



INTERNATIONAL CHINESE STATISTICAL ASSOCIATION

泛華統計協會

Short Courses

Two full-day short courses and four half-day short courses will be offered on Sunday, June 20.

Course 1 (Full Day): Recent Developments in Practical Bayesian Methods for Clinical Trials

Instructor: Dr. Peter F. Thall (rex@mdanderson.org), M.D. Anderson Cancer Center

Abstract: This one-day short course will cover a variety of practical Bayesian methods for clinical trial design and conduct. Some frequentist methods also will be discussed. The course will include numerous illustrations from actual clinical trials. Emphasis will be on newer methods that I have developed with colleagues in recent years. *As time permits*, the topics will include (1) designs that deal with multiplicities and heterogeneity in early phase trials, including individualized dose-finding in phase I/II, (2) using elicited utilities as a basis for trial design and conduct, (3) monitoring multiple outcomes, monitoring possibly right-censored event times and accounting for patient heterogeneity in phase II trials, (4) a method for computing the effective sample size of a parametric prior, including both standard Bayesian models and conditionally independent hierarchical models, (5) a phase III group sequential design that uses Bayesian model selection and controls overall frequentist error probabilities (6) designs to evaluate and compare multi-stage dynamic treatment regimes, rather than individual treatments, (7) geometric methods for settings with two-dimensional parameters, including a cord blood cell transplantation trial and a phase II-III trial of chemotherapies for pediatric brain tumors, (8) a phase II-III design of prophylactic agents for atrial fibrillation following lung surgery that accounts for patient heterogeneity and (9) adaptive randomization. Many of the illustrative applications will include examples of prior elicitation and calibration, incorporating historical data, and using computer simulation to establish a design's frequentist properties. Attendees should have at least a Masters degree in statistics, or equivalent experience, and an understanding of clinical trials and elementary Bayesian concepts.

About the Instructor:

Peter F. Thall is the Anise J. Sorrell Professor in the Department of Biostatistics at M.D. Anderson Cancer Center. Dr. Thall is an author of over 160 papers and book chapters in the statistical and medical literature, with research interests including Bayesian statistics, medical statistics and clinical trials. He has presented 21 short courses on statistical methods for clinical trials and over 130 invited talks. He has served as an associate editor of *Journal of the National Cancer Institute*, *Statistics in Medicine* and *Biometrics*, and currently is an associate editor of *Clinical Trials* and *Statistics in Biosciences*, serves on several external advisory boards and grant review panels, and is an American Statistical Association Media Expert.

Course 2 (Full Day): Modern Techniques in Data Mining

Instructor: David Banks, Professor in the Department of Statistical Science at Duke University

Abstract: This one-day short course surveys the development of an important new subfield at the intersection of statistics and computer science. It has important applications in many areas, especially bioinformatics and information technology. The course starts from the perspective of nonparametric regression, addressing the problems of variable selection, local fitting, model assessment and uncertainty, all in the context of the Curse of Dimensionality. Then the course moves to consider comparable issues in the case of classification, cluster analysis, and multidimensional scaling. Finally, the course gives a short summary of three areas of emerging theory that provide insight on when it is possible to make inference in high dimensions, and when there is no really no hope. Key topics include support vector machines, neural networks, boosting and bagging, random forests, overcompleteness, wavelets, sparsity, VC classes, and the LASSO and related methods.

About the Instructor:

David Banks is a professor in the Department of Statistical Science at Duke University. Before that, he held positions in the Food and Drug Administration, the Department of Transportation, the National Institute of Standards and Technology, and Carnegie Mellon University. He was editor of the Applications and Case Studies section of the Journal of the American Statistical Association (2007-2009), serves on the Board of the American Statistical Association, and has chaired the ASA Sections on Risk Analysis and Statistics in Defense and National Security. His research focuses on computer-intensive methods, complex data sets, dynamic network models, metabolomics, public policy, and adversarial risk analysis. He has published more than 60 papers, edited six books, and co-authored a monograph.

