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

Sponsored by
Deming Conference Organization
AMERICAN STATISTICAL ASSOCIATION: Biopharmaceutical Section

December 3 – December 8, 2023: Three-Day Conference plus Two-Day Short Course
Sonesta Philadelphia Rittenhouse Square, 1800 Market St, Philadelphia, PA

Three Keynotes on December 4-6, 2023

The Power of AI, Data Sciences, and Technology in Drug Development, **Venkat Sethuraman**, Bristol Myers Squibb
Interpreting Deep Neural Networks towards Trustworthy AI, **Prof. Bin Yu**, UC Berkeley
Deming's Contributions and Big Data, **Prof. David Banks**, Duke University

Twelve Sessions of Tutorials on December 4-6, 2023 and Two Short Courses on December 7-8, 2023

Short Course 1. Real-world Evidence in Medical Product Development
by **Weili He, Yixin Fang, and Hongwei Wang**, Abbvie

Short Course 2. Statistical Analysis with Missing Data
by **Prof. Rod Little**, University of Michigan, and **Prof. Qixuan Chen**, Columbia University

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 3rd and will be followed by a one-hour reception with cold drinks and snacks. It will continue at 6:30 AM Monday December 4th through Thursday December 7th.
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 15th 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 15, 2023. 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 (79th) 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 3, 2023 Registration: 6:00 ⇒ 7:30 PM and Reception 7:00 ⇒ 8:00 PM

Monday December 4, 2023 Registration: 6:30 ⇒ 8:00 AM and Hot Breakfast 7:00 ⇒ 7:50 AM

8:00 ⇒ 9:00 AM Keynote: **The Power of AI, Data Sciences, and Technology in Drug Development, Venkat Sethuraman, Bristol Myers Squibb**
Moderator: Ivan S. F. Chan

Session A (9am-12pm) An Introduction to Machine Learning Methods for Optimal Dynamic Treatment Decisions in Precision Medicine Prof. Donglin Zheng, UNC and Prof. Yuanjia Wang, Columbia University Moderator: Kalyan Ghosh	**Session B (9am-12pm)** Evaluating Predictive Accuracy of Survival Models Using the ROC Curve and Related Measures in Clinical Trial Applications Kassu Mehari Beyene and Ding-Geng (Din) Chen, ASU Moderator: Alfred H. Balch
Lunch (On Your Own) 12:00 ⇒ 2:00 PM	
Session C♣ (2pm-5pm) Cell and Gene Therapy: Introduction and Overview of Important Regulatory, Statistical and Operational Considerations Shihua Wen, Novartis and Patricia Anderson, ICON Moderator: Ivan S. F. Chan	**Session D ♣ (2-5pm)** Bayesian semi-parametric approaches to exposure-response modeling with time-to-event outcomes Tim Waterhouse, Statistics Metrum Research Group Moderator: Alfred H. Balch
7:00 PM Speaker's and Awards Dinner (Optional Added Fee Event)	

Tuesday December 5. 2022 Registration: 7:00 ⇒ 8:00 AM and Hot Breakfast 7:00 ⇒ 7:50 AM

11:00 ⇒ 12:00 PM: Keynote: Interpreting Deep Neural Networks towards Trustworthy AI, Prof. Bin Yu, UC Berkeley
Moderator: Alfred H. Balch

Session E ♣v(8am-11pm) Leveraging Real-World Data in Medical Product Clinical Trials Design and Analysis Chenguang Wang, Regeneron Moderator: Naitee Ting	**Session F ♣ (8am-11pm)** Subgroup Analysis and Causal Inference with Application in Medical Research Prof. Menggang Yu, University of Wisconsin-Madison Moderator: William Wang
Lunch (On Your Own) 12:00 ⇒ 2:00 PM	
Session G (2pm-5pm) Sequential monitoring of adaptive randomized clinical trials Hongjian Zhu, AbbVie Inc. Moderator: Weili He	**Session H (2pm-5pm)** Win statistics (win ratio, win odds and net benefit): introduction, properties, implementations, and applications Gaohong Dong, BeiGene and Margaret (Meg) Gamalo, Pfizer Moderator: Jingjing Ye

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

8:00 ⇒ 9:00 AM: Keynote: Deming's Contributions and Big Data, Prof. David Banks, Duke University
Moderator: Alfred H. Balch

Session I ♣ (9am-12pm) Statistical Strategies and Practical Considerations for Dose Optimization Prof. Ying Yuan, University of Texas, MD Anderson Cancer Center Moderator: Jerry Li	**Session J ♣ (9am-12pm)** Bayesian Adaptive Statistical Approaches for Accelerating Drug and Medical Device Approvals in Rare Disease Bradley P. Carlin, PharmaLex - US Moderator: Din Chen
Lunch (On Your Own) 12:00 ⇒ 2:00 PM	
Session K (2pm-5pm) Introduction to Adaptive Design Methods for Dose and Treatment Selection Prof. Haitao Pan, St. Jude Children's Research Hospital Moderator: Naitee Ting	**Session L (2pm-5pm)** Enhancing Treatment Effect Assessment through Covariate Adjustment Methods Margaret Gamalo, Jinma Ren, Wenjin Wang, Pfizer Inc Moderator: Li-An Xu

Thursday December 7, 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**

Real-world Evidence in Medical Product Development 🕮 Weili He, Yixin Fang, and Hongwei Wang, Abbvie Moderator: Jerry Li	Statistical Analysis with Missing Data Prof. Rod Little, University of Michigan, and Prof. Qixuan Chen, Columbia University Moderator: Alfred H. Balch

Friday December 8, 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

Patricia Anderson, MD, is currently Assoc. Director of Biostatistics and the Biometrics Lead for the ICON Centre for Cell and Gene Therapy. Her therapeutic experience spans diagnostic imaging (including national trials and registries), solid tumors, melanoma, blood disorders and cancers, stem cell transplant, cell and gene therapy, and others. Patricia began work in cell therapy and stem cell transplant in 2012 at MD Anderson Cancer Center. At ICON, Patricia developed a team of biometrics CGT subject matter experts and leads creation of new biometrics CGT training and standards. She received her undergraduate and graduate degrees from Brown University. Research interests have included adaptive randomization and early phase study design.

