PROGRAMME OF THE SEVENTY-EIGHTTH ANNUAL DEMING CONFERENCE ON APPLIED STATISTICS

Sponsored by
Deming Conference Organization
AMERICAN STATISTICAL ASSOCIATION: Biopharmaceutical Section

December 4 – December 9, 2022: Three-Day Conference plus Two-Day Short Course
Sonesta Philadelphia Rittenhouse Square, 1800 Market St, Philadelphia, PA

Three Keynotes on December 5-7, 2022
Walter Young Memorial Session
COVID 19 Vaccine Trials and Related Data Monitoring Issues by **Susan Ellenberg**, University of Pennsylvania
New Statistical Initiatives in the FDA CDRH by **Aloka Chakravarty**, FDA

Twelve Sessions of Tutorials on December 5-7, 2022 and Two Short Courses on December 8-9, 2022

Short Course 1. Combining Information from Different Studies with Meta-Analysis and Network Meta-Analysis
by **Christopher Schmid and Thomas Trikalinos**, Brown University

Short Course 2. Multi-regional Clinical Development and Safety/Benefit-Risk evaluation
by **Bruce Binkowitz**, Arcutis Biotherapeutics Inc, **Gang Li**, Eisai Inc, **Jim Buchanan**, Covilance LLC, **Judy Li**, BMS, and **Aloka Chakravarty**, FDA

A $5,000 college scholarship will be awarded to an undergraduate spouse, child, stepchild, or grandchild of a registrant

The registration will start at 6:00 pm on Sunday December 4th and will be followed by a one-hour reception with cold drinks and snacks. It will continue at 6:30 AM Monday December 5th through Thursday December 8th.
THREE-DAY REGISTRANTS WILL RECEIVE A BOUND COPY OF THE 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.org. This gives you an instant email acknowledgement. Payment must be paid by a credit card. E-Mail Cancellations sent to *registrar@demingconference.org* 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.

We are soliciting abstract proposals for posters. The Poster Presentation forum allows participants to submit their research concepts and issues of relevance for peer review in the area of biostatistics. Poster sessions, which will be held on all 3 days of the conference, allow 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 Saturday, October 1, 2022. Full details and tips for presentation, are on our website. We will hold poster sessions, providing a forum to attendees to present concepts and issues of relevance to their peers. Poster abstracts can be emailed to pinggao.zhang@takeda.com or submitted online for consideration. Students pursuing a doctorate degree in Biostatistics/Statistics may apply to receive a student scholar award and present a poster on their doctoral thesis at the conference. For further information, please contact the student scholar chair at sofia.x.paul@gsk.com

Sonesta Philadelphia Rittenhouse Square hotel is a premier choice among hotels in Philadelphia. Its 439 spacious, redesigned rooms and suites with AAA 3 Diamond rating in Philadelphia are thoughtfully appointed with all the comforts and amenities to help you rest and retreat. Located in Center City Philadelphia within the Financial District and just steps away from Rittenhouse Square where you will find from fine dining, upscale shopping, and treasured historic attractions, and all guest rooms have access to our fitness center. Hotel amenities include:

- 24-hour on-site fitness center
- Wireless high-speed internet access
- Seasonal Outdoor Heated Pool open daily 9:00 am – 9:00 pm

Seventy Eighth (78th) Annual Deming Conference on Applied Statistics
Sonesta Philadelphia Rittenhouse Square, 1800 Market St, Philadelphia, PA
Sponsored by the Biopharmaceutical Section of the ASA and the Deming Conference Organization

Sunday December 4, 2022 Registration: 6:00 ⇒ 7:30 PM and Reception 7:00 ⇒ 8:00 PM

Monday December 5, 2022 Registration: 6:30 ⇒ 8:00 AM and Hot Breakfast 7:00 ⇒ 7:50 AM

8:00 ⇒ 9:00 AM: **Walter Young Memorial Session**
Moderator: Alfred H. Balch

Session A	**Session B**
Hybrid Frequentist / Bayesian Power and Bayesian Power in Planning Clinical Trials 🕮 Andy P. Grieve, UCB Pharma Moderator: Din Chen	**Spatial Data Science Meets Bayesian Modeling and Inference** Sudipto Banerjee, UCLA Moderator: Naitee Ting

Lunch (On Your Own) 12:15 ⇒ 1:30 PM

Session C♣	**Session D ♣**
Incorporating Uncertainty in Power Considerations of Clinical Trials with Applications on Equivalence Trials Arne Ring and Rachid El-Galta, Sandoz Moderator: Din Chen	**Bayesian Methods for Sample Size Determinations** 🕮 Sujit K. Ghosh, NCSU and Fei Wang, Boehringer Ingelheim Moderator: Naitee Ting

7:00 PM Speaker's and Awards Dinner (Optional Added Fee Event)

Tuesday December 6. 2022 Registration: 7:00 ⇒ 8:00 AM and Hot Breakfast 7:00 ⇒ 7:50 AM

8:00 ⇒ 9:00 AM: Keynote: COVID 19 Vaccine Trials and Related Data Monitoring Issues by Susan Ellenberg, University of Pennsylvania
Moderator: Ivan S. F. Chan

Session E ♣	**Session F ♣**
Statistical Topics in Outcomes Research: Patient-Reported Outcomes, Meta-Analysis, and Health Economics 🕮 Joseph C. Cappelleri, Pfizer Inc and Thomas Mathew, UMBC Moderator: Wenjin Wang	**Adjust Overall Survival in Randomized Clinical Trials with Treatment Switching** Songzi Li, Hong Tian, and Kaifeng Lu, BeiGene USA Inc. Moderator: Kalyan Ghosh

Lunch (On Your Own) 12:15 ⇒ 1:30 PM

Session G	**Session H**
Estimand in Real-world Setting and Targeted Learning in Generating and Evaluating Real-world Evidence Jie Chen, Overland Pharmaceuticals and Susan Gruber, Putnam Data Sciences Moderator: Weili He	**Statistical Translation of Extrapolation: A Tutorial for Demonstrating Efficacy and Safety of Investigational Medicines in Pediatric Populations** James Travis, FDA; Margaret Gamalo, Pfizer Inc; and Jingjing Ye, BeiGene Moderator: Kalyan Ghosh

Wednesday December 7, 2022 Registration: 7:00 ⇒ 8:00 AM and Hot Breakfast 7:00 ⇒ 7:50 AM

8:00 ⇒ 9:00 AM: Keynote: New Statistical Initiatives in the FDA CDRH by Aloka Chakravarty, FDA
Moderator: William Wang

Session I ♣	**Session J ♣**
N-of-1 Trials for Personalized Healthcare Christopher Schmid, Brown University and Naihua Duan, Columbia University Moderator: Alfred H. Balch	**Machine Learning for Statisticians** Andy Liaw and Junshui Ma, Merck & Co., Inc Moderator: Ivan S. F. Chan

Lunch (On Your Own) 12:15 ⇒ 1:30 PM

Session K	**Session L**
Using SAS PROC BGLIMM and MCMC for Bayesian Analysis of Mixed Models 🕮 Walter Stroup, University of Nebraska Moderator: Alfred H. Balch	**Safety and Benefit-Risk Evaluation with Practical Visual Analytical Tools** Melvin Munsaka, AbbVie Inc and Jim Buchanan, Covilance LLC Moderator: William Wang

Thursday December 8, 2022 Registration: 6:30 ⇒ 8:00 AM and Hot Breakfast: 7:00 ⇒ 7:50 AM

Short Course 8:00⇒9:30 Lecture / **9:30⇒9:50** *Break* / **9:50⇒11:20 Lecture** / **11:20⇒12:40** *Lunch on Your Own* / **12:40⇒2:10 Lecture** / **2:10⇒2:30** *Break* / **2:30⇒4:00 Lecture** / **4:00⇒4:20** *Break* / **4:20⇒5:00 Lecture**

