PROGRAMME OF THE SEVENTIETH ANNUAL DEMING CONFERENCE ON APPLIED STATISTICS

Sponsored by
AMERICAN SOCIETY FOR QUALITY
NY/NJ Metropolitan Section ~ ~ Statistics Division
AMERICAN STATISTICAL ASSOCIATION: Biopharmaceutical Section
December 8 – December 10, 2014: Three-Day Conference
Tropicana Casino and Resort, Havana Tower, Atlantic City, NJ

Short Courses: – December 11-12, 2014

1. Patient-Reported Outcomes: Measurement, Implementation and Interpretation Dr. Joseph C. Cappelleri & Mr. Andrew G. Bushmakin Pfizer
2. Applied Predictive Modeling Dr. Kjell Johnson Arbor Analytics

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 7th and will be followed by a one-hour reception with cold drinks and snacks.
It will continue at 7:30 AM Monday December 8th through Wednesday December 10th and 8 AM Thursday December 11th.
ALL REGISTRANTS WILL RECEIVE A BOUND COPY OF THE AVAILABLE HANDOUTS FOR ALL SESSIONS.
RECEIPTS and a CERTIFICATE OF ATTENDANCE will be distributed at the conference. Register and pay for both the conference and the hotel online as early as possible at www.demingconference.com. This gives you an instant email acknowledgement. Only if absolutely necessary, mail a check with your completed registration form on page 7 in this program. If checks aren't postmarked on or before the early discounted registration date, you will be charged the next higher amount. 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 can't be cancelled. If a registrant cancels, his or her ordered books would be mailed.

The Deming Committee is soliciting abstract proposals for posters via email to the registrar. The Poster Presentation forum allows participants to submit their research concepts and issues of relevance for peer review in the area of biostatistics. The Poster session allows attendees to discuss the specifics of an abstract with the author in a small group setting. Accepted poster abstracts will be published on both the website and in the transactions. Submissions will be accepted through Friday, October 31, 2014. Full details are on our website.

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

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. Driving directions are on the last page.

- 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 NJ, with 2,079 rooms, elegant public areas, exclusive retail shops and 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 separate building connected by a bridge.
- A free Trop Advantage Card can offer rewards based on your play and may offer dining and shows discounts.

David Burt (PhD in Statistics from Virginia Polytechnic Institute and State University) has used simulation techniques to evaluate the properties of automatic bandwidth selection procedures in his dissertation work and has experience with PK/PD modeling and simulation as well as clinical trial simulation in the pharmaceutical industry. His other interests include Bayesian predictive methods using network meta-analyses and adaptive clinical trials.

Claudio Carini MD, PhD, FRCPath has more than 20 years experience in all stages of biomedical research from bench experimentation to clinical research. He is board certified in Internal Medicine, Pathology, Respiratory Medicine, and Clinical Immunology. He is serving at Pfizer as Global Clinical Immunology and Biomarkers Lead being responsible for the Immunology/Biomarkers strategy for the entire Biosimilars portfolio and other projects and holds an Honorary Faculty Position at King's College, London. In addition, he serves on several national and international scientific boards. He has over 200 publications in national and international peer reviewed journals.

Brad Carlin (PhD in Statistics from the University of Connecticut) is Mayo Professor of Public Health, and Professor and Head of Biostatistics in the School of Public Health at the University of Minnesota. In addition to his three textbooks, he is author of over 150 papers in refereed books and journals. He was the 2000 winner of the American Public Health Association's Mortimer Spiegelman Award, and served for three years as editor-in-chief of *Bayesian Analysis*, the official journal of the International Society for Bayesian Analysis (ISBA). He has won both teaching and mentoring awards from the University of Minnesota.

Mark Chang is Vice President, Biometrics; AMAG. Previously, he held various positions in Millennium Pharmaceuticals. He is a co-founder of the International Society for Biopharmaceutical Statistics, was an executive member of the ASA Biopharmaceutical Section, and a member of the Expert Panel for the Networks of Centres of Excellence (NCE), Canada. He is a co-chair of the Biotechnology Industry Organization (BIO) Adaptive Design Working Group. He has many publications including five books. He has taught over ten statistical short courses. He is an adjunct professor of Boston University and 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 100-refereed professional publications and co-authored five books in biostatistics.

Joshua Chen (PhD in Statistics from University of Wisconsin @ Madison) is the Global Head, Biostatistics and Programming at Sanofi Pasteur. Prior to that, he worked in Late Development Statistics at Merck Research Laboratories. His experience has spanned many therapeutic areas with focus on HIV antivirals and human vaccines. He has extensive experience in study design, conduct and reporting of international clinical trials from proof-of-concept through regulatory approvals and life cycle management. He has published 30+ papers in peer-reviewed clinical and statistical journals. His primary research interest is clinical trial designs, including group sequential methods, adaptive designs and multiregional clinical trials (MRCTs). He was a co-lead of the across-industry MRCT Consistency Working Group under PhRMA (2008-2011) and Society for Clinical Trials (2012-2014).

