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

Sponsored by
Deming Conference Organization
AMERICAN STATISTICAL ASSOCIATION: Biopharmaceutical Section

December 2 – December 6, 2019: Three-Day Conference plus Two-Day Short Course
Tropicana Casino and Resort, Havana Tower, Atlantic City, NJ

Two Keynotes on December 2-3, 2019 and a Special Session on December 4, 2019

Keynote 1: *Clinical Trials in the Twenty-First Century: Challenges and Opportunities*, **Professor Susan S. Ellenberg**, University of Pennsylvania
Keynote 2: *Practical and Challenging Statistical Issues in Regulatory Science*, **Professor Shein-Chung Chow**, Duke University
Special Session: *Non-Statistical Reflections on 50 Years Chairing the Deming Conference*, **Walter R. Young**

Twelve Sessions of Tutorials on December 2-4, 2019
Three Short Courses on December 5-6, 2019

1. Medical Product Safety Evaluation: Biological Models and Statistical Methods by **Dr. Jie Chen**, Merck Research Laboratories
2. Targeted Learning: Causal Inference for Observational and Experimental Data by **Prof. Mark J. van der Laan**, University of California at Berkeley
3. Combining Information from Different Studies with Meta-Analysis and Network Meta-Analysis by **Prof. Chris Schmid**, Brown University

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

ONSITE REGISTRATION WILL BE ON THE FOURTH FLOOR OF THE HAVANA TOWER.
It will start at 6:00 pm on Sunday December 1st and will be followed by a one-hour reception with cold drinks and snacks.
It will continue at 6:30 AM Monday December 2nd through Thursday December 5th.
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. Only if absolutely necessary, mail a check with your completed registration form on page 10 in this program. If checks aren't postmarked on or before the early discounted registration date, you will be charged the next higher amount. E-Mail Cancellations sent to 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 31, 2019. A $150 credit on registration will be issued to the early poster submittal and accepted by September 15, 2019. 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 on-line for consideration.

Meeting facilities are in the Tropicana's Havana Tower state-of-the-art complex with 502 nonsmoking rooms where attendees stay in soundproof climate controlled rooms with direct-dial phones, cable color TV, coffee makers, hairdryers, refrigerators, safe, iron and board, complimentary wireless internet and gorgeous views of the Atlantic City skyline.

- **There is a guest check in desk on the 3rd floor of the Havana Tower and meeting facilities are on the 4th floor.**
- **It's one of the largest NJ hotels, with 2,079 rooms, elegant public areas, exclusive retail shops and fine dining.**
- **It's on the beach with a complimentary heated indoor pool on the sixth floor of the South Tower.**
- **It has free Wi-Fi in the rooms and conference floor. The casino is in a separate building connected by a bridge.**
- **A free Trop Advantage Card can offer rewards based on your play and may offer dining and show discounts.**

The AtlantiCare Life Center is a fully equipped fitness facility located in the Havana Tower basement for a fee of $15/day. A complimentary one-day membership pass can be requested. A voucher for free parking will be given to all registrants. 3-day registrants will get a free ticket to the holiday show on Tuesday night.

Seventy Fifth (75th) Annual Deming Conference on Applied Statistics
Tropicana Casino and Resort, Havana Tower, Atlantic City, NJ
Sponsored by the Biopharmaceutical Section of the ASA and the Deming Conference Organization

Monday December 2, 2019 Registration: 6:30 ⇒ 8 AM Hot Breakfast 7 ⇒ 7:50 AM

8 ⇒ 9 AM Keynote 1: ***Clinical Trials in the Twenty-First Century: Challenges and Opportunities*, Professor Susan S. Ellenberg, UPenn**
Moderator: Alfred H. Balch

Session A 🕮 **Clinical Trial Data Monitoring Committees and Reporting Statistical Centers: Problems and Solutions** Professor Susan S. Ellenberg, University of Pennsylvania Matt Downs, MPH, Statistics Collaborative, Washington DC Moderator: Alfred H. Balch	**Session B** **Using Restricted Mean Survival Time for Classifications and Clinical Trials for Survival Endpoints** Professor Ying Lu, Stanford University Moderator: Naitee Ting

Lunch (On Your Own) 12:15 ⇒ 1:30 PM

Session C ♣ **Bootstrap Methods** Professor Wei-Yin Loh, University of Wisconsin, Madison Moderator: Ivan S. F. Chan	**Session D** ♣ Discrete Multiple Testing In Detecting Differential Methylation Using Sequencing Data Professor Nan Lin, Washington University in St. Louis Moderator: Xiaoming Li

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

Tuesday December 3. 2019 Registration: 6:30 ⇒ 8 AM Hot Breakfast 7 ⇒ 7:50 AM

8 ⇒ 9 AM: Keynote 2: *Practical and Challenging Statistical Issues in Regulatory Science*, Professor Shein-Chung Chow, Duke University
Moderator: Naitee Ting

Session E ♣ **Introduction to Instrumental Variables** Professors Nandita Mitra, UPenn and Jason Roy, Rutgers University Moderator: Kalyan Ghosh	**Session F** ♣ **Modern Dose Finding Designs - Advances and Hot Topics** Frank Fleischer, PhD, Boehringer-Ingelheim Pharma GmbH and Co. KG Moderator: Naitee Ting