Combining Information from Different Studies with Meta-Analysis and Network Meta-Analysis 🕮 : Christopher Schmid and Thomas Trikalinos, Brown University Moderator: Alfred H. Balch	**Multi-regional Clinical Development and Safety/Benefit-Risk evaluation** 🕮 Bruce Binkowitz, Arcutis Biotherapeutics Inc, Gang Li, Eisai Inc, Jim Buchanan, Covilance LLC, Judy Li, BMS, and Aloka Chakravarty, FDA Moderator: Ivan S. F. Chan and William Wang

Friday December 9, 2022 Hot Breakfast: 7:00 ⇒ 7:50 AM

Short Course (Continued) 8:00 - 9:30 Lecture / **9:30 - 9:50** Break / **9:50 - 11:20 Lecture** / **11:20 - 11:40** Break / **11:40 - 1:10 Lecture**

All tutorial and short course titles, presenters and moderators from 1970 onwards are on www.demingconference.org

🕮 Session is based on a recently published text that is available either for a discounted price or is included in the price of the short course registration

♣ Sessions will have their breaks extended by 15 minutes for Poster Presentations

Conference Speakers Biography

Sudipto Banerjee is currently Professor and Chair of the UCLA Department of Biostatistics and the 2022 President of the International Society for Bayesian Analysis. Dr. Banerjee has substantial experience in Bayesian modeling and inference for spatially-temporally referenced data. He has published over 160 peer-reviewed articles, two textbooks as leading author, one edited handbook and two committee reports for the National Academy of Sciences. He has produced open-source statistical software packages for fitting Bayesian hierarchical models for analysis of spatially and temporally indexed data. He has participated in a number of federally funded projects, both as PI and as co-PI, and has regularly served as PI on R01 grants from NIH and received continuous funding since 2007 from NSF as PI of projects advancing statistical methods for spatially oriented BIG DATA problems. He has graduated 15 doctoral students and has supervised 2 postdoctoral scholars. Dr. Banerjee has received many honors, including the Abdel El-Shaarawi Award from The International Environmetric Society (TIES), the Mortimer Spiegelman Award from the American Public Health Association and the George W. Snedecor Award from the Committee of Presidents of Statistical Societies (COPSS), elected membership of the International Statistical Institute, elected fellowships in the Institute of Mathematical Statistics (IMS), the American Statistical Association (ASA), the International Society for Bayesian Analysis and the American Association for the Advancement of Science (AAAS), a Distinguished Achievement Medal from the ASA's Section on Statistics and the Environment, and an ASA Outstanding Statistical Application Award.

James Buchanan, president of Covilance LLC, has 30+ years of drug safety experience in the pharmaceutical industry. He is a co-lead of the ASA Biopharmaceutical Safety Working Group and the Interactive Safety Graphics taskforce that is developing novel, open-source, interactive graphical tools to evaluate drug safety issues.

Joseph C. Cappelleri, PhD, MPH, MS is an executive director in the Statistical Research and Data Science Center at Pfizer Inc. He earned his M.S. in statistics from the City University of New York (Baruch College), Ph.D. in psychometrics from Cornell University, and M.P.H. in epidemiology from Harvard University. As an adjunct professor, Dr. Cappelleri has served on the faculties of Brown University, University of Connecticut, and Tufts Medical Center. 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 is lead author of the book *Patient-Reported Outcomes: Measurement, Implementation and Interpretation* and has co-authored or co-edited three other books (*Phase II Clinical Development of New Drugs, Statistical Topics in Health Economics and Outcomes Research, Design and Analysis of Subgroups with Biopharmaceutical Applications*). Dr. Cappelleri is a fellow of the American Statistical Association and president of the New England Statistical Society.

Jie Chen is Chief Scientific Officer at Elixir Clinical Research and Senior Vice President and head of Biometrics at Overland Pharmaceuticals. Before joining Elixir and Overland, Jie was a distinguished Scientist in the Biostatistics and Research Decision Sciences at Merck Research Laboratories (US). He also worked as a senior global group head in several multi-national biopharmaceutical companies. Jie has over 27 years of experience in biopharmaceutical R&D and has been invited to give short courses at national or international statistical conferences. He is a co-chair for the phase III projects of the American Statistical Association (ASA) Real-World Evidence Scientific Working Group. Jie has co-authored a book on *Medical Product Safety Evaluation: Biological Models and Statistical Methods* (with Heyse and Lai) and published over 40 papers in peer-reviewed statistical journals. He is an elected Fellow of the ASA and a visiting member of the Center for Innovative Study Design, Stanford University.

Naihua Duan is an accomplished practicing biostatistician with research interests in a variety of domains, including implementation research, quality improvement investigations, health services research, prevention research, sample design and experimental design, model robustness, transformation models, multilevel modeling, nonparametric and semi-parametric regression methods, environmental exposure assessment, etc. He has published more than 200 papers in leading journals in statistics, medicine, and public health. He is an Elected Fellow of the American Statistical Association (ASA) and the Institute of Mathematical Statistics, and the co-founding chair (with Robert Gibbons) for the Mental Health Statistics Section of the ASA. He received the Long-Term Excellence Award from the Health Policy Statistics Section of the ASA in 2013, and the Annual Harvard Award in Psychiatric Epidemiology and Biostatistics in 2016. He received a B.S. in Mathematics from National Taiwan University, an M.A. in Mathematical Statistics from Columbia University, and a Ph.D. in Statistics from Stanford University. He worked at RAND from 1979 to 2000, advancing from Associate Statistician to Corporate Chair and Senior Fellow in Statistics. From 2000 to 2007, he served as Professor in Residence, with tenure, in the Departments of Biostatistics and Psychiatry at UCLA. From 2007 to 2012, he served as Professor of Biostatistics (in Psychiatry), with tenure, in the Departments of Biostatistics and Psychiatry; Research Scientist in the New York State Psychiatric Institute; and Director for the Division of Biostatistics in the Department of Psychiatry at Columbia University and New York State Psychiatric Institute. He retired in 2012 from Columbia University and New York State Psychiatric Institute and continued to conduct research and consulting at a leisurely pace, while enjoying his golden years with his wife ChihMing Fan and their grandchildren, Alex, Evelina, and Theodore.

Andy P. Grieve studied Mathematics (BSc) and Applied Statistics (MSc) at Southampton University in the UK and received his Ph.D. in Statistics from Nottingham University also in the UK and an Honorary Doctorate from Kingston University for Services to Statistics. Dr Grieve has been with the Belgian pharmaceutical company, UCB, since 2017 and established the Center of Excellence for Statistical Innovation (CESI), where he is now a Statistical Research Fellow. Prior to joining UCB he was a Vice President in the Innovation Center of the Contract Research Organisation ICON/Aptiv Solutions. From 2006 to 2010 he was Professor of Medical Statistics at King's College London in the Department of Public Health Sciences. Before joining King's he spent over 30 years in the pharmaceutical industry working for CIBA-GEIGY, in the UK and Switzerland, ICI Pharmaceuticals (Zeneca) and Pfizer. Dr Grieve has worked in all areas of pharmaceutical R&D in which statistical methods and statisticians are intimately involved including drug discovery, pre-clinical toxicology, pharmaceutical development, pharmacokinetics and pharmacodynamics, phase I-IV of clinical development, manufacturing, health economics and clinical operations. He has served on advisory committees of both the MHRA and EMA, and has been a member of UK Government Panels on "Imaging Techniques as an alternative Measure of Efficacy in Cardiovascular Drug Development", "Personalised Medicine" and "Dose Response designs in Phase I and II" and has run in-house workshops for the US Food and Drug Administration. Dr Grieve is a Fellow, Chartered Statistician and former president of the Royal Statistical Society; Fellow of the American Statistical Association and honorary life-member of Statisticians in the Pharmaceutical Industry of which he is a past-Chairman and founder-member. Dr Grieve's statistical research has been primarily concerned with the application Bayesian ideas and techniques of statistics to the pharmaceutical industry. Latterly he has concentrated on the design and implementation of Bayesian adaptive trials, and the Probability of Success (PoS) of studies and drug development programs. He has published over 140 articles and is the author two books. The first, for non-statisticians involved in clinical trials is entitled "FAQ's on Statistics in Clinical Trials". The second will appear in May and is entitled "Hybrid Frequentist / Bayesian Power and Bayesian Power in Planning Clinical Trials. He has been an invited speaker at national and international conferences on over 300 occasions.

