BBSW2020 Virtual Symposium

 # 1 Embracing Challenges and Opportunities Posed by the COVID-19 Pandemic

A Showcase of Pragmatic Examples by Clinical Trial Statisticians

Program Book

BBSW Bay Area Biotech-Pharma Statistics workshop

BBSW Virtual Symposium #1

Day 1 (Aug 13)	● 8:30 – 8:45 Symposium Welcome *Cheng Su (BioMarin)* ● 8:45 – 9:20 Keynote: COVID-19 and the Evidence Generation System *Keynote Speaker: Robert Califf (Verily/Google)* ● 09:20 – 09:30 Q&A *Moderator: Tara Maddala (TMbiostats)* ● 9:35 – 10:55 Statistical and executional considerations for trials impacted by COVID-19 pandemic *Speakers: Marcel Wolbers, Chin-Yu Lin, Zoe Zhang, Xin Li (Roche/Genentech)* ● 10:55 – 11:15 Q&A *Moderator: Tara Maddala (TMbiostats)* ● 11:15 – 11:30 Closing remarks for Day 1 and RAFFLE *Cheng Su (BioMarin)*
Day 2 (Aug 14)	● 8:30 – 8:40 Second day welcome *Whedy Wang (Theravance Biopharma)* ● 8:40 – 9:05 Considerations and practices in monitoring COVID-19 impact *Speaker: Priscilla Yen (Amgen)* ● 9:10 – 9:35 Safety assessment for studies and submissions impacted by COVID-19 *Speaker: Greg Ball (Merck)* ● 9:40 – 10:05 Summaries of COVID-19 infections in clinical trials *Speaker: Mary Nilsson (Lilly)* ● 10:10 – 11:15 Round Table: How pharma/biotech navigates COVID-19 and what roles statisticians play during the crisis *Moderator: Julia Varshavsky (Occampoint)* ● 11:15 – 11:30 Symposium closing remark and RAFFLE *Whedy Wang (Theravance Biopharma)*

ABSTRACTS

Day 1, Aug 13

8:45-9:20 am
Keynote: COVID-19 and the Evidence Generation System
Speaker: Robert Califf

The pandemic has required major alterations in our evidence generation system. This lecture will review the following areas: Consent, regulatory and ethics review; contracts and liability; digital/virtual/hybrid trials; interoperability and access to health records; data integration; involvement of people, patients, families, careers; novel outcomes and safety assessment; clinician involvement; analytical methods; meta-organization of studies/questions; dissemination; purposefulness. The key issue is to initiate an approach to assessment of which changes to the system should be kept as the pandemic comes under control and which changes should be eschewed to return to the previous standards.

9:35-10:55 am
Statistical and Executional Considerations for Trials Impacted by COVID-19 Pandemic
Speakers: Marcel Wolbers, Chin-Yu Lin, Zoe Zhang, Xin Li

The COVID-19 pandemic has been having impacts on planned and ongoing clinical trials, impacts on trial conduct, data collection, statistical analyses and interpretation. The COVID-19 pandemic impact varies depending on the nature of diseases under study as well as trial designs. In this session, we will focus on both statistical and executional considerations.

In the beginning of the session, the discussion will be on efficacy analyses, the use of the estimand framework to assess and address pandemic-related disruptions as well as provide analysis strategies on how to handle pandemic-related missing and unobservable values based on the Pharmaceutical Industry Working Group white paper and the general guidance issued at Roche/Genentech. Detailed examples will be presented as well.

Then a few examples of tools developed to assess the impact of COVID-19 will be provided. With these tools, and the specific instructions to the sites on data entry requirements for COVID-19 related reasons, the Sponsor could track missing doses, missing assessments, treatment and study discontinuation that are due to COVID-19, either directly or indirectly. In addition, we will provide suggestion on definitions of major protocol deviations to incorporate COVID-19 related deviations that may impact efficacy and safety assessments; an example of a tool developed to help screening the COVID-19 related protocol deviations will be also discussed.