Lunch (On Your Own) 12:15 ⇒ 1:30 PM

Session G **Artificial Intelligence for Drug Development, Precision Medicine and Healthcare** Professor Mark Chang, Boston University Moderator: Wenjin Wang	**Session H** 🕮 **Clinical Trial Data Analysis Using R and SAS** Professor Din Chen, UNC and Pinggao Zhang, PhD, Takeda Moderator: Walter R. Young

Wednesday December 4, 2019 Registration: 6:30 ⇒ 8 AM Hot Breakfast 7 ⇒ 7:50 AM

8 ⇒ 9 AM: Special Session: *Non-Statistical Reflections on 50 Years Chairing the Deming Conference*, Walter R. Young 🕮
Moderator Alfred H. Balch

Session I ♣ **Targeted Maximum Likelihood Estimation (TMLE) for Machine Learning: A Gentle Introduction** Professor Mark J. van der Laan, University of California at Berkeley Moderator: Bill Wang	**Session J** 🕮♣ **Statistical Topics in Outcomes Research: Patient-Reported Outcomes, Meta-Analysis, and Health Economics** Joseph Cappelleri, PhD, Pfizer and Professor Thomas Mathew, UMBC Moderator: Ivan S. F. Chan

Lunch (On Your Own) 12:15 ⇒ 1:30 PM

Session K **Prediction In Event-Based Trials** Professor Daniel F. Heitjan, Southern Methodist University Moderator: Kalyan Ghosh	**Session L** **A Method to Evaluate the Validity of a Literature Claim** Stanley Young, PhD, CGSTAT Moderator: Alfred H. Balch

Thursday December 5, 2019 **Short Course** Registration and Hot Breakfast: 6:30 ⇒ 7:50 AM

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⇒5:50 Lecture**

S1: Medical Product Safety Evaluation: Biological Models and Statistical Methods 🕮 Dr. Jie Chen Merck Research Laboratories Moderator: Naitee Ting	**S2: Targeted Learning in Data Science: Causal Inference for Observational and Experimental Data** 🕮 Professor Mark J. van der Laan University of California at Berkeley Moderator: Bill Wang	**S3: Combining Information from Different Studies with Meta-Analysis and Network Meta-Analysis** Professor Chris Schmid, Brown University Moderator: Alfred H. Balch

Friday December 6, 2019, Short Course Continues and Hot Breakfast: 6:30 ⇒ 7:50 AM

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⇒5:50 Lecture**

All tutorial and short course titles, presenters and moderators from 1989 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

TRAVEL TO THE DEMING CONFERENCE

AIR: Check both Atlantic City (ACY) and Philadelphia (PHL) to search for the best fare and connections. The cheapest quick airport connection to PHL is the Tropiano shuttle, requiring reservations at least two days in advance at (215) 616-5370. It charges $55 from PHL directly to the Tropicana. A tip is expected. There is a $10 jitney from ACY as well as a $35 taxi service to the Tropicana. For both of these, call Ext 2002 from the Taxi and Shuttle Service Desk, located in the Baggage Claim Area, near the Exit door. You can also call 609-344-8642 or 609-576-2776 in advance**.** The cheapest connection from PHL is the below referenced SEPTA, but this will take more than two hours. One can rent a car (www.bnm.com) but it isn't necessary during one's stay. Also consider discount airlines not on the major search engines such as Spirit, www.spiritair.com (which is the only airline serving ACY); AirTran www.airtran.com, Frontier www.frontierairlines.com, and Southwest, www.southwest.com. These airlines offer the additional advantage that they sell one-way tickets without a premium that is useful if one is using the conference as a stopover. While we don't recommend Newark Airport except as a means of saving money and perhaps travel time on international flights, there is a #67 NJ Transit bus (requiring a change at Toms River) as well as several train service options to Atlantic City, including the one referenced below. This trip would take about three hours as opposed to about ninety minutes if one rented a car.

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

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

DRIVING: To get to the Tropicana from the Garden State Parkway, NJ Turnpike or Philadelphia, take the Atlantic City Expressway. Follow the Atlantic City Expressway to Exit 2. This will take you to the Black Horse Pike, Route 40/322, which you will take into Atlantic City. Turn left on Arctic Avenue, the first light over the bridge. Take Arctic Avenue to Brighton Avenue. Turn right on Brighton and cross Atlantic Avenue. The entrance to "The Quarter" Garage (Havana Tower) is on your left, off Atlantic Avenue. Self or valet (doesn't permit easy access to your car during your stay) parking is $10 per stay for hotel guests with unlimited in and out privileges. Don't park in the Tropicana's other garage, as it is tedious to get to the Havana Tower.

INFO: For general tourist info visit www.visitnj.org/city/atlantic-city that has an option for you to request a free visitor packet as well as an opportunity to e-mail questions that are promptly answered. Consider walking to and shopping in the upscale Atlantic City Outlets at the foot of the Atlantic City Expressway or strolling on the Boardwalk to the pier shops at Caesars. Remember there is no sales tax on apparel in NJ.