Margaret (Meg) Gamalo, PhD is Head of Statistics –Inflammation and Immunology, Pfizer Innovative Health. She combines expertise in biostatistics, regulatory and adult and pediatric drug development. She recently was a Research Advisor, Global Statistical Sciences at Eli Lilly and Company and prior to that was a Mathematical Statistician at the Food and Drug Administration. Meg leads the Pediatric Innovation Task Force at the Biotechnology Innovation Organization. She also actively contributes to research topics within the European Forum for Good Clinical Practice – Children's Medicine Working Party. Meg is Editor-in-Chief of the Journal of Biopharmaceutical Statistics and is actively involved in many statistical activities in the American Statistical Association. She received her PhD in Statistics from The University of Pittsburgh and master's in applied mathematics from the University of the Philippines.

Rachid El Galta holds a university degree in Mathematics from University of Rabat, MSc. in statistics from university of Amsterdam and PhD in Biostatistics from Leiden University. In February 2006 he joined as a biostatistician the institute of Cancer Research, London, before moving to the pharmaceutical industry in 2007. He is currently working at Sandoz.

Sujit Kumar Ghosh has over 25 years of experience in conducting, applying, evaluating, and documenting statistical analysis of biomedical and environmental data. Prof. Ghosh is actively involved in teaching, supervising, and mentoring graduate students at the doctoral and master levels. He has supervised over 40 doctoral graduate students and published over 125 peer-reviewed journal articles in various areas of statistics with applications in biomedical and environmental sciences, econometrics, and engineering. He has recently co-authored a book (with Dr. Reich) titled "Bayesian Statistical Methods," which is being used as a textbook at several universities. Prof. Ghosh has delivered over 180 invited lectures, seminars at national and international meetings. He has also delivered several short courses and served as short-term visiting professor at several institutions in various countries. Prof. Ghosh received the International Indian Statistical Association (IISA) Young Investigator Award in 2008; was elected a Fellow of the American Statistical Association (ASA) in 2009; was elected as the President of the NC Chapter of ASA in 2013 and elected as the President of the IISA in 2017. Currently, he is the interim Department Head of Statistics at NC State University.

Susan Gruber, PhD, MPH, MS, is the founder of Putnam Data Sciences, statistical consulting and data analytics consulting firm. Her work focuses on the development and application of data-adaptive methodologies for improving the quality of evidence generated by observational and randomized health care studies. Prior to forming Putnam Data Sciences, Dr. Gruber was the Director of the Biostatistics Center in the Department of Population Medicine at Harvard Pilgrim Health Care and Harvard Medical School, and former Senior Director of the IMEDS Methods program at the Reagan Udall Foundation for the FDA.

Songzi Li has over 7 years of experience in design and analysis of clinical trials. Currently he is an Associate Director of biostatistics at BeiGene, serving as a statistical lead for multiple clinical studies. Dr. Li's research interest includes treatment switching, go-no-go, sequential parallel comparison design (non-oncology), and clustering analysis. He co-developed SAS macros and R functions for RPSFTM, IPCW and two-stage method.

Prior to joining BeiGene, Dr. Li spent 4 years at PPD, working at the studies in multiple therapeutic areas including oncology, inflammatory bowel disease, and neurology, which support submission and successful approvals. He received a doctorate degree in Statistics from Bowling Green State University.

Andy Liaw has been doing research and applying Statistics and Machine Learning methods to drug discovery areas such as high throughput screening, pharmacology, cheminformatics, proteomics, and biomarkers for the past 22 years. He is the author of the R package randomForest and had made several contributions to the open-source R software for Statistics and Data Science. He is currently Senior Principal Scientist in Merck Research Laboratories. He received his Ph.D. in Statistics from Texas A&M University.

Kaifeng Lu has 20 years of experience in design and analysis of clinical trials. Currently he is a Senior Director of Biostatistics at BeiGene, leading Statistical Modelling & Simulations and the non-oncology drug development statistics. Dr. Lu has published more than 30 papers in peer reviewed statistical journals on a wide range of topics such as sample size estimation, missing data handling, multiple comparison procedures, adaptive designs, and survival analysis. His research interest also includes treatment switching, real-world data, estimand, and causal inference. Dr. Lu is a member of Oncology estimand working group. Prior to joining BeiGene, Dr. Lu has worked in late-stage statistics at Eli Lilly & Company, Merck & Co., Inc., Forest Laboratories/Actavis/Allergan/AbbVie, covering the areas of women's health, anti-inflammatory, respiratory, metabolic, and CNS, which led to several successful regulatory submissions and approvals. He received a doctorate degree in Biostatistics from North Caroline State University.

Junshui Ma is currently an Executive Director and head of Biometrics Research department at Merck. Junshui obtained his Ph.D. from the Ohio State University in 2001. After working shortly in Los Alamos National Lab, a biotech startup, and Ohio Supercomputer Center, he joined Merck in early 2005. In the past 17 years, he engaged in all phases of drug Research & Development (R&D), including preclinical discovery, clinical development, regulatory filing, and translational medicine. His research interests include machine learning in pharmaceutical R&D, stratified medicine, and survival analysis. He coauthored over 30 peer-reviewed journal papers, along with many conference abstracts and posters.

Thomas Mathew, PhD, is Professor, Department of Mathematics & Statistics, University of Maryland Baltimore County (UMBC). He earned his PhD in statistics from the Indian Statistical Institute in 1983 and has been a faculty member at UMBC since 1985. He has delivered numerous conference presentations, nationally and internationally, and has published extensively on methodological and applied topics, including cost-effectiveness analysis, bioequivalence testing, exposure data analysis, meta-analysis, mixed and random effects models, and tolerance intervals. He is the co-author of two books *Statistical Tests in Mixed Linear Models* and *Statistical Tolerance Regions: Theory, Applications and Computation,* both published by Wiley. He has served on the Editorial Boards of several journals, and is currently an Associate Editor of the *Journal of the American Statistical Association, Journal of Multivariate Analysis,* and *Sankhya*. Dr. Mathew is a Fellow of the American Statistical Association, and a Fellow of the Institute of Mathematical Statistics. He has also been appointed as Presidential Research Professor at his campus.

Melvin S. Munsaka is currently Senior Director and Head of Safety Statistics at AbbVie. He has more than 25 years of industry experience. He is a member of the ASA Biopharmaceutical Safety Scientific Working Group, DIA Bayesian Scientific Working Group, and the PHUSE Safety Analytics Working Group.

Arne Ring earned his Diploma in mathematics and his Ph.D. in pharmacometrics from the Martin-Luther-University Halle-Wittenberg. He started his professional career as an actuary in at GE ERC Frankona in Munich in April 2000. In August 2002, he moved to Boehringer Ingelheim as statistician and later as the head of the phase I-IIa statistics team. In 2011, he joined the Diabetes Trials Unit at the University of Oxford as head of the statistics and modelling group and in 2013 he moved to the Clinical Trials Unit at Leicester University. In 2015 he returned to the pharmaceutical industry at medac, and is currently head of biosimilar biostatistics at Sandoz. In addition, he was awarded the affiliated Professorship of Statistics at the University of the Free State, South Africa in 2014.

