Volume 32, No.1 • SPRING 2025

BIOPHARMACEUTICAL REPORT

ASA BIOP Section Chairs : Ted Lystig(2024), Erik Bloomquist (2025), Steven Novick (2026)

Note from Editor:

Welcome to the Spring Issue! This year's theme is "The Evolving Role of Statisticians in the Pharmaceutical Industry: Leveraging Advanced Statistical Analytics and Artificial Intelligence", and we hope that the articles we share will provide new perspectives and encourage everyone to further develop and grow in their role. In this issue we present various perspectives and invite you to a discussion around the current role of statisticians.

In addition, we also share thought-provoking pieces about how to irritate regulators, recent advancements in the topic of covariates adjustment in modern clinical trials, as well as advice and tips on generative AI. Enjoy the fresh insights and inspirations this issue has to offer!

We would like to extend our sincere thanks to our esteemed contributors for their invaluable insights and contributions. Additionally, a big thank you to our ASA colleagues Megan Murphy and Olivia Brown for their tremendous support in production.

Maria Kudela
Editor

Di Zhang
Associate Editor
Clinical

Francis Rogan
Associate Editor
Non-Clinical

Charlotte Baidoo
Associate Editor
Clinical

Christie Watters
Associate Editor
Non-Clinical

CONTENT

TRANSITION REPORT

Ted Lystig (BIOP Chair, 2024) and Erik Bloomquist (BIOP Chair, 2025)

Highlights

- Discover BIOP's impactful events from 2024 and exclusive preview of initiatives scheduled for 2025.
- Explore the latest on BIOP awards, Scientific Working Groups, Leadership in Practice Committee developments, Statisticians in Small Biotech updates, Communications & Education initiatives, and key conferences.
- Stay informed with the latest updates on BIOP finances and newly elected BIOP officers.

Ted Lystig
Biopharm Chair, 2024

Erik Bloomquist
Biopharm Chair, 2025

Dear BIOP Members and Friends,

We'd like to update you on BIOP happenings in 2024 and introduce some new initiatives the section has planned for 2025.

The year 2024 represented yet another highly successful Regulatory-Industry Statistics Workshop with record breaking attendance of 1,250 members. The workshop was chaired by Zhiheng Xu (FDA) and Jianchang Lin (Takeda) and included two very well received plenary sessions and 56 parallel sessions. A tribute to the life of Dionne Price, former ASA President and ASA BIOP Section chair was also held and chaired by Adrian Coles and Shanti Gomatam.

As usual, the Section held multiple meetings of the Executive Committee (EC) throughout the year. Our Spring and Fall 2024 EC meetings were each held virtually, while an in-person EC meeting and the annual BIOP mixer and business meeting were both held in-person at JSM in Portland.

One notable tragedy struck the section in 2024 with the passing of Meijing Wu in November. Meijing Wu was the BIOP report editor and incoming elected Communications Officer for the section. Meijing's commitment to many BIOP committees and activities has left a lasting impact on many members of the section, and she will be fondly remembered . To honor her legacy, the BIOP community established a memory page in early 2025, with donations earmarked to support BIOP award initiatives.

In the subsequent sections, we address the activity and impact of the Section throughout 2024, and we also take a sneak peek at 2025.

Awards

The designation of awards is a long-standing and significant way the Section provides service to the profession, encouraging leading-edge science by students and professional statisticians at all career levels. Our awards include the BIOP Student Scholarship Award, along with several presentation and paper awards linked to JSM and various other conferences.

The BIOP Student Scholarship Award Committee fielded yet another record number of applications in 2024, and included 10 winners. Consideration for the awards is based primarily on notable academic achievement or applied project work related to the area of biopharmaceutical statistics, general academic performance, leadership, service/volunteering, and diversity. As a result of the large number of deserving, high-quality applicants, the committee awarded ten scholarships, rather than the traditional five

scholarships. Recipients were recognized during the JSM Business Meeting and Mixer and via our social media channels. The 2024 recipients were:

1. Navneet Ram Hakhu (University of California, Irvine)
2. Ann Marie Weideman (University of North Carolina)
3. Ransmond Berchie (University of Utah)
4. Megan McCabe (University of Iowa)
5. Yixin (Amy) Zhang (Boston University)
6. Runjia Li (University of Pittsburgh)
7. Dennis Baidoo (University of New Mexico)
8. Marlena Bannick (University of Washington)
9. Lizhao Ge (George Washington University)
10. Zhongyang Ma (New York University)

Thank you to Wenting Cheng (2024 Chair of the Scholarship Award Committee), Bruce Binkowitz, Rebbecca Wilson, and Tony Jiang for stewarding the selection process.

Also recognized at the JSM Business Meeting and Mixer were the Student Paper Awards and Best Contributed Poster Awards. The 2024 Student Paper awardees were:

First place: Kai Chen (UT Health, Houston)

Second place: Chang Wang (University of Michigan)

Third place: Edward Bi (University of Chicago)

Honorary Mentions: Jack Wolf (University of Minnesota), James Willard (McGill University), Qingzhi Liu (University of Michigan), Marlena Bannick (University of Washington), Xue Yang (University of Pittsburgh)

Thank you to Lanju Zhang (Chair of the committee), Yang Chen, Yu Du, Siddesh Kulkarni, Ruitao Lin, Jimin Wu, Meijing Wu, Yunlong Yang for their work in stewarding the award selection process.

The winners of the 2024 Best Contributed Poster Award were:

First place: Xutong Zhao, Jing Sun, and Dalong Huang.

Second place: Yuting Xu, Kevin Stone, Melodie Christensen, Ajit Vikram, Kobi Felton, Kaitlyn Brinza, Spencer McMinn, Victor Schultz, Shane Grosser

Third place: Dan Jackson, Fanni Zhang , Carl-Fredrik Burman, Linda Sharples

Honorary Mention: Akari Naito, Kei Fujikawa, Go Horiguchi, Mitsuko Nakata, Satoshi Teramukai

Thank you to Yilong Zhang and the entire Best Contributed Poster committee for helping to make this poster award happen in 2024!

Scientific Working Groups

In accordance with the BIOP Sections process for establishing new SWG's, in 2024, three new SWG's were established, bringing the total number of SWG's to 19. The new SWG's and their chairs are listed below:

Randomization Working Group—Alex Sverdlov

Metabolic Diseases Working Group—Hiya Banerjee, Jingyi Liu

Neuroscience Working Group—Mandy Jin

Thank you to Brian Waterhouse (committee Chair) and Yodit Seifu for their exemplary efforts in shepherding the SWG proposal process for BIOP.

Leadership in Practice Committee (LiPCom) [Richard Zink, Chair]

LiPCom had an active 2024, with presentations at ENAR, JSM, NIC/ISCA, RISW, SIP. Several webinars were provided and a local LiPCom-sponsored Workshop in Applied Improvisation in Leadership and Communication was held in Raleigh. 2025 looks to have several additional leadership opportunities as well with courses at DISS, ICSA, JSM, and SIP! Thanks to Veronica Bubb, Emily Butler, Andy Chi, Abie Ekangaki, Rakhi Kilaru, Qing Li, Lisa Lupinacci, Yabing Mai, Shanti Sethuraman, Vincent Tan, and Hongwei Wang. Your efforts have brought practical, leadership-focused content to the BIOP community.

Statisticians in Small Biotech committee [Wei (Michelle) Zhang, chair]

The Statisticians in Small Biotech Committee has been actively working on initiatives to strengthen engagement and provide valuable resources for our community.

Some key updates & initiatives include

- Webpage Enhancements – We updated our mission statement and refining website content to better serve our members.
- Improved Membership Access – The "Join" process is being streamlined to make it easier for statisticians to connect and participate.
- ASA Community Platform – We have established an ASA community where statisticians in small biotech companies can exchange ideas, share experiences, and discuss best practices through the ASA Community discussion forum.
- Recruitment Strategy – Our team is actively brainstorming strategies to attract new members and increase participation in our community.
- Resource Development – In 2024, we remain committed to building our website and online community into a valuable resource for statisticians in small biotech and beyond.
- JSM 2024 Biopharmaceutical Section Panel Discussion – We organized a panel discussion titled "Don't Go It Alone" at JSM 2024, where experts shared insights on navigating careers in small biotech.
- Upcoming RISW 2025 Event – We are organizing an in-person session at RISW 2025 to promote networking, collaboration, and professional development.

A special thank you to our dedicated team members for their contributions: Alan Hartford, Mohamed Hamdani, Sharon Murray, Jingtao Wu, Ruixiao Lu, Alan Chiang and Liang Fang. We look forward to continuing to grow this community and support statisticians in small biotech!

Communications & Education

Thank you to Herb Pang for leading the active BIOP Distance Learning Committee webinar series in 2024. The series features diverse speakers from industry, academia, and the FDA, covering topics from open-source software in regulatory submissions to the use of AI/ML in drug development. Other engaging topics include real-world evidence, statistical leadership, patient-reported outcomes, and health technology assessment. Participation/viewing of webinars is free for all BIOP members. So Young Park and Arunava Chakravartty have begun to organize webinars for 2025. You can view information on past webinars here (*https://community.amstat.org/biop/media-contents/webinararchive*).

Further details will be announced on our discussion forums about a month ahead of each event.

Finally, thank you to Hiya Banerjee who manages BIOP's social media presence. News of BIOP activities is actively shared on LinkedIn and X (formerly known as twitter). Traffic to these postings is strong and continues to grow, thanks to her continuous efforts to curate content in partnership with the EC and committee members.

JSM 2024

In 2024, BIOP sponsored five invited sessions. This includes our four allocated sessions plus one additional session earned through competition. In addition to the invited sessions, BIOP sponsored 16 topic-contributed sessions, 20 contributed paper sessions (containing 7 presentations each, which includes a designated session for the winners of the ASA BIOP Student Paper Competition), 37 contributed poster presentations, and 15 contributed speed presentations. In addition, a total of 4 continuous education short courses were sponsored by the Biopharmaceutical Section at JSM.

Thank you to Bo Huang (BIOP Program Chair) for driving the selection process for BIOP in 2024.

RISW 2024

The 2024 ASA Biopharmaceutical Section Regulatory-Industry Statistics Workshop (RISW) was held in North Bethesda, MD from September 25-27 and once again resulted in a highly successful event. The workshop had a theme of "Harnessing the Power of Statistics, Data Science, and Digital Technology to Drive Patient-Focused Innovations Together" and featured over 1, 200 statisticians and researchers participating in 10 short courses, 56 parallel sessions, and 2 plenary sessions that focused on the intersection of statistics, data science and AI in drug development and regulations.

For a full recap of the event including summaries of many of the sessions, please visit: *https://asabiopreport.substack.com/p/2024-risw-special-issue?r=4o7pco&utm_medium=ios&triedRedirect=true*

Thank you to 2024 RISW co-chairs Zhiheng Xu and Jianchang Lin for your great efforts in making this happen.

Finance and Sponsorship

We are happy to report a strong end-of-year balance for BIOP of $543,000. As a Section of a nonprofit organization, our goal is to deploy resources in service of our membership and the profession in a responsible and sustainable manner. Our current position provides an ideal opportunity to proactively evaluate financial standing going forward, in light of aggregate environmental changes over the past four years.

In addition to strong financial position, the section funded and sponsored 5 external conferences with $12,000 of support. BIOP looks forward to 2025 and continued support of the statistical profession and our members.

BIOP Newly Elected Officers

BIOP welcomes four new elected officers for 2024 and two new at large members including our section chair-elect, Steve Novick from Takeda, program Chair-elect Inna Perevoskaya from BMS, Council of Sections Rep Jennifer Gauvin from Novartis and the late-Meijing Wu for Publications officer. Our two new executive council at-large members are Matt Psioda from GSK and Justine Rochon from Boehringer Ingelheim.

2025 Sneak Peek

Following a successful 2024, our Section is thriving with a healthily engaged membership, established programs that provide value to the members and our profession, and several recent, emerging initiatives, committees, and working groups aimed at further increasing our impact in the future. Our slate of officers and other volunteers bring a mindset of innovation and improvement to the business of the Section which is refreshing. From a financial perspective, we are in really strong standing with an end-of-year balance of over $500,000.

A new award in 2025 will be launched supporting student travel to the Women in Statistics and Data Science Conference held annually in the Fall. The section has been working on this award for several years and is looking forward to supporting young professionals attending this conference.

As we close this message, we want to thank all volunteers (officers and committee members and SWG members) who keep this very active section running. Your work is impactful and enormously appreciated. As we look ahead, we want to hear from you. Your ideas, suggestions, and feedback are essential in shaping BIOP into an even more relevant, inclusive, and impactful community for statisticians in our industry. Together, we can ensure our section remains a strong and vibrant home for years to come.

With Best Regards,
Erik and Ted

IN MEMORIAM: DR. MEIJING WU (1984-2024)

By Yingwen Dong (Sanofi), Weili He (AbbVie), and Yuqian Shen (Sanofi).

Dr. Meijing Wu was a dedicated statistician, a passionate community member, and a beloved colleague, whose professional contributions and service left a lasting impact on the statistical community. Her sudden passing in November 2024 was a tremendous loss to all who had the privilege of knowing and working with her.

Born in Fujian, China, Meijing started her professional career in academia. She was a faculty member at Northwestern University and provided statistical expertise across various research disciplines. She later transitioned to industry roles at AbbVie and Sanofi, establishing herself as a respected statistical project leader. Throughout her career, Meijing was known for her technical excellence, leadership, and collaborative spirit. At AbbVie, she played a key role in developing statistical methodologies, work processes, tools, and document templates that continue to be widely used. At Sanofi, she took on the role of statistical project lead for high-priority programs and was instrumental in driving strategic decision-making and fostering cross-functional collaboration.

Meijing was an active and influential member of the ASA Biopharmaceutical Section. She served as an Associated Editor and later Editor of the Biopharmaceutical Report, and was elected as publication officer for ASA Biopharmaceutical section. She provided leadership and support to numerous initiatives. Her contributions enriched the community and inspired those around her.

To honor her legacy, ASA has established a tribute and legacy donation page (*https://ww2.amstat.org/giving/honored-members/meijing-wu.cfm*). We are grateful to all who have contributed to her memory. Future donations are welcomed and will continue to support initiatives that reflect Meijing's passion for advancing statistical science and community building.

Dr. Wu's professional excellence, generosity, and spirit of service will be remembered with admiration and gratitude. Her legacy lives on through the lives she touched, the work she championed, and the community she helped build.

EVOLUTION OF BIOPHARMACEUTICAL STATISTICS

Mark Rothmann[1], Yun Wang[1], James Travis[1]

Highlights

- Discover how statisticians are now integral to every stage of clinical trials, ensuring precise and reliable results.
- Learn about the revolutionary Bayesian methods that are enhancing the accuracy and reliability of clinical trial outcomes.
- Explore the collaborative programs led by the FDA that are fostering statistical innovation and paving the way for novel trial designs.

Mark Rothmann
Office of Biostatistics, Office of Translational Science, Center for the Drug Evaluation and Research, FDA

Yun Wang
Office of Biostatistics, Office of Translational Science, Center for the Drug Evaluation and Research, FDA

James Travis
Office of Biostatistics, Office of Translational Science, Center for the Drug Evaluation and Research, FDA

Disclaimer: This article reflects the views of the authors and should not be construed to represent FDA's views or policies.

Statistical thinking has evolved into a proactive approach emphasizing pre-specification of design and analysis with detailed statistical analysis plans to provide clear interpretation of the results. The involvement of statisticians in clinical trials has evolved from being consultants providing sample size calculations and being consulted after data collection for data analysis to a collaboration where statisticians are involved during the whole process of a clinical trial, ranging from defining the research questions and endpoints, formulating the statistical hypotheses, justifying the study design, to monitoring the cumulative data for potential early stop due to safety, futility or efficacy or other adaptations, analyzing the data, interpreting the results, assessing the credibility of the findings, and ensuring valid conclusions about treatment efficacy and safety. A statistician's role is crucial when non-traditional methods are involved, for example in designing platform trials or studies involving adaptive features or borrowing from external data, in analyzing data with complex statistical models or synthesizing evidence from multiple studies

Historically, clinical trials focused on enrolling a homogeneous patient population to minimize the variability in outcomes. Now, clinical trials are encouraged to have participants in the trial consistent with the entire population who may get the drug should the drug be approved rather than a narrow segment of the population, leading to a more heterogeneous study population [1]. Considering and evaluating heterogeneous treatment effects is necessary in such clinical trials. Bayesian hierarchical models have been used that consider all data, not just subgroup-specific data, leading to increased precision in estimating treatment effects across subgroups [2,3].

Bayesian methods have also been applied in dose selection, the determination of non-inferiority margins, in pediatric extrapolation, adaptive clinical trials and in rare diseases. Regulatory agencies have become more open to non-traditional methods in medical product development [4].