Course 3 (Half Day): An Introduction to Propensity Score Methods in Observational Research

Instructor: Peter Austin, Sr. Scientist at the Institute for Clinical Evaluative Sciences (ICES) in Toronto, Canada

Abstract: This half-day workshop examines the use of propensity score methods in observational research. Confounding frequently occurs in observational studies of the effects of treatments and exposures on health outcomes. This workshop will address several statistical issues in estimating treatment effects in the presence of confounding. First, a theoretical framework for confounding will be developed and causal diagrams will be introduced. Second, the design of randomized controlled trials (RCTs) will be briefly reviewed. Third, issues in the design of observational studies will be highlighted. We will discuss designing observational studies so that their design mimics some of the characteristics of that of RCTs. Fourth, we will describe design-based and analysis-based methods for removing confounding when estimating treatment effects using observational data. Analysis-based methods include regression-based approaches. Design-based approaches include stratification and propensity score-based methods. Fifth, attendees will be introduced to the concept of the propensity score and how it can be used to

remove confounding in observational studies. Issues in propensity score analyses will be covered in more depth. The workshop will cover the following issues in propensity score analyses: specifying the propensity score model; balance diagnostics for assessing the adequacy of the specification of the propensity score model; different propensity score methods (matching, stratification, weighting, and covariate adjustment); and sensitivity analyses for propensity score analyses.

About the Instructor:

Peter Austin is a Senior Scientist at the Institute for Clinical Evaluative Sciences (ICES) in Toronto, Canada and an Associate Professor in the Department of Health Policy, Management and Evaluation at the University of Toronto. His research interests include propensity score methods for causal inference, predictive models for cardiovascular outcomes, statistical methods for provider profiling, and applied Bayesian methods in health services research. He has published actively on propensity score methods and frequently collaborates with investigators in health services research, pharmacoepidemiology, and clinical epidemiology.

Course 4 (Half Day): Post-Marketing Drug Safety Evaluation

Instructor: A. Lawrence Gould, Merck Research Laboratories

Abstract: Surveillance of drug products in the marketplace continues after regulatory approval for a variety of reasons, e.g., to identify rare potential toxicities that are unlikely to have been observed in the clinical trials carried out before approval. Conventional statistically based postmarketing surveillance traditionally has focused on the large number of spontaneous reports of adverse events in spontaneous report databases. There currently is considerable interest and effort being directed towards using large observational databases containing insurance claim information or routinely maintained electronic health records. Determining which drug-event associations, of which there may be many tens of thousands, are real reporting associations and which random noise presents a substantial problem of multiplicity because the resources available for medical and epidemiologic followup are limited. This presentation will address some of the issues associated with using these sources for postmarketing safety surveillance, and will describe and compare methods for identifying potential 'signals' from spontaneous reporting databases.

About the Instructor:

A. Lawrence Gould received his PhD degree in Biometry from Case Western Reserve University (1967). He is currently a Senior Director at Merck Research Laboratory. He was elected as Fellow of the American Statistical Association in 1988. He has served as Fellows Committee Chair and Publications Officer of the Biopharmaceutical Section. Member of Biometric Society ENAR, served as Secretary/Treasurer 1982-1986. Served as Editor of Journal of Biopharmaceutical Statistics 2001-2002. His areas of research interest include use of Bayesian methods to improve effectiveness of the drug development process, adaptive trial design (including group sequential methods), evaluation of safety data from clinical trials, application of data mining and Bayesian methods to pharmacovigilance, use of data mining to identify relationships that can be used to design future trials, meta-analysis, modeling and simulation techniques to reduce cost and unnecessary patient exposure in drug development, and application

of decision science methods to drug development strategy.