Day 2, Aug 14

8:40-9:05 am

Considerations & practices in monitoring COVID-19 impact – an illustrative example

Speaker: Priscilla Yen (Amgen)

Although the pharmaceutical industry has observed disruptions on trial conduct due to COVID-19, we as statisticians can use various tools to evaluate the impact on individual studies, followed by implementation of mitigation strategies to maintain high data quality and to minimize potential bias due to the pandemic in our analyses. Graphical display of data is useful in communicating the quantification of impact of the pandemic in a clinical trial. This presentation discusses three types of visualizations: the first illustrates whether patients receive investigational product; the second depicts whether patients fulfill disease assessments; the third combines information from the first two. The visualizations are a useful tool for broad audiences to quickly understand dosing and assessment patterns prior to and during the pandemic, which in turn help us as statisticians make well-informed decisions on appropriate mitigation strategies. An example of the three visualization types, their interpretations, and resulting potential sensitivity analyses are presented.

9:10-9:35 am

Safety Assessment for Studies and Submissions Impacted by COVID-19

Speaker: Greg Ball (Merck)

Standard safety analyses and reporting of clinical trial safety data may need to be modified, given potential impact from the COVID-19 pandemic. In 2012, PHUSE and the FDA started a collaboration that has resulted in three white papers and a workshop (PHUSE 2013, 2015, 2017, 2019) on recommended safety analyses for industry standardization and education. The white papers have gone through a robust, public peer-review process. Using these standard safety analyses as a framework, we examine potential impact from COVID-19 on the scientific evaluation of safety data from clinical trials overlapping in time and geography with the pandemic. We focus on safety planning for Phase 2-4 clinical trials and integrated summaries for submissions. Guidance is provided on how to simply and properly reframe the analyses.

9:40-10:05 am

Summaries of COVID-19 Infections in Clinical Trials

Speaker: Mary Nilsson

The pandemic of coronavirus disease (COVID-19) has had broad impact on ongoing clinical development programs. Challenges may arise from quarantines, site closures, travel limitations, or other considerations if site personnel or trial participants become infected with COVID-19. Guidance has been released by various stakeholders and regulatory agencies to address some of the challenges. Several guidance documents recommend enumerating, describing, and/or summarizing COVID-19 infections occurring in trial participants, as part of an overall impact summary and/or as part of the summary of safety findings. This presentation will discuss existing recommendations and will provide practical advice on if, when and how to summarize COVID-19 infections.

BIOGRAPHIES

Greg Ball, Ph.D.
Senior Principal Statistician
Clinical Safety Statistics, Biostatistics and Research Decision Sciences
Merck & Co, Inc

After graduating from Northwestern University with a bachelor's in economics, Greg served in the Navy for 4 years and taught high school math and physics for 5 years, before going back to school to get a master's in applied statistics from Purdue University. Eventually, while working as a statistician, he earned his PhD in biostatistics from the University of Texas. Greg's research on blinded safety monitoring procedures is being developed in collaboration with clinical, safety and statistical scientists from several pharmaceutical companies. Greg established, with Bill Wang, the ASA Biopharm Safety Monitoring working group and is pioneering the joint DIA-ASA Interdisciplinary Safety Evaluation (DAISE) scientific working group, to advocate for aggregate safety assessments and cross-disciplinary scientific engagement.

Robert Califf. M.D.
Head of Clinical Policy and Strategy at Verily/Google
Former FDA Commissioner

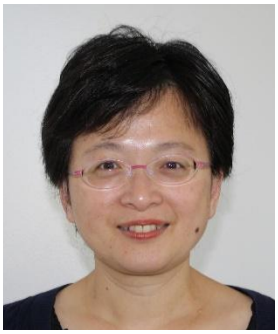
Robert M. Califf, MD, MACC, is the Head of Clinical Policy and Strategy for Verily and Google Health for Verily and Google Health. Prior to this Dr. Califf was the vice chancellor for health data science for the Duke University School of Medicine; director of Duke Forge, Duke's center for health data science; and the Donald F. Fortin, MD, Professor of Cardiology. He served as Deputy Commissioner for Medical Products and Tobacco in the U.S. Food and Drug Administration (FDA) from 2015-2016, and as Commissioner of Food and Drugs from 2016-2017. A nationally and internationally recognized leader in cardiovascular medicine, health outcomes research, healthcare quality, and clinical research, Dr. Califf is a graduate of Duke University School of Medicine. Dr. Califf was the founding director of the Duke Clinical Research Institute and is one of the most frequently cited authors in biomedical science.