David Banks obtained a **Ph.D**. in Statistics in 1984. He won an NSF Postdoctoral Research Fellowship in the Mathematical Sciences, which he took at Berkeley, working with David Blackwell. In 1986 he was a visiting assistant lecturer at the University of Cambridge, and then joined the Department of Statistics at Carnegie Mellon in 1987. In 1997 he went to the National Institute of Standards and Technology, then served as Chief Statistician of the U.S. Department of Transportation, and finally joined the U.S. Food and Drug Administration in 2002. In 2003, he returned to academics at Duke University. He was the coordinating editor of the *Journal of the American Statistical Association*. He co-founded the journal *Statistics and Public Policy* and served as its editor. He co-founded the American Statistical Association's Section on National Defense and Homeland Security, and has chaired that section, as well as the sections on Risk Analysis and on Statistical Learning and Data Mining. David Banks is past president of the Classification Society and of the International Society for Business and Industrial Statistics. He has twice served on the Board of Directors of the American Statistical Association. He is a fellow of the American Statistical Association, of the Institute of Mathematical Statistics, and of the American Association for the Advancement of Science. He won the American Statistical Association's Founders Award, the De Groot Award, and gave the William Sealy Gosset Lecture and the Deming Lecture. From January 2018 to September 2021, he was the director of SAMSI. His research areas include models for computational advertising, dynamic text networks, adversarial risk analysis (i.e., Bayesian behavioral game theory), human rights statistics, agent-based models, forensics, and certain topics in high-dimensional data analysis.

Kassu Mehari Beyene, PhD, is a postdoctoral research scholar in Biostatistics at the College of Health Solutions, Arizona State University at Phoenix. After earning a PhD in Biostatistics from Catholic University of Louvain (Belgium), he worked an assistant professor in biostatistics at the Department of Statistics, Wollo University, Ethiopia. His research interest includes the ROC curve and other related approaches for evaluating predictive accuracy of biomarkers, survival data analysis, infectious disease modeling, and longitudinal data analysis. He has three research publications in ROC curve estimation for censored time-to-event data and also published an R package for ROC curve and related measures estimation in the context of survival data. He presented talks about ROC curve and related measures estimation and survival data analysis at various professional conferences and seminars.

Brad Carlin, PhD, is a statistical researcher, methodologist, consultant, and instructor. In addition to serving as founder and president of Counterpoint, he is also Senior Advisor for Data Science and Statistics at PharmaLex, an international pharmaceutical consulting firm. Prior to this, he spent 27 years on the faculty of the Division of Biostatistics at the University of Minnesota School of Public Health, serving as division head for 7 of those years. He has also held visiting positions at Carnegie Mellon University, Medical Research Council Biostatistics Unit, Cambridge University (UK), Medtronic Corporation, HealthPartners Research Foundation, the M.D Anderson Cancer Center, and AbbVie Pharmaceuticals. He has published more than 185 papers in refereed books and journals and has co-authored three popular textbooks: "Bayesian Methods for Data Analysis" with Tom Louis, "Hierarchical Modeling and Analysis for Spatial Data" with Sudipto Banerjee and Alan Gelfand, and "Bayesian Adaptive Methods for Clinical Trials" with Scott Berry, J. Jack Lee, and Peter Muller. From 2006-2009 he served as editor-in-chief of Bayesian Analysis, the official journal of the International Society for Bayesian Analysis (ISBA). During his academic career, he served as primary dissertation adviser for 20 PhD students. Dr. Carlin has extensive experience teaching short courses and tutorials and won both teaching and mentoring awards from the University of Minnesota. During his spare time, Brad is a health musician and bandleader, providing keyboards and vocals in a variety of venues.

Din Chen received his **Ph.D**. in Statistics from the University of Guelph (Canada) in 1995 and is now the executive director and professor in Biostatistics at the College of Health Solutions, Arizona State University, USA. He is also an extraordinary professor and the DST-NRF-SAMRC SARCHI research chair (Tier 1) in biostatistics, at the Department of Statistics, University of Pretoria, South Africa. Dr. Chen served as the Wallace H. Kuralt distinguished professor in biostatistics at the University of North Carolina-Chapel Hill from 2005 to 2021, a biostatistics professor at the University of Rochester Medical Center from 2020 to 2025, the Karl E. Peace endowed eminent scholar chair in biostatistics from the Jian-Ping Hsu College of Public Health at the Georgia Southern University from 2019 to 2020. Dr. Chen is an elected fellow of the American Statistical Association and a senior expert consultant for biopharmaceuticals and government agencies with extensive expertise in clinical trial biostatistics. Dr. Chen has more than 200 scientific publications and co-authored/co-edited 38 books on clinical trials, survival data, meta-analysis, causal inference and structural equation modeling, Monte-Carlo simulation-based statistical modelling. His research has been funded as PI/Co-PI from NIH R01s and other governmental agencies.

Gaohong Dong, PhD, has 20 years of experience in the pharmaceutical industry. He is a Director of Biostatistics at BeiGene. Prior to joining BeiGene, he worked at Novartis, then worked as a consultant under his own entity of iStats Inc. Gaohong has been supporting drug development in multiple therapeutic areas including solid organ transplant, stem-cell transplant, infection disease, and oncology. He is a co-author of many highly cited medical papers. Gaohong has a great passion on statistical research. He published peer-reviewed statistical journal papers and book chapters on Bayesian-Frequentist design, adaptive design, missing data imputation, meta-analysis, and composite of prioritized multiple outcomes. During the recent years, he has been focusing on the win statistics (win ratio, win odds, and net benefit). His research of the stratified win ratio and the win odds have been applied to designs and analyses of clinical trials including phase III studies. Gaohong has been serving as an Associate Editor of the Journal of Biopharmaceutical Statistics since 2017.

Margaret (Meg) Gamalo, PhD, is Statistics Head for Inflammation and Immunology in Pfizer Global Product Development. She combines expertise in biostatistics, regulatory science and adult and pediatric clinical development. Prior to joining Pfizer, she was Research Advisor, Global Statistical Sciences at Eli Lilly and Company and as Mathematical Statistician at the Food and Drug Administration. Meg leads the Complex Innovative Design 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 currently Editor-in-Chief of the Journal of Biopharmaceutical Statistics and is actively involved in many statistical activities in the American Statistical Association. Recently, she was elected Fellow of the American Statistical Association.

Haitao Pan, PhD, is an Associate Professor of Biostatistics at St. Jude Children's Research Hospital. His research is primarily focused on developing innovative clinical trial designs, particularly for oncology, from early to late phases. Since joining St. Jude in 2017, Dr. Pan has served as the Primary Study Statistician for 32 St. Jude investigator-initiated clinical trials and is a member of the Clinical Trials – Scientific Review Committee at St. Jude. He has authored over 50 publications in peer-reviewed journals, spanning across medical and statistical journals, and has published a book through Springer Nature. Dr. Pan has also developed 16 R software packages, with a specific focus on adaptive clinical trial design and sample-size calculation. Many of these have been used to develop clinical trial protocols at St. Jude. Additionally, Dr. Pan is an adjunct faculty member at Florida State University and The University of Memphis. Dr. Pan holds two Ph.D. degrees: one in Preventive Medicine from China, and another in Biostatistics from MD. Anderson Cancer Center.