Christy Chuang-Stein is Vice President, Head of Statistical Research and Consulting Center She has supported multiple drug development programs and participated in the filings of multiple new drug applications. She has experience in infectious diseases, central nervous system, cardiovascular diseases, and women health areas. She is an ASA Fellow and was a vice president in 2009-2011 and received their Founders Award in 2012. She has 138 publications in peer-reviewed journals and book chapters, including two books. Her current research interests include adaptive design, non-inferiority trial, subgroup analysis, quantitative decision making in drug development, multi-regional trials, multiple co-primary endpoints, safety analysis, benefit/risk assessment and cost-effectiveness analysis.

Greg Cicconetti (PhD in Statistics from University of Connecticut) was an Assistant Professor of Statistics at Muhlenberg College before joining GlaxoSmithKline in 2005. In his published research, he used simulation to study point and interval estimation problems following sequential sampling. At GlaxoSmithKline, he has used simulation extensively in support of the design, monitoring, and analysis of clinical trials. He has experience working in the cardiovascular, osteoporosis, osteoarthritis therapeutic areas. His other interests include graphics and statistical learning.

Chen Hu (PhD in Biostatistics from the University of Michigan) is the lead biostatistician of the Lung Cancer Committee, NRG Oncology, an integrated entity of three legacy National Cancer Institute-sponsored multi-center cancer clinical trials groups (NSABP, RTOG and GOG). He is also an adjunct faculty member at Center for Clinical Epidemiology and Biostatistics, University of Pennsylvania School of Medicine. He has broad methodological research interests including clinical trial design, competing risks analysis, event history analysis, semi-parametric regression models for time-to-event data, missing data analysis, and surrogacy evaluation. He has been actively publishing in the Journal of Clinical Oncology, Proceedings of National Academy of Sciences, Biostatistics, and Lifetime Data Analysis.

Ilya Lipkovich (PhD in Statistics from Virginia Tech) is Senior Director at Center for Statistics in Drug Development at Quintiles Innovation. He has 17 years of statistical consulting experience working in various areas including econometrics, manufacturing and quality control, and pharmaceutical industry. His research interests include clustering, predictive modeling and subgroup identification in clinical data using recursive partitioning, missing data and multiple imputation, and causal inference for observational data including marginal structural models and propensity-based estimation. He is a co-developer of novel subgroup identification methods (SIDES and SIDEScreen) and chairs the QSPI Subgroup Analysis Working Group sponsored by the Society of Clinical Trials.

Erica Moodie (PhD in Biostatistics from the University of Washington) is an Associate Professor of Biostatistics in the Department of Epidemiology, Biostatistics, and Occupational Health at McGill University. Her main research interests are in causal inference and longitudinal data with a focus on methods for HIV research. She is an Associate Editor of Biometrics and the Journal of the American Statistical Association. She is the recipient of a Natural Sciences and Engineering Research Council University Faculty Award and a Chercheur-Boursier junior 2 career award from the Fonds de recherche du Quebec-Sante (FRQ-S).

Daniel Scharfstein (ScD in Biostatistics from the Harvard School of Public Health) is Professor of Biostatistics at the Johns Hopkins Bloomberg School of Public Health. His research is focused on how to report results of randomized trials with informative missing or censored data and of observational studies with non-random treatment assignment. He recently served on the National Academy panel, which issued the report The Prevention and Treatment of Missing Data in Clinical Trials. He is the principal biostatistician of the METRC Consortium, which is funded by the Department of Defense to conduct multicenter research relevant to the treatment and outcomes of orthopedic trauma sustained in the military. He is president of Saphire Consulting, Inc., which provides expertise on the design, analysis and monitoring of randomized and observational studies. He is an ASA Fellow and received the 1999 George W Snedecor Award for Best Paper in Biometry. In 2010, he was awarded the Distinguished Alumni Award from the Department of Biostatistics at the Harvard School of Public Health.

Noah Simon (PhD in Statistics from Stanford University) is an Assistant Professor in the Department of Biostatistics at the University of Washington. He works on problems at the intersection of statistics, biology and computer science, developing algorithms to build scientific knowledge from modern high-throughput technologies. His interests include high dimensional modeling and inference, selection-bias in high-throughput experiments, biomarker development, and adaptive clinical trial design. He was a Weiland Fellow and currently holds the Genentech Endowed Professorship in Biostatistics at the University of Washington.