Cheng Su, Ph.D.
BBSW President-Elect, Biomarin Pharmaceutical

Cheng is currently Executive Director of Data Sciences & Analytics at BioMarin. Cheng has two decades of industry experiences spanning from drug discovery to clinical development. His areas of expertise include high throughput screening, drug combination, assay development, predictive modeling, biomarker, early clinical trials and statistical monitoring. Cheng has led several cross-functional efforts and developed many standard approaches and automated analysis systems for the evaluation of in vivo experiments, immunogenicity assays, and centralized statistical monitoring.

Cheng received his dual-major B.S. in International Trade and Computer Sciences from Shanghai Jiao Tong University, and Ph.D. in statistics from NCSU.

Xin Li, Ph.D.
Vice President, Roche/Genentech
Xin currently is a Vice President at Roche/Genentech, she is the Global Head of Biostatistics focusing on Immunology, Infectious Disease, Ophthalmology, and NeuroScience (I2ON). Xin is a member of the Pharmaceutical Industry Biostatistics Working Group on COVID-19 and a co-author of the white paper entitled "Statistical Issues and Recommendations for Clinical Trials Conducted During the COVID-19 Pandemic" in Statistics in Biopharmaceutical Research. Xin has a Ph.D. in Statistics from Rutgers University. Prior to Roche/Genentech, she also worked in the Pharmaceutical Research Institute of Johnson & Johnson as well as Sequus Biopharmaceuticals.



Chin-Yu Lin, Ph.D.
Biostatistics Director, Roche/Genentech
Chin-Yu received her PhD in statistics with emphasis on biostatistics from University of Wisconsin-Madison. She is a Biostatistics Director at Genentech supporting late stage ophthalmology. Chin-Yu joined Genentech in 2004 and after a brief period away at Achaogen in 2013/14, leading their Biometrics activities for antibiotic studies, she re-joined Genentech in 2014. She has experiences in multiple disease areas including oncology, hematology, ophthalmology and respiratory. Her research interests include innovative clinical trial designs and statistical methods for drug development. She is involved in clinical trials facing challenges due to COVID-19.

Tara Maddala
TMbiostats
Tara is an independent statistical consultant and principal of TMBiostats LLC, specializing in clinical development strategy for pharmaceutical and diagnostic companies. Tara is also an expert statistical consultant with NDA Partners. From 2016 to 2019, Tara was the Vice President of Biometrics at GRAIL, leading a team of statisticians, clinical data scientists, data managers, and biosample managers. Before GRAIL, Tara led the Biostatistics team at Genomic Health (GHI) responsible for design and analysis of large-scale oncology biomarker studies. Prior to GHI, Tara was Director of Biostatistics at Clinimetrics, a CRO, working in drug development. She is co-inventor on several cancer genomic patents and has co-authored approximately 20 peer-reviewed publications and over 30 congress presentations. In addition to BBSW, Tara volunteers with Young Women in Bio, regularly lectures for the UCSF-Berkeley Translational Medicine program, and coaches high school JV boy's tennis. She holds a PhD in Biostatistics from The University of Texas and Engineering BS and MS degrees from The University of Florida and Georgia Tech.

Mary Nilsson, M.S.
Research Advisor, Safety Analytics, Global Statistical Sciences,
Eli Lilly and Company
Mary received a MS degree in statistics from Iowa State University in 1989. She has been employed at Lilly since 1989 and is currently a research advisor in the Safety Analytics group within the Statistical Sciences function. She consults with compound teams on safety analysis planning for Phase 2-3 studies and integrated submission documents. Her primary interests include analyses of adverse event data, analyses of laboratory data, statistical analysis plans, and collection and analysis of suicide-related events. Additionally, she co-leads a PhUSE Safety Analytics Working Group involved

with creating cross-functional education and cross-industry recommendations for standard safety analyses and displays.

Julia Varshavsky, Ph.D.
Occampoint

Dr. Varshavsky is the founder and managing director of OccamPoint. She has over 15 years of drug development experience spanning areas from drug discovery through commercialization and life-cycle management. During her tenure in the industry, Dr. Varshavsky served in a variety of leadership roles in both large R&D (Eli Lilly, Genentech) and small-to-midsize pharma (Jazz Pharmaceuticals, Corcept Therapeutics) organizations, building and leading Biostatistical, Biometrics and Development teams.