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

*** Walter R. Young has chaired the Deming Conference for fifty consecutive years. There is a special session this year on December 4th to celebrate his contributions to this conference.**

Conference Speakers Biography

Joseph C. Cappelleri (PhD in psychometrics from Cornell University and MPH in epidemiology from Harvard University) is an executive director in the Statistical Research and Data Science Center at Pfizer. As an adjunct professor, he has served on the faculties of Brown University, University of Connecticut, and Tufts Medical Center. He has published extensively on clinical and methodological topics (approximately 1,500 co-authored publications and conference presentations), including regression-discontinuity designs, meta-analyses, and health measurement scales. Dr. Cappelleri is a Fellow of ASA.

Mark Chang (PhD in in Civil Engineering from University of Massachusetts in Amherst) is founder of AGInception, a research organization for artificial general intelligence. He was Sr. Vice President, Strategic Statistical Consulting at Veristat and Vice President of Biometrics at AMAG Pharmaceuticals. Chang is a fellow of the American Statistical Association and an adjunct professor of Biostatistics at Boston University. He is a co-founder of the International Society for Biopharmaceutical Statistics, co-chair of the Biotechnology Industry Organization (BIO) Adaptive Design Working Group, and a member of the Multiregional Clinical Trial (MRCT) Expert Group. Chang has served associate editor for Journal of Pharmaceutical Statistics. Dr. Chang has published 10 books.

Din Chen (PhD in Statistics from University of Guelph) is the Wallace H. Kuralt distinguished professor in Biostatistics at University of North Carolina-Chapel Hill. Dr. Chen is an elected fellow of American Statistical Association (ASA), an elected member of the International Statistics Institute (ISI) and a senior expert consultant for biopharmaceuticals and government agencies with extensive expertise in clinical trial biostatistics. Dr. Chen has more than 200 referred professional publications and co-authored/co-edited 25 books on biostatistics clinical trials, biopharmaceutical statistics, interval-censored survival data analysis, meta-analysis, public health statistics, statistical causal inferences; statistical methods in big-data sciences and Monte-Carlo simulation based statistical modeling. Dr. Chen is a committee member of the Deming Conference and has been invited to give various tutorials at Deming Conference since 2011.

Shein-Chung Chow (PhD in Statistics from University of Wisconsin at Madison) is a Professor of Biostatistics and Bioinformatics at Duke University School of Medicine, Durham, NC. He is also a special government employee (SGE) appointed by the FDA as an Advisory Committee voting member and Statistical Advisor to the FDA. He is Editor-in-Chief of the *Journal of Biopharmaceutical Statistics* and Editor-in-Chief of the *Biostatistics Book Series* at Chapman and Hall and CRC Press, Taylor & Francis. Dr. Chow is Fellow of the American Statistical Association, an author or co-author of over 300 methodology papers and 30 books.

Matt Downs (MPH in Epidemiology and Biostatistics from the University of California, Berkeley) is a statistical scientist at Statistics Collaborative. Since 1999, he has served as the independent reporting statistician to DMCs for multinational Phase 2 and 3 trials in many disease areas. Mr. Downs speaks at professional meetings on a range of statistical topics, including dynamic allocation methods, conditional power, and implementation of treatment assignment algorithms. He is a member of the American Statistical Association and the Society for Clinical Trials.

Susan S. Ellenberg (Ph.D. in Mathematical Statistics from The George Washington University) is a professor in Biostatistics and Epidemiology at the Hospital of the University of Pennsylvania. Her research has focused on practical problems and ethical issues in designing, conducting and analyzing data from clinical trials. She is a Fellow of the American Statistical Association, the Society for Clinical Trials and the American Association for the Advancement of Science, and is an elected member of the International Statistical Institute. She is the 2019 recipient of the Florence Nightingale David Award.

Frank Fleischer (PhD in statistics from Ulm University) is the Head of Methodology Statistics, Boehringer-Ingelheim Pharma GmbH & Co. KG. He is leading a global team of statisticians at Boehringer Ingelheim focusing on statistical methodology and the implementation of innovative statistical designs into practice. In that role, Frank and his team are considered with methodological questions regarding adaptive designs, statistical decision making, dose finding and Bayesian borrowing designs as well as with piloting these methods in clinical trials. Formerly he has been a lead project statistician for different projects in oncology, immunology and the biosimilars.

Daniel F. Heitjan (PhD in Statistics from The University of Chicago) is a Professor of Statistical Science at Southern Methodist University and Professor of Population & Data Sciences at UT Southwestern Medical Center, both in Dallas, TX. His research interests include clinical trial design and analysis, incomplete data, modeling cancer survivorship, and statistical methods in health economics. Dr. Heitjan is a fellow of the American Statistical Association, the Institute of Mathematical Statistics, and the Society for Clinical Trials.

Nan Lin (PhD in Statistics from University of Illinois at Urbana-Champaign) is a professor in the Department of Mathematics and Statistics at Washington University in St. Louis and has a joint appointment in the Division of Biostatistics, Washington University in St. Louis, School of Medicine. His research focuses on developing statistical methodologies for big data, quantile regression, multiple testing, bioinformatics, Bayesian statistics, longitudinal and functional data analysis. His work on Bayesian Elastic Net was awarded as *the most promising paper published in Bayesian Analysis* in 2016 by the International Society for Bayesian Analysis.