Richard Simon (PhD in Applied Mathematics and Computer Science from Washington University in St. Louis Missouri) is Chief of the Biometric Research Branch of the NCI where he is chief statistician for the Division of Cancer Diagnosis & Treatment. He established the Molecular Statistics & Bioinformatics Section of the NCI, a multi-disciplinary group of scientists developing and applying methods for the application of genomics to cancer therapeutics. He is the architect of BRB-ArrayTools software for the analysis of microarray expression and copy number data; with over 13,000 registered users in 65 countries it has been cited in over 1500 publications. In recent years he has been involved in development of clinical trial designs for the development of new drugs and companion diagnostics.

Edward Vonesh (PhD in biostatistics from the University of Michigan) is Professor in Preventive Medicine-Biostatistics in the Department of Preventive Medicine at Northwestern University and Managing Member of Vonesh Statistical Consulting, LLC. His research interests are in longitudinal data analysis and in the theory and application of generalized linear and nonlinear models for correlated data including both marginal and mixed-effects models. He has written two books on linear and nonlinear models for correlated data.

Xiao-Hua (Andrew) Zhou (PhD in Statistics from Ohio State University) is Professor in the Department of Biostatistics and Associate Director of National Alzheimer's Coordinating Center at University of Washington. He is also Director of Biostatistics Unit and Research Career Scientist in of the VA Seattle Medical Center and President of the VA Statisticians' Association. He was elected to the International Statistical Institute in 1999 and an ASA Fellow in 2004. He served as Chairs of the ASA's Section on Statistics in Epidemiology and the Health Policy Statistics Section. He is currently Chair of the Mental Health Statistics Section of the ASA and a voting member of Radiological Health Advisory Committee of the FDA. In 2007, he received a Research Career Scientist Award from the VA. He has published over 190 refereed papers. He is an Associate editor for Statistics in Medicine. His research has focused on the statistical methods for diagnostic medicine and health services research, and causal inference.

Monday December 8, 2014 8:30 – 11:30 AM

Session A

Global Sensitivity Analysis of Randomized Trials with Missing Data: Recent Advances

Prof. Daniel Scharfstein, Johns Hopkins University

Moderator: Ivan Chan

In 2010, the National Research Council issued the report: "The Prevention and Treatment of Missing Data in Clinical Trials." This report, commissioned by the FDA, provides 18 recommendations. Since inference in the presence of missing data requires untestable assumptions, Recommendation 15 states: "Sensitivity analyses should be part of the primary reporting of findings from clinical trials. Examining sensitivity to the assumptions about the missing data mechanism should be a mandatory component of reporting."

Broadly speaking, there are three main types of sensitivity analysis. Ad-hoc sensitivity analysis involves analyzing the data using a few different methods and evaluating whether the inferences are consistent. Local sensitivity analysis evaluates how inferences vary in a small neighborhood of a benchmark identification assumption, such as missing at random. Chapter 5 of the report emphasizes global sensitivity analysis, which considers how inferences vary over a much larger neighborhood of identification assumptions.

We present a global sensitivity analysis methodology for drawing inference about the mean at the final scheduled visit in a repeated measures study with dropout. A recently developed semi-parametric approach and associated freely available, open source software (available at www.missingdatamatters.org) is discussed. We present a detailed case study to illustrate the methodology.

Session B 🕮

Generalized Nonlinear Models for Correlated Response Data: Overcoming Apparent Limitations in SAS®

Professor Edward Vonesh, Northwestern University

Moderator: Wenjin Wang

Correlated response data, either discrete (nominal, ordinal, counts), continuous or a combination thereof, occur in numerous disciplines and more often than not, require the use of statistical models that are nonlinear in the parameters of interest. In this tutorial we briefly describe the different types of correlated response data one encounters in practice as well as the types of models used to analyze such data. Such models include generalized linear models and generalized nonlinear models both of which can be further classified according to whether they are marginal or mixed-effects models. The course's focus will be on illustrating how one can overcome apparent modeling limitations within SAS®. Specifically, we will show through a number of applications how to 1) conduct likelihood-based inference for nonlinear mixed-effects models with intra-subject correlation; 2) fit nonlinear mixed-effects models to data assuming non-Gaussian random effects; and 3) fit marginal generalized linear models to correlated response data using second order generalized estimating equations or maximum likelihood estimation. In each case, standard SAS® procedures such as GLIMMIX and NLMIXED are used so that one can easily adapt these techniques to other applications.