Christopher Schmid is Professor of Biostatistics at Brown University School of Public Health where he co-founded the Center for Evidence Synthesis in Health. He directs the Biostatistics, Epidemiology and Research Design (BERD) Core of the Rhode Island Center to Advance Translational Science. He is a Fellow of the American Statistical Association, founding Editor of the journal *Research Synthesis Methods*, long-time statistical editor of the *American Journal of Kidney Diseases* and former member of the Drug Safety and Risk Management Committee for FDA. His research focuses on Bayesian methods for meta-analysis, methods for developing and accessing predictive models using data from multiple sources and on methods for design and analysis of N-of-1 trials. He has a long record of collaborative research in diverse areas of medicine and health with academia, government and industry and nearly 300 peer-reviewed publications. He has coauthored consensus CONSORT reporting guidelines for N-of-1 trials and single-case designs, and PRISMA guidelines extensions for meta-analysis of individual participant studies and for network meta-analyses as well as the Institute of Medicine report that established US standards for systematic reviews. He is lead statistician on several N-of-1 trial consortia. Dr. Schmid graduated from Haverford College with a BA in Mathematics and received his PhD in Statistics from Harvard University.

Walt Stroup is Emeritus Professor of Statistics at the University of Nebraska-Lincoln. He served on the University of Nebraska faculty from 1979 until 2020. His responsibilities included teaching statistical modeling, design of experiments, and research specializing in mixed models and their applications in agriculture, natural resources, medical and pharmaceutical sciences, education, and the behavioral sciences. He is the founding chair of Nebraska's Department of Statistics and served as chair from 2001 until 2010. In 2020, he received the University of Nebraska's Outstanding Teaching and Innovative Curriculum Award, the university's highest teaching honor. He was a member of PQRI's Stability Shelf-Life Working Group from its inception in 2006 until its disbanding in 2019. He received PQRI's *Excellence in Research* award in 2009. He co-authored *SAS for Mixed Models, SAS for Linear Models, 4th ed.*, and authored *Generalized Linear Mixed Models: Modern Concepts, Methods and Applications*. He has conducted numerous short courses on mixed and generalized linear models for industry and professional organizations in Africa, Europe, Australia and North America. He is a Fellow of the American Statistical Association.

Hong Tian is Head of Global Statistics at BeiGene, responsible for ensuring adequate statistical support BeiGene's growing portfolio including clinical development for solid tumor, hematology and non-oncology, quantitative evidence generation post approval and statistics for discovery, biomarker, and manufacturing. Hong joined BeiGene in June 2021, following more than 15-year career at Johnson & Johnson Pharmaceutical R&D. Her past roles including Head of Early Development Statistics for Oncology, Global Clinical Team Statistical Lead for the BCMA CAR-T Program and Functional Manager for Statistical Modeling and Methodology group for Janssen oncology. Hong has supported various stages of drug development across therapeutic areas has contributed to multiple global marketing authorizations across oncology, cardiovascular and metabolic diseases and infectious diseases areas. Her research interests are in the areas of multiple comparison, enrichment design and composite endpoint. Hong obtained her Ph.D. in Biostatistics from Columbia University.

James Travis is a statistical team leader in the Office of Biostatistics within the Center for Drug Evaluation and Research at the US Food and Drug Administration and leads the team supporting the Division of Pediatric and Maternal Health. James joined the Agency in 2014 following completion of his PhD at the University of Maryland, Baltimore County. He is a representative on the Pediatric Review Committee for the Office of Biostatistics. He has interests in Bayesian methods, particularly the use of informative priors in implementing extrapolation in pediatric clinical trials.

Fei Wang is a Senior Principal Data Scientist at Boehringer Ingelheim Pharmaceuticals, US. Her research interests are Bayesian design and modeling; Simulation-based Bayesian sample size determination; Translational medicine and biomarkers. She has more than 10 years' experience in biopharmaceutical industry and 5 years' experience in academic research and teaching. She worked in various therapeutic areas and supported submission projects. Before working in pharmaceutical industry, she was an Assistant Professor in the School of Public Health at Boston University for 5 years. She was in the Department of Health Policy and Management and worked in collaboration with the Center for Health Quality, Outcomes, & Economic Research. Her research interests are Bayesian hierarchical modeling in health policy, medical tests, and sample size determination. She did her postdoctoral work at Brown University after graduating from the Department of Statistics at the University of Connecticut.

Jingjing Ye is an executive director and currently leads a global team, Data Science and Operational Excellence (DSOE), with Global Statistics and Data Sciences (GSDS) in BeiGene. She has over 16 years' experience in pharmaceutical industry and US FDA, with focus in cancer drug discovery and development. Her statistical and regulatory experience expands full spectrum on patients' treatment journey from diagnosis, treatment to living with the condition. Before BeiGene, she was most recently a statistics team leader in the Office of Biostatistics in CDER. At CDER, she supervised a team of statistical analysts and reviewers for designing, reviewing and analyzing clinical trials to support drug approvals throughout preIND, IND, NDA/BLA and post-approval studies in oncology and hematology. She was statistical representative within the Oncology Center of Excellence (OCE) Pediatric Review sub-committee, responsible for overseeing all pediatric review operations within the OCE. She is currently the co-lead on several working groups, including ASA Biopharmaceutical Section (BIOP) Pediatric Working Group (pediatric extrapolation sub-team), ASA BIOP Statistical Considerations in Oncology Pediatric Trials subgroup under ASA BIOP Stats Methods in Oncology working group, and DIA-ASA Master Protocol Patient Engagement Sub-team. She received her PhD degree in statistics from University of California, Davis and B.S. in Applied Mathematics from Peking University in China.

Monday December 5, 2022 9:00 – 12:15 PM

Session A

Hybrid Frequentist / Bayesian Power and Bayesian Power in Planning Clinical Trials 🕮

Instructor: Andy P. Grieve, UCB Pharma
Moderator: Din Chen

Abstract

For the most part the planning of clinical trials is based on considerations of the power of a test of a given alternative hypothesis based on ideas introduced by Neyman and Pearson in 1933. As early as 1939, Jeffreys pointed out that if the true value was unknown, so was the power. Jeffreys suggested that to understand the true power of a study the conditional power values should be averaged with respect to their prior probabilities, an unconditional power. This idea was taken up in the 1980's by Spiegelhalter and colleagues and in the early 2000s by O'Hagan and Stevens who introduced the concept of assurance. All of this work uses unconditional as opposed to conditional probabilities. Topics covered in the course include:

- Expected Power, Average Power (AP), Predicted Power, Probability of Success and Assurance for a Simple Normal Model with Known Variance
  - Bounds on AP and Assurance
  - Sample Size for a Given AP/Assurance and Normalized Assurance.
  - Applying Assurance to a Series of Studies
  - Assurance for a Clinical Trial with a Single Interim Analysis
  - Non-Inferiority Trials
- AP in Non-Normal Settings – Unknown variance, Binary Data, Survival Analysis
- Bayesian Power (BP)
  - Bounds on BP
  - Sample Size for a Given BP/Normalized BP
  - Posterior Conditional Success Distributions
  - Prior Distributions for Power and sample Size
- Interim Predictions and Links to AP

  AP with Multiple Decision Criteria – Normal Model with Known Variance
  - Bounds on AP and Assurance
  - Generalized Assurance
  - Bayesian Approach to Multiple Decision Criteria.
  - Posterior Conditional GO/NOGO/Pause/Distributions
- Surety and Assurance in Estimation
  - An Alternative to Power in sample Size Determination
  - Unconditional Sample Sizing Based on CI width