Wei-Yin Loh (PhD in Statistics from University of California at Berkeley) is a professor of Statistics at the University of Wisconsin, Madison. His research interests are in bootstrap theory and methodology and algorithms for classification and regression trees. Loh is a fellow of the American Statistical Association and the Institute of Mathematical Statistics, and a consultant to government and industry. He is a recipient of the Reynolds Award for teaching, the U.S. Army Wilks Award for statistics research and application, an Outstanding Science Alumni Award from the National University of Singapore, and visiting fellowships from AbbVie, IBM and the Bureau of Labor Statistics.

Ying Lu (PhD in Biostatistics from University of California at Berkeley) is a professor of Biomedical Data Science, of the Health Research and Policy and of Radiology, co-director of the Center for Innovative Study Design and Biostatistics Core of the Stanford Cancer Institute, Stanford University School of Medicine. Professor Lu's current research interests include the statistical design and analytic methods for clinical trials, validation of biomarkers/medical diagnoses, meta-analysis, and medical decision making. He is the author of 245 peer-reviewed publications and editor of several books. He is the 2019 President Elect of WNAR, the 2014 President of the International Chinese Statistical Association (ICSA) and served as a member of DSMBs for clinical trials and FDA PCNS Drug Advisory Committee. Professor Lu was a fellow of ASA and biostatistics editor of JCO Precision Oncology.

Thomas Mathew (PhD in Statistics from Indian Statistical Institute) is a Professor at the Department of Mathematics & Statistics, University of Maryland Baltimore County (UMBC). 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. Dr. Mathew is a Fellow of the American Statistical Association, and a Fellow of the Institute of Mathematical Statistics.

Nandita Mitra (PhD in Biostatistics from Columbia University) is a Professor of Biostatistics, Vice-Chair of Faculty Professional Development, Chair of the Graduate Group in Epidemiology and Biostatistics, and Co-Director of the Center for Causal Inference at the University of Pennsylvania. Her primary methodological research focuses on propensity score and instrumental variables approaches to the analysis of observational data and causal inference approaches to cost-effectiveness estimation. Her collaborative research areas include cancer outcomes, cancer genetics, health policy, and health economics.

Jason Roy (PhD in Biostatistics from University of Michigan) is a Professor and Chair of the Department of Biostatistics and Epidemiology at Rutgers University, Co-Director of the biostatistics core for the New Jersey Alliance for Clinical and Translational Science, and Co-Director of the Center for Causal Inference. He has expertise in Bayesian methods, causal inference, and missing data. His primary recent methodological research has focused on developing flexible Bayesian models for complex observational data, especially from large healthcare databases.

S. Stanley Young (PhD in Statistics and Genetics from North Carolina State University) is currently the CEO of CGStat. His current interest is studying methods used in the evaluation of observational studies. He worked in the pharmaceutical industry on all phases of pre-clinical research. Dr. Young is a Fellow of the American Statistical Association and the American Association for the Advancement of Science. He is an adjunct professor of statistics at North Carolina State University, the University of Waterloo, and the University of British Columbia. He is also an adjunct professor of biostatistics in the Jiann-Ping Hsu College of Public Health at Georgia Southern University. Dr. Young is on the Scientific Advisory Board of the U.S. Environmental Protection Agency.

Walter R. Young (BChE from CUNY; MChE and MSOR from NYU; NY Professional Engineering license; ASQ Quality and Engineering Certification) is an elected ASQ fellow and founder and chair for 3 years of the Tappan Zee section. He was awarded the Deming Silver Medal and the Ellis R. Ott award. He chaired the ASTM E-11 nonparametric methods subcommittee and the working group that rewrote its outlier standard. He worked for 31 years for Lederle Labs until Wyeth acquired it and retired as a Principal Clinical Programmer in 2005. He published more than 2-dozen professional papers and gave numerous talks. He is an expertise in a number of programming languages and graphics.

Pinggao Zhang (PhD in Epidemiology from University of Guelph) is a team lead and director of biostatistics in Takeda Pharmaceutical Company Limited, Cambridge, MA. Dr. Zhang has been leading biostatistics activities in support of clinical research across all development phases, regulatory submissions, and publications. He has worked in various therapeutic areas and has contributed to several successful drug approvals. Dr. Zhang is a committee member of the Deming Conference and has served as an invited speaker at various occasions.

Monday December 2, 2019 9:00 – 12:15 PM

Section A 🕮

Clinical Trial Data Monitoring Committees and Reporting Statistical Centers: Problems and Solutions

Professor Susan S. Ellenberg, University of Pennsylvania and Matt Downs, MPH, Statistics Collaborative, Washington DC

Moderator Alfred H. Balch

The number of clinical trials that are overseen by independent Data Monitoring Committees/Data and Safety Monitoring Boards is ever-increasing. A recent survey of DMC members showed that almost none had had training in DMC practices prior to their first time on a DMC, and most of those felt that such training would have been beneficial. Additionally, while many statistical centers and contract research organizations have substantial experience in developing DMC reports and presenting them at DMC meetings, many others are new to these processes; further, many DMC reports even from experienced centers are currently far from optimal.

This course will be divided into 2 sections: first, we will cover the basics of DMC operations, including: typical responsibilities of DMCs; DMC composition; structure of DMC meetings; statistical aspects of data monitoring; and regulations and policies regarding operation of DMCs. We will also address ongoing and emerging issues about DMC operations, about which there is less current consensus. Points in the discussion will be illustrated with case studies. The second section of the course will address operational issues for statistical centers reporting to DMCs. This section will cover the basic responsibilities of the statistical center and describe best operational practices, with many examples of optimal reports.