Jinma Ren, PhD and MD, is a director of biostatistics in the Statistical Research & Data Science Center (SRDC) and its Health Economics & Outcomes Research (HEOR) Statistics Group at Pfizer Inc., where he has provided statistical support to oncology and other areas on HEOR projects, mainly for health technology assessment (HTA). Currently, as statistics lead, he is helping design and analyze externally controlled studies to support HTA submissions for Elranatamab. Jinma is also leading the analyses of patient-reported outcomes (PRO) in Paxlovid trials. Prior to join Pfizer, Jinma has 15+ years of outcomes research experience from both academia and industry, and he serves on the editorial board of two major peer-reviewed journals. Jinma holds both PhD degree in epidemiology and health statistics and MD degree in preventive medicine.

Venkat Sethuraman, PhD, serves as the senior vice president of Global Biometrics and Data Sciences at Bristol Myers Squibb, where he oversees the data and digital strategy by utilizing data science, advanced clinical trial solutions and robust digital tools to accelerate our pipeline.Venkat and his team are working at the forefront of how Bristol Myers Squibb is utilizing digital innovation to revolutionize drug development by harnessing the power of big data, artificial intelligence (AI) and machine learning approaches to power prediction from the earliest inception of our programs. In his role, Venkat is one of the driving minds behind the way Bristol Myers Squibb leverages advanced machine learning to accelerate early assets and clinical trials.

Chenguang Wang, PhD, is a Senior Director and the Head of Statistical Innovation at Regeneron. Previously, Dr. Wang was an Associate Professor with Johns Hopkins University and an FDA Mathematical Statistician at CDRH. Dr. Wang has extensive experience in clinical trial design and analysis in the regulatory setting. Dr. Wang also holds B.S. and M.S. degrees in Computer Science and has abundant experience developing user-friendly statistical software.

Wenjin Wang, PhD, is a senior director in Global Biometrics & Data Management within Pfizer Research & Development division, Pfizer Inc. Currently he is leading the statistical group for the development of gastrointestinal therapeutic products. With over two decades of experience in the pharmaceutical industry, Wenjin has played a pivotal role in driving the success of developing several products that are in the market today by merging statistical expertise and regulatory insight. Wenjin is also actively serving in professional activities. He is a co-founder and esteemed board member of the International Society for Biopharmaceutical Statistics. He serves executive and program committee roles for the Annual Deming Conference on Applied Statistics since 2005. He is a book review editor for Journal of Biopharmaceutical Statistics. He was an ASA president appointed member of the inauguration committee for the ASA Conference on Statistical Practice and contributed to the program organization over four years. He was also a representative of the Biotechnology Industry Organization (BIO) Adaptive Design Working Group.

Yuanjia Wang, PhD, works on developing data-driven approaches to uncover complex relationships between biomarkers, clinical markers, environmental variables and health outcomes to assist studies of disease etiology, diagnostic capabilities and optimal treatments. Her methodological interests include machine learning, analytics for precision medicine, network analysis, and novel design and analysis of clinical trials and electronic health records. Her substantive applied research area includes psychiatric disorders and neurological disorders.

Tim Waterhouse, PhD, has worked at Metrum since 2019, in both PK/PD and statistics. He attained his Ph.D. in Statistics from the University of Queensland, where he applied optimal design methods to PK/PD models. He then worked at Eli Lilly and Company in pharmacometrics before joining Metrum. His work involves using modeling and simulation to inform decision making in all phases of drug development across a range of therapeutic areas.

Shihua Wen, PhD, is currently a Sr. director of biostatistics in Novartis Pharmaceuticals Corp. (US). He joined Novartis in 2016 and started to work in gene therapy area in the recent years. Dr. Wen has rich experience in late phase clinical development across multiple therapeutic areas. At Novartis, he served as the statistical lead for multiple global clinical development programs in neurology area and successfully supported regulatory submissions with major health authorities. Prior to Novartis, he worked in Abbott Laboratory / AbbVie Inc. as a biostatistician as well with increasing responsibility. Dr. Wen received his doctoral degree in statistics at University of Maryland, Collage Park, in 2007. His research interests are drug development, benefit-risk assessment, innovative trial design, data fusion, etc.

Bin Yu, PhD, is Chancellor's Distinguished Professor and Class of 1936 Second Chair in the Departments of statistics and EECS, and Center for Computational Biology at UC Berkeley. She obtained her BS Degree in Mathematics from Peking University, and MS and PhD Degrees in Statistics from UC Berkeley. She was Assistant Professor at UW-Madison, Visiting Assistant Professor at Yale University, Member of Technical Staff at Lucent Bell-Labs, and Miller Research Professor at Berkeley. She was a Visiting Faculty at MIT, ETH, Poincare Institute, Peking University, INRIA-Paris, Fields Institute at University of Toronto, Newton Institute at Cambridge University, and the Flatiron Institute in NYC. She was Chair of the Department of Statistics at UC Berkeley. She has published more than 170 publications in premier venues and these papers not only investigate a wide range of research topics from practice to algorithms and to theory, but also seek deep insights. The breadth and depth of her research experience enabled unique and novel solutions to interdisciplinary data problems in audio and image compression, network tomography, remote sensing, neuroscience, genomics, and precision medicine.Bin Yu is a Member of the U.S. National Academy of Sciences and of the American Academy of Arts and Sciences. She is Past President of the Institute of Mathematical Statistics (IMS), Guggenheim Fellow, Tukey Memorial Lecturer of the Bernoulli Society, Rietz Lecturer of IMS, and a COPSS E. L. Scott Prize winner. She has been selected to deliver the Wald Memorial Lectures of IMS at JSM in 2023.

Menggang Yu, PhD, is a professor at the Department of Biostatistics and Medical Informatics, University of Wisconsin – Madison and Director of the Biostatistics Shared Resources at the UW Carbone Cancer Center. He is an elected fellow of the American Statistical Association (ASA). Dr. Yu conducts broad statistical methodology research, all motivated by his daily collaborative experience with medical investigators. His methodological publications cover extensive topics including joint modeling of longitudinal and survival data, missing data, clinical trial design and analysis, causal inference, and personalized medicine. Dr. Yu is also a devoted statistical collaborator. One of his career goals is to make integral contributions to scientific research that has direct impact on human health. His scientific collaboration is mainly in the areas of cancer and health care research. He has also co-authored over 80 collaborative medical papers, among which over 25% are in highly impactful medical journals (with 2017 impact factors range from 10.0 to 244.6). These publications introduce ground-breaking and practice-changing results to many areas of oncology and health services.