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

1:00 - 4:00 PM

Session C

Statistical Simulation In Drug Development

Drs. David Burt & Greg Cicconetti GSK

Moderator: Kalyan Ghosh

Simulation methods have become an increasingly important tool in the search for more efficient clinical trial designs and/or statistical analysis procedures. During our short course we will provide a road map to developing and executing a successful simulation plan and communicating these results with a broader team. We will begin with a survey of problems one might encounter during the design, monitoring and analysis stages of a clinical trial for which a simulation study may provide some insight. We continue with an introduction to standard methods for generating random data. This discussion will include methods to mimic real-world data that do not adhere to standard statistical distributions, methods to introduce correlation among endpoints, parametric and non-parametric bootstrapping techniques, a brief introduction to importance sampling and rejection sampling and the use of sparse historical data to simulate future data. Having established this foundation, we return to some of our motivating problems and discuss their simulation-based solutions in greater depth. This deeper dive will include various approaches to enrollment modeling, simulating data to mimic a cross-over study, simulating data to explore the robustness of an efficacy endpoint to missing data in an outcomes trial and the evaluation of competing statistical methodologies for specific applications. Though some R and SAS® code will be provided to supplement this tutorial, the emphasis will not be on code or syntax.

Session D

Subgroup Analysis In Clinical Trials

Exploratory Subgroup Analysis in Clinical Trials

Dr. Ilya Lipkovich (Center for Statistics in Drug Development) Quintiles

Moderator: Ivan Chan

Vast literature has been generated in medical and statistical journals over the last 15 years concerning exploratory subgroup analysis methodology and the assessment of validity/credibility of subgroup analysis methods for clinical trial data. We see a shift from presenting checklists of "good practices" for subgroup analysis to developing more aggressive subgroup identification and biomarker discovery strategies under the umbrella of "personalized medicine/tailored therapeutics". This tutorial will present and discuss methods of exploratory analysis that can be applied in late-phase clinical trials to identify promising biomarkers and subgroups that can be validated using independent historical data or future studies. The discussion of exploratory subgroup analysis methods begins with a detailed review of recent approaches to subgroup identification in the context of personalized medicine and then focuses on the SIDES method (Subgroup Identification based on Differential Effect Search) introduced in Lipkovich et al. (2011), Lipkovich and Dmitrienko (2014).

SIDES is based on recursive partitioning and can be used in prospective and retrospective subgroup analysis. Key elements of SIDES will be discussed, including (1) generation of multiple promising subgroups based on different splitting criteria, (2) choice of optimal values of complexity parameters via cross-validation, (3) evaluation of variable importance and using variable importance indices for pre-screening covariates, and (4) addressing Type I error rate inflation using a resampling-based method. Case studies will be used to illustrate the principles and statistical methodology. Software tools for implementing subgroup analysis methods in clinical trials will be presented, including the SIDES package developed by the authors.

Upon completion of this short course, participants should be able to:

- Define statistical methods for analyzing subgroup effects in exploratory settings and describe their properties.
- Identify the factors to consider in selecting appropriate statistical methods for exploratory subgroup analysis.
- Apply the statistical methods discussed in the tutorial using statistical software (Excel and R).

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

Tuesday December 9, 2014 8:30 – 11:30 AM

Session E

Choosing Appropriate Metrics to Enable Sound Decision Making at Different Stages of Drug Development

Dr. Christy Chuang-Stein Pfizer

Moderator: Naitee Ting

Drug development is a continuous process with many stages. There are many decision points along this development continuum. Sound decisions begin with asking the right questions and choosing appropriate metrics to help set up the decision framework. In this tutorial, we will look at metrics that address the unique needs at various stage gates such as proof of concept, dose-response relationship, transition to late stage development and the decision to file for marketing authorization. We will illustrate how existing information should be used to construct the metrics at these stage gates and to help develop the decision criteria. Prior information and the go/no go criteria have important implications in designing subsequent trials that, together with earlier trials, form the evidential basis for product approval. We will also illustrate why early observed treatment efficacy often represents an inflation of the true treatment efficacy and should be discounted when used to estimate the true treatment efficacy. We will discuss sources of the inflation and recommend possible approaches to discount the observed treatment efficacy when using it to design future trials or to project product efficacy in the market place. The interplay between decision criteria and design features will jointly determine the operating characteristic of the design and the quality of our decisions. We will use examples to illustrate these points.

Session F 🕮

Competing Risks in Cancer Clinical Trials

Prof. Din Chen University of Rochester & Dr. Chen Hu American College of Radiology

Moderator: Walter R Young

A brief summary of the book aimed to honor the contributions of the Deming conference in clinical trials and biopharmaceutical industries for the last decades by compiling the cutting-edge developments in biostatistical methodologies in clinical trials and biopharmaceutical applications will be given. This will be followed by the fundamental concepts and practical applications of competing risks, with a highlight of the theoretical and practical distinctions between commonly used statistical analysis methods, and how to choosing appropriate methods to address specific research questions in Chapter 10. The impacts on study design in presence of competing risks, such as sample size calculation, type I error and power, are reviewed. Software implementations of competing risks methods using SAS® and R software are illustrated accordingly. This will be a well-balanced mix of theoretical results and implications in applications, with recommendations and case studies for real oncology clinical trials. An elementary knowledge of survival analysis will be a plus but not required.