Session B

Using Restricted Mean Survival Time for Classifications and Clinical Trials for Survival Endpoints

Professor Ying Lu, Stanford University

Moderator: Naitee Ting

Because of the censoring, analyses of survival data have been focused on the difference in hazards function. For example, in a prospective clinical study that compares the difference between two groups in the time to a specific event (for example, disease progression, death), a hazard ratio estimate is routinely used to empirically quantify the between-group difference. Similarly, for a classification algorithm, we want to have subgroups that have the most different hazards function. When the hazard ratio of the two hazard functions is approximately constant over time, Cox model is a very powerful tool for these problems. However, the clinical meaning of such a ratio estimate is difficult, if not impossible, to interpret when the underlying proportional hazards assumption is violated. When the assumption is not plausible, the hazard ratio is not a good metric to evaluate the treatment efficacy or classification efficiency. In this tutorial lecture, we will discuss several critical concerns regarding this conventional practice and propose an attractive alternative for quantifying the underlying differences between groups based on restricted mean survival time (RMST). I will discuss various issues in employing RMST in practical analysis including the benefits of RMST in interpretation, using it as a classification efficiency metrics, using it in clinical trials, including statistical inference, selecting the truncation point, study design, power comparison, regression adjustment and extensions to competing risk and recurrent events settings. We will discuss the pros and cons of the RMST-based analysis and demonstrate that it is competitive to its hazard ratio-based conventional counterparts in many real world applications. This is a joint work with Professor Lu Tian in the Department of Biomedical Data Science, Stanford University.

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

1:30 - 5:00 PM

Session C ♣

Bootstrap Methods

Professor Wei-Yin Loh, University of Wisconsin, Madison

Moderator: Ivan S. F. Chan

Introduced exactly 40 years ago (Efron, 1979, Ann. Statist.), the bootstrap is a widely-used statistical technique. Its popularity is due to two main factors: (i) in a large number of problems amenable to mathematical analysis, the bootstrap is shown to perform as well as, if not better than, classical methods and (ii) enabled by the widespread availability of computers, the bootstrap technique is often applicable and its solutions are useful even when no other solution exists.

The first part of the tutorial reviews the motivation, underlying concepts, and fundamental assumptions that ensure the asymptotic validity of the bootstrap. The second part considers an extension of the bootstrap idea to that of "bootstrap calibration" (Loh, 1987, JASA; 1991, Statist. Sinica) and its application to a previously unsolved problem of post-selection inference: assessing statistical significance of subgroup treatment effects in randomized trials where the subgroups are obtained from complex search algorithms such as regression trees (Loh et al., 2015, 2016, 2019, Statist. Med). To keep things simple, the main focus throughout is on confidence interval estimation, as it is by far the most important area of application of the bootstrap.

Session D ♣

Discrete Multiple Testing In Detecting Differential Methylation Using Sequencing Data

Professor Nan Lin, Washington University in St. Louis

Moderator: Xiaoming Li

DNA methylation, as one of the most important epigenetic mechanisms, is critical for deciding cell fate, and hence tightly relevant to understanding disease processes, such as cancer. It is expected that epigenetic tests will be widely used for selecting personalized treatments in cancer and other diseases. We will discuss the multiple testing issue arising in detecting differential methylation in next generation sequencing studies. The detection requires comparing DNA methylation levels at millions of genomic loci across different genomic samples and statistically can be viewed as a large-scale multiple testing problem. Due to low read counts at individual CpG sites, asymptotic tests are often inadequate as discreteness in the test statistics is nonignorable. This brings up many intriguing statistical issues on proper control of false discovery rates (FDRs). Popular FDR control procedures often assume the test statistics are continuously distributed. Consequently, direct applications of such methods are often underpowered in methylation sequencing data analysis due to the discreteness. As discrete multiple testing is a generic statistical problem, methods discussed in this tutorial are also widely applicable in scenarios beyond methylation sequencing data analyses. The first part of the tutorial will review background issues in multiple testing and next generation sequencing data. The second part will discuss various FDR control methods for discrete multiple testing developed recently, and provide R demonstrations on real methylation sequencing data.

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

Tuesday December 3, 2019 9:00 – 12:15 PM

Session E ♣

Introduction to Instrumental Variables

Professors Nandita Mitra, UPenn and Jason Roy, Rutgers University

Moderator: Kalyan Ghosh

The goal of this tutorial is to provide a practical introduction to instrumental variables and how they are used for the analysis of observational studies. We will begin with a brief overview of causal inference concepts including simple directed acyclic graphs, the potential outcomes framework, average causal effects, and identifying assumptions. We will then briefly review standard approaches to analyzing observational data such as propensity score matching and inverse probability of treatment weighting. We will then motivate the need for using instrumental variable (IV) approaches to account for unmeasured confounding. We will define what an IV is and describe the underlying assumptions. We will provide examples of common IVs used in the clinical literature and discuss their limitations. We will also demonstrate how to use IVs to estimate average treatment effects using two-stage models, such as two-stage predictor substitution and two-stage residual inclusion, and how to interpret the results. Strengths and limitations of these methods will be discussed as well. Throughout, we will use examples from our own work in cancer comparative effectiveness studies. We will demonstrate how to implement IV estimation using the R package *ivreg*. The instructors have a long-standing interest in developing causal inference methodology and are co-directors of the Center for Causal Inference (with Dr. Dylan Small): https://www.cceb.med.upenn.edu/cci