Ying Yuan, PhD, is Bettyann Asche Murray Distinguished Professor and Deputy Chair in the Department of Biostatistics at University of Texas MD Anderson Cancer Center. Dr. Yuan is an internationally renowned researcher in innovative Bayesian adaptive designs, with over 140 statistical methodology papers published on early phase trials, seamless trials, biomarker-guided trials, and basket and platform trials. The designs and software developed by Dr. Yuan's lab (www.trialdesign.org) have been widely used in medical research institutes and pharmaceutical companies. The BOIN design, developed by Dr. Yuan's team, is a groundbreaking oncology dose-finding design that has been recognized by the FDA as a fit-for-purpose drug development tool. Dr. Yuan was elected as the American Statistical Association Fellow, and is the leading author of two books, "Bayesian Designs for Phase I-II Clinical Trials" and "Model-Assisted Bayesian Designs for Dose Finding and Optimization," both published by Chapman & Hall/CRC.

Donglin Zeng, PhD, is a professor at the Gillings School at University of North Carolina at Chapel Hill. Dr. Zeng is an expert on modern empirical process theory and semiparametric efficiency theory. He has made important contributions to survival analysis, causal inference, missing data, semiparametric models, statistical genetics, personalized medicine, machine learning and high-dimensional data.He has published over 100 papers, most of which have appeared in first-tier statistical journals. Dr. Zeng is a Fellow of the American Statistical Association and a Fellow of the Institute of Mathematical Statistics.

Hongjian Zhu received his Ph.D. in Statistics from the University of Virginia in 2010 and subsequently completed postdoctoral training at Yale University in 2012. Then he joined UTHealth and was promoted to tenured Associate Professor. Currently, he is a Director in the Statistical Innovation Group at AbbVie Inc. In this role, he offers strategic, innovative thinking and develops novel statistical methodology for various Therapeutic Areas, including Immunology, Oncology, and Eyecare. His primary research focuses on adaptive clinical trial designs. He has published papers in top-tier journals such as *The Journal of the American Statistical Association (JASA), The Annals of Statistics, Biometrics, The Journal of the American Medical Association (JAMA), and The Journals of the American College of Cardiology (JACC).* He received funding from the National Science Foundation as the Principal Investigator. He is an Elected Member of the International Statistical Institute (ISI) and president-elect of the Houston Area Chapter of the ASA (HACASA).

Monday December 4, 2023 9:00 – 12:00 PM

Session A

An Introduction to Machine Learning Methods for Optimal Dynamic Treatment Decisions in Precision Medicine

Prof. Donglin Zheng, UNC and Prof. Yuanjia Wang, Columbia University

Moderator: Kalyan Ghosh

Abstract

This tutorial provides a comprehensive introduction to the development and application of machine learning methods for making optimal treatment decisions in personalized or precision medicine. In the first part, the tutorial begins by introducing causal inference under a potential outcome framework and then describes the concepts of heterogeneous treatment effects and dynamic treatment regimens. Next, the tutorial will illustrate how to use observational studies and sequentially randomized trials to estimate these quantities. Machine learning methods for estimating optimal dynamic treatment regimens or decisions will be introduced, with a focus on Q-learning and O-learning. The second part of the tutorial focuses on recent advancements in more complex settings, providing participants with a comprehensive overview of real-world applications. These advancements include the integration of real-world evidence (e.g., electronic health records), analysis of multi-domain outcomes, and consideration of the benefit-risk balance in decision-making.

Session B

Evaluating Predictive Accuracy of Survival Models Using the ROC Curve and Related Measures in Clinical Trial Applications

Kassu Mehari Beyene and Ding-Geng (Din) Chen, ASU

Moderator: Alfred H. Balch

Abstract:

In clinical trials, one of the common endpoints is time-to-event, which can be defined as the duration between randomization and the occurrence of a well-defined event of interest. The event, for example, can be death due to certain disease, disease progression, treatment failure or the recurrences of a disease. In such follow-up studies, the event of interest is not necessarily experienced by all study participants at the end of the study, so the actual event times for some subjects are unknown. This loss of information on time-to-event is known as censoring, which may occur when a subject withdraws from the study, lost to follow-up, or the study ends before the event has occurred. Survival analysis, or more generally, time-to-event analysis, is a standard tool to take this unique feature into account. Survival models, for example, Cox proportional hazards model, can be used to identify significant survival-related biomarkers or compare the efficacy between a new treatment and a placebo or an active treatment.

Like many other statistical models, however, ensuring their validity is crucial before using them in routine clinical practice. Assessing the validity of survival models often involves measuring the predictive accuracy, the ability of a model to predict the risk of a future event given a set of baseline factors. In literature, there are several ways for assessing the predictive accuracy of survival models which are often described by two components: calibration and discrimination. Discrimination characterizes how well the model can classify subjects into one of the two groups (e.g., diseased and non-diseased), whereas calibration measures the degree of closeness between the predicted probabilities and the observed outcome. There are a variety of methods to evaluate the discriminatory ability of a survival model. The most commonly used are the receiver operating characteristic (ROC) curve and the associated summary measures.

This tutorial is to discuss the ROC curve and its associated summary measures in the context of censored data with detailed step-by-step illustrations and implementations using the R software from R package ***cenROC***. In this tutorial, we will use publicly available dataset from the Mayo Clinic trial in primary biliary cirrhosis (PBC) of the liver and other clinical trial datasets to illustrate the ROC curve and the associated summary measures analysis.

Monday Lunch (On Your Own) 12:00 PM – 2:00 PM

2:00 - 5:00 PM

Session C♣

Cell and Gene Therapy: Introduction and Overview of Important Regulatory, Statistical and Operational Considerations

Shihua Wen, Novartis and Patricia Anderson, ICON

Moderator: Ivan S. F. Chan

Abstract

As the science of advanced therapy medicinal products continues to evolve, the impact of cell and gene therapies (CGT) on patients around the globe is increasing. In this half-day short course, presenter(s) from the American Statistical Association's Cell and Gene Therapy Scientific Working Group will provide an overview on cell and gene therapy concepts, as well as highlight important regulatory, statistical (e.g., using historical information in clinical trials, estimand, data monitoring, etc.), and operational considerations during the clinical development of the CGT. The course will also include case studies from approved therapies or investigational products.

Session D ♣

Bayesian semi-parametric approaches to exposure-response modeling with time-to-event outcomes

Tim Waterhouse, Statistics Metrum Research Group

Moderator: Alfred H. Balch

Abstract

The importance of exposure-response (ER) analyses in the realm of drug development cannot be overstated. These analyses serve to understand how varying doses or levels of a drug correlate with the therapeutic outcomes, side effects, and overall patient response.

In the conventional landscape, parametric ER time-to-event (TTE) models have been widely adopted. These models, which rely on a fixed form for the hazard function, make assumptions about the shape of the underlying distribution. While they can be straightforward and computationally less demanding, their restrictive nature can sometimes limit the ability to capture the underlying complexity in the data.