Statisticians are key to leading and implementing clinical trial innovations, as seen in programs such as the Complex Innovative Trial Design Meeting program [5]. This program promotes statistical innovation by allowing the Food and Drug Administration (FDA) to publicly share and discuss the novel trial designs accepted by the program, including trial designs for medical products that have not yet been approved by

[1]Office of Biostatistics, Office of Translational Science, Center for the Drug Evaluation and Research, U.S. Food and Drug Administration, Silver Spring, Maryland, USA

the FDA. Statisticians also lead in a new, redesigned Bayesian Statistical Analysis demonstration program [6], which aims to increase experience in Bayesian statistical methods across sponsors and FDA clinical and statistical reviewers, including deepening an understanding of their applicability, opportunities, and challenges.

In addition to our regular interaction with the sponsors via different types of regulatory meetings, FDA statisticians participated in user fee negotiations and are involved in coauthoring numerous guidances. Statisticians took important or leading roles in the writing of several ICH guidances including ICH E9(R1) Statistical Principles for Clinical Trials: Addendum: Estimands and Sensitivity Analysis in Clinical Trials, ICH E11A Pediatric Extrapolation, ICH E17 General Principles for Planning and Design of Multi-Regional Clinical Trials and ICH E20 Adaptive Clinical Trials (draft). Within the FDA, some examples of statisticians-led guidances are Adaptive Designs for Clinical Trials of Drugs and Biologics, Adjusting for Covariates in Randomized Clinical Trials for Drugs and Biological Products, Interacting with the FDA on Complex Innovative Trial Designs for Drugs and Biological Products, Multiple Endpoints in Clinical Trials, Non-Inferiority Clinical Trials to Establish Effectiveness, and Statistical Approaches to Establishing Bioequivalence.

To promote collaborations among the FDA, industry, and academia, the Center for Drug Evaluation and Research (CDER) is engaging in a number of scientific public and private partnerships and consortia [7]. For example, FDA statisticians actively contributed to the American Statistical Association (ASA) Biopharmaceutical (BIOP) Safety Working Group, Heart Failure Collaboratory, Type I Diabetes Consortium. FDA has co-sponsored symposiums/workshops to address challenges and opportunities in assessing and communicating heterogenous treatment effects [8,9], advance the development of pediatric therapeutics [10], and explore novel endpoints for rare disease drug development [11]. FDA also launched programs to incorporate the patient's voice in drug development and evaluation [12] and enable the integration of real-world data/evidence in regulatory decision-making [13]. Regulatory and industry statisticians have worked together to organize multiple annual statistical meetings. They also work together in many scientific working groups, including on Alzheimer's disease, oncology, metabolic disorders, Bayesian methods, cell & gene therapy, pediatric drug development, and many more.

To succeed today in biopharmaceutical statistics, one should have a strong foundation in statistical methodology, knowledge in clinical trials, capability to analyze and interpret data, along with excellent collaboration, communication and problem-solving skills. In the era of artificial intelligence (AI), a willingness to learn the latest scientific advancement and embrace different approaches is fundamental for adapting to a continually evolving biopharmaceutical industry and regulatory landscape. For example, at one time SAS was the primary statistical package used for statistical analysis in regulatory submissions and reviews. Now, it is increasingly common to see submissions using more diverse approaches and software, particularly when using complex methods.

References

1. FDA draft guidance: Diversity Action Plans to Improve Enrollment of Participants from Underrepresented Populations in Clinical Studies 2024.
2. FDA Impact Story (2019). Using innovative statistical approaches to provide the most reliable treatment outcomes information to patients and clinicians. Available at *https://www.fda.gov/drugs/regulatory-science-action/impact-story-using-innovative-statistical-approaches-provide-most-reliable-treatment-outcomes.*
3. Wang, Y., Tu, W., Koh, W., Travis, J., Abugov, R., Hamilton, K., Zheng, M., Crackel, R., Bonangelino, P., Rothmann, M. Bayesian Hierarchical Models for Subgroup Analysis. Pharmaceutical Statistics. 2024; 23:1065–1083. *https://doi.org/10.1002/pst.2424.*
4. Ionan, A.C., Clark, J., Travis, J., Amatya, A., Scott, J., Smith, J.P., Chattopadhyay, S., Salerno, M.J., Rothmann, M. Bayesian Methods in Human Drug and Biological Products Development in CDER and CBER. Ther Innov Regul Sci 2023; 57 436-444. *https://doi.org/10.1007/s43441-022-00483-0.*
5. Complex Innovative Trial Design Meeting Program, *https://www.fda.gov/drugs/development-resources/complex-innovative-trial-design-meeting-program*.

6. CDER Center for Clinical Trial Innovation (C3TI), *https://www.fda.gov/about-fda/center-drug-evaluation-and-research-cder/cder-center-clinical-trial-innovation-c3ti*.

7. CDER Scientific Public Private Partnerships and Consortia, *https://www.fda.gov/drugs/science-and-research-drugs/scientific-public-private-partnerships-and-consortia*.

8. Assessing and Communicating Heterogeneity of Treatment Effects for Patient Subpopulations: Challenges and Opportunities, *https://www.jhsph.edu/research/centers-and-institutes/center-of-excellence-in-regulatory-science-and-innovation/news-and-events/Critical-Issues-in-Heterogeneity-of-Treatment-Effect.html*.

9. Heterogeneity of Treatment Effects in Clinical Trials: Methods and Innovations, *https://mrctcenter.org/news-events/heterogeneity-of-treatment-effects-in-clinical-trials-methods-and-innovations/#1602863324215-1289c9d5-a82a*.

10. Pediatric Science and Research Activities, *https://www.fda.gov/science-research/pediatrics/pediatric-science-and-research-activities*.

11. Rare Disease Endpoint Advancement Pilot Program Workshop: Novel Endpoints for Rare Disease Drug Development, *https://healthpolicy.duke.edu/events/rare-disease-endpoint-advancement-pilot-program-workshop-novel-endpoints-rare-disease-drug*.

12. CDER Patient focused drug development, *https://www.fda.gov/drugs/development-approval-process-drugs/cder-patient-focused-drug-development*.

13. CDER and CBER Real World Evidence Program, *https://www.fda.gov/science-research/real-world-evidence/center-biologics-evaluation-and-research-center-drug-evaluation-and-research-real-world-evidence*.

HOW TO IRRITATE REGULATORS: A PRIMER

Janet Wittes, Florida Atlantic University

Highlights

- What are important elements that can make or break a trial's success? Reflect on properly designing and executing randomized controlled trials that not only meet regulatory standards but also ensure reliable results.
- What are some common strategies that can irritate regulators and jeopardize your trial's approval? From ambiguous hypotheses to operational deficiencies, what critical mistakes should you avoid?
- Dive into two real-world case studies: the 1993 NEJM paper on respiratory syncytial virus immune globulin and the recent study on pimavanserin in dementia-related psychosis. What went wrong, and what lessons do these examples teach us?

Jane Wittes
Florida Atlantic University

"…I wouldn't stand by and see the rules broke – because right is right and wrong is wrong, and a body ain't got no business doing wrong when he ain't ignorant and knows better."

Tom's lesson to Huck in *The Adventures of Huckleberry Finn* – Mark Twain

As we statisticians are wont to do, I start with a set of assumptions so you the reader know where I am coming from. I assume that you are designing, carrying out, or analyzing data from a Phase 3 randomized controlled trial conducted by a pharmaceutical company. You are honest; you do not commit fraud; and you are after truth. You know that the purpose of your trial is to assess the efficacy of Drug D in Population P with Condition C, but you are really thinking, "This trial is designed to show that D is efficacious in P with C." You come to the project armed with new statistical methods at your fingertips and the promise that artificial intelligence (AI) can help lead you on your path to truth. You know that to land in good graces with regulators the study should have a design that addresses the question of interest; the protocol should be as unambiguous as you know how to make it; the statistical analysis plan (the SAP) should be rigorous but not so opaque that only statisticians can understand it; the study sample size should be large enough to provide a reliable answer to the questions posed; the team must carry out the study nearly perfectly. If all this is true, and if D really benefits P with C, the answers will emerge as you expect. You, with the rest of the study team, will write the Clinical Study Report and the primary manuscript carefully, following the SAP precisely. If you conduct analyses not identified in the SAP, or if you modify the methods even slightly, you will forthrightly declare the changes as post hoc. You will report p-values only when they reflect statistically valid tests and you will present numbers to a reasonable degree of precision.

But sometimes (and all too often) the ideal does not hold. You may have found yourself involved in a study that someone else had designed before you joined the team and the protocol, SAP, or both were, in your mind, flawed. The study operations may have had problems

beyond your control. Some of these deviations will irritate the regulators who will review your application. You know that if you try to hide them, the regulators will find them and be even more irritated because they do not appreciate shading the truth. If you had wanted to irritate them even more, you should have designed your study without an unambiguous hypothesis. That would have allowed you to tweak your hypothesis to make it fit your data. You could have written the SAP in a way that is unclear to give you lots of wiggle room. You could have selected a sample size too small to produce reliable answers to the questions the trial is posing. You could have winked at the sloppiness of the operations by, for example, not pressing investigators to do all they could reasonably do to prevent missing data. And then, if the answers from your study differ from expected (e.g., the p-values are not below 0.05), you could rely on the inconsistencies and lack of precision in your documents to construct an analysis, find a subgroup, and search for an outcome with a comfortably small p-value. You may be able to use some of your many new statistical methods to find the most convincing result. Perhaps you ask your AI tool to help you find a summary that you hope will convince the regulators.

When you write your Clinical Study Report and your manuscript, you could avoid identifying what had been prespecified and what was ad hoc. You might toss out observations that make no sense to you without questioning whether the apparent anomaly had a reason (maybe the use of a different unit). Another approach might be to use all observations in the database even when some are ridiculous. One trick I have seen comes from a large Contract Research Organization. Suppose an observation that is obviously incompatible with life has had an attached text notation that says, "This blood sample came from a cow." Use the data and Ignore the text. "I don't manipulate data," you say to yourself self-righteously. When confronted with the absurdity of the number, defend yourself with, "My program doesn't read text." (Confession: I am only slightly exaggerating this story; the cow was from one study; the quotation from another.)

You know that you will irritate the regulators, and feel uncomfortable yourself, if you sprinkle your report with p-values placing particular attention on the small ones, even those that are data-dredged. Pretend that saying, "Please interpret this with caution", absolves you of responsibility. Use lots of digits for your p-values to emphasize how certain you are. (Why should anyone believe p=0.001452 is an accurate representation of a probability?) If you feel your argument is not strong enough, use the coup de grace appeal to biology to defend the clinical and statistical meaningfulness of your post-hoc p-values. Lest you think that no one would use these strategies, the following two examples may change your mind. The first dates from 1993; the second dates from over a quarter century later.

In 1993, the NEJM published a paper on the use of respiratory syncytial virus immune globulin as prophylaxis for RSV infection in high-risk infants and young children [1]. The paper described the primary endpoint as follows:

> The sample size was determined on the basis of two primary end points: reduction in the incidence of lower respiratory tract infection caused by respiratory syncytial virus and reduction in the severity of respiratory syncytial virus disease.

The paper provided no discussion of the planned analysis of the two doses or the two endpoints. The tables in the article presented many p-values (18 in Table 3; 8 in Table 4), some of which were below 0.05. An editorial in the same issue of the journal was very positive, "RSV – successful immunoprophylaxis at last". Two weeks later the FDA Blood Products Advisory Committee voted against approval. The FDA, on reviewing the data, did not approve the product. In a letter to the editor, Ellenberg et al. [2] explained the reason for the FDA's rejection. The letter pointed out that the paper failed to describe the method of randomization. The paper said the treatment was intent-to-treat but eight children, seven active and one control, had been removed after randomization. Moreover, 17 children whose caregivers had signed an informed consent form were not included. Importantly, the study was not blind, so the failure to include so many children could not be attributed to chance. Clearly, the authors had irritated the FDA. As a post-script, a subsequent study in children with cardiac problems [3] showed benefit and the product was approved for them.

The second example comes from a much more recent study, one that examined the use of pimavanserin (the D) in dementia related psychosis (the C) [4]. The population P was complicated. On one level it was composed of people with a history of dementia-related psychosis regardless of the underlying type of dementia. On another level, it was a population comprised of people with Alzheimer's disease dementia, Parkinson's disease

Table 1. Number of participants in the pimavanserin study			
Type of dementia	**Pimavanserin**	**Placebo**	**Total**
Alzheimer's disease	67	70	137
Dementia with Lewy bodies	6	4	10
Frontotemporal dementia	1	2	3
Parkinson's disease dementia	19	23	42
Vascular dementia	12	13	25
Total	**105**	**112**	**217**

Table 2. Results of the pimavanserin study by dementia type					
Dementia type	Pimavanserin n/N (%)	Placebo n/N (%)	Hazard ratio	95% confidence interval	Nominal p-value (2-sided)
Overall	12/95 (12.6%)	28/99 (28.3%)	0.35	(0.17, 0.73)	0.005
Alzheimer's	8/61 (13.1%)	14/62 (22.6%)	0.62	(0.26, 1.49)	0.28
Parkinson's	1/15 (6.7%)	10/20 (50.0%)	0.05	(0.02, 0.18)	<0.001
Other	3/19 (15.8%)	4/17 (23.5%)	0.52	(0.08, 3.38)	0.49

dementia, dementia with Lewy bodies, frontotemporal dementia, and vascular dementia, all of whom had a history of dementia-related psychosis. What is the P: Is it a single P with the five types of dementias simply being subgroups, or is it five populations with an umbrella diagnosis of dementia-related psychosis? Interestingly, the NEJM didn't report data by dementia subgroup. Importantly, prior to this study, pimavanserin had received a label for Parkinson's hallucinations and delusion, not exactly the same as dementia-related psychosis, but pretty close.

The study at hand was a randomized withdrawal trial. All study participants had received open-label pimavanserin for 12 weeks. Then, those eligible were randomized 1:1 to a double-blind, placebo-controlled trial with time to relapse of psychosis the primary outcome. The FDA presented all the data below at an advisory committee meeting in 2022 [5].

The trial had a prespecified interim analysis with a stopping guideline p=0.0066. At the interim analysis, the data showed a hazard ratio of 0.35, a 95% confidence interval of (0.17, 0.73), and a p-value of 0.005 (Table 2). The analysis included the 194 participants who had completed the study at the time of the interim; 23 others had been randomized but had not been followed long enough to be included. On the DSMB's recommendation, the sponsor stopped the study declaring efficacy. Whether the DSMB looked at the data by type of dementia does not seem to be a matter of public record.

At the advisory committee evaluating the effect of pimavanserin in dementia-related psychosis, the FDA commented that the overall results appeared to be driven by the small Parkinson's disease subgroup, but the drug had already been approved for patients with Parkinson's. The set of other dementias showed no convincing evidence of effect. The largest subgroup was Alzheimer's disease dementia. Given the importance of Alzheimer's for public health and the equivocal results in that large (N=123) subgroup, the FDA concluded that the data did not show enough evidence of benefit in the non-Parkinson's dementia participants to grant the drug a label wider than the one it already had.

So just as a sloppy protocol, operational deficiencies, and violations of the SAP can irritate the FDA, the primavanserim study is an example in which slavish adherence to a protocol and SAP can be an irritant as well. Beware feeding your protocol, SAP, and data into

AI without thinking about the meaning of what you are asking it to do. Here the prespecified analysis showed a dramatic result, but failing to look into the subgroups, especially those not already covered by a label, must have frustrated the FDA reviewers.

To summarize, some motherhood and apple pie principles to prevent you from irritating reviewers and, in addition, keeping yourself in your own good graces:

- Believe in the importance of randomization (don't just give it lip service). That will make you worry about missing data and prevent you from believing that post-randomization subgroups provide causal information.
- Work really hard to write a sensible, rigorous, doable, protocol and SAP. And if you join a study that already has a flawed SAP, do what you can to correct it before unblinding the data.
- List your assumptions clearly. If you are using complicated methodology, make sure that you understand the assumptions implicit in the model. If you are using AI, be especially careful that you check it is not following the rules too literally.
- Don't hide the warts in your study or your analyses. A reviewer will find them – far better for you to expose them and then, if they do not worry you, explain why you find the data convincing if, in fact, you do.
- And the hardest principle of all: resist getting seduced by your prior convictions. Be honest to yourself and others about your findings. Remember Tom's advice to Huck, "a body ain't got no business doing wrong when he ain't ignorant and knows better."

Comments: This paper is based on a talk I gave as part of a Master Class in Statistics at the 2023 meeting of the CardioVascular Clinical Trials (CVCT) meeting. My thanks to Faiez Zannad, MD, and Stuart Pocock, PhD, for inviting me to participate in the class and to Vijay Kumar, MD, of the FDA for encouraging me to write it up.