Session F ♣

Modern Dose Finding Designs - Advances and Hot Topics

Frank Fleischer, PhD, Boehringer-Ingelheim Pharma GmbH and Co. KG

Moderator: Naitee Ting

Approaches to dose finding designs have improved a lot both for parallel group as well as for up-and-down designs. Multiple-comparison procedures and modelling (MCPMod) and Bayesian logistic regression models (BLRM]) have become standard techniques in these settings leading to more efficient and precise dose and MTD determination. This short course will start with an introduction into the elementary principles of dose finding and the two approaches. Exposure-based and other possibilities for incorporating different schedules and regimens are discussed and compared. A fully Bayesian approach to MCPMod (BMCPMod) will be introduced that is able to combine the advantages of MCPMod with Bayesian data augmentation. We will show simulation results as well as case studies in the normal and binary data setting for BMCPMod demonstrating the benefits of the approach. For the BLRM different extensions are discussed like combination models with more than two combination partners and the integration of covariates. A joint model for BLRMs will be explained that can simultaneously cope with parallel dose escalations in different mono and combination settings. The course will conclude with some examples of applications for these techniques in clinical trials and some practical issues and experiences related to that.

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

1:30 - 5:00 PM

Session G

Artificial Intelligence for Drug Development, Precision Medicine and Healthcare

Professor Mark Chang, Boston University

Moderator: Wenjin Wang

Artificial intelligence (AI) or machine learning (ML) has been used in drug discovery in biopharmaceutical companies for nearly 20 years. More recently AI has also been used for the disease diagnosis and prognosis in healthcare. In analysis of clinical trial data, predicted individual patient outcomes for precision medicine, similarity-based machine learning (SBML) has recently been proposed for clinical trials for oncology and rare disease without the requirement of big data. The course will focus on supervised learning, including similarity-based learning and deep learning neural networks. We will also introduce unsupervised, reinforcement, and evolutionary learning methods. The short course aims at conceptual clarity and mathematical simplicity. Provide R code for implementation with examples. The course materials are based on instructor's upcoming book: Artificial Intelligence in *Drug Development, Precision Medicine, and Healthcare*.

The course will cover:

(1) Introduction to AI, topics including: Classic Statistics versus AI Approach; Weak AI versus Strong AI (AGI); Past, Current, and Future of AI in Drug Development, Medicine, and HealthCare

(2) Similarity Based Method: Similarity-Based Machine Learning; Kernel Method; Nearest-Neighbors Method; Support Vector Machine

(3) Deep Learning Neural Networks: Convolutional Neural Network (CNN); Recurrent Neural Network (RNN); Long Short-term Memory Networks (LSTMs) ; Deep Belief Network (DBN)

(4) Overview of unsupervised, Reinforcement, and Evolutionary Learning Methods

Goals: attendees will learn common AI methods in drug development and medicine, be able to use the AI methods with R for clinical trial and other data, and be able to interpret the results.

Session H 🕮

Clinical Trial Data Analysis Using R and SAS

Professor Din Chen, UNC and Pinggao Zhang, PhD, Takeda

Moderator: Walter R. Young

This tutorial is based on the book: "Clinical Trial Data Analysis Using R and SAS" co-authored by (Din) Ding-Geng Chen, Karl E. Peace and Pinggao Zhang, published by Chapman and Hall/CRC Biostatistics Series in 2017, which uses R and SAS to design and analyze clinical trials. This tutorial provides a thorough presentation of biostatistical analyses of clinical trial data with detailed step-by-step illustrations on their implementation using R and SAS. Examples of clinical trials based on the authors' actual experience in clinical trials in various therapeutic areas are presented. After understanding the application, various biostatistical methods appropriate for analyzing data from the trials are identified. Then statistical programming code is developed using appropriate R/SAS packages to analyze the data. The code development and results are presented in a stepwise fashion. This stepwise approach should enable students to follow the logic and gain an understanding of the analysis methods and the R/SAS implementation so that they may use R/SAS to analyze their own clinical trial data.

Topics To Be Covered:

1. Fundamentals of clinical trial design: a brief introduction will be given to design factors including randomization, blinding, bias source and control, endpoint, patient selection, sample size and power.
2. Basics of clinical trial data interpretation: a high-level discussion will be given to protocol, statistical analysis plan, topline results, and clinical report.
3. Treatment comparisons with continuous/categorical endpoints: We start with simple two treatment comparisons using t-test and extend the analysis to multiple treatment comparisons (analysis of variance) and then to analysis of covariance with clinical covariates.
4. Longitudinal clinical trials: We will illustrate longitudinal trials and their analysis using linear mixed models for continuous endpoints, generalized linear mixed model and GEE for categorical endpoints.
5. Bayesian analysis in clinical trials using MCMC.