A more flexible alternative is the Bayesian semi-parametric approach to TTE modeling. This tutorial introduces this methodology, particularly focusing on models that account for time-varying exposure. One such model discussed in detail is the piecewise exponential model, which divides the timeline into intervals and allows the hazard rate to change at each interval boundary. This allows for a more adaptable fit to the data, especially when there are sudden changes or non-uniform patterns in the exposure levels or response over time.

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

Tuesday December 5, 2023 8:00 – 11 AM

Session E ♣

Leveraging Real-World Data in Medical Product Clinical Trials Design and Analysis

Chenguang Wang, Regeneron

Moderator: Naitee Ting

Abstract

Incorporating real-world data (RWD) in regulatory decision-making demands much more than "mixing" RWD with investigational clinical trial data. The RWD has to undergo appropriate analysis for deriving the right real-world evidence (RWE). Moreover, such analysis has to be integrated with the design and analysis of the investigational study for regulatory decision-making. The standard clinical trial toolbox does not offer ready solutions for incorporating RWD. Therefore, there is an unmet need for sound clinical trial design and analysis for leveraging RWE in clinical evaluations.

In this course, the instructor will cover a series of methods they have developed for leveraging real-world data in clinical trial design and analysis. Noteworthy, these work has been recognized by the FDA and received The FDA CDRH Excellence in Scientific Research Award and The FDA Scientific Achievement Award for extraordinary achievements in the timely development and active promotion of novel statistical methods for leveraging real-world evidence to support regulatory decision-making.

In Part I of the course, the instructor will introduce a method for proposing performance goals—numerical target values pertaining to effectiveness or safety endpoints in single-arm medical product clinical studies—by leveraging RWE. The method applies entropy balancing to address possible patient dissimilarities between the study's target patient population and existing real-world patients and can take into account operation differences between clinical studies and real-world clinical practice.

In Part II of the course, the instructor will introduce a method that extends the Bayesian power prior approach for a single-arm study to leverage external RWD. The method uses propensity score methodology to pre-select a subset of RWD patients that are similar to those in the current study in terms of covariates, and to stratify the selected patients together with those in the current study into more homogeneous strata. The power prior approach is then applied in each stratum to obtain stratum-specific posterior distributions, which are combined to complete the Bayesian inference for the parameters of interest.

In Part III of the course, the instructor will describe an R package, psrwe, that implements a PS-integrated power prior (PSPP) method, a PS-integrated composite likelihood (PSCL) method, and a PS-integrated weighted Kaplan-Meier estimation (PSKM) method for the methods in Part II. Illustrative examples are provided to demonstrate each of the approaches.

Session F ♣

Subgroup Analysis and Causal Inference with Application in Medical Research

Prof. Menggang Yu, University of Wisconsin-Madison

Moderator: William Wang

Abstract

Modern therapeutic studies typically involve subgroup analysis, whether it is pre-specified or post hoc. A key aspect of subgroup analysis is to identify clinically relevant patient characteristics for estimation of treatment effect heterogeneity and for treatment recommendation that may optimize treatment effectiveness or generate interesting research questions.

In this short course, we will introduce two general frameworks that encompass many recent statistical methods for subgroup analysis. These methods focus on modeling treatment effect modification, instead of the potential outcomes. The causal effect of treatment effect modifiers will be examined mainly based on the no-unmeasured confounders assumption. However instrumental variable approach will also be discussed to deal with possible unmeasured confounders. The proposed methods are quite flexible and can be used for analysis of both randomized clinical trials and observational studies. They also link nicely with the estimand framework laid out in the International Council for Harmonisation (ICH) E9 (R1) document that aims to provide guidance for statistical analysis for clinical trials.

We will examine the empirical performance of several procedures belonging to the proposed framework through numerical studies and real data analyses. In particular, we will discuss our experience in intervention recommendation for a transitional care program at the University of Wisconsin Health system and in a breast cancer screening study where we use health behavioral constructs, comorbidity variables, and social economic factors as treatment effect modifiers.

Prerequisites

The course is accessible to anyone with a knowledge of statistical inference at the level of introductory graduate level courses in mathematical statistics and probability. Exposure to causal inference (based on the potential outcomes), statistical learning theory (e.g. regularization method) can be helpful, but is not required.

Tuesday Lunch (On Your Own) 12:00 AM – 2:00 PM

2:00 - 5:00PM

Session G

Sequential monitoring of adaptive randomized clinical trials

Hongjian Zhu, AbbVie Inc.

Moderator: Weili He

Abstract

Clinical trials are intricate endeavors with multiple objectives, including controlling the type I error rate, enhancing the power to detect treatment differences, allocating more patients to superior treatments, achieving balance in covariates across treatments, and more. To fulfill these objectives, the literature proposes two distinct families of techniques: (i) the analysis approach—where observed data is analyzed sequentially, and (ii) the design approach—where the allocation probability is altered sequentially. Sequential monitoring has administrative, ethical, and economic advantages. Response adaptive randomization (RAR) can also achieve ethical and efficient objectives by skewing the allocation proportion. In addition, it is well known that an imbalance of the confounding covariates across treatments may bias the study results. This imbalance can be mitigated by covariate adaptive randomization (CAR). CAR can also reduce the selection bias, minimize the accidental bias, and improve statistical efficiency. This tutorial delves into the fundamentals of sequential monitoring, responses adaptive randomization, and covariate adaptive randomization. Additionally, we present theoretical and numerical findings from sequential monitoring in various adaptive randomized clinical trials.

Session H

Win statistics (win ratio, win odds and net benefit): introduction, properties, implementations, and applications.

Gaohong Dong, BeiGene and Margaret (Meg) Gamalo, Pfizer

Moderator: Jingjing Ye

Abstract

Over the past decade, the win ratio (ratio of win proportions, Pocock et al. 2012), the net benefit (difference in win proportions, Buyse 2010) and the win odds (odds of win proportions by dividing a tie into two half wins and assigning a half win to each treatment group, Dong et al. 2020) have been developed and comprehensively studied. The concept of "win" from Pocock et al. (2012) is very intuitive and attractive. The pioneering work of Finkelstein and Schoenfeld (1999) is equivalent to the test of the difference in the number of wins between the two treatment groups. The win statistics (win ratio, win odds and net benefit) hierarchically analyze prioritized multiple outcomes. "Wins" are determined by comparing each patient in the Treatment group with every patient in the Control group. Each pairwise comparison starts with the most important outcome (e.g., death), then less important endpoints (e.g., a non-fatal outcome such as disease progression in oncology studies) are considered only if the higher priority outcomes do not result in a win. Therefore, the win statistics have advantages compared to the conventional time-to-first-event analyses (e.g., Kaplan-Meier estimates, log-rank test, and Cox models).Moreover, as nonparametric methods, the win statistics can avoid multiplicity issue of multiple outcomes, they can handle semi-competing risk situations (i.e., fatal outcomes plus non-fatal outcomes) and non-proportional hazards situations (e.g., delayed treatment effect typically seen in Immuno-Oncology). Their flexibility allows a composite of multiple endpoints in any (mixture) data type (e.g., time-to-event, binary, ordinal, continuous). The win ratio and the win odds have been applied in practice (e.g., design and analysis of Phase III trials) and the win ratio as the primary analysis has been used to support regulatory approvals (e.g. tafamidis for treatment of cardiomyopathy per the ATTR-ACT trial).In this short course, we will focus on introduction, properties, implementations, and applications of win statistics.