References

[1] Groothuis JR, Simoes EA, Levin MJ, Hall CB, Long CE, Rodriguez WJ, Arrobio J, Meissner HC, Fulton DR, Welliver RC, et al. Prophylactic administration of respiratory syncytial virus immune globulin to high-risk infants and young children. The Respiratory Syncytial Virus Immune Globulin Study Group. N Engl J Med. 1993 Nov 18;329(21):1524-30. doi: 10.1056/NEJM199311183292102. PMID: 8413475.

[2] Ellenberg SS, Epstein JS, Fratantoni JC, Scott D, Zoon KC. A trial of RSV immune globulin in infants and young children: the FDA's view. N Engl J Med. 1994 Jul 21;331(3):203-5. doi: 10.1056/NEJM199407213310315. PMID: 8054049.

[3] Simoes EA, Sondheimer HM, Top FH Jr, Meissner HC, Welliver RC, Kramer AA, Groothuis JR. Respiratory syncytial virus immune globulin for prophylaxis against respiratory syncytial virus disease in infants and children with congenital heart disease. The Cardiac Study Group. J Pediatr. 1998 Oct;133(4):492-9. doi: 10.1016/s0022-3476(98)70056-3. PMID: 9787686.

[4] Tariot PN, Cummings JL, Soto-Martin ME, Ballard C, Erten-Lyons D, Sultzer DL, Devanand DP, Weintraub D, McEvoy B, Youakim JM, Stankovic S, Foff EP. Trial of Pimavanserin in Dementia-Related Psychosis. N Engl J Med. 2021 Jul 22;385(4):309-319. doi: 10.1056/NEJMoa2034634. PMID: 34289275.

[5] The information had been on the FDA's website in the past but on 11-April-2025 the documents from the advisory committee were no longer available (or, to be more accurate, I couldn't find them). So the data I am presenting come from my records – I would have checked their accuracy had I found the data on the website.

EXPLORING THE ROLE OF COVARIATE ADJUSTMENT IN MODERN CLINICAL TRIALS: INSIGHTS AND IMPLICATIONS – **DISCUSSION WITH DR. TING YE**

Erik Bloomquist (Merck), Maria Kudela (Pfizer)

Highlights

- Discover how Dr. Ting Ye's innovative research in covariate adjustment is transforming the efficiency and precision of randomized clinical trials.
- Learn about the RobinCar R package, a comprehensive toolkit developed by Dr. Ye's team, which is widely used in ongoing registrational trials.
- Explore Dr. Ye's journey and the impactful contributions her work has made to regulatory thinking and modern clinical trials

Ting Ye
University of Washington

Ting Ye is an Assistant Professor in Biostatistics at the University of Washington. Her research aims to accelerate human health advances through data-driven discovery, development, and delivery of clinical, medical, and scientific breakthroughs, spanning the design and analysis of complex innovative clinical trials, causal inference in biomedical big data, and quantitative medical research. Ting is a recipient of the School of Public Health's Genentech Endowed Professorship and the NIH Maximizing Investigators' Research Award (MIRA). She is a leader in covariate adjustment for randomized clinical trials and has published over ten papers, including four in top-tier journals such as JASA, JRSSB, and Biometrika. Prior to joining UW, Dr. Ye completed a PhD in Statistics at the University of Wisconsin-Madison in 2019 and a postdoctoral fellowship in Statistics at the University of Pennsylvania in 2021.

We recently spoke with Dr. Ye about advancements in covariate adjustment analysis and her journey in that field.

Everyone remembers covariates as part of that basic regression course we all took in school. Yet when we joined pharma and industry, no one ever used covariates for clinical trials. "Randomization will take care of it" our bosses would say. Now, with the FDA guidance coming out, your advances, and the start of the covariate working group, it seems we were wrong. What's going on here?

Reply: That's a great question! It is true that randomization would balance everything out and unadjusted analysis (like difference in outcome means) can correctly estimate the unconditional treatment effect.

In traditional regression courses, we're taught that a coefficient's interpretation is conditional on the other variables in the model and relies on correct model specification. This has understandably led to some hesitation around regression-based approaches, as the results can be sensitive to the choice of covariates and the correctness of the model.

However, advances in causal inference and the establishment of the estimand framework in ICH E9(R1) have begun to clearly disentangle the concept of the estimand from the choice of statistical analysis methods. In clinical trials, thanks to randomization,

many researchers have proposed robust, model-assisted approaches to improve efficiency. These developments address the two concerns associated with classic regression. Specifically, one can now define the estimand based on the clinical question of interest first, then apply pre-specified covariate adjustment methods that target that same estimand under the same assumptions used in unadjusted analyses. Methods along this line are transparent, robust, and have real, practical value in improving power and precision.

How did you get involved in this area? Was it related to the FDA guidance coming out?

Reply: In grad school, I really liked the 2010 Biometrika paper by Prof. Jun Shao on covariate-adaptive randomization, so I started working on theory for survival analysis under covariate-adaptive randomization (e.g., stratified permuted block) as part of my dissertation in 2018. That work culminated in a paper (Ye and Shao, 2020; JRSSB) where we examined the behavior of common tests under covariate-adaptive randomization. We found that the log-rank test and Lin and Wei's score test tended to be conservative under these designs. To address this, we proposed adjustments to correct the conservativeness. But what really surprised us was an elegant twist: the stratified log-rank test, contrary to what one might expect, turned out to be valid—not conservative—under covariate-adaptive randomization. This insight was exciting, as it suggested a way to handle the complexities of Pocock and Simon's minimization without directly confronting its intricate theoretical properties. Instead, we could leverage statistics whose asymptotic behavior remains invariant to the randomization schemes.

Building on this idea, we extended our analysis to non-censored outcomes and demonstrated that the post-stratification estimator remains valid under covariate-adaptive randomization. While post-stratification is a form of covariate adjustment, it isn't fully general. As we dug deeper, I became intrigued by the broader field of covariate adjustment, inspired in particular by the influential 2008 papers by Freedman and Lin. Motivated by their ideas, we explored model-assisted estimation, where models are used to improve efficiency, but validity holds even if the models are misspecified. This led to our second paper (Ye et al., 2022; *Biometrika*), which we developed at full speed during December 2019 and quickly submitted.

After completing that project, a new idea took shape. We realized that post-stratification estimators could be viewed as special cases within a broader class of linearly-adjusted estimators. What began as an attempt at a brief follow-up evolved into a much deeper study. We ended up characterizing a complete class of linearly-adjusted estimators, deriving their joint asymptotic distribution for multiple treatment arms, and identifying the most efficient estimator of this class—the ANHECOVA estimator (Analysis of Heterogeneous Covariance). We also uncovered the interplay between covariate adjustment at the design and analysis stages. This project was a turning point for me. I learned so much while writing this paper with Qingyuan Zhao, whose deep insights and style in writing truly elevated the work. We posted the preprint on arXiv in September 2020, and it was later published in JASA in 2023. Alongside it, we released the RobinCar package on GitHub to make these tools accessible to practitioners.

In May 2021, the FDA released its draft guidance on covariate adjustment. We submitted a public comment (*https://www.regulations.gov/comment/FDA-2019-D-0934-0034*), and two years later, the final guidance cited two of our papers. It was a meaningful moment—seeing our statistical contributions influence regulatory thinking.

Despite the progress we had made in linear adjustment, we weren't satisfied. Nonlinear methods like G-computation and covariate adjustment for time-to-event data lacked some of the desirable properties we had come to appreciate—guaranteed efficiency gains, robustness, and universal applicability. Realizing that ANHECOVA could serve as a unifying core, we extended its use to calibrate predictions from nonlinear models (Bannick et al., 2025; *Biometrika*) and to develop covariate adjustment methods for survival outcomes (Ye et al., 2024; *Biometrika*). Together, this body of work provides a comprehensive toolkit for improving precision in treatment effect testing and estimation.

For those new to covariate adjustment, is it the same thing we learned in graduate school? For example for continuous endpoints, can I just use the R command (lm~x1+x2+x3) command in R? Or is it more advanced?

Reply: Covariate adjustment is generally not the same as simply obtaining coefficient estimates from a fitted regression model. For continuous or discrete outcomes, covariate adjustment typically involves two steps: first, fitting a linear or nonlinear regression model; and second, using the fitted model to construct an estimator of the treatment effect (such as the g-computation estimator described in the FDA's final guidance).

For example, when using an ANCOVA model of the form lm(Y ~ A + X), where A is the treatment indicator and X represents covariates, the covariate-adjusted estimator coincides with the coefficient on A. However, when fitting an ANHECOVA model with treatment-by-covariate interactions, such as lm(Y ~ A + X + A:X), the covariate-adjusted estimator is no longer simply one of the coefficient estimates. (A fun fact: it can be retrieved as a coefficient if the covariates X are centered.)

That said, even in these models, variance estimates for the covariate-adjusted treatment effect cannot be directly obtained from standard linear model output in R.

What types of packages in R and SAS are available for this adjustment? Do I need to start from scratch or can I rely on existing software?

Reply: To make these methods widely accessible, our group initiated the development of RobinCar, an open-source R package that consolidates tools for linear and nonlinear covariate adjustment, as well as methods for time-to-event outcomes (available on CRAN and GitHub, >400 downloads/month on CRAN). The R package is rigorously validated to comply with good clinical and software practices, actively maintained based on user feedback, and includes comprehensive documentation and vignettes. As far as I know, RobinCar has been used in numerous ongoing registrational trials.

More recently, the ASA biopharmaceutical section (ASA-BIOP) covariate adjustment scientific working group is developing a lite version of RobinCar, called RobinCar2. Together, these form the RobinCar family: RobinCar is designed to be the most comprehensive, keeping pace with the latest methods in the literature and tested actively by users, while RobinCar2 will include a curated subset of well-validated methods.

I work in the area of oncology and hematology, where survival analysis is still the primary methodology, e.g. log-rank tests and coxph? Is there anything different here?

Reply: You're absolutely right—covariate adjustment in survival analysis is different from that in standard settings. The first step is to clearly define the estimand of interest: for example, the unconditional survival functions for each treatment arm, the unconditional hazard ratio, or the stratified hazard ratio. Once the estimand is identified, covariate adjustment can be applied to improve efficiency—reducing variability without changing the estimand or requiring additional assumptions.

To give a concrete example: the log-rank test is commonly used to compare unconditional hazard functions between two arms. Covariate adjustment methods proposed by Lu and Tsiatis (2008, Biometrika) and Ye et al. (2024, Biometrika) work by linearizing the score equation (i.e., the numerator of the log-rank test statistic) to generate "derived outcomes," to which ANHECOVA adjustment is then applied. As another example, if the estimand of interest is the unconditional hazard ratio defined by a Cox model with only a treatment indicator, the unadjusted estimator solves the corresponding score equation. In this case, one can linearize the score equation, apply ANHECOVA adjustment to the resulting estimating equations, and solve the adjusted score equation to obtain the covariate-adjusted estimator of the unconditional hazard ratio. Similar approaches can be extended to stratified log-rank tests and stratified Cox models, as shown in Ye et al. (2024, Biometrika). A key feature of these methods is their ability to disentangle the estimand from the analysis method. These methods are also implemented in the RobinCar R package.

If I bring this up to my team, and they ask "what are the advantages of adjustment?" what should I say? For example, can I say we'll see a 15% reduction in sample size? Quicker milestones?

Reply: Adjusting for pre-specified baseline covariates that are prognostic of the outcome is generally a robust approach and often leads to efficiency gains. The extent of the gain depends on how strongly the covariates are associated with the outcome. If historical data on outcomes and covariates are available, one can estimate the potential relative efficiency gain or sample size reduction—and even construct confidence intervals for these estimates (Li et al. 2023; JRSSB).

Ultimately, it is up to the sponsor to decide whether to base the sample size calculation on the unadjusted analysis and treat covariate adjustment as a source of additional efficiency, or to base it on the adjusted analysis, or take an approach somewhere in between.

Even if the sample size is calculated based on the unadjusted analysis, covariate adjustment can still lead to higher power for detecting a treatment effect. In trials with planned interim analyses, this gain in power can translate into a higher probability of rejecting the null hypothesis early, potentially leading to faster conclusions about efficacy.

Ok let's say I want to incorporate this into my protocol, what things should I consider when choosing these covariates? Any downsides or risks to doing this?

Reply: Covariates used for adjustment should be measured at baseline and pre-specified. Ideally, a small number of covariates that are most prognostic of the outcome should be selected, along with any stratification factors used in stratified or covariate-adaptive randomization, especially if they are believed to be related to the outcome. The selection of covariates can be informed by prior knowledge of the disease or condition, or by analysis of historical data.

With a small number of carefully-chosen covariates and if one uses methods that have guaranteed efficiency gain over unadjusted estimator (e.g., the ANHECOVA estimator), the risk is minimal.

However, if a large number of covariates are considered and it's not possible to narrow down the list, including too many covariates may lead to type I error inflation or a loss of power. In such cases, data-adaptive variable selection methods can be applied when fitting the regression models. To maintain valid inference, cross-fitting should be used to ensure consistency of the estimator (Bannick et al., 2025; Biometrika). How to best use data-adaptive procedures in covariate adjustment is still an active research topic; see Van Lancker (2024) for a recent preprint on this topic.

Any additional resources or written material available for those who want to learn more?

Reply: Our ASA-BIOP covariate adjustment scientific working group has posted very nice blogs and tutorials, which are available at: https://carswg.github.io/blog.html. There are also great review papers on the topic, e.g. Van Lancker et al. (2024).

Where do you see this area moving in the next 5 years? Will covariate adjustment become the standard for clinical trials?

Reply: I believe there is still a need for further research on covariate adjustment in more complex settings, such as interim analyses, data-adaptive variable selection, and more complex trial designs. It would also be valuable to see more papers that address the practical implementation of covariate adjustment, including empirical evaluations using realistic simulations or real-world data.

As covariate adjustment continues to gain traction, I expect it will become the standard approach in clinical trials.

As we conclude our discussion, it's evident that Dr. Ye's innovative contributions have significantly impacted the field of randomized clinical trials. Her work on covariate adjustment and the development of the RobinCar R package are not only advancing the efficiency and precision of trials but also shaping the future of clinical research. Dr. Ye's dedication and pioneering spirit continue to inspire progress, promising a more robust and reliable landscape for clinical trials. Thank you for sharing your invaluable insights and experiences with us.

References:

Shao, J., Yu, X. & Zhong, B., (2010). A theory for testing hypotheses under covariate-adaptive randomization. *Biometrika*, 97(2), pp.347-360.

Ye, T., & Shao, J. (2020). Robust Tests for Treatment Effect in Survival Analysis under Covariate-Adaptive-Randomization. *Journal of the Royal Statistical Society:* Series B, 82(5):1301-1323.

Lin, W. (2013). Agnostic notes on regression adjustments to experimental data: Reexamining Freedman's critique. *Ann. Appl. Stat.* 7(1): 295-318.

Freedman, D. A. (2008). On regression adjustments to experimental data. *Adv. in Appl. Math.* 40 180–193.

Freedman, D. A. (2008). On regression adjustments in experiments with several treatments. *Ann. Appl. Stat.* 2 176–196

Ye, T., Yi, Y., & Shao, J. (2022). Inference on Average Treatment Effect under Minimization and Other Covariate-Adaptive Randomization Methods. *Biometrika,* 109(1):33–47.

Ye, T., Shao, J., Yi, Y., & Zhao, Q. (2023). Toward better practice of covariate adjustment in analyzing randomized clinical trials. *Journal of the American Statistical Association,* 118(544):2370–2382.

Bannick, M. S., Shao, J., Liu, J., Du, Y., Yi, Y., & Ye, T. (2025). A General Form of Covariate Adjustment in Randomized Clinical Trials. *Biometrika* (accepted).

Lu, X. and Tsiatis, A.A., (2008). Improving the efficiency of the log-rank test using auxiliary covariates. *Biometrika*, 95(3), pp.679-694.

Ye, T., Shao, J., & Yi, Y. (2024). Covariate-Adjusted Log-Rank Test: Guaranteed Efficiency Gain and Universal Applicability. *Biometrika*, 111(2):691-705.

Li, X., Li, S. and Luedtke, A., (2023). Estimating the efficiency gain of covariate-adjusted analyses in future clinical trials using external data. *Journal of the Royal Statistical Society* Series B: Statistical Methodology, 85(2), pp.356-377.

Van Lancker, K., Díaz, I. and Vansteelandt, S., (2024). Automated, efficient and model-free inference for randomized clinical trials via data-driven covariate adjustment. arXiv preprint arXiv:2404.11150.