Wednesday December 4, 2019 9:00 – 12:15 PM

Session I ♣

Targeted Maximum Likelihood Estimation (TMLE) for Machine Learning: A Gentle Introduction

Professor Mark J. van der Laan, University of California at Berkeley

Moderator: Bill Wang

During this half-day tutorial, we will delve into the utility of the roadmap of targeted learning for translating real-world data applications to a mathematical and statistical formulation of the relevant research question of interest. Participants will perform hands-on implementation of state-of-the-art targeted maximum likelihood estimators using the tlverse software ecosystem in the R programming language. Participants will actively learn and apply the core principles of the Targeted Learning methodology, which (1) generalizes machine learning to any estimand of interest; (2) obtains an optimal estimator of the given estimand, grounded in theory; (3) integrates modern ensemble machine learning techniques; and (4) provides formal statistical inference in terms of confidence intervals and testing of specified null hypotheses of interest. It is highly recommended for participants to have an understanding of basic statistical concepts such as confounding, probability distributions, confidence intervals, hypothesis tests, and regression. Advanced knowledge of mathematical statistics may be useful but is not necessary. Familiarity with the R programming language will be essential.

Session J 🕮 ♣

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

Joseph Cappelleri, PhD, Pfizer and Professor Thomas Mathew, UMBC

Moderator: Ivan S. F. Chan

Based in part on the recently published co-edited volume *Statistical Topics in Health Economics and Outcomes Research*, 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, exploratory factor analysis, confirmatory factor analysis, person-item maps, and reliability. Regarding analysis of aggregate data, several areas are elucidated: traditional meta-analysis, network meta-analysis, model validation, meta-regression, 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. Emerging topics of contemporary importance and interest will be highlighted. 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.

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

1:30 - 5:00 PM

Session K

Prediction In Event-Based Trials

Professor Daniel F. Heitjan, Southern Methodist University

Moderator: Kalyan Ghosh

Randomized clinical trials often include planned interim analyses, at which external reviewers assess the accumulated data to determine whether the study should continue. With time-to-event endpoints, it is often desirable to schedule the interim analyses at the times of occurrence of specified landmark events, such as the 100th event, the 200th event, and so on. Often one wishes to predict the times of such events, together with other trial outcomes, as an aid to real-time logistical planning.

Traditional prediction methods use data only from previous trials and give inaccurate projections if, as often happens, historical enrollment or event rates differ from those in the current trial. Contemporary data management systems allow us to create accurate and complete study databases in real time, making it possible to use the accumulating data from the trial itself to make predictions about its future. Over the last several years, the presenter and colleagues have developed a suite of statistical methods for real-time prediction of the future course of a clinical trial. In this short course, I will describe these methods and train potential users in their application.

Session L

A Method to Evaluate the Validity of a Literature Claim

S. Stanley Young, PhD, CGSTAT

Moderator: Alfred H. Balch

Well over 80% of claims made in observational studies fail to replicate. The problems appear systemic. There is a need to be able to evaluate the reliability of literature claims; some are true, but most have no valid statistical support. Our idea is to evaluate the claim of interest by examining a meta-analysis study. A SAS JMP Add-In, MetaEval starts with table of risk ratios and their confidence limits and computes a p-value for each meta-analysis base paper. A p-value plot completes the analysis. About 400,000 meta-analysis studies have been published since 2015. Our evidence is that many/most of these studies exhibit heterogeneity, which strongly implies that positive base studies are the result of excessive model searching, p-hacking. The benefit of our evaluation strategy is the easy evaluation of the claim coming from a meta- analysis. Our results indicate that most meta-analysis studies based on observational studies and the base papers used therein have no valid statistical support.

THREE SIMULTANEOUS SHORT COURSES THURSDAY AND FRIDAY, DECEMBER 5-6, 2019

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

8:00⇒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⇒5:50 Lecture**

S1: Medical Product Safety Evaluation: Biological Models and Statistical Methods 🕮

Dr. Jie Chen
Merck Research Laboratories
Moderator: Naitee Ting

This cource provides cutting-edge biological models and statistical methods that are tailored to specific objectives and data types for safety analysis and benefit-risk assessment. Some frequently encountered issues and challenges in the design and analysis of safety studies are discussed with illustrative applications and examples.

Specifically, the short course will first give an overview of regulatory requirements on product safety and some general considerations for the design and analysis of safety studies. Biological models will be introduced with focuses on pharmacokinetic-pharmacodynamic models, predictive toxicology and regulatory framework in predictive toxicology. Statistical methodologies in benefit-risk assessment will be presented. Some design and analysis consideration for clinical trials that use pre-identified safety events as a primary endpoint will be discussed. Statistical methods handling multiplicity, one of the most challenging issues in safety data analysis, will also be presented. Causal inference methodologies will be introduced for use to establish causal relationship of a treatment with safety outcomes using observation studies and real-world data. Finally, some recent advances in pharmacovigilance (e.g., meta-analysis, likelihood ratio test, and pharmacoepidemiolige methods) and sequential surveillance methods will be discussed.