Wednesday December 6, 2023 9:00 – 12:00 PM

Session I ♣

Statistical Strategies and Practical Considerations for Dose Optimization

Prof. Ying Yuan, University of Texas, MD Anderson Cancer Center

Moderator: Jerry Li

Abstract

The US Food and Drug Administration (FDA) launched Project Optimus with the aim of shifting the paradigm of dose-finding and selection towards identifying the optimal biological dose that offers the optimal balance between benefit and risk, rather than the maximum tolerated dose. However, achieving dose optimization is a challenging task that involves a variety of factors and is considerably more complicated than identifying the maximum tolerated dose, both in terms of design and implementation. This tutorial provides a comprehensive review of various design strategies for dose optimization trials, including phase I/II and II/III designs, and highlights their respective advantages and disadvantages. Additionally, practical considerations for selecting an appropriate design and planning and executing the trial are discussed. The tutorial also presents freely available software tools that can be used for designing and implementing dose optimization trials. Real-world examples are used to illustrate the approaches and their implementation.

Session J ♣

Bayesian Adaptive Statistical Approaches for Accelerating Drug and Medical Device Approvals in Rare Disease

Bradley P. Carlin, PharmaLex - US

Moderator: Din Chen

Abstract

It is estimated that more than 30 million people in the U.S. are impacted by acknowledged rare diseases, which now number over 7000. Sadly, the development of clinical trials to study such diseases has been hampered by the inherently small patient populations available for study, as well as poor understanding of the natural history of such diseases. Since August 2018, the use of Bayesian and other nontraditional approaches in this area has been fostered by the FDA's Complex Innovative Trial Design (CID) Pilot Meeting Program. More recently, in May 2022, the FDA Center for Drug Evaluation and Research (CDER) launched its Accelerating Rare disease Cures (ARC) Program, which seeks to speed and increase the development of effective and safe treatment options addressing the unmet needs of patients with rare diseases. Thanks to the emergence of Markov chain Monte Carlo (MCMC) computational methods in the 1990s, Bayesian methods now have a more than 25-year history of utility in statistical and biostatistical design and analysis. Such methods are especially useful in the area of rare disease, where the inherently small sample sizes mean that standard approaches are either unethical, hopelessly underpowered, or both. In this tutorial, after a brief review of some Bayesian basics, we consider recent developments in Bayesian adaptive methods for cautiously borrowing strength from historical datasets, an approach now commonly used to boost power in rare disease trials. Here, the notion of effective sample size is important to judge the relative importance and impacts of the various data sources. Techniques specific to rare and pediatric diseases will be discussed, as will an approach for optimally selecting the timing of an interim look at the data. On the drug side, the use of PK/PD data to expand the range of useful auxiliary information will be explored. We will offer an application of such borrowing to platform trials, and also describe methods for borrowing from a subject's own disease natural history data. We also consider the problem of borrowing strength from observational and other real-world data (RWD), where propensity score matching offers a way to correct for possible biases arising from the lack of randomization. Throughout, we illustrate with practical examples from the instructor's own consulting practice, which has included both device and drug approvals. We also comment on relevant recent developments in Bayesian computing, especially the R-INLA package, an approximate Bayesian approach that offers a two-order of magnitude speed-up over traditional MCMC approaches, enormously helpful when simulating design operating characteristics for sponsors and regulators.

Wednesday Lunch (On Your Own) 12:00 AM – 2:00 PM

2:00 - 5:00 PM

Session K

Introduction to Adaptive Design Methods for Dose and Treatment Selection

Prof. Haitao Pan, St. Jude Children's Research Hospital

Moderator: Naitee Ting

Abstract

This tutorial is divided into three parts, with a duration of three hours. In the first part, we will introduce model-assisted dose-finding design methods used to identify the maximum tolerated dose (MTD), and the SEARS (Seamless Phase I/IIa with Early Analysis for Response and Safety) framework, which helps identify the optimal biological dose (OBD). We will demonstrate how to implement these methods using the BOIN and SEARS R packages. Moving on to the second part, we will discuss two-stage designs for single-arm phase IIa trials, including Simon's two-stage design for binary endpoints and its extension for time-to-event endpoints. We will also demonstrate how to implement these methods using the clinfun and OneArm2Stage R packages.

In the third and final part of the tutorial, we will introduce platform design methods. We will discuss the concept of multi-arm design and present an optimal platform design. Using the PlatformDesign R package, we will demonstrate how to implement these methods. By the end of this tutorial, you will have gained a comprehensive understanding of model-assisted dose-finding, two-stage designs for single-arm phase IIa trials, and platform design methods. You will also be equipped with the skills to implement these methods using the R packages BOIN, SEARS, clinfun, OneArm2Stage, and PlatformDesign.

Session L

Enhancing Treatment Effect Assessment through Covariate Adjustment Methods

Margaret Gamalo, Jinma Ren, Wenjin Wang, Pfizer Inc

Moderator: Li-An Xu

Abstract

Assessing treatment effects in clinical trials frequently encounters bias due to unbalanced baseline characteristics. Absent use of appropriate statistical techniques or comprehensive measurement of potential prognostic factors can introduce biases in various scenarios. These include comparing single-arm trials with external controls, evaluating effects in observational studies, or even within randomized clinical trials (RCTs), and investigating treatment effects in subgroup analyses.

Effective mitigation of such biases and improvement of accuracy and test power necessitates adjusting for baseline prognostic factors. The literature offers a range of covariate adjustment methods. In this informative tutorial session, we embark on a comprehensive journey:

1. We will commence by reviewing guidelines issued by regulatory authorities and health technology assessment bodies. Understanding the regulatory landscape and insight is crucial for robust analyses.
2. Subsequently, we will delve into prevalent covariate adjustment methods. This will encompass:
   - Techniques leveraging individual participant data (IPD), such as propensity-score-based weighting, g-computation, and doubly robust estimators.
   - Approaches applicable when only partial trial IPD and summary data from external sources are available, namely simulated treatment comparison (STC) and matching-adjusted indirect comparison (MAIC).
   - Exploring Bayesian strategies for incorporating external controls.
3. Throughout the session, we will substantiate concepts through comparative simulations, offering a hands-on understanding of the presented methods' strengths and limitations.
4. To bring theory to life, we will illustrate an application involving the assessment of differential placebo response proportions between two pivotal clinical trials.