Session B

Spatial Data Science Meets Bayesian Modeling and Inference

Instructor: Sudipto Banerjee, UCLA
Moderator: Naitee Ting

Abstract:

Geographic Information Systems (GIS) and related technologies such as remote sensors, satellite imaging and portable devices that are capable of collecting precise positioning information, even on portable hand-held devices, have spawned massive amounts of spatial-temporal databases. Spatial "data science" broadly refers to the use of technology, statistical methods, computational algorithms to extract knowledge and insights from spatially referenced data. Applications of spatial-temporal data science are pervasive in the natural and environmental sciences; economics; climate science; ecology; forestry; and public health. With the abundance of spatial BIG DATA problems in the sciences and engineering, GIS and spatial data science will likely occupy a central place in the data revolution engulfing us. This tutorial will introduce participants to the various challenges data scientists are encountering in analyzing massive spatial-temporal data sets in diverse applications. The approach of the tutorial will be fully oriented toward a data science audience linking model development and computations through the R statistical computing environment and software packages such as BUGS/JAGS and STAN. We will begin with a description of different types of spatial data structures and the relevant data analytic questions they pose. We will show, with several examples, the importance of formal statistical inference and, in particular, the many benefits of Bayesian modeling for spatial and spatial-temporal data. We will elucidate recent developments in Bayesian statistical science that harness high performance scientific computing methods for spatial-temporal BIG DATA analysis and emphasize how such methods can be implemented on very modest computing architectures (such as a laptop). The talk will include specific examples of Bayesian hierarchical modeling in diverse scientific disciplines including environmental sciences; economics; and public health.

Monday Lunch (On Your Own) 12:15 PM - 1:30 PM

1:30 - 5:00 PM

Session C ♣

Incorporating Uncertainty in Power Considerations of Clinical Trials with Applications on Equivalence Trials

Instructors: Arne Ring, Sandoz, Martin-Luther-University and Rachid El-Galta, Sandoz
Moderator: Din Chen

Abstract

The application of the standard "fixed parameter approach" for sample size considerations often yields a sample size that leads to lower actual power than desired. This may happen when estimate of the true but unknown parameter is subject to reasonably large amount of uncertainty, as the loss in power for a parameter change to one side is not symmetric to the gain in power to the other side.

With a Bayesian power consideration, the quantified uncertainty can be incorporated by integrating the power function over the expected distribution of the parameter, so that an overall "probability of success" can be derived [1, 2]. This method has been widely adopted in the pharmaceutical industry, e.g. for optimizing sequential superiority trials [3].

We demonstrate how to apply the approach to equivalence trials of two treatments, Test (T) and reference (R). The objective of such trials typically is to demonstrate that the 90% confidence interval of the T/R-ratios of the primary endpoints are fully included in a given acceptance interval [4]. For quantitative endpoints we show how the uncertainty about the two relevant parameters (mean ratio and CV) can be incorporated simultaneously. Furthermore, we illustrate applications for other types of endpoints.

Session D ♣

Bayesian Sample Size Determination Methods for Hypotheses Testing 🕮

Instructors: Sujit K. Ghosh, NCSU and Fei Wang, Boehringer Ingelheim
Moderator: Naitee Ting

Abstract

Sample size determination is one of most widely used methods in bio-pharmaceutical applications. The primary goal is to determine minimal sample size that would achieve a desired sampling precision for statistical estimation and/or maintain a pre-specified Type-I and Type-II error rates for hypotheses testing. However, Bayesian methods are not usually designed to achieve such desired precision or control error rates despite the need for such desired characteristics from regulatory perspectives. On the other hand, the success of classical sample size determination methods crucially depends on finding a pivotal quantity which becomes increasingly difficult for general composite null hypothesis (e.g., bio-equivalence and non-inferiority tests) involving nuisance parameters. Modern clinical trial design features require simulations to show operating characteristics. Thus, a unified methodological framework is needed that not only provide theoretical guarantees for controlling desired level of errors but is also broadly applicable for composite null hypothesis. This tutorial will focus on presenting recent Bayesian methodologies for sample size calculation primarily for hypotheses testing framework.

In summary, the tutorial presents (i) a general Bayesian/Classical framework for sample size determination for estimation and testing hypotheses (ii) theoretical and numerical illustrations of controlling two types of error rates for hypotheses testing; and (iii) applications of the methodologies for a few popular clinical trials and some recent developments on adaptive methods. Selected software demos (R packages: BAEssd, BDP2, ph2bayes, gsbDesign, BayesPPD) will also be illustrated with working examples and use cases and supporting literature will also be provided.

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

Tuesday December 6, 2022 9:00 – 12:15 PM

Session E ♣

Statistical Topics in Outcomes Research: Patient-Reported Outcomes, Meta-Analysis, and Health Economics 🕮

Instructors: Joseph C. Cappelleri, Pfizer Inc, and Thomas Mathew, University of Maryland Baltimore County

Moderator: Wenjin Wang

Abstract

Based in part on the recently published co-edited volume *Statistical Topics in Health Economics and Outcomes Research* (Alemayehu et al.), this four-hour short course recognizes that, with ever-rising healthcare costs, evidence generation through health economics and outcomes research (HEOR) plays an increasingly important role in decision-making about the allocation of resources. This course highlights three major topics related to HEOR, with objectives to learn about 1) patient-reported outcomes, 2) analysis of aggregate data, and 3) methodological issues in health economic analysis. Key themes on patient-reported outcomes are presented regarding their development and validation: content validity, construct validity, and reliability. Regarding analysis of aggregate data, several areas are elucidated: traditional meta-analysis, network meta-analysis, assumptions, and best practices for the conduct and reporting of aggregated data. For methodological issues on health economic analysis, cost-effectiveness criteria are covered: traditional measures of cost-effectiveness, the cost-effectiveness acceptability curve, statistical inference for cost-effectiveness measures, the fiducial approach (or generalized pivotal quantity approach), and a probabilistic measure of cost-effectiveness. Illustrative examples are used throughout the course to complement the concepts. Attendees are expected to have taken at least one graduate level course in statistics.

Learning Objectives

To understand and critique the major methodological issues in outcomes research on the development and validation of patient-reported outcomes, traditional meta-analysis and network meta-analysis, and health economic analysis.

Session F ♣

Adjust Overall Survival in Randomized Clinical Trials with Treatment Switching

Instructors: Songzi Li, Hong Tian, and Kaifeng Lu, BeiGene USA Inc

Moderator: Kaylan Ghosh

Abstract

Treatment switching is commonly allowed in randomized clinical trials on novel interventions driven by ethical considerations. When control group patients switch to experimental arm and benefit from the experimental treatment, statistical inference on overall survival based on data according to the arms to which patients were randomized will be biased. The question of clinical interest "what is the overall survival benefit of treatment" cannot be addressed adequately without proper adjustment.

Rank preserving structural failure time model, inverse probability of censoring weights and two-stages were most widely used model to adjust overall survival for treatment switching. However, there is no available validated SAS macro/R package for those statistical models. In this course, we will introduce the traditional treatment adjustment models (RPFSTM, IPCW, and Two-stage) and walk through the SAS macro/R package with audience. Furthermore, we pick a few typical industry case studies which represent difference scenarios of K-M curve.