Day 1 of the source will cover:

- A brief history of medical product regulation and relevant regulatory guidelines
- Biological models and associated statistical methods
- Design and analysis of clinical trials with safety endpoints
- Multiplicity issue in safety evaluation

Day 2 of the course will cover:

- Benefit-risk assessment
- Statistical methods in pharmacovigilance
- Sequential surveillance
- Benefit-risk analysis

S2: Targeted Learning in Data Science: Causal Inference for Observational and Experimental Data 🕮

Professor Mark J. van der Laan,
University of California at Berkeley
Moderator: Bill Wang

This 2-day short course will provide a comprehensive introduction to the field of targeted learning for causal inference and corresponding tlverse software ecosystem. We will focus on targeted minimum loss-based estimators of causal effects, including those of static, dynamic, optimal dynamic, and stochastic interventions. These multiply robust, efficient plug-in estimators use state-of-the-art, ensemble machine learning tools to flexibly adjust for confounding while yielding valid statistical inference. Estimators will be explored under various real-world scenarios: when the outcome is subject to missingness, when mediators are present on the causal pathway, in high dimensions, under two-phase sampling designs, and in right-censored survival settings possibly subject to competing risks. We will discuss the utility of this robust estimation strategy in comparison to conventional techniques, which often rely on restrictive statistical models and may therefore lead to severely biased inference.

In addition to discussion, this course will incorporate both interactive activities and hands-on, guided R programming exercises, to allow participants the opportunity to familiarize themselves with methodology and tools that will translate to real-world analyses. It is highly recommended for participants to have an understanding of basic statistical concepts such as confounding, probability distributions, confidence intervals, hypothesis tests, and regression. Advanced knowledge of mathematical statistics may be useful but is not necessary. Familiarity with the R programming language will be essential.

S3: Combining Information from Different Studies with Meta-Analysis and Network Meta-Analysis

Professor Chris Schmid
Brown University
Moderator: Alfred H. Balch

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

Jie Chen is a Distinguished Scientist in Methodology Research at Merck Research Laboratories, Merck & Co., Inc. He has nearly 25 years of experience in biopharmaceutical R&D with research interest in the areas of innovative trial design, data analysis, Bayesian methods, multiregional clinical trials, data mining, machine learning methods, and medical product safety evaluation.	**Mark van der Laan** is the Jiann-Ping Hsu/Karl E. Peace Professor of Biostatistics and Statistics at the University of California, Berkeley. He has made contributions to survival analysis, semiparametric statistics, multiple testing, and causal inference. He also developed the targeted maximum likelihood methodology and general theory for super-learning. He is a founding editor of the Journal of Causal Inference and International Journal of Biostatistics. He has authored 4 books on targeted learning, censored data and multiple testing, and authored over 300 publications, and graduated 45 Ph.D. students. He received his Ph.D. from Utrecht University in 1993 with a dissertation titled "Efficient and Inefficient Estimation in Semiparametric Models". He received the COPSS Presidents' Award in 2005, the Mortimer Spiegelman Award in 2004, and the van Dantzig Award in 2005.	**Christopher Schmid** is Professor and Chair 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.

TWO KEYNOTES AND ONE SPECIAL SESSION
(Monday, Tuesday, and Wednesday Morning, December 2-4, 8-9am)

Keynote 1: Clinical Trials in the Twenty-First Century: Challenges and Opportunities	*Keynote 2: Practical and Challenging Statistical Issues in Regulatory Science*	*Special Session: Non-Statistical Reflections on 50 Years Chairing the Deming Conference* 🕮
Professor Susan S. Ellenberg, U of Penn Moderator: Alfred H. Balch	Professor Shein-Chung Chow, Duke University Moderator: Naitee Ting	Walter R. Young Moderator: Alfred H. Balch
The practice of clinical trials has evolved substantially in the 70+ years since the modern era of clinical trials was ushered in with randomized trials of streptomycin to treat tuberculosis. Many trial designs and new methods of analysis have been developed to meet emerging needs, and many pitfalls in the early approaches to trial design, conduct and analysis have been recognized and methods developed to avoid them. But the clinical trials community faces many new challenges, such as using "real world data" to enhance the generalizability of results and lower trial costs; making optimal use of sophisticated imaging and mobile health technology; and engaging with attacks on our traditional inferential approaches. These are interesting times for clinical trialists!	During drug and biologic product development, some practical and challenging issues are evitably encountered. These issues have an impact on the process of regulatory review and approval. These issues include, but are not limited to, (i) the use of 90% confidence interval approach for generics/biosimilars versus the use of 95% confidence interval approach for new drugs, (ii) the selection of study endpoints, (iii) the selection of non-inferiority (similarity) margin, (iv) sample size requirement, and (v) design and analysis for rare diseases clinical trials. Most recently, United States Food and Drug Administration (FDA) has kicked off several critical clinical initiatives to not only improve but also to shorten drug and biologic product development. These clinical initiatives include big data analytics, real world data/evidence, complex innovative design (including adaptive design and n-of-1 trial design), model-informed drug development, biomarker development for precision medicine, master protocols in cancer research. This presentation intends to cover practical and challenging issues that are commonly seen in regulatory review and approval process and introduce FDA clinical initiatives regarding drug research and development.	I first attended the Princeton Conference (as it was then known) in December 1964 and have attended every conference since, which must be somewhat of a record for a single symposium. I serendipitously assumed its chair several weeks after the 1969 meeting. There have been ups and downs but on the whole I've really enjoyed this experience, especially working with a top-notch organizing committee and consider it to be one of the major achievements in my life. This talk will describe the conference's history as well as some amusing anecdotes and is an update of the similarly titled paper in the text.

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Two Day Short Course (December 5-6)					
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