sent to registration@demingconference.com will be accepted until November 16th for a separate $50 fee for both the conference and courses. Afterwards, there will be no refunds but substitution of another registrant is permissible. Book orders cannot be cancelled. If a registrant cancels, his or her ordered books will be mailed.

❑ American Express ❑ Master Card ❑ Visa ❑ Discover Card Number: _____ Expiration Date: _____ Security Code: _____

Card Holder Signature: _____

TRAVEL TO THE CONFERENCE

AIR: Check both Atlantic City (ACY) and Philadelphia (PHL) to search for the best fare and connections. The cheapest quick airport connection to PHL is the Tropiano shuttle, requiring reservations 2 days in advance at 1-800-559-2040. It charges $55 cash (no credit cards) from PHL directly to the Tropicana. A tip is expected. There currently is a $10 jitney from ACY to the Tropicana. The cheapest connection from PHL is the below referenced SEPTA, but this will take more than two hours. One can rent a car (www.bnm.com) but it isn't necessary during one's stay. Also consider discount airlines not on the major search engines such as Spirit, www.spiritair.com (which is the only airline serving ACY); AirTran www.airtran.com, Frontier www.frontierairlines.com, and Southwest, www.southwest.com. These airlines offer the additional advantage that they sell one-way tickets without a premium that is useful if one is using the conference as a stopover. While we don't recommend Newark Airport except as a means of saving money and perhaps travel time on international flights, there is a #67 NJ Transit bus (requiring a change at Toms River) as well as several train service options to Atlantic City, including the one referenced below. This trip would take about three hours as opposed to about ninety minutes if one rented a car.

RAIL: NJ Transit has relatively frequent local (14 daily trips with 6 stops) service to Philadelphia connecting with Amtrak, NJ Transit to NYC, and SEPTA at 30th Street and PATCO at Lindenwold. Free shuttle busses meet all trains and provide direct service to the Tropicana. www.njtransit.com/pdf/rail/R0090.pdf has a schedule that also shows the R1 SEPTA connections from PHL to 30th Street. Direct service from NYC with a stop in Newark is available www.acestrain.com, Friday through Sunday only.

BUS: Call the Tropicana casino bus transportation department, (888) 275-1212 # 1 to find if there is service from your local neighborhood since some of these buses travel as far as 200 miles. Most allow you to return on a different day for a charge or a space available basis. Cost of the trip will be offset by casino cash back rebates and other offers. One may take a bus to any casino, collect their coins and coupons and use a $2.25 jitney on Pacific Avenue to quickly get to the Tropicana. Explore Greyhound, which has open return service with a slot play bonus from 13 cities www.luckystreakbus.com. While there are fewer trips, travel time is less than with a train as there are no transfers.

DRIVING: To get to the Tropicana from the Garden State Parkway, NJ Turnpike or Philadelphia, take the Atlantic City Expressway. Follow the Atlantic City Expressway to Exit 2. This will take you to the Black Horse Pike, Route 40/322, which you will take into Atlantic City. Turn left on Arctic Avenue, the first light over the bridge. Take Arctic Avenue to Brighton Avenue. Turn right on Brighton and cross Atlantic Avenue. The entrance to "The Quarter" Garage (Havana Tower) is on your left, off Atlantic Avenue. Don't park in the Tropicana's other garage, as it is tedious to get to the Havana Tower. We don't recommend valet parking, as this doesn't permit easy access to your car during your stay.

POSTERS: We will have poster session(s) to provide a forum for attendees to present concepts and issues of relevance to their peers. The abstract submission rules and presentation tips are on our website. Accepted abstracts will be posted on our website and in our transactions.

INFO: For maps, an events schedule, casino shows and general tourist info visit the Atlantic City Convention and Visitors Authority website at www.atlanticcitynj.com that has an option for you to request a free visitor packet as well as an opportunity to e-mail questions that are promptly answered. Consider walking to and shopping in the upscale Atlantic City Outlets at the foot of the Atlantic City Expressway or strolling on the Boardwalk to the pier shops at Caesars. Remember there is no sales tax on clothes in NJ.

MEALS: Take the time to explore www.tropicana.net. It contains complete details of the meeting facility and gives descriptions of the 22 restaurants and other attractions. We provide a full hot breakfast on Monday and a continental breakfast on Tuesday and Wednesday before our morning sessions as well as afternoon refreshment breaks. There is a subsidized Speaker Dinner on Monday and a free one-hour reception on Sunday with cold drinks, snacks, and a cash bar where you can meet with fellow attendees.

WALTER YOUNG SCHOLARSHIP: The ASQ Metropolitan Section will award one $4,000 college scholarship to an undergraduate spouse, child, stepchild, or grandchild of a registrant. The application, complete rules, and background information are on the conference website. The application must be submitted after the conference and before April 1, 2013. The award will be announced and paid directly to the applicant on May 15, 2013. The applicant must be accepted or matriculated at an accredited college or university in the United States and have at least a 2.75 grade point average. The Scholarship Committee, whose decision is final, reserves the right to distribute the amount of the scholarship to multiple recipients at their discretion.

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*** Walter R. Young has chaired the Deming Conference for forty-four consecutive years.**