1. Why and when to consider competing risks in cancer clinical trials
2. How to formulate competing risks in clinical trial biostatistics
3. Statistical methods for estimation and inference
4. Distinctions and relationship between "competing" methods
5. Impacts on study design
6. Case studies in cancer clinical trials
7. Computations and software implementations

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

1:00 - 4:00 PM

Session G

Developing Prognostic and Predictive Biomarkers with High Dimensional Data

Drs. Richard Simon & Noah Simon University of Washington

Moderator: Alfred Balch

Modern medicine has graduated from broad-spectrum treatments to targeted therapeutics. Continuing advances in high throughput biotechnology make it increasingly feasible to use whole genome assays to develop biomarkers for use in targeting therapies. Specialized methodology must be used for such development because the number of candidate features is generally much greater than the number of patients and because the problem is one of classification, prediction and decision, not hypothesis testing. The goal of this short course will be to discuss methodology for the development of predictive models that are actionable for aiding treatment selection using high dimensional data such as gene expression profiles, exome sequence based mutation data or metabolomics profiles. Penalized regression methods as well as probabilistic and machine learning classifiers will be covered. We will discuss the application of resampling methods for evaluating the accuracy of such models for predicting outcome, informing treatment decisions and for partitioning the patients based on relative treatment benefit involving non-standard applications of resampling methods. The course will provide hands-on experience with tools for building predictive biomarker models using real, high-dimensional datasets with a variety of endpoints including binary and censored survival. Issues of multiplicity, and selection bias and relationship to modeling to clinical trials will be discussed. Participants will gain experience applying these methods in R.

Session H

Multi-Regional Clinical Trials: Issues and Methods

Dr. Joshua Chen Sanofi Pasteur

Moderator: Naitee Ting

In recent years, many biopharmaceutical companies are moving toward global simultaneous development and registration of new drugs/vaccines across the world. Global clinical development strategy utilizing multi-regional clinical trials (MRCTs) plays a crucial role to ensure the success of such an approach. MRCTs are most often conducted as a single trial focusing on the overall results, but when such trials are submitted to health authorities, the scope and concern often broaden to include the "local" results. Although it comes with great opportunities, there are also tremendous challenges in the design, conduct and interpretation of MRCTs. This tutorial will introduce the statistician to these issues, and describe methods to help handle such issues. Topics to be covered include specific MRCT concerns at the design stage, including simultaneous global development strategy vs bridging strategy, methods for assessing consistency of treatment effect across regions and sample size planning. Monitoring the regional difference in an ongoing MRCT and additional methods involving adaptive designs will be described. Both fixed and random effect models and Bayesian methods will be discussed with application to the MRCT setting. Analysis and interpretation will be discussed including graphics and methodology to evaluate consistency of effect. Case studies will be presented and the methods introduced will be applied to those case studies.

Student Scholar and Attendee Poster Session Moderator: Nandita Biswas

Convolutional Autoregressive Model for Functional Time Series and Its Applications by Xialu Liu & Rong Chen; Rutgers University

A Decision Theoretic Approach to Multiple Testing of Grouped Hypotheses by Yanping Liu, Sanat K Sarkar & Zhigen Zhao; Temple University

Combining Propensity Scores, Regression, & Matching for Robust Estimation of Treatment Effects by Edward Kennedy; University of Pennsylvania

Instrumental Variables Estimation with Some Invalid Instruments & its Application to Mendelian Randomization by Hyunseung Kang, Anru Zhang, T Tony Cai & Dylan S Small; Wharton School; University of Pennsylvania

Wednesday December 10, 2014 8:30 – 11:30 AM

Session I 🕮

Statistical Methods in Diagnostic Medicine
Professor Andrew Zhou, University of Washington
Moderator: Kalyan Ghosh.

Diagnostic medicine is the process of identifying the disease, or condition that a patient has, and ruling out conditions that the patient does not have, through assessment of the patient's signs, symptoms, and results of various diagnostic tests. Diagnostic. Diagnostic accuracy studies are research studies that examine the ability of diagnostic tests to discriminate between patients with and without the condition.

Diagnostic test studies are conducted to tell us how diagnostic tests perform and, thus, how they should be interpreted. Diagnostic testing plays an important role in medical care and contributes significantly to health care costs, yet the quality of many studies of diagnostic tests has been poor. There is no question that studies of the accuracy of diagnostic tests are challenging to design; they also require specialized statistical methods for their analysis.

In the tutorial we will present and illustrate concepts and methods for designing, analyzing, interpreting, and reporting studies of diagnostic test accuracy. Specifically, we will define various measures of diagnostic accuracy, describe strategies for designing diagnostic accuracy studies. We will then present the basic statistical methods for estimating and comparing test accuracy. Finally, we will present more advanced statistical methods for estimating test's accuracy when accuracy is affected by patient characteristics, for correcting for verification bias and imperfect gold standards. We will illustrate applications of these methods in real-world examples.