Course 5 (Half Day): Principles and Techniques of Multiple testing and Multiple Comparisons

Instructor: Jason C. Hsu, The Ohio State University

Abstract: This half-day short course is about fundamental concepts and techniques of multiple testing, in clinical trials and bioinformatics. We will discuss Familywise Error Rate (FWER), generalized Familywise Error Rate (gFWER), and various versions of False Discovery Rate (FDR, Fdr). Issues to consider in error rate control include

- True, average, or worst case scenario (to sup or not to sup)
- Number or proportion of incorrect rejections
- Conditional or unconditional
- Tail probability or expectation

We will describe the multiple test construction techniques of closed testing and partition testing. Familiar methods such as Holm's and Hochberg's step-wise tests turn out to be special cases of partition testing. Using clinical trial with Multiple Endpoints as an illustration, we will show Partition Testing requires drastically fewer tests than Gatekeeping, and is more powerful.

The rush to meet the challenge of Bioinformatics seems to have occasionally overlooked fundamental principles of multiple testing. Using testing for association between biomarkers and drug response or adverse events as an example, we will show that common permutation tests do not control multiple testing error rate (unless assumptions are made on the joint distributions of gene expression levels or SNP alleles between phenotypes). We will illustrate the application of fundamental principle and techniques in multiple primary-secondary endpoints efficacy testing and genome-wide association studies (GWAS). The objective of this course is to help the participant decide on an error rate to logically control, and to confidently control it.

About the instructor:

Jason Hsu is a professor in the Department of Statistics at the Ohio State University. He works in the area of multiple testing and multiple comparisons. Since 1998, the approach he has emphasized is to connect methodological development with emerging biomedical issues. Besides fundamental concepts and techniques, his current interests include analysis of multiple endpoints data, and pharmacogenomics.

Course 6 (Half Day): Pharmacogenomics Clinical Trials: Genomic Biomarker Associated Design and Analysis Issues

Instructor: Dr. Sue-Jane Wang (suejane.wang@fda.hhs.gov), U.S. Food and Drug Administration

Abstract: In recent years, early phase clinical studies have begun to incorporate mRNA microarrays or whole genome DNA scanning high throughput biotechnologies as a means to explore the potential genomic associations between high dimensional genomic data and clinical outcome. There are high expectations on the use of such biotechnologies to develop and validate genomic composite biomarker with prognostic, diagnostic screening, and predictive potential for drug treatment in complex disease area, such as psychiatric, cardio-renal diseases or

life-threatening diseases, such as AIDS and oncology. This half-day short course will provide an overview of many considerations and challenges in incorporating pharmacogenomics in a clinical drug development program ranging from development of a genomic composite biomarker to implementation of personalized medicine. The topics will include statistical concepts in pharmacogenomics exploratory studies and evaluation of confirmatory pharmacogenomics clinical trials. The course outlines include • Development of a genomic composite biomarker

- Multiplicity issues on false discovery
- Establishment and validation of a genomic predictive model
- Genomewide association study
- Clinical utility of genomic biomarker and biomarker qualification
- Diagnostics performance characteristics assessment: companion or co-developed
- Convenience samples and confounding issues
- Evaluation of study designs and analysis methods in confirmatory PG trials
- Probability of imbalance and design issues with biomarker negative patient subset
- Reproducibility issues

The course will include clinical trial examples mimicking new drug application submissions. Literature overview and the instructor's collaborative research will be introduced. Attendees should have at least a Masters degree in statistics, or equivalent experience, and an understanding of clinical trials.

About the Instructor:

Sue-Jane Wang is Office Associate Director for Pharmacogenomics and Adaptive Design in the Office of Biostatistics under Office of Translational Sciences, Center for Drug Evaluation and Research (CDER), U.S. Food and Drug Administration. She is an elected member of the International Statistical Institute. She has served as an Editor-in-Chief of Pharmaceutical Statistics, and currently is an Associate Editor of Statistics in Medicine and Statistics BioSciences. Based on her collaborative research publications, Dr.Wang had given short courses on adaptive design, pharmacogenomics, multi-regional clinical trials, non-inferiority and bioinformatics, and has served numerous (co)chair, discussant, and keynote roles in addition to invited talks at the professional meetings.