Van Lancker, K., Bretz, F. and Dukes, O., (2024). Covariate adjustment in randomized controlled trials: General concepts and practical considerations. Clinical Trials, 21(4), pp.399-411

GENERATIVE ARTIFICIAL INTELLIGENCE AS MODERN-DAY ELECTRICITY – ONE STEP AT A TIME

Hong Tian and Tony Guo, BeOne Medicines USA, Inc. (formerly BeiGene USA, Inc.)

Highlights

- Discover how AI tools like Open AI GPT are reshaping the role of statisticians in pharma and biotech - boosting efficiency, accelerating learning, and sparking innovation.
- See real-world examples of AI assistants designed as medical and regulatory experts, providing domain-specific support.
- Explore how prompt engineering and generative AI can accelerate knowledge acquisition, enhance productivity, and uncover deeper insights

Hong Tian
VP, Head of Global Statistics

Tony Guo
SVP, Head of Global Statistics and Data Science

In pharma and biotech, statisticians play a pivotal role in shaping data generation strategies to answer scientific questions around safety, efficacy, and quality. Their work spans study design, data collection, analysis, and interpretation—requiring both strategic vision and operational excellence.

Today, AI tools such as Open AI GPT can assist with nearly every aspect of that work. With minimal effort, statisticians can create custom AI assistants to enhance efficiency, accelerate learning, and spark new ideas. We aim to share practical examples and inspire broader applications.

"*The best thing about being a statistician is that you get to play in everyone's backyard*." — John Tukey

To make a meaningful impact, statisticians must understand the evolving context of their work: disease biology, treatment algorithms, risk stratification, competitive landscapes and regulatory policy. These "backyards" are data-rich—and constantly changing.

Chat GPTs can dramatically speed up knowledge acquisition and elevate both productivity and creativity. For statisticians already fluent in programming, learning prompt engineering is a natural and rewarding next step. White et al. (2023) outlines many helpful prompt patterns.

It takes surprisingly little effort to bring expert-level AI support to your fingertips. In this article, we share a few simple use cases—hoping to inspire many more.

The first two examples demonstrate how Chat GPTs can be configured to act as a medical assistant and a regulatory assistant, delivering domain-specific, reliable support. The following three examples highlight how to enhance efficiency and quality through conversational prompting—drawing clear parallels to R programming constructs to make prompt engineering more intuitive for statisticians.

Example 1: Medical Expert Specialized in Lymphoma

 # Persona

You are a digital medical expert specializing in lymphoma. You integrate current clinical practice, trial data, and regulatory guidelines to produce the most reliable and explainable answers.

 # Output Expectations

- Respond concisely and clearly.
- Justify conclusions using trial data or official guidance.
- Include links to references for every key claim (e.g., PubMed, FDA, NCCN, ASCO).
- State when no definitive evidence exists.

 # Upload files

Include latest disease and treatment guidelines.

Example 2: Global regulatory strategist

 # Persona

You are a global regulatory strategist with deep expertise in oncology drug and device development. You are highly knowledgeable about regulations, processes, and precedents across major health authorities: FDA (U.S.), EMA (Europe), PMDA (Japan), and Health Canada. You synthesize current guidance documents, historical approvals, and jurisdiction-specific practices to deliver reliable, evidence-based regulatory insights.

 # Output Expectations

- Provide **clear**, **concise**, and **well-reasoned** responses.
- Ground all conclusions in **official regulatory guidance**, **publicly available review documents**, or **historical approval records**.
- **Cite and link to primary sources**, prioritizing the following approval databases:

  - **PMDA (Japan)**
    - [Approved Drugs (English)] (*https://www.pmda.go.jp/english/review-services/reviews/approved-information/drugs/0001.html*)
    - [Japanese Drug Search (in Japanese)] (*https://www.pmda.go.jp/PmdaSearch/iyakuSearch/*)
  - **Health Canada**
    - [Clinical Information Portal] (*https://clinical-information.canada.ca/search/ci-rc*)
  - **FDA (U.S.)**
    - [Drugs@FDA Database] (*https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm*)
  - **EMA (Europe)**
    - [EMA Medicines Search] (*https://www.ema.europa.eu/en/search?f%5B0%5D=ema_medicine_bundle%3Aema_medicine&f%5B1%5D=ema_search_categories%3A83*)

- Use **regulatory terms and timelines correctly**, and specify **jurisdictional differences** when applicable (e.g., Fast Track vs. PRIME vs. Sakigake).
- If no definitive guidance exists, **state this clearly**, and offer relevant analogs or case precedents.

Generative AI has made learning and knowledge acquisition remarkably more accessible. With genuine curiosity and a basic grasp of prompt engineering, anyone can unlock its potential.

Yet, hallucination remains a persistent challenge. It quickly becomes clear that links may be inaccurate, and responses—though confident—can shift under scrutiny. In this era, human expertise and critical thinking are more essential than ever.

GPT models offer useful coding support—and better yet, we can use a conversational style to carry out tasks that mimic programming logic.

Example 3: Repetitive Task — Iterating Through Multiple Drug Approvals

```
for (i in 1:n) {
  # repeat task for each element
}
```

I will provide links to three FDA drug approvals. For each, please summarize the following in a table: medication name, indication, study objectives, primary and key secondary endpoints, and main efficacy results.

Links:1…, 2… and 3…

Example 4: Conditional Logic — Tailoring Search Based on Region

```
if (condition) {
  # code if condition is TRUE
} else {
  # code if condition is FALSE
}
```

Example: If I ask about drug approval in Japan, please first search:

site: *https://www.pmda.go.jp/PmdaSearch/iyakuSearch/*

If I ask about drug approval in countries other than Japan (e.g., U.S.), please first search:

site: *https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm*

Example 5: Conditional Loop — Repeating a Behavior Based on Ongoing Instruction

```
while (condition) {
  # code to run
}
```

Example:

From now on, please whenever I ask you a question. Please write me alternative prompts to address my question.

We encourage statisticians to explore generative AI tools—not just as users, but as builders. Using your own GPT assistant can accelerate domain understanding and unlock deeper insights, ultimately contributing to more efficient drug development.

The barrier to entry is lower than many assume. With just curiosity and a willingness to experiment, statisticians can begin integrating AI into their daily work.

By sharing our early experiences, we hope to spark more use cases, foster collaboration, and inspire others to share their journeys. In a rapidly evolving landscape, the ability to adapt and embrace new technologies is as vital as technical skill. When combined thoughtfully, human expertise and artificial intelligence can propel us further than alone.

Reference:

White, Jules, et al. "A prompt pattern catalog to enhance prompt engineering with chatgpt." arXiv preprint arXiv:2302.11382 (2023).

A PERSPECTIVE ON THE EVOLVING ROLE OF STATISTICIANS IN THE PHARMACEUTICAL INDUSTRY: **LEVERAGING ADVANCED STATISTICAL ANALYTICS AND ARTIFICIAL INTELLIGENCE**

Vijay Yadav (Merck)

Highlights

- The pharmaceutical industry is experiencing a rapid shift driven by generative AI (GenAI) and advanced analytics, transforming statisticians from data analysts to strategic partners in the areas of their business functional support.
- GenAI-powered knowledge management systems enable statisticians to search and leverage institutional knowledge stored in unstructured formats, reducing report preparation time while improving consistency and regulatory compliance.
- Advanced statistical approaches enhanced by AI allow for more efficient integration of real-world evidence, predictive modeling, and continuous learning systems sourcing data from all formats unstructured (e.g. .pdfs), semi-structured (e.g. excels), and structured (databases)
- As statisticians evolve into strategic partners, they must balance technical expertise with business acumen while maintaining methodological rigor and addressing ethical considerations in AI implementation.

Vijay Yadav
(Merck) Director, Data Science - Advanced Analytics (AI/ML)

Abstract

The pharmaceutical industry is witnessing a fundamental transformation as generative artificial intelligence (GenAI) and advanced analytics reshape traditional roles. This article examines how statisticians are evolving from data analysts into strategic partners who build AI-driven innovation that delivers business value at scale and speed. By automating routine workflows, GenAI frees up valuable time to focus on high-impact activities like faster drug discovery and development, efficient manufacturing operations and regulatory affairs support. The integration of GenAI-driven knowledge bases allows statisticians to efficiently search institutional knowledge stored in unstructured formats, significantly improving workflow efficiency. Through case studies and industry examples, we explore how this shift is creating productivity gains, and modernizing industry practices. As pharmaceutical development continues to evolve, statisticians who successfully blend statistical rigor with AI literacy will drive innovation and ultimately improve patient outcomes through faster, more efficient processes in the pharma value chain.

Introduction

The pharmaceutical industry is undergoing a paradigm shift driven by generative artificial intelligence (GenAI) and advanced analytics. Statisticians, traditionally tasked with manual data processing can now transition into strategic roles as architects of AI-driven solutions. By automating routine workflows, GenAI enables statisticians to focus on high-impact tasks such as drug discovery, development, trial design, complex data interpretation, and regulatory strategy development.

This transformation represents more than just a change in daily activities—it's a fundamental reimagining of how

statisticians contribute to drug development. As the industry embraces digital transformation, statisticians are increasingly becoming the bridge between complex data science and critical business decisions that impact patient care.

The catalyst for this change has been the rapid advancement of AI technologies that can automate routine tasks while enhancing statisticians' ability to extract meaningful insights from increasingly complex datasets. Where statisticians once spent weeks manually processing clinical trial data, AI-powered systems now complete these tasks in hours, allowing focus on strategic questions about trial design, endpoint selection, and regulatory strategy.

The Transformation of Statistical Roles: From Data Analysis to Strategic Partnership

Historically, pharmaceutical statisticians have spent a significant amount of time on data cleansing, validation, and routine analyses. Today, AI-powered tools are beginning to automate these processes, allowing statisticians to evolve into strategic partners who drive critical decision-making.

The FDA's discussion paper "Using Artificial Intelligence and Machine Learning in the Development of Drug and Biological Products" (2023) acknowledges this transformation, noting the exponential growth in AI/ML-related regulatory submissions from 1 in 2016 to 132 in 2021 (Liu et al., 2023).

Modern Contributions of Pharmaceutical Statisticians

Modern pharmaceutical statisticians can now focus on high-impact areas such as:

Research & Development

- Optimizing experimental designs for biomarker discovery using adaptive algorithms
- Developing predictive models to accelerate candidate molecule selection
- Analyzing high-dimensional genomic data to identify therapeutic targets

Clinical Development

- Designing innovative trial designs using simulation and predictive modeling
- Implementing Bayesian approaches for dose-finding and adaptive trials
- Developing analytical methods for complex endpoints and biomarkers

Regulatory Affairs

- Creating statistical analysis plans that satisfy evolving regulatory requirements
- Collaborating with agencies on novel methodologies for accelerated approvals
- Developing statistical approaches for real-world evidence submissions

Commercial & Market Access

- Modeling pricing strategies based on comparative effectiveness data
- Analyzing patient subgroups to identify high-value market segments
- Developing predictive models for treatment adoption and market penetration

Technology Transfer

- Ensuring statistical consistency between clinical and commercial manufacturing
- Developing statistical process control methods for technology scale-up
- Creating risk-based statistical approaches for comparability assessments

Manufacturing

- Implementing advanced process control algorithms for quality optimization
- Developing multivariate statistical methods for continuous manufacturing
- Creating predictive maintenance models to prevent production disruptions

Supply Chain

- Optimizing inventory levels through demand forecasting models
- Developing risk models for supply chain resilience and disruption mitigation
- Creating statistical approaches for shelf-life determination and stability testing

Augmenting Statistical Expertise with AI

Modern statisticians are increasingly leveraging machine learning to enhance traditional statistical methods. This hybrid approach combines the rigor of classical statistics with the pattern-recognition capabilities of AI, creating new methodologies for analyzing complex data.

As Hunter and Holmes (2023) note in the New England Journal of Medicine, "AI algorithms largely remove the need for analysts to prespecify features for prediction or manually curate transformations of variables. These attributes are particularly beneficial in large, complex data domains such as image analysis, genomics, or modeling of electronic health records."

The integration of AI into statistical workflows has enabled more sophisticated approaches to:

- Subgroup identification and personalized medicine
- Signal detection in safety monitoring
- Biomarker discovery and validation
- Synthetic control arm development

Knowledge Management Revolution

Unlocking Institutional Knowledge

One of the transformative applications of generative AI for pharmaceutical statisticians is the ability to query vast repositories of unstructured data. Traditional knowledge management systems struggled with the complexity of statistical reports, protocols, and regulatory submissions stored as PDFs or in disparate databases.

Modern GenAI systems can index, contextualize, and retrieve relevant information from these documents, creating a searchable institutional memory. This capability is particularly valuable in an industry where staff turnover can result in significant knowledge loss.

When a statistician begins work on a new analysis, GenAI-powered knowledge bases can:

- Identify methodologically similar reports from past studies
- Surface relevant regulatory precedents and feedback
- Highlight common analytical challenges and solutions
- Provide templates and code snippets for efficient implementation

Advanced Analytics Application

Real-World Evidence Integration

The FDA's increasing acceptance of real-world evidence (RWE) has created new opportunities for statisticians to influence drug development and post-approval monitoring. GenAI tools now enable statisticians to integrate clinical trial data with electronic health records, claims databases, and patient-reported outcomes.

This integration requires sophisticated statistical approaches to address data heterogeneity, missing information, and potential biases. Statisticians equipped with AI tools can develop robust methodologies that satisfy regulatory requirements while extracting meaningful insights from diverse data sources.

Example use cases include:

- Synthetic control arm development for rare disease trials
- Post-marketing safety surveillance and signal detection
- Label expansion through real-world comparative effectiveness studies
- Understanding treatment patterns and adherence in clinical practice

Predictive Modeling for Trial Optimization

AI-enhanced predictive modeling allows statisticians to simulate trial outcomes under various design parameters. These models incorporate historical trial data, disease progression patterns, and patient characteristics to optimize sample sizes, endpoint selection, and inclusion criteria.

Challenges and Ethical Considerations

Maintaining Statistical Rigor

As AI tools become more integrated into statistical workflows, maintaining methodological rigor remains paramount. The "black box" nature of some machine learning approaches presents challenges for regulatory acceptance and scientific validity.

Forward-thinking statisticians are developing frameworks for validating AI-derived insights, ensuring transparency in methodologies, and establishing appropriate boundaries for automation. These frameworks emphasize that AI should augment rather than replace statistical expertise, particularly for critical decisions affecting patient safety.

Key considerations include:

- Validation of AI-derived insights against traditional methods
- Documentation of model development and validation processes
- Transparency in reporting limitations and uncertainties
- Appropriate use of AI tools within regulatory frameworks

Data Privacy and Ethical AI Use

The integration of diverse data sources raises important privacy considerations. Statisticians must navigate complex regulatory requirements like GDPR and HIPAA while leveraging the full potential of available data.

Ethical considerations extend beyond privacy to questions of bias, fairness, and representation in AI-enhanced analyses. Statisticians are uniquely positioned to identify and mitigate these issues through careful study design and analytical approaches that account for demographic and socioeconomic factors.

Responsible AI implementation requires:

- Rigorous data governance and privacy protection
- Evaluation of potential algorithmic bias
- Ensuring diverse representation in training data
- Transparent reporting of limitations and uncertainties

Future Directions

Continuous Learning Systems

The future of pharmaceutical statistics lies in continuous learning systems that adapt to emerging data. Rather than the traditional model of discrete analyses at predetermined timepoints, these systems continuously incorporate new information to refine predictions and recommendations. One potential technology innovation is Agentic AI where different agents can work together to make predictions and recommendations.

This approach is particularly valuable for long-term safety monitoring, where rare adverse events may only become apparent after extensive real-world use. AI-enhanced statistical methods can detect subtle safety signals earlier than traditional approaches, potentially improving patient outcomes.

Emerging applications include:

- Adaptive safety monitoring across the product lifecycle
- Continuous benefit-risk assessment incorporating real-world data
- Dynamic dosing recommendations based on patient characteristics
- Automated signal detection and validation

Cross-Functional Integration

As statisticians evolve into strategic partners, their collaboration with other functions is intensifying. Modern statistical leaders work closely with data science, clinical operations, regulatory affairs, and commercial teams to ensure that analytical insights drive decision-making throughout the product lifecycle.

This integration requires statisticians to develop communication skills that translate complex analytical concepts into actionable insights for non-technical stakeholders. The most successful statistical leaders combine technical expertise with business acumen and strategic vision.

Key areas of cross-functional collaboration include:

- Translating clinical insights into commercial strategy
- Partnering with regulatory affairs on innovative approaches
- Working with data science on advanced analytics implementation
- Collaborating with medical affairs on evidence generation

Summary

The transformation of statistical roles in the pharmaceutical industry represents both an opportunity and a challenge. By embracing AI-enhanced tools and methodologies, statisticians can dramatically increase their impact on drug development while focusing their expertise on the most complex and consequential questions.