In 2019 Dr. Varshavsky founded OccamPoint, a consortium of drug and combination product development professionals, to aid assessment of investment risk in healthcare and digital health products during due diligence and business development. As a Life Sciences Council member for Springboard Enterprises, Dr. Varshavsky works with peers in finance, legal and investment communities to foster success of female-led healthcare and digital health startups, coaching on a broad range of topics including indication-specific product development, use of AI in patient selection and diagnostics, as well as scalable and efficient data aggregation and sharing strategies.

Dr. Varshavsky holds a Ph.D. in Statistics from Purdue University.

Whedy Wang, Ph.D.
Theravance

Whedy has over 20 years of experience in the biopharmaceutical industry, including directing biometrics efforts in more than ten NDA and sNDA submissions, three advisory committee meetings and multiple EX-US submissions, all leading to successful approvals. Whedy is currently VP of Biometrics at Theravance Biopharma, a company focusing on creating medicines that help improve the lives of patients suffering from serious illness. Prior to joining Theravance Biopharma, she held several senior positions including Vice President of Biometrics at Gilead Sciences Palo Alto (formerly CV Therapeutics), Senior Vice President of Bioinformatics at Orexigen, and Executive Director of Biometrics at Affymax.

At her current as well as previous job postings, Whedy provided strategic input and biometrics oversight to U.S. and EU development and commercial efforts. As a member of executive team at CV Therapeutics and Orexigen, Whedy contributed to the development of corporate strategy and led life cycle management planning. Additionally, Whedy was the global project leader for Lexiscan® and Ranexa® where her contributions included presenting development rationale and product life cycle management plan to the Board of Directors, and potential EU and Asia partners. Whedy also played a key role in business development discussions that led to successful collaborations such as royalty financing of $185 million for Lexiscan® Injection with TPG-Axon Capital, and license agreement for Ranexa® in 68 countries including EU with the Menarini Group. Whedy holds a M.P.H. in Epidemiology, and a Ph.D. in Biostatistics, both from the University of Michigan.

Whedy thrives to be a leader who inspires and empowers others to be their best!! She lives in Palo Alto with her husband and 3 toddler girls. Her favorite daily routine includes reading bedtime stories and singing off-key with her daughters.

Marcel Wolbers, Ph.D.
Expert Statistical Scientist, Roche/Genentech

Marcel Wolbers received his PhD in mathematical statistics from ETH Zurich in 2002. Between 2002 and 2005, he worked in the biostatistics department of Roche, primarily in the area of hematology. In 2005, Marcel returned to academia, first to the Institute for Clinical Epidemiology and Biostatistics of the University Hospital of Basel and then to the Oxford University Clinical Research Unit, Ho Chi Minh City, Vietnam, as Head of Biostatistics. In 2016, he returned to Roche and is currently an expert statistician working in the Methods, Collaboration, and Outreach group (MCO) of Roche's biostatistics department. His research interests include innovative statistical methods for clinical trial designs and drug development, prognostic models, and competing risks. He is a member of two COVID-19 cross-industry working groups and leads the Roche-internal methodological efforts to address COVID-19-related disruptions of clinical trials.

Priscilla Yen, Ph.D.
Biostatistics Manager
Center for Design & Analysis, Amgen Inc

Priscilla received her doctoral degree in biostatistics at the University of California, Los Angeles in 2019, where her research included decision-making in adaptive design. She joined Amgen's Center for Design and Analysis in 2018, where she has worked on Phase 2 and Phase 3 studies and is a member of the Estimand Technical Subteam Working Group. Her interests include adaptive design, missing data, and how to present data effectively. In her spare time, she enjoys the company of her two dogs, hiking, cooking, and traveling.

Zoe Zhang, Ph.D.
Principal Statistical Scientist, Roche/Genentech

Zoe Zhang received her PhD in statistics from North Carolina University. She has worked in the biostatistics department of Genentech since 2016, primarily in the area of oncology. Prior to joining Genentech, she worked as a statistician at Quintiles in Beijing, China, and Duke Clinical Research Institute (DCRI) in Durham, North Carolina. Before becoming a statistician, she held a Master degree in Molecular Biology and worked as a research analyst at Duke University Medical School.
Her research interests include innovative clinical trial designs for efficient drug development. She is a member of the Roche-internal taskforce to address COVID-19-related disruptions of clinical trials.