Join us for an illuminating tutorial that equips you with invaluable insights into the world of covariate adjustment methods, ensuring robust and accurate treatment effect assessment in clinical trials.

TWO SIMULTANEOUS SHORT COURSES THURSDAY AND FRIDAY, DECEMBER 7-8, 2023

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**

Real-world Evidence in Medical Product Development 🕮

Instructors: Weili He, Yixin Fang, and Hongwei Wang, Abbvie

Moderator: Jerry Li

Abstract

The organic and evolving nature of real-world data (RWD) and real-world evidence (RWE) responding to the fit-for-purpose requirements for expanding applications of RWE to address payers, patients, physicians' need along with supporting regulatory decisions is a defining characteristic of this arena. Randomized controlled clinical trials (RCTs) have been the gold standard for the evaluation of efficacy and safety of medical interventions. However, the costs, duration, practicality, and limited generalizability have incentivized many to look for alternative ways to optimize the process and address unique real-world research questions. In recent years, we have seen an increasing usage of RWD and RWE in clinical development and life-cycle management. The major impetus behind the interest in the use of RWE is the increased efficiency in drug development, resulting in savings of cost and time, ultimately getting drugs to patients sooner. However, even with the encouragement from regulators and available guidance and literature on the use of RWD and RWE in recent years, many challenges remain. In this short course, based on a to be published book in June 2023 by Springer Nature: "Real-World Evidence in Medical Product Development", will address these challenges by providing an end-to-end guidance including strategic considerations, state-of-the-art statistical methodology reviews, organization and infrastructure considerations, logistic challenges, and practical use cases. The target audience who may be interested in this short course is anyone involved, or with an interest, in the use of RWE in their research for drug development and healthcare decision making. In particular, the audience may include statisticians, clinicians, pharmacometricians, clinical operation specialists, regulators, and decision makers working in academic or contract research organizations, government, and industry.

Outline of the Short Course

Day 1 Morning: RWE to Accelerate Medical Product Development and Fit-for-Use RWD Assessment

- Introduction and background on the need for RWE and RWD in clinical development and life-cycle management along with future directions.
- Existing guidance documents and precedents related to RWE by major regulatory agencies across the world and compare similarities and differences in those concepts in guidance documents from different countries.
- key considerations in forming research questions in RW setting.
- Principles in the assessment of assess fit-for-use RWD sources.
- Advanced analytics for key variables ascertainment, including disease status, exposure, or outcomes.

Day 1 Afternoon: RWD Standard, Linkage, and Estimand in RW Setting

- Introduction of different RWD standards and importance of common data model
- Enhancing RWD capacities via privacy-preserving linkage

Statistical Analysis with Missing Data

Instructors: Prof. Rod Little, University of Michigan, and Prof. Qixuan Chen, Columbia University

Moderator: Alfred H. Balch

Abstract

Missing data are a common challenge in health and social science research. Statistical methods and tools can be used to handle missing data to achieve valid statistical inference. This short course will integrate the principle concepts and methods commonly used in statistical analysis with missing data and their applications in surveys, longitudinal studies, and clinical trials. On Day 1 of the course, we first define missing data, patterns of missing data, and missing mechanisms. We then introduce the weighted complete-case analysis, reviewing methods for creating weights and conducting weighted analysis. Finally, we will present incomplete data analysis using maximum likelihood and Bayes methods. On Day 2, we first discuss using multiple imputation (MI) to handle missing data. We cover both implicit and explicit MI procedures. We then discuss likelihood methods for missing not at random (MNAR) models, based on both selection and pattern-mixture models. Finally, we discuss missing data in clinical trials.

The short course will integrate lectures with case studies and hands-on computer lab sessions to put concepts into practice. We include a wide variety of examples to illustrate the techniques and approaches, focusing on weighting in surveys on Day 1 and on MI by chained equations and sensitivity analysis under MNAR on Day 2.

Outline of the Short Course

Day 1 Topics Covered

- Introduction and overview
- Complete-case analysis
- Methods for creating weights
- Inverse-probability weighting
- Doubly-robust methods
- Likelihood methods with incomplete data
- Bayes for missing data

Day 2 Topics Covered

- Multiple imputation inference
- Hot-deck imputation
- MI based on joint distribution of incomplete data
- MI using chained equations
- Likelihood methods for MNAR models
- Pattern-mixture models
- Missing data in clinical trials

Roderick J. Little is Richard D. Remington Distinguished University Professor of Biostatistics at the University of Michigan, where he also holds appointments in the Department of Statistics and the Institute for Social Research. From 2010-21012 he was the inaugural Associate Director for Research and Methodology and Chief Scientist at the U.S. Census Bureau. He has over 250 publications, notably on methods for the analysis of data with missing values and model-based survey inference, and the application of statistics to diverse scientific areas,

- Key considerations in applying estimand framework to RW studies
- Advanced analytics for personalized medicine using RWD

Day 2 Morning: Causal Inference and Sensitivity Analysis

- Introduction to potential outcomes, directed acyclic graphs, identifiability assumptions, and causal inference.
- Review of commonly used methods for conducting causal inference: g-formula, inverse probability of treatment weighting (IPTW), doubly robust methods, and targeted learning.
- Overview of sensitivity analysis methods for the missing-at-random assumption, the assumptions made for handing intercurrent events, and identifiability assumptions made for causal inference.
- Causal inference roadmap for deriving RWE from the analysis of RWD.

Day 2 Afternoon: Case Example Studies

- Application of causal-inference roadmap to RW studies via examples.
- Six application examples with analysis on regulatory contexts, quality of data sources, statistical methods, and regulatory decisions.
- Conclusion and future directions

Dr. Weili He has over 25 years of experience working in the biopharmaceutical industry. She is currently a Distinguished Research Fellow and head of Medical Affairs and Health Technology Assessment (HTA) statistics at AbbVie. She has a PhD in Biostatistics. Weili's areas of expertise span across clinical trials, real-world studies and evidence generations, statistical methodologies in clinical trials, observational research, innovative adaptive designs, and benefit-risk assessment. She is the lead or co-author of more than 60 peer-reviewed publications in statistics or medical journals and lead editor of three books on adaptive design, benefit-risk assessment, and RWE, respectively. She is the co-founder and co-chair of the American Statistical Association (ASA) Biopharmaceutical Section (BIOP) Real-world Evidence Scientific Working Group (SWG) from 2018 to 2022. She is also the founder and co-chair of a newly formed ASA BIOP HTA SWG. Weili is the BIOP Chair-Elect, Chair, and Past Chair from 2020-2022. She is also an Associate Editor of Statistics in Biopharmaceutical Research since 2014, and an elected Fellow of ASA since 2018.