The knowledge management revolution enabled by GenAI creates unprecedented opportunities to leverage institutional experience and avoid repeating past mistakes. As the industry continues to evolve, statisticians who combine traditional statistical rigor with AI literacy will be uniquely positioned to drive innovation and improve patient outcomes.

The future statistician is not merely an analyst but a strategic partner who harnesses the power of advanced analytics to accelerate drug development, enhance decision-making, and ultimately bring life-changing therapies to patients more efficiently than ever before.

References

1. Liu Q, Huang R, Hsieh J, et al. Landscape Analysis of the Application of Artificial Intelligence and Machine Learning in Regulatory Submissions for Drug Development From 2016 to 2021. *https://pubmed.ncbi.nlm.nih.gov/35707940/*

2. FDA. Using Artificial Intelligence and Machine Learning in the Development of Drug and Biological Products. Discussion Paper. 2023. *https://www.fda.gov/media/167973/download*

3. FDA. Artificial Intelligence/Machine Learning (AI/ML)-Based Software as a Medical Device (SaMD) Action Plan. 2021. *https://www.fda.gov/media/145022/download*

4. Hunter DJ, Holmes C. Where medical statistics meets artificial intelligence. N Engl J Med. 2023 *https://pubmed.ncbi.nlm.nih.gov/37754286/*

5. Heads of Medicines Agencies and European Medicines Agency. Guiding principles on the use of large language models in regulatory science and for medicines regulatory activities. September 5, 2024. *https://www.ema.europa.eu/en/documents/other/guiding-principles-use-large-language-models-regulatory-science-medicines-regulatory-activities_en.pdf*

A perspective on the evolving role of statisticians in the pharmaceutical industry: leveraging advanced statistical analytics and artificial intelligence

ML/AI INNOVATION IN REGULATORY: INTERVIEW WITH ANDREA MANFRIN

Di Zhang (Teva), Maria Kudela (Pfizer)

Andrea has over 30 years of international experience as an academic, consultant, and entrepreneur in the healthcare sector. He joined the Medicines and Healthcare products Regulatory Agency (MHRA) in June 2023 as Deputy Director of Clinical Investigations and Trials. His ambition is to facilitate regulatory change, making the UK one of the best places for sponsors and patients to conduct clinical research. Before working at the MHRA, Andrea was at the University of Central Lancashire (UCLan, UK) as the Faculty Director of Research and Innovation in the Faculty of Clinical and Biomedical Sciences and Chair Professor of Pharmacy Practice, where he led the conceptualization and development of clinical trials in medicine, dentistry, pharmacy, and health services research. He continues to hold a visiting professor position at UCLan.

Andrea Manfrin
Deputy Director of Clinical Investigations and Trials at MHRA

We were grateful to have the opportunity to sit down and talk about the exciting developments at MHRA with Andrea.

1. What are some of the AI/ML related initiatives in MHRA?

We are now planning to test and deploy AI/LLM in three different areas: 1) support assessors during the clinical trial review, 2) support training of new assessors, 3) support sponsors by providing AI-driven assistance for common regulatory queries via the MHRA Web system.

We manage a significant volume of clinical investigation and trial applications. Last year alone, we processed more than 5300 applications, including 83 initial clinical investigations and 290 amendments, and 761 initial clinical trials, and over 4200 amendments to existing applications. These documents are often extensive and detailed, requiring a considerable amount of time for our assessors to review and extract critical information. To address this challenge, we focused on clinical trials and spent the summer of 2024 exploring various digital tools to enhance our efficiency. We tested several off-the-shelf AI tools but found none that met our specific needs. Consequently, we partnered with a company through our digital and technology team to develop a custom AI tool from scratch. This tool was designed to help assessors quickly locate necessary information, significantly reducing the time spent on this task from hours to just 34.5 seconds. This frees up assessors to focus on more complex and knowledge-intensive activities, such as evaluating the safety and benefit-risk profiles of the trials.

We also developed a training tool to help new assessors onboard more efficiently to not only help assessors get up to speed but alleviate the pressure on senior staff who were previously responsible for mentoring new employees.

We are also creating a tools for sponsors to pre-check regulatory concerns, which helps to strengthen their submissions.

Our AI tools will continuously improve, using some sources of information held in our data bank such as a dataset including 110,000 grounds for non-acceptance (GNAs, questions raised to the sponsors) that we use to train the system. This dataset helps the AI identify potential issues and improve its accuracy over time. The evidence from the literature shows that AI and natural language processing, save up to 70% of the time required to find information. By adopting this approach, our assessors should have more time to engage in more valuable activities, such as providing scientific advice to sponsors.

On April 22nd, following two successful proof of concept studied conducted between October 2024 and March 2025, we deployed the first two AI/LLM tools: 1) General Manufacturing Practice (GMP) compliance checker, 2) The knowledge hub using the searchable data base for past GNAs and assessment reports. Overall, our efforts should lead to significant improvements in efficiency and effectiveness in managing clinical trial applications, benefiting both our team and the sponsors we work with.

It's important to understand that while AI can provide valuable insights, we to ensure that humans, our assessors, are ultimately responsible for making the final decisions. For instance, consider a medical doctor conducting a brain or body scan on a patient. The machine performs the scan and generates the information, but the doctor interprets the data and makes the final decision, determining whether treatment is needed or if the scan is clear. We're using AI to support our assessment activities, not as a replacement. Only the assessors will make the final decision.

2. What unique challenges do you face when implementing AI/ML in a regulatory environment?

I must say we ventured into uncharted territory, as we've never done this before in our division and in my career. It was entirely new for us, and to the best of my knowledge ge we're among the few divisions in the MHRA testing this kind of activity, especially while supporting the assessment of submissions. Given our funding constraints and workload pressures, we knew we needed to find innovative ways to support our work. This led us to explore new avenues.

While I've used machine learning before, for example artificial neural networks, I had never applied it at this level. Fortunately, my colleagues, who are open-minded and passionate about AI, helped us start looking for solutions. The collaboration with the external partner was fundamental. The biggest challenge was realising we needed to create a solution from scratch, as there wasn't an off-the-shelf option available.

Through my colleagues in the digital team, we connected with an external , which has a great multidisciplinary with diverse skills. Statistics and machine learning were the common themes that united us, as we aimed to develop something truly innovative and new in our field. We followed the law of diffusion of innovation, starting with early innovators who think outside the box, and gradually building interest across the agency. Now, many people are involved in this programme, and it has been a great experience.

3. What trends do you see shaping the future of AI/ML in regulatory settings?

Currently, there are numerous AI projects underway across the MHRA, although I'm not familiar with the specifics of each programme. So far, we've focused on controlled pilots to ensure the tools are consistent and reliable. Now, we're branching out - into areas like assessment support, training, , with more branches to come. These "branches" are all part of the same tree: a regulatory system supported by AI.

We see potential in using AI for various purposes, including finding solutions for clinical investigations and improving team efficiency. For instance, one of our teams, the Clinical Investigation and Trials Operation team, is already using basic AI tools like Copilot to manage workload and data analytics handling vast amounts of information and data. They are involved in many areas, such as developing clinical trial guidance

for the new clinical trials regulations supporting point-of-care manufacturing, .

Our AI programme aims to create evidence, develop new regulatory pathways in life sciences, address gaps and challenges, and ensure long-term sustainability – all while co-creating tools and systems with others. The above examples show how we started to use AI , machine learning, and related technologies.

One exciting example is our involvement in the creation of Centre of Excellence for Regulatory Science Innovation (CERSI). Within this, we (Clinical Investigations and Trials at the MHRA) supports the CERSI on in-silico trials, - virtual simulations of how medical products and devices might behave. In-silico trials could help us move faster from preclinical to clinical testing, and address issues like recruitment delays. This CERSI initiative involves 85 organisations, including regulators, universities, and pharmaceutical companies. It's amazing how these entities have come together to develop new approaches for clinical investigations and trials testing.

While I can only speak for my division, I believe AI has significant potential within the regulatory environment. This includes leveraging AI to enhance our activities and supporting sponsors using AI for trials, data collection, and device usage. Another specialized team within our group, focuses on these aspects.

4. How do you foster collaboration and communication among team members from different disciplines?

Within our Clinical Investigations and Trials unit, we have three teams: the Clinical Trials team, the Clinical Investigations team, and the Clinical Investigations and Trials Operation team (CIT OPS). We've created a culture that is very flat, with no hierarchy, allowing everyone to express their ideas and concerns easily. Information flows quickly, which is essential since we are legally required to complete (for example) the initial clinical trial review within 30 days. This short timeframe necessitates agility and rapid information exchange.

We share information through various methods, including face-to-face meetings and data exchanges. For instance, the CIT OPS team developed new tools last year that provide real-time data analysis, which we didn't have before. This advancement allows the heads of different disciplines such as clinical non-clinical and pharmaceutical to view workflows immediately and plan work allocation more efficiently.

Although we are still under pressure, these tools give us a better overview of the situation and help us identify triggers for action more quickly.

Outside of our internal collaborations, we are also involved in the Access Consortium. It's a collaboration of five regulators from Australia, Singapore, Canada, Switzerland and us, representing around 150 million people. The diverse population helps achieve generalizable data. Since summer 2024, we have worked with colleagues across these jurisdictions aiming to safely enhance clinical trial delivery. We aim to start this program in autumn 2025, benefiting both us and patients. The first challenge was the time zone differences, but we've adapted. Working in a consortium requires a lot of open communication and collaboration to achieve our goals and address various country-specific regulations.

5. What advice would you give to someone aspiring to lead interdisciplinary teams in AI and machine learning?

Leading in AI and machine learning doesn't necessarily require a completely different skill set than leading in other areas. Leadership isn't solely about technical knowledge; it's a more holistic approach. I'd like to provide three examples of leadership.

Firstly, anyone leading AI and machine learning programs needs to have an open mind and shouldn't be intimidated by technology. They should work with people who can explain the technology simply, which has been invaluable to me. My colleagues have helped me understand complex concepts in a digestible way.

In terms of leadership overall, even when focusing on AI and machine learning, I believe leadership can be summarised through three individuals. The first is Simon Sinek, a cultural anthropologist and TED speaker, who famously said, "Managers eat first, leaders eat last." To be a good leader, you need to listen more and talk less, paying close attention to your team. You don't have to know everything - and pretending you do won't get you far.

Secondly, I'm inspired by Harvard Business School professor Linda Hill, who suggests moving from a

vision-based leadership to shaping the culture. This modern approach is necessary because achieving complex goals requires collaboration with diverse teams and the key element is co-creation. Hill outlines three functions of leadership called the ABC of leadership:

A, the architect builds the company's culture and capabilities for innovations, leveraging different people's skills and capabilities ("Collective Genius"). For example, we created something that did not exist before, the AI/LLM tools.

B, the bridger, knows that its company lacks all the talent and tools it needs to innovate quickly and efficiently. This is why we wanted to work with an external company that has a great and talented team of people with a completely different skillset to enable us to innovate and create the AI/LLM

C, the catalyst, accelerates the co-creation across the entire eco-system. A good example is the collaboration with the CERSI for in-silico trials, which could improve patient safety, reduce the time and costs for device and drug development and therefore, bring new devices and medications to patients faster. This activity could reshape the entire clinical trials eco-system

Creating something new is often a bumpy ride, requiring multiple iterations, but maintaining momentum and positivity is key to eventually achieving results.

Finally, Steve Jobs famously once said that it's pointless to hire smart people and then tell them what to do. Instead, it's better to hire them so they can tell us what to do. This means listening to a range of views, but ultimately making the decision and taking responsibility for it. A good leader takes responsibility for the outcomes: if the decision is right, the credit goes to the team; if it's wrong, the leader takes the blame. That's what leadership is.

In essence, this captures my view of what makes a good leader. I don't claim to be a perfect leader myself, but these are the qualities I believe are essential.

6. Where do you see the role of statistician within AI/ML related initiatives?

My Ph.D. focused on developing randomised control trials and the applications of advanced statistics. However, the statistics I've encountered in the past year have gone far beyond that. Interestingly, until a few years ago, statistics was often seen as a supporting discipline. Now, data science, machine learning, and AI have become the new currency and vocabulary, with other disciplines supporting AI and machine learning as the new cornerstone.

I believe AI and machine learning should be integrated into everyone's training, because our future work will increasingly involve these tools. That said, we'll always need true experts in AI, as it will become crucial for exchanging information and analytics.

7. You will be publishing one of your articles in the summer issue. Could you tell us more about the upcoming article?

Thank you so much for this opportunity to share our work. The paper has several goals: sharing what we've learned, including our challenges, and to show that we brought together many skillsets, including software engineers, data scientists, assessors, and more. We will also describe our methodology and process, making AI and machine learning work more accessible and applicable to other regulators.

The paper will have a simple structure: an introduction, a straightforward method section, a narrative description with pictures of our journey, and a discussion of our experiences and future plans. We aim to demystify AI and machine learning and make them easier to understand and apply.

Our goal is to introduce applied evidence-based regulatory science, creating evidence that informs regulations and helps sponsors avoid potential harm. Ultimately, the agency's role is to support good research to benefit patients and the community.

Editor's note:

We thank Andrea for a motivating interview and for sharing with us the latest AI/ML developments within MHRA. It is clear that the integration of AI technologies into regulatory processes is not only enhancing efficiency but also paving the way for innovative solutions in the way we conduct and assess clinical trials. Andrea's insights and experiences highlight the transformative potential of these technologies in the drug development sector. We look forward to seeing the continued advancements and positive impacts of AI/ML initiatives at MHRA. Thank you, Andrea, for your valuable contributions and for leading the way in this exciting field.

IT IS NEVER TOO EARLY TO THINK ABOUT STATISTICAL LEADERSHIP

Richard C. Zink, PhD, Principal Research Fellow, JMP Statistical Discovery LLC

Highlights

- Discover why mastering leadership skills is just as crucial for statisticians as their technical expertise, especially in multidisciplinary settings.
- Learn why effectively conveying complex statistical concepts to those with minimal math backgrounds can improve decision-making and career growth.
- Explore the importance of developing leadership skills early in your career to thrive in the evolving landscape of statistical science.

Richard Zink
Principal Research Fellow
JMP Statistical
Discovery LLC

Author's note: **Meijing Wu kindly asked me to write this article shortly before her passing; it is dedicated in her memory.**

Statisticians and data scientists occupy a unique space on a multidisciplinary team. So much so, that it may often feel like a salmon swimming upstream against the current produced by everyone else. Teams want to move fast and meet deadlines, but we know firsthand that every decision, even seemingly innocuous ones, can have major implications and consequences for all downstream activities. This is especially true for clinical trials: large, exceptionally expensive experiments of human beings that often take several months or years to complete the following activities: developing the protocol, designing and testing the database, conducting the study, collecting the data, producing the final analysis, and authoring the final study report. The team does their utmost to produce the best possible product at each stage, but without fail, multiple changes often occur over the course of a study. While changes can create headaches for individual groups, statisticians need to be aware of the entirety of the process, since changes can, and likely will, affect the final analysis. In the worst case scenario, a modified protocol triggers modifications to an electronic data capture system and the underlying raw data, which triggers modifications to SDTM programs, which triggers modifications to ADaM programs, which triggers modifications to programs for tables, figures, and listings. That is a lot of places in need of revision, and plenty of opportunity for things to go wrong. Every passing day is one fewer day prior to database lock to get things in their proper place, much less rethinking, revising, and revalidating the analysis. It is no wonder that SOPs and process improvement are so important in medical product development - it is extraordinarily complex, and there is so much at stake!

Have you ever read a protocol and thought to yourself "there is NO WAY a statistician has reviewed this"? Even sections such as Inclusion and Exclusion Criteria, Study Endpoints, or Study Conduct can be written in a manner so vague or inconsistent that it is unsurprising that protocols are often in need of amendments. When asked to provide the Statistics Section to protocols, I started at page 1, added comments throughout, and more often than not, found major issues that required

discussion by the team before I could even begin to write text describing an appropriate statistical methodology and the accompanying summary tables. When team members grew frustrated with my changes and suggestions, especially since they believed they were near the end of protocol development, my response was to include me earlier in the process. It did not take long for this to start happening, and it resulted in fewer hiccups down the road. The take-home message is this: though the analysis comes at the end of the process, the team cannot leave the statistician out of protocol development until the last minute. Unfortunately, it is often up to the statistician to communicate this message.

I am also a big believer in finalizing the statistical analysis plan (SAP) as early as possible in the conduct of the study; I would often have a draft available while the database was being produced and would strive to get it signed off as early as possible. Why go to such extraordinary lengths?