Session J 🕮

Bayesian Evidence Synthesis and Network Meta-Analysis
Professor Brad Carlin University of Minnesota
Moderator: Xiaoming Li

As the era of "big data" arrives in full force for health care and pharmaceutical development, researchers in these areas must turn to increasingly sophisticated statistical tools for their proper analysis. Bayesian statistical methods, while dating in principle to the publication of Bayes' Rule in 1763, have only recently begun to see widespread practical application due to advances in computation and software. This tutorial will provide an overview of Bayesian statistical methods and computation, and then explore their use in evidence synthesis and network meta-analysis (NMA), especially with regard to drug safety. We will demonstrate methods via case examples and discuss the impact of utilizing these approaches throughout pharmaceutical development. Broad application of these methods has been driven by an increased need for quantitative health technology assessment (HTA), especially comparative effectiveness research (CER). In particular, Bayesian methods facilitate borrowing of strength across treatments, trials, and outcomes (say, both safety and efficacy), as well as provide a natural framework for filling in missing data values that respect the underlying correlation structure in the data. This tutorial will focus on principles and understanding of critical assumptions, while still indicating where interested users can obtain corresponding technical details. It has the following objectives:

- Present the key concepts of Bayesian statistical methods, computation, and software
- Discuss the use of Bayesian evidence synthesis techniques when applied to network (multiple treatment) meta-analysis for drug safety and efficacy
- Identify how compounds fare statistically in relation to others, and adjusting for key confounders
- Compare "contrast-based" and "arm-based" NMA methods, as well as approaches that use aggregate versus individual-level patient data, and handle mixed outcome types (say, both binary and continuous)
- Mention how these methods may be used in conjunction with adaptive clinical trial designs and how inconsistency between direct and indirect evidence can be diagnosed and remedied.

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

1:00 - 4:00 PM

Session K 🕮

Clinical and Statistical Considerations in Personalized Medicine
Drs. Mark Chang AMAG Pharmaceutical Inc. & Claudio Carini Pfizer
Moderator: Xiaoming Li

A new strategy is needed for the development of validated biomarkers (BMs), which will assist in optimal decision-making process during pre-clinical phase in drug development as well as in effective execution of personalized medicine in different clinical phases across complex disease areas. A systems biology approach that views biology as an information science to examine biological systems as a whole and their interactions with the environment is certainly one way to approach for the discovery and development of BMs that can address these needs. This approach has particular power in the search for network-based informative BMs of diseases and treatment as well as BMs for selection of right patients, who will likely respond to a specific treatment. Recent advances in multiple omics technologies including epigenetics, genomics, transcriptomics, proteomics, cytometry, metabolomics, microbiome and imaging with the help of bioinformatics and biostatistics have improved the discovery and development of robust BMs for complex chronic diseases. However, a consistent framework for the validation, acceptance and qualification of BMs for regulatory use is still required to promote innovative research and application of BMs in preclinical and clinical phase of drug development.

In additional to clinical aspects, the second part of the talk will be on the statistical aspects. We will discuss the biomarker utilities in the adaptive design settings, including biomarker enrichment design, biomarker-informed adaptive design with single-level and hierarchical biomarker models. These models will be compared with the classic Dunnett procedure, drop-loser and add-arm designs for dose-finding trials. Examples and simulation programs in SAS and R will be provided. By attending this session, we hope the audients will learn some recent developments in biomarker study from both clinical and statistical aspects and share their experiences and practical problems concerning the biomarker utility in drug development.

Session L 🕮

Statistical Methods for Dynamic Treatment Regimes
Professor Erica Moodie McGill University, Montreal
Moderator: Alfred Balch

Effective treatment of chronic disorders such as mental illnesses, cancer, and HIV infection typically requires ongoing interventions where clinicians make repeated (sequential) therapeutic decisions, adapting the type, dosage and timing of treatment according to evolving patient characteristics. Dynamic treatment regimes (DTRs) operationalize this sequential decision-making process, and can be viewed as decision support systems for clinicians. Constructing data-driven DTRs from longitudinal observational data or sequential multiple-assignment randomized trials (SMARTs) comprise a cutting-edge area of biostatistical research.

In this tutorial, we will provide an overview of the area, beginning with a discussion of relevant data sources for constructing DTRs and design of efficient studies to produce such data. We will then turn our attention to estimation using a method called Q-learning that was originally developed in the computer science literature but later adapted to statistics; continuous, discrete, time-to-event, and composite outcome types will be covered within the Q-learning framework. Next, we will discuss inferential challenges and solutions. We will demonstrate estimation of optimal DTRs using Q-learning and associated inference using the R package 'qLearn'. Prerequisites for the course are a thorough grasp of regression analysis and familiarity with elementary linear algebra and basic large-sample theory. Demonstrations will be performed using the R computing environment.