Dr. Yixin Fang, After he received his PhD in Statistics from Columbia University in 2006, Yixin Fang had been working in academia before he joined AbbVie in 2019. Currently, he is a Research Fellow and Director of Statistics in Medical Affairs and Health Technology Assessment Statistics (MA&HTA Statistics) at AbbVie. Within MA&HTA Statistics, he is Head of the therapeutics areas (TAs) of Eye Care and Specialty and Head of Causal Inference Center (CIC). In this role, he is involved with the design and analysis of Phase IV studies and real-world studies in medical affairs and leading HTA submissions in the TA of Eye Care. In addition, he is active in the statistical community with over 100 peer-reviewed manuscripts and his research interests are in real-world data analysis, machine learning, and causal inference. Currently, he serves as a co-chair for the phase III of the ASA-BIOP Real-world Evidence Scientific Working Group and a journal associate editor for *Statistics in Biopharmaceutical Research*.

Dr. Hongwei Wang has close to 20 years' experience working in the biopharmaceutical industry. He is currently a Research Fellow and Director at Medical Affairs and Health Technology Assessment Statistics of AbbVie. Prior to that, Hongwei worked at Sanofi and Merck with increasing responsibilities. He has been leading evidence planning and evidence generation activities across various therapeutic areas in the fields of real-world studies, network meta-analysis and post-hoc analysis with a mission to support medical affair strategy and optimal reimbursement. Hongwei received his PhD in Statistics from Rutgers University, conducts active methodology research and their applications to different stages of drug development. He serves as coauthor of about 40 manuscripts in peer reviewed journals and over 100 presentations at scientific congresses.

including medicine, demography, economics, psychiatry, aging and the environment. His book "Statistical Analysis with Missing Data" with Donald Rubin is now in its 3rd edition, and has over 30,000 google scholar citations. Little is an elected member of the International Statistical Institute, a Fellow of the American Statistical Association and the American Academy of Arts and Sciences, and a member of the Institute of Medicine of the U.S. National Academies. In 2005, Little was awarded the American Statistical Association's Wilks Medal for research contributions, and he gave the President's Invited Address at the Joint Statistical Meetings. He was the COPSS Fisher Lecturer at the 2012 Joint Statistics Meetings.

Qixuan Chen is Associate Professor of Biostatistics at Columbia University. Her research focuses on statistical methods development for handling missing data and measurement error arising from health studies. She has also made important contributions in developing novel methods for the analysis of complex survey data. She has been actively engaged in building analysis tools to promote the use of novel statistical methods in health research, with applications to environmental health sciences, psychiatry and mental health, substance abuse, and traffic safety. She is an Associate Editor for Biometrics.

THREE KEYNOTES

(Monday, Tuesday, and Wednesday Morning, December 4-6, 2023)

Keynote 1: The Power of AI, Data Sciences, and Technology in Drug Development

Presenter: Venkat Sethuraman,
Bristol Myers Squibb
(8-9am, December 4, 2023)
Moderator: Ivan S. F. Chan

Abstract

Pharmaceutical drug development is a complex and costly process that involves extensive research and development, clinical trials, and regulatory approval. In recent years, the power of AI, data sciences, and cutting-edge technology has revolutionized this process and opened up new possibilities for the pharmaceutical industry.

AI algorithms and machine learning have enabled researchers to analyze vast amounts of data and identify new drug targets and biomarkers. By using machine learning to analyze data from clinical trials, researchers can identify patient subgroups that are more likely to respond positively to a particular drug. This can help optimize clinical trial design, leading to faster and more efficient drug development. In addition to machine learning, natural language processing (NLP) has also been used in drug development. NLP algorithms can extract valuable insights from scientific literature and clinical trial data, helping researchers to accelerate clinical development process.

Radiomics imaging is a field of medical imaging that uses advanced algorithms to analyze images and extract quantitative features. These features can provide valuable insights into the underlying biology of diseases and help drug developers identify disease progression. By analyzing radiomics data from clinical trials, researchers can identify patient subgroups that are more likely to respond positively to a particular drug, allowing for faster and more efficient drug development.

The power of AI and other cutting-edge technologies in drug development is not limited to the laboratory. Digital health technologies are also being used to monitor patients in real-time and collect valuable data on drug efficacy and safety. This data can be used to optimize drug dosages and improve patient outcomes. Overall, the power of AI, data sciences, and cutting-edge technology is transforming the pharmaceutical industry and accelerating the pace of drug development. As these technologies continue to evolve and become more sophisticated, we can expect to see even more groundbreaking discoveries in the years ahead.

Keynote 2: Interpreting Deep Neural Networks towards Trustworthy AI

Presenter: Prof. Bin Yu
UC Berkeley
(11-12pm, December 5, 2023)
Moderator: Alfred H. Balch

Abstract

In this talk, I describe adaptive wavelet distillation (AWD) interpretation method for pre-trained deep learning models. AWD is shown to be both outperforming deep neural networks and interpretable in the motivating cosmology problem and an external validating cell biology problem. Moreover, I discuss an investigation into the effects of pre-training data distributions on large language models (LLMs) for fine-tuning pathology report classification. Finally, I address the need to quality control the entire data science life cycle to build any model for trustworthy interpretable data results throughout Predictability-Computability-Stability (PCS) framework and documentation for veridical data science.

Keynote3: Deming's Contributions and Big Data

Presenter: Prof. David Banks,
Duke University
(8-9am, December 6, 2023)
Moderator: Alfred H. Balch

Abstract

Dr. Deming was one of the foundational leaders in industrial statistics, with contributions to experimental design, sampling, and process control. More importantly, he changed the culture of business leadership in two nations, and implicitly, around the world. But the industries of his day focused on manufacturing, while today's industries reflect the knowledge economy. This talk asks the industrial statistics community to consider how to update and apply Dr. Deming's ideas in the Big Data era. There are some very direct correspondences, and this talk reviews Deming-like innovations in computational advertising, autonomous vehicles, and operations management.

Committee Members

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Speaker Dinner (Optional, Monday 7:00 PM)	$60 ❑	$60 ❑	$60 ❑	$60 ❑	
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❑ **Real-world Evidence in Medical Product Development**	$1180 ❑	$1380 ❑	$1450 ❑	$1650 ❑	
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Registration for a short course is required and independent of the registration for the tutorial sessions.

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