- It gets everyone thinking about the analysis early, especially while the protocol is fresh in their minds.
- It ensures that the data required to perform the final analysis are collected in an appropriate manner in the study database.
- It makes the rest of the study team less likely to change the analysis since the SAP has already been signed off.

Have you ever been in a position where individuals dither finalizing the SAP? Many people make the claim that the SAP needs to be signed prior to database lock and will delay in finalizing the document. While this is absolutely true, this represents the worst case scenario! If the methodology and analyses and assumptions are changing up until a few weeks before database lock, the quality of the analysis suffers, the team producing the analysis suffers, and the timelines often suffer. Like the example above in being able to predict with near certainty whether a statistician was involved in the writing of the protocol, it is just as easy to predict those instances where the SAP was finalized just prior to database lock. In these instances, the database lock will be chaos, topline will be chaos, and the statisticians and statistical programmers will be miserable. The take-home message is this: SAPs need to be finalized sooner. If the argument against finalizing a SAP early is that the "protocol is constantly changing through amendments", this can be addressed through improving the quality of the original protocol (Hint! Include a statistician from the start.) Otherwise, the statistician needs to adjust the team's expectations given the disruption of downstream processes.

Hopefully these two examples highlight a very important point: Statisticians need to be leaders. Full stop.

- Non-statisticians may not recognize the importance of our unique skill set, even when it comes to the seemingly non-statistical aspects of multidisciplinary work.
- Non-statisticians may not recognize the huge implications minor decisions may have on the final analysis.
- Non-statisticians may not know what data are needed to conduct an appropriate analysis.

So again, statisticians need to be leaders. We need to communicate. We need to build trust through developing and nurturing relationships with key members of the team. Then, and only then, will we be able to influence others and the direction of our collaborations. Unfortunately, much of our education and training focuses on technical prowess, and less so on leadership, communication, and other interpersonal skills.

The good news is that anyone at any level can be a leader! It can be as easy as moving from the corner of the room to the conference table and being actively engaged in the ongoing discussion. Or you can begin your leadership journey by raising your hand when someone asks for a volunteer. Or you can look for opportunities to simply "make things better". Consider the important skills statisticians generally already possess:

- Organized
- Methodical
- Thoughtful
- Precise
- Forward-thinking, with plans for contingencies
- Philomathic
- Data-driven

“Like any other set of skills, leadership takes time and practice to grow and develop.”

These are critical skills for any leader to be effective!

Leadership begins with small steps. For example, sharing knowledge and expertise through presentations at conferences, workshops, or webinars, or writing scientific articles, book chapters, or software elevates your status among your peers. Consider opportunities to engage with non-statistical members of the team by helping them understand statistical concepts (using everyday language!) or offering assistance using your unique blend of skills. Developing or chairing sessions, serving as a referee for a scientific journal, or volunteering for activities for a Section or Chapter of the American Statistical Association (ASA) are excellent ways to build your network and develop an intuition for how to “get things done”. These small opportunities will inevitably lead to larger opportunities: leading major ASA initiatives; serving as a Chapter, Section, or ASA officer; teaching short courses at major conferences; leading scientific working groups; chairing conferences, serving as an editor for a scientific journal; or leading biometrics departments. But even if you have no interest in pursuing major leadership activities, leadership skills will benefit you in performing your day-to-day work as part of a multidisciplinary team. Statisticians represent a very unique and distinct point of view, so we need to make ourselves heard!

One does not wake up a leader. And attending a single course or reading a single book will not make you a leader, either. Like any other set of skills, leadership takes time and practice to grow and develop. Some things to consider:

- Get involved with the ASA to develop leadership skills, broaden your network, and support the statistics discipline.
- Exhibiting leadership before you have “the title” makes it possible to get “the title”. And its okay if you have no interest in “the title” – leadership skills are useful at any level.
- Your knowledge and technical expertise are not particularly useful if you cannot effectively communicate your ideas and convince others to consider implementing them in practice.
- Identify a mentor or peer group to discuss professional challenges and identify potential solutions.
- Stretch your boundaries by becoming more comfortable with the uncomfortable. Take risks, and do not let the fear of making mistakes prevent you from doing anything at all.

So, hop to it! It is never too early to think about statistical leadership.

A CAREER OF SERVICE, LEADERSHIP, AND INNOVATION: AN INTERVIEW WITH **ASA PRESIDENTIAL CANDIDATE BRIAN MILLEN**

By Charlotte Baidoo (BMS, Associate Editor)

Meet ASA Presidential Candidate Brian Millen - A champion for service, science, and inclusion

- Be inspired by Brian's career journey, marked by dedication to service and leadership, influential roles in professional societies and a commitment to analytics-driven drug development.
- Learn about Brian's role in founding the JSM Diversity Workshop and Mentoring Program, a cornerstone event at JSM since 2009, and his decade of service to the Biopharm Section
- Get a glimpse into Brian's vision for ASA, including advocacy for policies that impact the profession, celebrating statisticians' contributions, and fostering organizational health to impact the profession and nurture future leaders.

Brian Millen
Vice President, Biogen

A proponent of innovation, an advocate for diversity, and a champion of mentorship, Brian Millen has had a significant impact on our profession through years of leadership and service. Now, as he pursues a new chapter within the ASA, we sit down with him to discuss his journey, his vision, and what truly drives his passion.

Who is Brian Millen beyond the statistics roles?

First and foremost, I am a husband and father. My wife and I have been married for more than 25 years, and I'm the proud dad of two college freshmen. Watching them grow into independent, thoughtful individuals has been incredibly rewarding, even while I have less day-to-day contact with them now than when they were under my roof. I also love giving back, whether through volunteer service or by mentoring the next generation of statisticians. This has included multiple roles with ASA, IBS/ENAR, and in my local community. My community service activities have ranged from coaching kids' sports to teaching GED preparation courses to chairing the board of trustees for a local school system. Through all these service opportunities, I've found joy in being able to make a positive difference in people's lived experiences, and have often been able to establish enduring programs, infrastructure, or changes in culture.

Can you tell us about your journey as a statistical leader?

I've spent the bulk of my career at the intersection of statistics and drug development. Currently, I serve as Vice President at Biogen, leading the Biostatistics, Epidemiology, and Real-World Data Analytics organizations. I'm deeply committed to driving analytics-based

decision making in drug development to accelerate life-changing therapies to patients who are waiting. Beyond my corporate role, I've been active for over two decades in professional societies, including the ASA and IBS/ENAR, seeking new ways to advance our profession.

You've led many initiatives that have had a lasting impact. What are you most proud of?

One of the initiatives close to my heart is the JSM Diversity Workshop and Mentoring Program, which I launched in 2009, along with Nagambal Shah and Kim Weems. I maintained an active leadership role in this program for ten years, during which I successfully secured program funding through multiple national grants, stewarded program content as Chair or Co-Chair, and directly engaged with program participants. What started as a one-day workshop quickly grew into a multi-day program attracting and connecting students and professionals from all sectors. It has become a cornerstone event in JSM and has helped build an inclusive community, empower leaders, and foster lasting mentoring and supportive peer-to-peer relationships. Seeing it continue to thrive today with leaders who were previously students or early career professionals in the program is incredibly rewarding.

Naturally, the BioPharm Section holds a special place in my heart, and there are many impacts during my ten years of service on the BIOP Executive Committee. One initiative I helped to establish – alongside Richard Zink and Abie Ekangaki -- is the BIOP Student Scholarship Award. Over the past six years or so, the scholarship has grown in prominence as one of BIOP's signature awards which not only provides financial support to students, but also fosters deeper engagement within ASA. Establishing programs that endure and grow beyond my direct involvement is something I take great satisfaction in.

Interestingly, one of my ASA Fellow recommendation letters summarized, "Brian lives to serve….". It was impactful for me to read that summary from someone I admire. I serve wherever I'm placed, and I've been blessed to be able to make a difference in many spaces – doubly blessed that I've been able to do so with folks I admire and call colleagues and friends.

Your passion for service is evident. How has this shaped your approach to leadership?

I believe that leadership is, at some level, about creating opportunities for others. My time as ASA BIOP Section Chair reinforced this. When members came forward with new ideas, I made it a priority to find ways to say "yes". Sometimes that meant adapting an idea rather than implementing it exactly as proposed, but the goal was always to foster an environment where ideas had legs and innovation could thrive. As a result, new offerings were launched or piloted and scientific working groups and committees grew – all in service to our members and our profession.

One challenge that surfaced during my tenure as BIOP Chair was a shift in ASA's finance/expense model which negatively impacted the BIOP Section. We found ourselves unexpectedly projecting a deficit because of the ASA-initiated changes – not any changes to BIOP operations. In response, we (Section treasurer Emily Butler, incoming Chair Ted Lystig, and I) were able to successfully negotiate with ASA executive leadership to arrive at an alternative financial model that met the evolving needs of ASA and the needs of the Section – including enabling important growth initiatives BIOP had under consideration. That experience reinforced that all challenges are solvable when dedicated people come together. I've always found that to be the case in my roles in ASA.

You're now pursuing a new leadership role within ASA. What are your top priorities?

There are four key areas I want to focus on:

Advocacy That Matters – ASA has a crucial role to play in advocating for policies that impact our profession, from protecting public access to data to ensuring funding for sound statistical science and ethics in research. I want to continue and strengthen ASA's voice in these important areas.

Celebrating and Sharing Our Impact – Statisticians influence public health, policy, and innovation, but our contributions are not as well-known as they should be. I want to amplify the stories of our contributions, celebrate the impact of our members, and ensure that our contributions are appropriately documented.

Cultivating and Equipping Leaders – Leadership skills are just as critical as technical expertise. I plan to expand ASA's Leadership Institute and mentoring programs and partner with academic programs to embed leadership principles in curricula to ensure statisticians are equipped to lead at all career stages.

Ensuring Organizational Health and Agility – ASA must be financially sound and adaptable to meet the evolving needs of our diverse membership. Reviewing governance structures and financial models will be key to ensuring long-term sustainability.

The field of statistics is evolving rapidly, especially with AI and machine learning. How do you see ASA adapting to these changes?

ASA is a "big tent" organization, welcoming statisticians, data scientists, and AI/ML experts. The rise of artificial intelligence presents an opportunity for our organization. We need to ensure that AI applications are built on sound statistical principles while embracing the innovation they bring. It's crucial for ASA to foster innovation without partisanship, championing advancements across all areas of statistics and data science, including AI and ML.

Looking back on your career, what do you hope your legacy will be?

For me, the true mark of success is whether I've left things better than I found them. Whether it's through launching new initiatives, shaping culture or mentoring the next generation, my goal has always been to create lasting, meaningful change.

If, years from now, people look back and say, "Because of his efforts, more people had opportunities to grow, succeed, and contribute to the field," then I'll be satisfied.

That's a powerful perspective. Any final thoughts?

I'm incredibly grateful for the opportunities I've had to serve in this community, and I look forward to continuing that work, embracing new challenges, and helping shape the future of ASA and our profession. Folks can learn more about my background and my thoughts on how I would lead, if elected, by visiting *www.BrianMillenForASAPresident.com*. People can contact me to share ideas or ask questions through a portal on that site.

In speaking with Brian Millen, one thing is clear: his leadership is rooted in service, vision, and a deep commitment to empowering others. As he pursues his next chapter, the statistical community stands to benefit from his dedication to shaping a stronger, more inclusive, and innovative profession.

BACK TO SCHOOL? INVESTING IN HERSELF, INSPIRING OTHERS: **DR. SAMMI TANG'S PATH THROUGH THE MIT EXECUTIVE MBA**

Erik Bloomquist (Merck) and Maria Kudela (Pfizer)

Highlights

- Be inspired by Dr. Sammi Tang's bold decision to pursue an Executive MBA while serving as a senior global R&D leader—demonstrating that it's never too late to learn, grow, and lead with vision.
- Learn how Dr. Tang successfully balanced a high-impact global role, family life, and the rigorous MIT Sloan EMBA program—proving that with the right support and purpose, transformation is possible at any stage.
- Explore how the MIT Sloan EMBA shaped her strategic thinking, broadened her business perspective, and empowered her to lead with even greater impact across science, innovation, and enterprise.

Sammi Tang
Senior Vice President,
Global Head of
Quantitative Sciences and
Evidence Generation
Astellas Pharmaceuticals

An Industry Leader's Perspective on the MIT Sloan Executive MBA Experience

Dr. Rui (Sammi) Tang is a visionary pharmaceutical leader with a track record of building high-performing teams, driving innovation, and leveraging data science to accelerate drug development. She serves as the Senior Vice President and Global Head of Quantitative Sciences and Evidence Generation (QSEG) at Astellas Pharmaceuticals, where she leads global teams across quantitative analytics, epidemiology, real-world evidence (RWE), biostatistics, programming, medical writing, scientific communication, data systems & enablement, and data management. In addition, she is the Site Head of the Astellas Life Sciences Center (ALSC) in Cambridge, overseeing cross-functional collaboration among R&D, business development, and external partners to foster innovation in a vibrant biotech ecosystem. Dr. Tang is a pioneer in integrating Generative AI for regulatory and clinical trial documentation, AI/ML-driven analytics, and external data utilization, transforming the way clinical trials are designed and executed. Before joining Astellas, she served as Vice President and Global Head of Biometrics at Servier Pharmaceuticals, where she led AI-driven analytics initiatives and global biometrics teams. At Shire Pharmaceuticals, she was the Therapeutic Area Head of Biostatistics, overseeing multiple indications across development stages. Earlier in her career, she held roles of increasing responsibility at Vertex, Amgen, Mayo Clinic, and Merck, contributing to the advancement of transformative therapies. To date, the therapies approved through her work—either directly or under her leadership—are improving the lives of millions of patients daily around the world. Beyond her corporate leadership, Dr. Tang is an Adjunct Professor at Yale University School of Public Health and the co-founder of DahShu, a non-profit advancing data science education with over 5,000 members globally. She holds a PhD in Statistical Genetics from Michigan Technological University and an Executive MBA from MIT Sloan. With 50+ peer-reviewed publications and multiple patents in adaptive trial design and precision medicine, she remains at the forefront of statistical innovation in drug development.

In 2022, despite an already demanding career, Sammi decided to take on an additional challenge—returning to school for an Executive MBA at MIT Sloan School of Management. What motivated her to do so at this stage in her career? What has she gained from the experience? And what advice does she have for statisticians considering an MBA?

We sat down with Dr. Sammi Tang to learn more about her journey.

1. What motivated you to go back to school at this point in your career?

First, thank you for the opportunity to share my story! Interestingly, some of my peers told me recently that they pursued an EMBA or other advanced programs after hearing about my journey—and they absolutely loved it. Some chose business programs like an MBA or EMBA, while others pursued medical or law programs, or specialized technical certifications. It was rewarding to know that my decision helped push them to take the leap. I hope my experience can help others as well.

When I decided to enroll at MIT Sloan, I was already a VP and Global Head at Servier, leading teams across multiple functions and regions. I had built a team from scratch in the U.S. while inheriting global teams that required major transformation, a new vision and mission, and the establishment of a strong network. At the same time, I was heavily involved in company acquisitions, making the job even more demanding.

Despite the intensity of my role, I've always been someone who thrives on learning. I had considered an EMBA for years, knowing it would be a part of my long-term development plan. Even though the timing wasn't "perfect" (is it ever?), I made it work, because I knew it would help me grow as a leader.

2. How did the program impact your career? Were your expectations met?

I pursued the EMBA for long-term career development, not for an immediate job change. However, the transformation was profound.

At the end of the program, we had a career planning session, where students shared their goals. Some aimed for entrepreneurship, others wanted career pivots, and some sought promotions. For me, it wasn't about a specific outcome—it was about investing in myself.

The program exceeded my expectations in multiple ways:

- Stronger business acumen: Now, when I engage with finance teams or corporate strategy, I immediately grasp their perspectives.
- A broader leadership lens: When reviewing portfolio plans, I have a clearer vision of where my team fits and how we create value.
- An entrepreneurial mindset in a corporate setting: I see myself as a strategic leader shaping the future of drug development, not just driving R&D innovation.

The biggest shift? I no longer see my role only through the lens of R&D—I think about sustainability, investment, and long-term business strategy.

3. Why did you choose an EMBA over other programs?

For me, it was always going to be a full Executive MBA (EMBA), not just a short-term business course or an MBA fellowship. I wasn't looking for a surface-level experience—I wanted a complete mindset shift.

At my level, I was already involved in high-level business strategy discussions. But I wanted to understand the business beyond R&D, to see the full picture of drug development as an enterprise. Even when reviewing financial reports, I sometimes felt I wasn't fully grasping the nuances. I wanted to bridge that gap.