Course Structure

- Overview existed statistical model and result to adjust overall survival (RPFSTM, IPCW, and Two-stage) (60 mins)
- SAS/R program example (30 mins)
- Break (15 mins)
- Industry Case Study (60 mins)
  - K-M curves diverges then parallel in the tail
  - K-M curves diverges then cross in the tail
  - K-M curves overlaps across time

Tuesday Lunch (On Your Own) 12:15 AM - 1:30 PM

1:30 - 5:00 PM

Session G

Estimand in Real-world Setting and Targeted Learning in Generating and Evaluating Real-world Evidence

Instructors: Jie Chen, Overland Pharmaceuticals and Susan Gruber, Putnam Data Sciences

Moderator: Weili He

Abstract

Constructing the right estimand—the target of estimation—which reflects the research question and the study objective, is one of the key components in formulating a clinical study. ICH E9(R1) describes statistical principles for constructing estimands in clinical trials with a focus on five attributes—population, treatment, end- points, intercurrent events, and population-level summary. However, defining estimands for clinical studies using real-world data (i.e., real-world evidence studies) requires additional considerations due to, for example, heterogeneity of study population, complexity of treatment regimes, different types and patterns of intercurrent events, and complexities in choosing study endpoints. In the first half of this tutorial, we will review the essential components of estimands and causal inference framework, discusses considerations in constructing estimands for real-world evidence (RWE) studies, highlights similarities and differences in traditional clinical trial and RWE study estimands, and provides a roadmap for choosing appropriate estimands for RWE studies.

Targeted Learning (TL) provides a template for efficient learning from data. TL can improve the quality of real-world evidence (RWE) generated from clinical studies using real-world data (RWD) and help assess the level of support for sound decision-making. The TL estimation roadmap is a step-by-step guide for causal effect estimation that produces a rich trove of information for assessing whether the RWD are adequate to address selected study questions, and whether study findings provide robust scientific evidence. In the second half of the tutorial, we will present the roadmap and use case studies to showcase its utility for developing a statistical analysis plan, generating RWE, and evaluating results from prior studies.

Session H

Statistical Translation of Extrapolation: A Tutorial for Demonstrating Efficacy and Safety of Investigational Medicines in Pediatric Populations

Instructors: James Travis, FDA; Margaret Gamalo, Pfizer; Jingjing Ye, BeiGene

Moderator: Kalyan Ghosh

Abstract

Pediatric drug development often faces substantial challenges, including economic, logistical, technical, and ethical barriers, among others. Pediatric drug development lags adult development by about 8 years and often faces infeasibility of trials, resulting in children being a large, underserved population of "therapeutic orphans," as an estimated 80% of children are treated off-label (Mulugeta et al. in Pediatr Clin 64(6):1185-1196, 2017). Among many efforts to mitigate these feasibility barriers and as an ethical approach to minimizing exposing pediatric patients to the research risks, increased attention has been given to extrapolation; that is, the leveraging of available data from adults or older age groups to draw conclusions for the pediatric population. Recent ICH harmonization on a pediatric extrapolation framework provides a clearer path forward for pediatric drug development programs leveraging some degree of extrapolation despite uncertainties. In this framework, the degree to which extrapolation can be used lies along a continuum representing the uncertainties to be addressed through generation of new pediatric evidence (Gamalo et al. 2021). This tutorial is structured as a combination of pediatric drug development process and statistical methodologies.

Outline of the tutorial:

Part I: Pediatric drug development regulatory history and ICH guidelines, including extrapolation strategy, process, concept, and plan. Regulatory implications and optimize pediatric drug development programs.

Part II: The applicability of Bayesian methodology within the framework of extrapolation and the incorporation of a "validate" approach within process. A discussion on related references is provided, e.g., Gamalo et al. (2017) for a review of Bayesian methods to the extrapolation of adult data to support drug approvals in a pediatric population.

Part III: The extent of development relating to safety and assessment of safety in pediatric patients

Wednesday December 7, 2022 9:00 – 12:15 PM

Session I ♣

N-of-1 Trials for Personalized Healthcare

Instructors: Christopher Schmid, Brown University and Naihua Duan, Columbia University
Moderator: Alfred Balch

Abstract

Personalized (N-of-1) trials hold great promise for broadening the clinical knowledge production enterprise to engage individuals in trial design, creation and use of personal data, and decision making. N-of-1 trials use a multi-crossover design in which each individual receives two or more treatments multiple times in a randomized order. In contrast to traditional clinical trial designs, N-of-1 designs can measure individual treatment efficacy to create personalized knowledge. By combining individual trials in a multilevel structure, they can also assess average treatment effects in populations and subgroups and measure treatment effect heterogeneity to create generalizable knowledge. N-of-1 trials may be deployed in a variety of ways. Individuals may create unique, personal designs focused on treatments and outcomes of interest carried out in a manner best suited to them. Or trials may be coordinated to have similar protocols facilitating the sharing and combining of information to learn about groups of individuals as well. Such designs may better inform individuals too through borrowing of strength from the findings of exchangeable group members. Such group designs may be particularly valuable in clinical settings such as healthcare organizations which provide personalized care to groups of individuals. We discuss the promise and challenges of N-of-1 trials, including the use of software to design and analyze trials, the use of mobile apps to facilitate participation, retain interest, collect data and provide interpreted results to participants, and some of the research barriers that need to be overcome, particularly the challenges of accommodating personalized protocols. These issues are illustrated by several of our recent projects each involving many N-of-1 trials in which we combined mobile device applications with server-driven statistical analytics using an R package to return results to individuals. We discuss defining treatments and sequences of treatments, synthesizing treatment networks, incorporating patient-specific prior information, automating the choice of appropriate statistical models and assessment of model assumptions, and automating graphical displays and text to facilitate appropriate interpretation by non-technical users.

Session J ♣

Machine Learning for Statisticians

Instructors: Andy Liaw, Junshui Ma, Merck & Co., Inc
Moderator: Ivan S. F. Chan

Abstract

Both Machine Learning (ML), which is loosely called Artificial Intelligence in the media, and Statistics are the fields of learning from data. The fact that they share many underlying mathematical theories and computational tools overshadow the fact that they are based on different philosophies. Ignoring the differences caused confusion among some statisticians and prevented them from effective use of some ML technologies.

This tutorial is uniquely designed as an introduction to ML for statisticians. It avoids dwelling on topics that statisticians are already familiar. Instead, it puts emphasis on the areas unique in ML, and draws connections between the two fields for those with superficial similarity.

The presentation has 4 sections: (1) What is ML? This section shows similarities and differences between ML and Statistics and provides an overview of ML. (2) Supervised learning workflow and (3) methods. These two sections explain the workflow, along with key concepts, related to supervised learning tasks, and introduce the popular ML methods, such as SVM, boosting machine, random forests, etc. (4) Model inference. This section explains how to use the trained models to predict, to select/rank variables, and to gain insights into the data. Throughout the tutorial examples from drug development will be used to demonstrate the points.

Wednesday Lunch (On Your Own) 12:15 AM - 1:30 PM

1:30 - 5:00 PM

Session K

Using SAS PROC BGLIMM and MCMC for Bayesian Analysis of Mixed Models 🕮

Instructor: Walter Stroup, University of Nebraska- Lincoln
Moderator: Alfred H. Balch

Abstract

Recent advances in statistical methodology and software capability have made Bayesian analysis of statistical models more accessible to data analysts. As a result, Bayesian methods have become more important. Many academic journals now discourage significance testing in favor of Bayesian inference. More importantly, the ability to use what we know prior to, or in the early stages of an investigation allow us to improve the accuracy and efficiency of statistical analysis. This tutorial introduces the SAS® system BGLIMM and MCMC procedures for Bayesian analysis. PROC BGLIMM uses syntax similar to PROC GLIMMIX to implement linear mixed models (LMMs) and generalized linear mixed models (GLMMs). PROC MCMC uses syntax similar to PROC NLMIXED and can implement non-linear, zero-inflated and semi-parametric mixed models in addition to LMMs and GLMMs. This tutorial uses examples from *SAS for Mixed Models: Introduction and Basic Applications* (Stroup, et al., 2018) and examples to appear in *SAS for Mixed Models: Advanced Applications* to introduce these two procedures and show participants what they need to know to get started with the SAS system for Bayesian analysis.