TWO SIMULTANEOUS SHORT COURSES THURSDAY AND FRIDAY, DECEMBER 11-12, 2014

Registration includes (1) a hot breakfast and two refreshment breaks each day; (2) handouts and (3) the text. 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

Patient-Reported Outcomes: Measurement, Implementation and Interpretation

Dr. Joseph C. Cappelleri & Mr. Andrew G. Bushmakin Pfizer

Moderator: Ivan Chan

Text: Patient-Reported Outcomes: Measurement, Implementation and Interpretation

This short course 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 and 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 mainly through real-life examples and also through simulated examples using SAS®.

Day 1 Topics:

- Introduction – perspectives and clinical research
- Development of a Patient-Reported Outcome – item generation and wording
- Validity – content and construct validity
- Reliability – intraclass correlation coefficient, kappa, Cronbach's alpha
- Exploratory and Confirmatory Factor Analysis – models and concepts
- Classical Test Theory & Item Response Theory – assumptions, item characteristics curve, item information, item fit

Day 2 Topics:

- Cross-sectional analysis – types of data, descriptive and regression analysis
- Longitudinal Analysis – repeated measures model, random coefficient model
- Mediation Models – single mediator models, model invariance, multiple mediators
- Missing Data – study design, patterns, mechanism, models
- Enriching Interpretation – anchor-based, distribution-based, multiple testing

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

- Understand key aspects of PRO methodology, including exploratory and confirmatory factor analysis, item response theory, cross-sectional analysis, longitudinal analysis, mediation models
- Highlight practices and advances in the assessment of instrument development, reliability, validity, missing data, and multiple testing
- Explain how to enhance the interpretation of scores from PRO measures
- Illustrate concepts with real-world applications
- Value the learning experience by appreciating practical examples with simulated data and analytic implementations using SAS®
- Be aware of relevant references

Joseph C. Cappelleri earned his MS in Statistics from the City University of New York (Baruch College), PhD in Psychometrics from Cornell University, and his MPH in Epidemiology from Harvard University. He is a Senior Director of Statistics at Pfizer Inc. and Fellow of the American Statistical Association. He has delivered numerous conference presentations and published extensively on clinical and methodological topics, including regression-discontinuity designs, meta-analysis, and health measurement scales.

Andrew G. Bushmakin earned his MS in Applied Mathematics and Physics from the National Research Nuclear University (former Moscow Engineering Physics Institute, Moscow, Russia). He has more than 20 years of experience in mathematical modeling and data analysis. He is an Associate Director of Statistics at Pfizer Inc. He has coauthored numerous articles and presentations on topics ranging from mathematical modeling of neutron physics processes to patient-reported outcomes.

Applied Predictive Modeling

Dr. Kjell Johnson Arbor Analytics

Moderator: Alfred Balch

Text: Applied Predictive Modeling

As data has become more readily available, organizations desire to harness potentially predictive information within the data to their benefit. Uncovering predictive patterns requires the appropriate tools and processes to ensure that the patterns are relevant and valid for generating predictions on other "out of sample" or future data. This course will provide an introduction to the foundations of model building, as well as an understanding of a number of traditional and modern predictive models. It is specifically designed for statisticians and practitioners who desire to extend their expertise in this area. Also, the course illustrates the predictive modeling process using examples from real data.

Day 1: Part 1: Foundations and basics of regression (3 hours)

- Introduction: Review of necessary terminology and an overview of examples
  - The importance understanding problem context: predictive modeling efforts must be paired with subject matter expertise
  - We can't always get what we want: model complexity comes at the cost of interpreting model results.
  - Watch out for pitfalls! Inadequate data pre-processing, inadequate model validation, and unjustified extrapolation lead to erroneous decisions.
- Data Pre-Processing: Why pre-process? The need for data transformations, filtering, and dimension reduction
- Model Tuning: Approaches to splitting data for the purpose of selecting optimal tuning parameters
- How to measure model performance for regression problems
- A survey of the varieties of predictive models

Part 2: Modern regression techniques and pitfalls to avoid

- Linear regression techniques (partial least squares and penalized methods)
- Nonlinear regression techniques (multivariate adaptive regression splines, support vector machines)
- Tree-based techniques (CART, boosted trees)
- A few more pitfalls to avoid: inclusion of non-informative data, and effects of measurement error in the predictors and the response

Day 2: Part 3: Modern classification techniques (3 hours)

- How to measure model performance for classification problems
- New techniques and extensions to regression techniques:
  - Linear techniques (partial least squares)
  - Nonlinear regression techniques (support vector machines, naïve Bayes)
  - Tree-based techniques (CART, boosted trees)