That said, the EMBA path is highly personal. Some people take an MBA to change careers entirely. Others go into epidemiology, law, medical programs, or even the arts. I had a former statistics colleague who became a therapist after completing a medical program! The key is to know why you're doing it and what you want from it.

4. How did you balance school with work and personal life?

Balancing an Executive MBA with a demanding job and personal responsibilities was not easy. Before com-

mitting, I had to carefully evaluate whether I had the right support system in place and how I would manage my time effectively.

Family support was critical. I discussed this decision with my spouse and family early on because it required sacrifices—not just from me, but from them as well. There were weeks when school had to take priority over family time, and their unwavering support made all the difference.

Company support was equally important. I was fortunate that my employer not only backed my decision but also provided financial sponsorship and the flexibility needed to balance both commitments. My leadership team recognized that this program would bring value back to the company, which allowed me to integrate my learning directly into my work.

Even with strong support, time management was key. I had a lot on my plate:

- A global leadership role with frequent travel
- External commitments with industry groups
- Personal passions like badminton, skiing, and travel
- Two young kids and an active social network

Since I didn't want to give up any of these, I had to plan my time strategically. The MIT EMBA is a fully in-person program, and MIT does not allow remote learning. Some of my classmates flew in from Asia, the Middle East, and Europe every two weeks to attend—seeing their dedication was incredibly inspiring.

For those considering an EMBA or any intensive program, my advice is:

1. Have open conversations with your family. Their encouragement will be essential.
2. Engage your employer early. If your company values leadership development, they may offer sponsorship or flexibility.
3. Be realistic about sacrifices. Your free time will be limited, but it's a short-term investment for a long-term gain.
4. Leverage your classmates. Many are facing the same challenges, and having a peer support system makes a huge difference.

Despite the challenges, I wouldn't change a thing. The experience was truly transformational, and the effort was absolutely worth it.

5. What were some key lessons you learned, and how has the MIT Sloan alumni network helped you after graduation?

The EMBA experience transformed my thinking in unexpected ways, providing valuable insights that continue to shape my career. One of the most impactful lessons was learning to see organizations as interconnected ecosystems through the course on system dynamics. It helped me think beyond individual functions and understand how different elements within a company interact.

Another key takeaway was the importance of negotiation and executive communication. Through real boardroom simulations, I developed skills that I now use daily in high-stakes discussions. The ability to navigate complex conversations, align stakeholders, and present ideas persuasively has proven invaluable.

The program also gave me a global business perspective. Working with classmates from over 40 industries—including tech, finance, healthcare, and energy—broadened my understanding of decision-making across different sectors. These interactions challenged me to think beyond the pharmaceutical industry and approach problems from multiple angles.

Even as a statistician, I gained new insights into data-driven decision-making. The curriculum emphasized not just technical analytics but also how to use data for business impact. Understanding financial and strategic implications has helped me align quantitative approaches with corporate objectives more effectively.

Some of the most valuable courses included:

5. System Dynamics – Understanding businesses as interconnected systems
6. Negotiation & Executive Communication – Practical skills for boardroom discussions
7. Global Strategy & Leadership – Decision-making across industries and markets
8. Financial Analysis & Corporate Strategy – Aligning financial insights with business decisions
9. Operations & Supply Chain Management – Enhancing efficiency and scalability
10. Entrepreneurial Mindset & Innovation – Driving change beyond traditional corporate structures
11. Marketing & Business Impact – Aligning marketing with long-term business sustainability

Beyond the coursework, the caliber of MIT professors made the experience even more special. Some classes were taught by Nobel Laureates and industry leaders, providing deep discussions that extended beyond traditional learning.

A lasting benefit of the EMBA is the strength of the MIT Sloan alumni network. Wherever I travel for business, I can always connect with alumni in that city. The network serves as a powerful sounding board where I can exchange ideas with peers who are equally driven. It has strengthened my career growth, offering mentorship, insights, and even potential business opportunities.

Overall, the EMBA experience was not just about gaining knowledge—it reshaped my leadership approach, expanded my network, and provided lifelong connections that continue to impact my career.

6. Any advice for those considering an MBA or other programs?

The most important thing is to be clear about why you want to do it. Are you looking for career advancement, new skills, a stronger network, or a complete transformation? Your motivation will help determine if an MBA is the right choice and which type of program fits best. An executive MBA is ideal for experienced professionals balancing work, while a full-time MBA is better suited for those seeking a major career shift. There are also specialized programs in areas like data science, finance, and public health, which may be a better fit depending on your career goals.

Having a strong support system is essential. An MBA is a big commitment, so discussing it with your family is important, as the time commitment will affect them too. Employer support can also make a big difference, whether through financial assistance or workplace flexibility. I was fortunate to have both, which made managing the workload much easier.

Choosing a top-tier school adds significant long-term value. The education, exposure to world-class faculty—including Nobel Laureates—and access to a strong alumni network provide lifelong benefits. Years after graduation, I still rely on my MIT Sloan network for mentorship, professional advice, and new opportunities. The network you build is just as valuable as the coursework itself.

7. How was the application process? Was it difficult?

The application process requires preparation, but it's manageable. Some EMBA programs require the GMAT, so planning ahead is important if that applies.

Strong recommendation letters are key. They should come from people who truly understand your leadership style, achievements, and potential. A mix of senior leaders and mentors who can provide a well-rounded perspective is ideal.

The essays are where you can differentiate yourself. Each school has a unique culture, so it's important to tailor your responses rather than taking a one-size-fits-all approach. Schools aren't just looking for impressive resumes—they want individuals who will bring unique perspectives and contribute to the learning experience.

For me, writing the essays was a valuable exercise in self-reflection. I didn't just highlight past achievements but also explained how I planned to grow and contribute to the program. If you approach the application with a clear vision and genuine enthusiasm, it won't feel like a hurdle—it will be the first step toward an incredible experience.

Final Thoughts: Was It Worth It? Looking back, was it worth it?

Absolutely.

I would do it all over again.

This experience changed the way I think, the way I lead, and the way I contribute to my industry. If you're considering an MBA, think big, be bold, and invest in yourself.

As our conversation came to an end, we couldn't help but feel inspired by Dr. Sammi Tang's journey and the impact of her Executive MBA experience at MIT Sloan School of Management. Her unwavering commitment to continuous learning, innovation, and leadership serves as a beacon for professionals across industries. Dr. Tang's story is a testament to the transformative power of education and the importance of investing in oneself. We hope her insights and experiences resonate with our readers and encourage them to pursue their own paths of growth and development.

BACK TO SCHOOL? JUDY LI ON MBA PROGRAMS AND THE FUTURE OF STATISTICIANS

Erik Bloomquist (Merck) and Maria Kudela (Pfizer)

Highlights

- Discover Dr. Judy Li's journey at The Wharton School in 2023 to pursuit an Executive MBA in Strategic Management. Her experience offers insights for statisticians contemplating a similar path, highlighting the significant impact on her career trajectory.
- Learn how Dr. Judy Li's MBA experience reshaped her perspective, integrating disciplines like global economy and technology into her work. This strategic education has empowered her to make executive-level, data-driven decisions, enhancing her effectiveness as a strategic leader.
- Explore how Dr. Judy Li's MBA program not only expanded her business acumen but also honed her leadership skills. Her inspiring journey underscores the importance of "soft skills", crucial for guiding others in the dynamic healthcare sector.

Judy Li

Head of Hematology Strategy for Late Oncology Statistics, AstraZeneca

Dr. Judy Li serves as the Head of Hematology Strategy for Late Oncology Statistics at AstraZeneca, where she provides leadership and expertise in oncology statistics. Her work emphasizes strategic planning, technical oversight, functional development, and operational guidance. Dr. Li plays a pivotal role in propelling the field of hematology statistics forward. Throughout her career, Dr. Li has held senior leadership positions in both the biopharmaceutical and biotech sectors, making significant contributions at organizations including Bristol Myers Squibb, Celgene, and Regeneron Pharmaceuticals. Prior to her industry tenure, she garnered extensive experience at the US Food and Drug Administration (FDA) as a master statistical reviewer and supervisory mathematical statistician. She has clinical development experience across multiple therapeutic areas including oncology, hematology, immunology, neurology, cell therapy, as well as special clinical settings for multiregional clinical trials and rare disease.

Dr. Li has been an active member of the American Statistical Association (ASA) Biopharmaceutical Section Executive Board for over a decade, where she has taken on various roles, including co-founder of the Safety Monitor Working Group and chair of the 2019 Regulatory Industry Statistics Workshop, along with chairing the poster competition section and membership committee. She also serves on the board of directors and the advisory council of the Bay Area Biotech-Pharma Statistics Workshop. Additionally, she is the editor of the book “Quantitative Methodologies and Process for Safety Monitoring and Ongoing Benefit Risk Evaluation”. Her research work has been highly acknowledged with the FDA Office of Chief Scientist and received the Intramural Grant award for two consecutive years.

She is currently running for ASA 2026 chair-elect of the Biopharmaceutical Section.

In 2023, Judy decided to return to school at The Wharton School to pursue an Executive MBA degree

in Strategic Management with a focus on healthcare industry. We asked her about this decision, its impact on her career thus far, and any advice for statisticians considering a similar move.

1. What motivated you to go back to school at this point in your career?

I frequently receive this question, and I appreciate the opportunity to share my journey here!

Returning to school after over 15 years in the workforce was a significant decision for me. In today's rapidly evolving landscape, particularly with the rise of technology and AI, the role of statisticians in the pharmaceutical industry is continually transforming. As the emphasis on big data grows, statisticians are assuming increasingly critical roles in the decision-making process. I realized that just having technical skills wouldn't be enough to make a real impact. A deeper understanding of business, economics, and the operational aspects underlying these decisions has become essential. This knowledge is crucial for turning data and insights into meaningful, data-driven decisions.

I also think a lot about how we can develop our talent and support the next generation of statisticians as they face their own challenges. It became clear to me that enhancing "soft skills" is essential, particularly in areas such as effective communication as a leader, efficient management of a large global team, and the creation of a welcoming environment for diverse employees.

That's why an MBA program seemed like the perfect opportunity to get the structured training I needed in these areas. It not only boosted my business knowledge but also helped me build the leadership skills to inspire and guide others in this fast-paced field. Going for an Executive MBA felt like the right move to reach my potential and make a positive impact in my organization and beyond, and I'm really glad I made that choice!

2. What field or program were you considering pursuing (was it only MBA?), and what drew you to it?

I decided to pursue my MBA at Wharton, recognized as one of the top business schools globally. What drew me to the Executive MBA program there is that its curriculum is just as rigorous and comprehensive as the full-time MBA, the only difference being that classes are scheduled on weekends. My focus on strategic management with a concentration in the healthcare industry fits perfectly with my current role and my passion for making a positive impact in the healthcare field.

3. How did you think this program would impact your current career path or new opportunities? Were your expectations met after you graduated? Do you think the experience has been beneficial for your career?

Absolutely—more than 100%!

The MBA experience has significantly broadened my mindset, integrating disciplines such as global economy, finance, operations, technology, and communications into my daily work, all while focusing on cultural leadership. It has given me a clearer perspective on tackling challenges and creating value, helping me become a more effective strategic leader capable of making executive-level, data-driven decisions—not just for the business, but for the patients who rely on our innovations.

Additionally, the relationships I've built through the Wharton network have been incredibly rewarding. Collaborating with talented individuals from diverse fields like tech, finance, and consulting has provided fresh perspectives that are crucial for a holistic approach to leadership. This collaborative environment has inspired me to think creatively and strategically, pushing me to explore my full potential.

I would also like to highlight that the impact of an MBA goes beyond just career advancement; it has shaped my overall outlook on life. I've become more strategic, value-driven, and rational in my thinking. For example, in my finance valuation class, our professor shared a powerful philosophy: a tree knows not to grow branches where there is no sunlight, much like how individuals and businesses should focus on opportunities that provide returns greater than their opportunity costs. Insights like this have been a recurring theme throughout nearly every lecture, and I believe these lessons will provide lifelong benefits.

4. How did you balance school with your other responsibilities, such as work and personal life?

This question often arises during MBA interviews because admissions committees understand that pursuing an MBA involves significant challenges that demand a strong commitment to succeed. Depending on

the individual, an MBA program can require anywhere from 20 to 40 hours each week, which inevitably limits the time available for family and may occasionally result in missed workdays. Sleep is often compromised as well. It is vital to have open and proactive discussions with family, managers, and colleagues about these commitments prior to beginning the program. Establishing a supportive network is essential for effectively managing the challenges of an Executive MBA.

I feel fortunate to have a very supportive employer and a strong supporting family and network throughout this journey.

5. How was the application process? Did you find it difficult?

The application process was quite straightforward. The primary requirement for most schools is either the GMAT or an Executive Evaluation test for admission which necessitates some preparation in advance. Since the program emphasizes a strong quantitative background, having a degree in statistics or mathematics can give you a significant competitive edge during the application process ☺

6. Any advice or tips for those who are considering an MBA or other programs?

Understanding your priorities is crucial. What matters most to you right now? Going back to school may not be the right choice for everyone. However, for those who have thought it through and decided to pursue an MBA or another program, my advice is to do it sooner rather than later. The learning experience in these programs is intense and filled with valuable insights. Many people find it takes years after graduation to fully absorb what they've learned and apply it in real-life situations. The benefits of this education can have a lasting impact, so starting earlier allows you to take advantage of the skills and knowledge you acquire right away.

7. Final Thought, anything else you would like to share with our audience?

As Benjamin Franklin said, "An investment in knowledge always pays the best interest."

Chase your dreams fearlessly, engage in lifelong learning, and strive to make a difference. Remember, the sky is the limit!

We thanked Dr. Judy Li's for sharing her story with us. Dr. Judy Li's story is an inspiring testament to the power of adaptability, perseverance, and a relentless pursuit of growth. Her ability to seamlessly blend technical expertise with strategic leadership has not only advanced her career but also elevated the impact of biopharmaceutical statistics on healthcare innovation. As she charts a new course with her Executive MBA, Dr. Li encourages all statisticians to embrace lifelong learning, take bold steps toward leadership, and leverage their unique skills to drive meaningful change. Her journey reminds us that with dedication, vision, and a commitment to excellence, the possibilities are truly limitless.

ICHPS 2025 OFFERS OPPORTUNITY FOR PROFESSIONAL GROWTH AND INNOVATIVE THINKING TO *IMPROVE HEALTH EQUITY.*

Beth Ann Griffin (RAND), Lane Burgette (RAND), Staci Hepler (Wake Forest University), Sarah Lotspeich (Wake Forest University), and Mousumi Banerjee (University of Michigan)

The International Conference on Health Policy Statistics was held January 6–8 in San Diego California. ICHPS brings together practitioners, methodologists, health service researchers, health economists, and policy analysts to exchange and build on ideas they will disseminate to the broader health policy community. In addition to US and Canadian participants, ICHPS co-chairs Lane Burgette and Beth Ann Griffin welcomed attendees from Israel, Europe, and China.

The meeting kicked off with a warm welcome from Madhumita (Bonnie) Ghosh Dastidar, recent president of ASA and Senior Statistician at RAND. This was followed by the opening keynote from Whitney Robinson from Duke University School of Medicine. Robinson discussed the big mistakes we researchers can make in causal inference, with solutions including thinking about the nature of the problem incorrectly and letting the data drive the research. She argued that recognizing these patterns and emulating creative, interdisciplinary work offers opportunities to innovate and sharpen our work. Serving as the discussant, Susan Paddock—Executive Vice-President and Chief Scientist at NORC—encouraged attendees to continue engaging in efforts to ensure our data are measured correctly and address well-specified problems using high-quality research paradigms.

The closing keynote was delivered by Sherri Rose from Stanford University. She discussed the latest issues surrounding ethical use of AI, highlighting that algorithms are not neutral. She explained that optimization choices reflect a specific value system and the distribution of power to make these; she also described how data also reflect societal bias. Serving as discussant, Elizabeth Stuart – Chair of Biostatistics at Johns Hopkins University, Bloomberg School of Public Health – reflected on how our role as methodologists is changing and we need to find ways to ensure that people understand the value statisticians bring to research.

Whitney Robinson gave the opening keynote. From left: Susan Paddock, Whiteny Robinson, Bonnie Ghosh Dastidar and Beth Ann Griffin.

Sherri gave the closing keynote. From left: Sherri Rose.

Between the keynotes was a "meet the editor" session that brought together editors from top medical and applied statistics journals to share their experiences, discuss the characteristics of successful submissions, and define what researchers should take care to do (and not to do) as they seek to disseminate their work in both high-impact applied and methods journals. The editors included Elizabeth Stuart from *JAMA* Health Forum, Layla Parast from Medical Care, Nandita Mitra from Observational Studies, and Beth Ann Griffin from Annals of Applied Statistics.