Session L

Safety and Benefit-Risk Evaluation with Practical Visual Analytical Tools

Instructors: Melvin Munsaka, AbbVie and Jim Buchanan, Covilance LLC
Moderator: William Wang

Abstract

The exploration of drug safety and the evaluation of benefits vs. risks requires the collaboration of multiple disciplines - biostatistics, medical scientists, safety scientists and data managers, to name a few. This tutorial will highlight some of the planning processes to facilitate such evaluations, such as the Aggregate Safety Assessment Plan (ASAP) and the Benefit-Risk Assessment Plan (BRAP), which involves the contribution of multiple stakeholders. The tutorial will also include an overview of quantitative methodological approaches and visual analytics for drug safety monitoring and evaluation at either pre- or post-marketing settings. These methodologies include blinded and unblinded monitoring, Bayesian and frequentist approaches, trial-level and meta-analytical analyses. In addition, practical tools will be described that can assist drug safety data exploration, visual analytics, evaluation, and reporting and benefit-risk assessment.

TWO SIMULTANEOUS SHORT COURSES THURSDAY AND FRIDAY, DECEMBER 8-9, 2022

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.

Thursday Schedule 8:00⇒9:30 Lecture / **9:30⇒9:50** *Break* / **9:50⇒11:20 Lecture** / **11:20⇒12:40** *Lunch on Your Own* / **12:40⇒2:10 Lecture** / **2:10⇒2:30** *Break* / **2:30⇒4:00 Lecture** / **4:00⇒4:20** *Break* / **4:20⇒5:00 Lecture**

Friday Schedule 8:00 - 9:30 Lecture / **9:30 - 9:50** Break / **9:50 - 11:20 Lecture** / **11:20 - 11:40** *Break* / **11:40 - 1:10 Lecture**

Combining Information From Different Studies with Meta-Analysis and Network Meta-Analysis 🕮

Instructors: Professors Christopher Schmid and Thomas Trikalinos, Brown University

Moderator: Alfred Balch

Abstract

Policymakers, scientists, and health care providers increasingly cite evidence-based decision-making as the basis for their choices. For a defined research question focusing on the effects of interventions, exposures or treatments on defined outcomes, systematic reviews provide a scientifically valid approach to synthesize all of the available evidence from research studies. Meta-analysis applies statistical models to estimate the size and direction of the comparative effects derived from multiple studies designed to determine the effect of a treatment, device or test. This course introduces the major principles and techniques of the statistical analysis of meta-analytic data for both summary data available from reports and individual data from studies.

The first part of the course focuses on comparisons of two treatments under a variety of different outcome types and using a variety of statistical models that incorporate within and between-study heterogeneity. The second part of the course extends the models for data that may involve more than two interventions and more than one outcome measured at different times. Reviews with three or more treatments combine data from studies that may each use only a subset of the treatments. These studies form a treatment network, combining direct evidence from studies with head-to-head comparisons and indirect evidence from studies that compare treatments indirectly through a directed path. The network models provide estimates of the relative effectiveness or harms of all included treatments, and a ranking with associated probability estimates. These methods depend on a crucial assumption that the direct and indirect evidence are compatible (consistency) and that treatments are mutually exchangeable across studies (transitivity).

The presentation will combine principles and intuition about the proper application of the methods as well as technical information about the models employed. Although most of the examples will be taken from healthcare, the methods are applicable in any discipline where meta-analysis is undertaken including education, psychology, economics, etc. Examples in each of these areas will be given and discussion is welcomed.

The short course will summarize the parts of a systematic review and the data necessary to carry out meta-analysis

- present different models for analyzing summary data from multiple studies in order to estimate and compare treatment effects in populations and subgroups
- discuss how to model individual participant data from trials
- identify and evaluate concepts and assumptions of network meta-analysis, such as heterogeneity, transitivity, and consistency
- present models for network meta-analysis and how heterogeneity and inconsistency can be explored

Multi-Regional Clinical Development and Safety/Benefit-Risk Evaluation - A Short Course for Statisticians and Non-statisticians 🕮

Instructors: Bruce Binkowitz, Arcutis Biotherapeutics Inc, Gang Li, Eisai Inc, Jim Buchanan, Covilance LLC, Judy Li, BMS, and Aloka Chakravarty, FDA

Moderators: Ivan Chan and William Wang

Abstract

This two-day short course will cover the topics of safety/ benefit risk assessment and multi-regional clinical development. The short course will be based on two recently published books: (1) **The book: "*Multi-Regional Clinical Development After E17*"** expands on the ICH E17 guidance, with more insight from the experts who were involved with creating ICH E17. It further brings examples from real MRCT trials and discusses development of methodology to improve the design and analysis of MRCTs; *(2)* **The book: *"Quantitative Drug Safety and Benefit Risk Evaluation - Practical and Cross-Disciplinary Approaches"*** provides a comprehensive coverage of safety monitoring methodologies, recognizing emerging global trends. Pharmacovigilance during clinical development has traditionally focused on the handling of individual adverse event reports; however, recently there has been a shift towards emphasizing aggregate analysis on an ongoing basis to better understand the scope of product risks.

Even though these two books focus on different perspectives of drug development, in this two-day short course we will connect them by the same clinical development case studies. In particular, we plan to use a cardiovascular drug development program to illustrate the concepts. A workshop style discussion will also be arranged on Day 2 on these case studies.

This is a short course for both statisticians and non-statisticians. Crossdisciplinary audience participation will be highly encouraged.

Outline of the Short Course

Day 1 Morning: MRCT and ICH E17

- ICH E17: Seven (7) principles of Good MRCT Design and Explanation in Each of Them
- Statistical Methodologies for Sample Size and Consistency
- Case Studies in Therapeutic Areas such as CV and Oncology

Day 1 Afternoon: Safety Monitoring and Evaluation

- Regulatory Landscape in Safety Monitoring
- Aggregate Safety Assessment Planning, Safety Signaling and Evaluation, including the use of open-source Interactive Safety Graphics
- Safety Monitoring Methodologies in RCT and RWE

Day 2 Morning: Case Based Examination on MRCT Consistency and Benefit-Risk Evaluation

- Introduction of the Case Studies in Type II Diabetes

- describe efficient tabular and graphical summaries of findings
- include examples from case studies and their interpretation for decision making
- demonstrate how to implement the methods using statistical software

Day 1 Topics Covered

- Systematic Reviews; Types of Data in Meta-Analysis; Estimating a Common Effect; Heterogeneity in Meta-Analysis; Meta-Regression; Bayesian Meta-Analysis; Individual Participant Analysis; Multivariate Meta-Analysis

Day 2 Topics Covered

- Background for network meta-analysis; Direct and indirect comparisons; Exchangeability; Heterogeneity; Consistency; Models under consistency assumption; Ranking of Treatments; Evaluating Network Assumptions: Exchangeability, Consistency

Christopher Schmid is Professor of Biostatistics at Brown University School of Public Health where he co-founded the Center for Evidence Synthesis in Health. Before that he worked for many years directing the Biostatistics Research Center at Tufts Medical Center in Boston. He has a long record of collaborative research in diverse areas of medicine and health with academia, government and industry and has more than 200 peer-reviewed publications. He has coauthored consensus CONSORT reporting guidelines for N-of-1 trials and single-case designs, and PRISMA guidelines extensions for meta-analysis of individual participant studies and for network meta-analyses as well as the Institute of Medicine report that established US standards for systematic reviews. His research focuses on Bayesian methods for meta-analysis, including networks of treatments and N-of-1 designs, as well as open-source software tools. He has developed predictive models for heart attack risk and the risk of dehydration in children suffering from diseases in the developing world. He also led analyses for the CKD-EPI consortium that developed the most commonly used formulas to estimate kidney function (GFR) based on the biomarkers serum creatinine and serum cystatin. He is lead statistician on several N-of-1 trial consortia. Professor Schmid is a Fellow of the American Statistical Association, founding Editor of the journal *Research Synthesis Methods,* long-time statistical editor of the *American Journal of Kidney Diseases* and served for several years on the FDA Drug Safety and Risk Management Committee.