Part 4: Practical issues in many predictive modeling problems (3 hours)

- Which models are best? Choosing the final model or set of models
- Extracting interpretation from some black-box models
- How to conduct feature selection without over-fitting to the training data
- How to approach problems with severe class imbalance (i.e. 90+% of samples in one class)

Time permitting: a start-to-finish example of the predictive modeling process and an explanation of the thought process at each stage

Kjell Johnson, PhD, has over 15 years of statistical consulting and predictive modeling experience in pharmaceutical R&D and other industries. He is co-founder of Arbor Analytics, a firm specializing in predictive modeling, and is a former Director of Statistics at Pfizer R&D. He has taught numerous short-courses, and has collaborated on many publications. He is a contributor to CRAN and is a co-author for the ada package for stochastic boosting.

Payment must accompany this form either by a check (payable to "ASQ NY/NJ Metropolitan Section" & mail to Manoj Patel; 114 Doric Court; Cary, NC 27519) or by a credit card. The ASQ is a tax-exempt organization. Federal Tax ID #39-09-12502.

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Conference Registration	Payment Must Be Made On or Before October 1st	November 1st	December 1st	Onsite	Amount
Three Day Conference	$550	$670	$800	$850	_____
One Day Registration Circle Mon, Tue, or Wed	$275	$325	$380	$430	_____
Student (Full time status proof needed) or Retiree	$225	$275	$325	$375	_____
1-Hour Sunday Reception with cold drinks & snacks	**Free**			**√ Box**	❑
Speaker Dinner, Monday 7:00 PM	$45	$50	$60	$60	_____
Courses ❑ Patient-Reported Outcomes	$740	$850	$970	$1,020	_____
❑ Applied Predictive Modeling	$740	$850	$970	$1,020	_____

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

Havana Tower Rate: **($62+ 14% Tax + $10 Resort Fee) $80.68/Room/ Night. Only short course attendees can register for Friday 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

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 ($) List	Price ($) Our	# of Copy	Total ($)
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Vonesh EF; **Generalized Linear and Nonlinear Models for Correlated Data: Theory and Applications Using SAS®**	548	2012	1-59994-647-4	90	57		
Springer							
Chakraborty B & Moodie EEM; Statistical Methods for Dynamic Treatment Regimes	204	2013	1-4614-7427-2	70	45		
Chang M; Modern Issues and Methods in Biostatistics	307	2011	1-4419-9841-5	109	68		
Kuhn M & Johnson K; Applied Predictive Modeling	600	2013	1-4614-6848-6	90	57		
Taylor and Francis							
Berry SM, Carlin BP, Lee JJ & Muller P; Bayesian Adaptive Methods for Clinical Trials	323	2010	1-4398-2548-8	105	66		
Cappelleri, Zou, Bushmakin, Alvir, Alemayehu & Symonds; Patient-Reported Outcomes: Measurement, Implementation and Interpretation	351	2013	1-4398-7367-0	100	63		
Carini C, Menon SM & Chang M; Clinical and Statistical Considerations in Personalized Medicine	358	2014	1-4665-9386-2	90	57		
Carlin BP & Louis TA; Bayesian Methods for Data Analysis 3rd Ed.	552	2008	1-5848-8697-6	80	51		
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Chang M; Adaptive Design Theory and Implementation using SAS® and R 2nd Ed.	700	2014	1-5848-8962-5	105	66		
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Chen D-G, Sun J & Peace KE; Interval-Censored Time-to-Event Data: Methods and Applications	421	2012	1-4665-0425-7	105	66		
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Chow S-C & Chang M; Adaptive Design Methods in Clinical Trials 2nd Ed.	374	2011	1-4398-3987-4	94	59		
Young WR & Chen D-G; Clinical Trial Biostatistics and Biopharmaceutical Applications	616	2014	1-4822-1218-1	120	75		
Wiley							
Bleavins MR, Carini C, Jurima-Romet M & Rahbari R; Biomarkers in Drug Development: A Handbook of Practice, Application and Strategy	800	2010	0-470-16927-8	192	112		
Chang M; Classical and Adaptive Clinical Trial Designs Using ExpDesign Studio	260	2008	0-470-27612-9	145	86		
Zhou X-H, Obuchowski NA & McClish DK; Statistical Methods in Diagnostic Medicine 2nd Ed.	592	2011	0-470-18314-4	130	77		
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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 besides United that has one daily nonstop round trip to its hubs at Houston and Chicago); 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 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 it has fewer trips, travel is easier than with the 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. Self or valet (doesn't permit easy access to your car during your stay) parking is $10 per stay for hotel guests with unlimited in and out privileges. Don't park in the Tropicana's other garage, as it is tedious to get to the Havana Tower.

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, 2015. The award will be announced and paid directly to the applicant on May 15, 2015. 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-five consecutive years.**