Thomas Trikalinos is Professor of Health Services, Policy and Practice at Brown University School of Public Health where he co-founded the Center for Evidence Synthesis in Health. Tom studied medicine in Greece. Currently he directs the Center for Evidence Synthesis in Health at Brown University -- CESH for short. CESH faculty and staff work on novel methodologies for comparative effectiveness research, with emphasis on the steps of evidence synthesis (by means of systematic review and meta-analysis), and evidence contextualization (by means of decision and economic analysis). Trikalinos and his colleagues strive to modernize and optimize the processes of evidence-synthesis by porting methodologies from computer science and applied mathematics. His current research is on decision making under deep uncertainty.

- Statistical Methodologies for Pooling and Consistency
- Benefit-risk Evaluation and Visualization

Day 2 Afternoon: Workshop Presentation and Panel Discussion

- Break up for attendees into subgroup with pre-arranged discussion topics
- Presentations by each of the working groups
- Panel discussion

Dr. Bruce Binkowitz is the Vice President of Biometrics at Arcutis Biotherapeutics Inc. Bruce has more than 30 years of pharmaceutical industry experience across many therapeutic areas as well as from early phase through phase IV clinical trials. He has experience in study design, conduct, analysis, and interpretation of results for clinical trials, as well as many interactions with health authorities worldwide. Dr. Binkowitz is active in the Statistical Community. Bruce is currently in his second term as co-leader of the cross-industry Multi-Regional Clinical Trial Consistency Expert Group. Dr. Binkowitz was elected a fellow of the American Statistical Association in 2015, and was awarded the 2022 Distinguished Alumni Award by the Rutgers School of Public Health.

Dr. Gang Li is Senior Director, Real World Evidence (RWE) and Medical Value, the Neurology Business Group of Eisai Inc. He received his PhD in Mathematical Statistics from the State University of New York at Binghamton. He co-authored over 60 publications on statistical methodologies, and research on psychiatry, obesity, and diabetes. He served as the Executive Director of the International Statistical Association (2017–2019). Dr. Li is a Fellow of the American Statistical Association.

Dr. James Buchanan, president of Covilance LLC, has 30+ years of drug safety experience in the pharmaceutical industry. He is a co-lead of the ASA Biopharmaceutical Safety Working Group and the Interactive Safety Graphics taskforce that is developing novel, open-source, interactive graphical tools to evaluate drug safety issues.

Dr. Judy X. Li is currently Senior Director, Biostatistics Lead for San Diego site Bristol Myers Squibb. She also has extensive experience working at the US Food and Drug Administration as a master statistical reviewer and supervisory mathematical statistician. She is the founding co-chair of the ASA Biopharmaceutical Safety Working Group.

Dr. Aloka Chakravarty is currently the Senior Statistical Advisor in the Office of the Commissioner, FDA for real-world data and evidence activities related to collaborations on COVID-19 and others. She is also working on select strategic data initiatives at FDA with the Chief Data Officer. Prior to that, she was the Deputy Director of the Office of Biostatistics in CDER, FDA. She is an internationally recognized thought leader in multi-regional clinical trials, safety evaluation, real world data and evidence, surrogate markers and biomarkers in drug development. Dr. Chakravarty served as an Adjunct Faculty in Department of Statistics, FAES, NIH and has been on Advisory Board of multiple academic institutions. Dr. Chakravarty has received numerous awards, including the FDA Award of Merit and Dr. Frances O. Kelsey Drug Safety Excellence Award. She received her Ph.D. in Statistics from Temple University, and M. Stat from Indian Statistical Institute. Dr. Chakravarty is a Fellow of the American Statistical Association and an Associate Editor of Statistics in Biomedical Research.

THREE KEYNOTES

(Monday, Tuesday, and Wednesday Morning, December 5-7, 2022, 8-9am)

Walter Young Memorial Session

Moderator: Alfred H. Balch

Abstract

Walter Richard Young, as the past chair of Deming conference, made significant contributions to shape this conference into today's format in the past 50 years. Walter passed away at the age of 83 on Friday, February 11th, 2022. He was survived by his wife, Lolita; his daughter, Katharine; his two sons, Peter and Walter (Albert); and their wives, Melissa and Maria. The 78th Deming conference organizing committee is hosting a special memorial session to commemorate Walter Young for his life-long contributions to this conference.

Keynote 2: Harnessing the Power of Statistics: Big Challenges, Big Opportunities

Susan Ellenberg, University of Pennsylvania

Moderator: Ivan S. F. Chan

Abstract

Vaccines to protect against the worldwide COVID-19 pandemic were developed in an astoundingly short time. The rapid sequencing of the virus SARS-COV-2 allowed vaccine manufacturers to formulate vaccine candidates very quickly, and after initial phase 1 studies were able to launch large scale trials by July 2020, only 6 months after the virus was initially identified. Five vaccine candidates were selected by the U.S. government for "Operation Warp Speed;" trials of these vaccines were conducted with the involvement of the National Institute of Allergy and Infectious Diseases and the Biomedical Advanced Research and Development Authority, and were overseen by a single Data and Safety Monitoring Board (DSMB). The Board faced a number of challenges during the monitoring process, primarily due to the urgent need for safe and effective vaccines, and to the fact that each vaccine manufacturer contracted with its own independent statistical/data management groups to perform interim analyses and present them to the DSMB.

Following the Emergency Use Authorization of vaccines shown to be safe and effective in the clinical trials, the vaccines were rapidly deployed; and just as rapidly, misinterpretation of the emerging post-marketing safety data entered into circulation. In this presentation I will discuss the challenges of monitoring the vaccines both prior to and after the vaccines became available to the public.

Keynote3: New Statistical Initiatives in the FDA CDRH

Aloka Chakravarty, FDA

Moderator: Bill Wang

Abstract

Clinical data collected outside of traditional clinical trials—also known as "real-world data"— can provide insights to FDA on how COVID-19 treatments, diagnostics, and vaccines are performing in a variety of clinical settings. The reliability and utility of real-world data depend on the application of rigorous analytical methods as well as validation and cross-checking of analyses. Through the Evidence Accelerator and other initiatives in the therapeutics and devices domains, FDA has collaborated to provide a unique venue for major data organizations, government and academic researchers, and health systems to share quickly insights, compare results, and answer curated key questions about COVID-19 treatment and response. In addition, the collaboration provided insights into understanding of disease, severity categorization, treatment characterizations and outcomes ascertainment. In this presentation, we will highlight, through use case examples, how FDA utilized parallel analysis, rapid-cycle queries, and other collaborative mechanisms simultaneously to respond to the evolving questions during the pandemic.

Committee Members

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Three Day Conference (December 7-10)	$900 ❑	$1050 ❑	$1250 ❑	$1450 ❑	
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Student (Full time status proof needed) or Retiree	$425 ❑	$475 ❑	$675 ❑	$775 ❑	
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Speaker Dinner (Optional, Monday 7:00 PM)	$60 ❑	$60 ❑	$60 ❑	$60 ❑	
Two Day Short Course (December 11-12)					
❑ Combining Information from Different Studies with Meta-Analysis and Network Meta-Analysis	$1030 ❑	$1180 ❑	$1380 ❑	$1450 ❑	
❑ Multi-regional Clinical Development and Safety/Benefit-Risk evaluation	$1030 ❑	$1180 ❑	$1380 ❑	$1450 ❑	

Registration for a short course is required and independent of the registration for the tutorial sessions.

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