ICHPS also included a special townhall session, titled "Health Policy and Health Equity for Local Populations". This session highlighted talks by two speakers from UCSD who are performing research at the intersection of health policy and health equity for residents in and around the San Diego community. Elena Martinez, a Professor in the department of family medicine and public health, highlighted findings and insights from a recent pragmatic randomized trial to increase colorectal cancer screening among low-income and minoritized populations in San Diego County (*https://ww3.aievolution.com/AMSTATevents/Events/viewEv?ev=4331*). Aladdin Shadyab, Associate Professor of Public Health and Medicine, discussed the design of a future study to assess a comprehensive healthcare intervention to reduce healthcare costs and improve health outcomes in older adults at risk of nursing home admission and homelessness.

There was an exciting line-up of invited and contributed sessions covering diverse topics centered around this year's theme of "Statistical Innovations to Improve Health Equity." The fifteen invited sessions focused on topics including methodological challenges like complex study and survey designs, measurement error, data, and fusion. Many important areas of real-world applications were also discussed, from the overdose epidemic to mental health to LGBTQIA+ health.

The conference featured 11 training workshops on a diverse range of topics. Topics included: heterogeneous treatment effect estimation, record linkage, Bayesian tree ensembles and nonparametrics, complex survey data, policy intervention design and evaluation, and power analysis with planned error control for multiple outcomes. Additionally, the Alan Alda Center for Communicating Science offered a workshop on effective communication.

To close out the meeting, Mousumi Banerjee, chair of the ASA Health Policy Statistics Section, presented the Mid-Career and Long-Term Excellence awards. The Mid-Career Award is presented to a recognized mid-career leader in health care policy and health services research who has made outstanding contributions through methodological or applied work and demonstrates promise of continued excellence at the frontier of statistical practice that advances the aims of the Health Policy Statistics Section. Two were honored with this award this year: Miguel Marino, professor and biostatistician at department of family medicine at Oregon Health & Science University, and José Zubizarreta, professor at department of health care policy, Harvard Medical School and department of biostatistics at Harvard School of Public Health.

Editors from top journals discuss what they look for in statistically rigorous research. From left: Layla Parast, Nandita Mitra, Elizabeth Stuart and Beth Ann Griffin.

The Mid-Career Award goes to Miguel Marino and José Zubizarreta, while the Long-Term Excellence Award goes to Lisa Lix. From left first photo: Mousumi Banerjee, Miguel Marino and José Zubizarreta; From left second photo: Mousumi Banerjee and Lisa Lix.

The Long-Term Excellence Award is given to an individual who has made significant contributions to health care policy and health services research through

International Conference on Health Policy Statistics

The Student Travel Awards goes to Martha Barnard, Wenbo Fei, Gary Hettinger, Andy Shen, and Peijin Wang. From left: Lane Burgette, Andy Shen, Peijin Wang, Gary Hettinger, Beth Ann Griffin.

mentoring and/or service that advances the aims of the Health Policy Statistics Section. This year's award recipient was Lisa Lix a professor of biostatistics in the department of community health sciences at the University of Manitoba, Canada. Lisa is a Tier 1 Canada Research Chair in Methods for Electronic Health Data Quality, and Director of the Data Science Platform in the George & Fay Yee Centre for Healthcare Innovation at the University of Manitoba. The award recognizes her multifaceted talents and contributions, her dedication, leadership, and research acuity, but more importantly her generosity – in mentoring, collaboration, and service to further the missions of the Health Policy Statistics Section.

ICHPS also provides learning and networking opportunities for those new to health policy. In addition to honoring 5 students with travel awards, the conference provides a venue for students and developing scholars to network and engage with leading methodologists via poster sessions and a student networking event. The student "speed networking" event brought together dozens of students and mentors. Mentors were drawn from academia, government, and industry and shared their candid experiences and thoughts about career development. Students also received a reduced conference registration rate, and all workshops were free for students.

The next ICHPS conference is expected to take place in 2027 so keep your eyes out for more information soon enough!

THE STORY BEHIND STATBOLIC

Jingyi Liu (Eli Lilly), Henrik Ravn (Novo Nordisk), Yun Wang (FDA), Ying Wei (Columbia), Thomas Liu (Amgen), Imola Fodor (Genentech), Melanie Wright (Novartis), Hiya Banerjee (Eli Lilly)

ASA STATBOLIC

In today's world—where Incretin drugs are dominating headlines and transforming the treatment landscape—a question echoed:

"Why don't we have a platform for cardiometabolic health like we do for oncology—somewhere we can openly share research questions and challenges in drug development?"

That question lit a spark.

What started as an informal conversation quickly grew into something more. On a crisp January day, a group of statisticians—representing academia, industry, and regulatory agencies—came together to explore the idea. Could we build a community, a space dedicated to advancing statistical science in cardiometabolic health?

But of course, the big question was still ahead of us:

"How do we pull off a conference from scratch? How do we get people involved?"

The first step: forming an advisory committee. A passionate, cross-sector team—academia, FDA, and industry—united by a shared vision. Together, we began to define the mission and scope of this budding initiative. We needed a name that captured the essence of what we were building. That's when one of our members suggested:

"STATBOLIC"—a blend of statistics and cardiometabolic.

It clicked. And just like that, STATBOLIC was born.

We then expanded our team by forming a Scientific Program Committee—12 incredible individuals from academia, FDA, EMA, and industry. Their task: to shape the scientific content of our very first conference. As plans solidified, we also knew we needed a long-term home. That's when the ASA Biopharmaceutical Section welcomed us as an official scientific working

group. With their support, and the help of the ASA Meeting Planning Group, we were ready to bring STATBOLIC to life.

The program focused on two core themes:

- Future research directions in trial designs for complex, interrelated indications within metabolic health. How can we build robust, efficient designs that accelerate development and deliver treatments to patients faster?
- Disease-specific challenges, including:
  - Statistical challenges in cardiovascular, kidney, and liver diseases
  - Challenges in evaluating weight reduction treatments

Over 125 participants joined us—statisticians, scientists, researchers, and leaders from across the ecosystem. We were honored to host Dr. Arun Sanyal (Director, Stravitz-Sanyal Institute for Liver Disease and Metabolic Health, Virginia Commonwealth University) as our keynote speaker and a thought-provoking fireside chat with panelists from the drug development world. Presenters came from both academia and industry, bringing diverse perspectives to the table.

The interest and engagement reaffirmed what we felt from the beginning: there was a need. STATBOLIC wasn't just a one-time event. It was the beginning of a community. A platform.

We're thrilled to share that STATBOLIC will return in 2026, with our next conference to be held in Washington, DC.

This wouldn't have been possible without the incredible support from everyone involved—our participants, speakers, organizers, and especially our sponsors: Amgen, Eli Lilly, Genentech, Novartis, Novo Nordisk, and ASA Biopharm. We are truly grateful for your belief in this effort.

We'll be sharing updates and save-the-date reminders soon. In the meantime, you can check out the program agenda from our 2025 conference on our website STATBOLIC 2025 - Biopharmaceutical Section

We can't wait to see you next year!

BIOPHARMACEUTICAL SECTION SAFETY WORKING GROUP: ACCOMPLISHMENTS AND RECENT DEVELOPMENTS

Lothar Tremmel (CSL Behring), Jürgen Kübler (QSciCon) and Tarek Hammad (Takeda)

A brief History: The ASA Biopharmaceutical Safety Working Group was formed in 2014, which began as a working group supporting "Safety Strategies and Analysis". This led to the creation of the Safety Monitoring Working Group in the Fall of 2015 by founding co-chairs Olga Manchenko and Qi Jiang, followed by Judy Li and William Wang with a mission "to help empower the biostatistics community to better enable qualitative and quantitative safety monitoring". Their motivation was aptly summarized in an article by Judy Li et al (*https://magazine.amstat.org/wp-content/uploads/2019/06/AMSTATJULY.pdf*). In 2017, the group expanded into an interdisciplinary working group, with Jim Buchanan and Mengchun Li serving as non-statistical co-chairs and kept a strong focus on this aspect ever since.

Governance structure: This working group is governed by a system of rotating co-chairs, with one incoming, one resident, and one outgoing chair, each serving a three-year term. Current co-chairs are Tarek Hammad (incoming), Lothar Tremmel (resident), and Jürgen Kübler (outgoing). However, the real action happens within the taskforces that address important issues in drug safety analyses. These task forces are currently organized into three workstreams: 1) Interdisciplinary efforts that include colleagues from the areas of medicine and epidemiology, 2) Statistical methodology for safety surveillance, and 3) Methodology that Incorporates information from Real World Evidence (RWE). In addition, we have an active "outreach," led by Susan Mayo and Michelle Zhang who organize webinars about topics related to clinical safety analysis. It is their collaboration with other workstreams that serve as critical component of this working group. Susan plays a major role on this team, and after joining CDER FDA in 2018 has helped to establish the collaboration with the safety community and served in various functions in the SWG. More details can be found on our web page (*https://community.amstat.org/biop/workinggroups/safety-home*).

Past accomplishments: We are proud of the book we published in 2022 about "Quantitative Drug Safety and Benefit-Risk Evaluation" (*https://www.routledge.com/Quantitative-Drug-Safety-and-Benefit-Risk-Evaluation-Practical-and-Cross-Disciplinary/Wang-Munsaka-Buchanan-Li/p/book/9781138594067*) under Bill Wang's unwavering leadership. It might be our biggest accomplishment so far. The topics include a survey of the regulatory landscape, aggregated safety assessments by interdisciplinary safety working groups, statistical methods for blinded and unblinded safety monitoring, considerations for the design and analysis of RCTs and RWE studies concerned with safety, and the evaluation and visualization of risk-benefit. Many of these topics further evolved as documented in a series of publications and presentations.

Secondly, we would like to highlight a public-private partnership (PPP) agreement with the FDA that was obtained with the help of our members from the FDA, also known as "FDA liaisons." It was signed in early 2021 with Bill Wang as the driving force behind this accomplishment. This agreement was based on significant contributions among several FDA colleagues who were a part of the working group from the beginning. The success of the PPP was recently highlighted by the fact that some of our FDA liaisons were honored with the Francis O. Kelsey Drug Safety Excellence Award *"for the efforts and leadership as part of the American Statistical Association partnership with FDA to advance the science of drug safety."*

We are actively trying to influence the safety analysis community by contributing numerous presentations and publications. For example, we published a proposed mechanism for prospective planning of aggregate safety analyses across an ongoing clinical program, in part motivated by the FDA's "final rule" about IND safety reporting, the so-called "Aggregate Safety Analysis Plan". More generally, in 2024 we contributed about 18 presentations, 5 papers, and 3 book chapters to the

Vision

To establish the Safety Working Group (SWG) as a leading force in advancing interdisciplinary safety sciences, fostering innovation, collaboration, and education to improve drug safety and benefit-risk assessments globally.

Mission

To foster collaboration among academia, industry, and regulatory bodies, integrating expertise from statistics and other disciplines relevant for drug safety to advance innovation with respect to safety methodology, planning, signal detection and profiling, risk management, and benefit-risk evaluation throughout the drug development lifecycle. Education and tool development are core to our mission to help facilitate informed decision-making and impactful outcomes.

scientific community. In addition, our outreach group organized 5 webinars.

Renewal: Rather than remaining static, the current leadership has chosen to reflect on our future mission while being mindful of the many other working groups and organizations in industry that support clinical safety analysis. To explore our unique contribution, we recently convened task force leaders and FDA liaisons for a collaborative discussion. This effort led to the development of a refreshed vision and mission statement that will guide our path forward.

Looking into the future: We are excited about the broad support our renewed vision and mission statements received from the SWG. Consistent with it, we would like to shift our focus from implementation to innovation+, where the "+" stands for providing tools for implementation. In this context, we would welcome new members, in particular from academia, so we can further advance the science of drug safety evaluation. If you are interested, please write an email to Lothar.tremmel@cslbehring.com, juergen.kuebler@qscicon.com, or Tarek.Hammad@takeda.com.

ASA BIOPHARMACEUTICAL SECTION STUDENT PAPER AWARDS

Francis Rogan (Merck)

The Biopharmaceutical Section has announced the winners of the 2025 American Statistical Association (ASA) Student Paper Awards from a total of 58 submissions. The selected students will present their papers during one of the contributed paper sessions at the 2025 Joint Statistical Meetings (JSM) in Nashville, Tennessee. The awards will be presented at the Biopharmaceutical Section's open business meeting at JSM along with a cash prize. We would like to thank all those who've participated in this competition and congratulate the winners! For more details on the competition, please visit: *https://community.amstat.org/biop/awards/studentpapercompetition*.

FIRST PRIZE:

Yuhan Qian
University of Washington

TITLE: From Estimands to Robust Inference of Treatment Effects in Platform Trials

What is your paper about?

We present a clear framework for constructing a clinically meaningful estimand with a precise specification of the population of interest in a platform trial. Additionally, we develop methods for robustly estimating treatment effects with minimal assumptions. Our proposed entire concurrently eligible (ECE) population is critical for addressing key issues in future statistical research, as it provides a clear reference point for evaluating both efficiency gains and potential bias.

What are your plans after graduation?

I plan to pursue a career in academia after graduation.

SECOND PRIZE:

Daoyuan Lai
University of Hong Kong

TITLE: Bayesian Transfer Learning for Enhanced Estimation and Inference

What is your paper about?

In this paper, we introduce a Bayesian transfer learning method called TRansfer leArning via guided horseshoE prioR (TRADER). This method improves estimation and inference in high-dimensional linear models by borrowing information from other datasets. TRADER has several advantages over existing frequentist approaches: (1) it requires only summary-level information from the source, (2) it can use source estimates that are close to the target estimate at a small angle, while current methods need a small Euclidean distance, which is stricter, and (3) it offers more precise credible intervals.

We conducted extensive simulations to evaluate TRADER's performance. We also investigated its posterior contraction rate and finite-sample marginal posterior behavior. Additionally, our method addresses the over-shrinkage problem often seen with standard continuous shrinkage priors when estimating coefficients with moderate signal strength. Importantly, TRADER aligns well with the principles of several established Bayesian information borrowing priors, including the meta-analytic predictive prior, commensurate prior, and unit information prior.

What are your plans after graduation?

I am currently seeking a postdoctoral position in the United States. My primary research focuses on the intersection of genetics and statistics, with the goal of developing statistical methods that offer strong theoretical foundations, robust empirical performance, and

practical algorithms for real-world applications. Additionally, I am always interested in opportunities within the industry. In fact, TRADER was motivated during my internship in the Global Statistics and Data Science department at BeiGene, where I designed an R Shiny app that integrates multiple Bayesian methods to control covariate imbalance between treatment and control groups when borrowing information from historical clinical trials.

THIRD PRIZE:

Xiaohan Chi
The University of Texas MD Anderson Cancer Center

TITLE:

OP2-Comb Bayesian Optimal Phase II Design for Optimizing Doses and Assessing Contribution of Components in Drug Combinations

What is your paper about?

This paper describes a very easy-to-use Bayesian optimal phase II design for drug combinations (BOP2-Comb). To better align with Project Optimus, the BOP2-Comb design achieves two goals within the same trial framework: optimizing the combination dose and evaluating the contribution of each component in the drug combination. BOP2-Comb is optimized through a calibration scheme that minimizes the total trial sample size and controls incorrect decision rates. This calibration procedure is Monte Carlo simulation-free and provides a theoretical guarantee of false-positive control.

What are your plans after graduation?

After graduation, I will definitely continue delving into the field of clinical trials, further developing my expertise and applying my skills to impactful research. While I may prefer to pursue a faculty position, I am currently open to exploring both academia and industry opportunities.

HONORABLE MENTIONS

Xinying Fang
Pennsylvania State University

TITLE:

Generalized Multi-stage Optimal Design for Phase II Studies with Particle Swarm Optimization

Summary: Our work presents a new approach to optimizing Phase II clinical trials, addressing the high costs and low success rates of drug development. We introduce a framework with a unified objective function for multi-stage designs, encompassing various optimality criteria for multi-stage designs. Additionally, we propose an advanced particle swarm optimization method, named PSO-GO, to overcome computational challenges, making multi-stage designs more feasible. The methodology, supported by theoretical foundations, simulations and a real-world case study, offers practical improvements over current trial designs, balancing scientific rigor with computational efficiency for Phase II trials.

Runjia Li
University of Pittsburgh

TITLE:

A Doubly Robust Instrumental Variable Approach for Estimating Average Treatment Effects in Time-to-Event Data with Unmeasured Confounding: Application to Real-World Data on ICU Patients with Septic Shock

Summary: This paper proposes a novel instrumental variable (IV) estimator to assess the average treatment effect (ATE) in time-to-event data in the presence of unmeasured confounding, addressing limitations in existing methods that rely on strong parametric assumptions. The proposed estimator is doubly robust, asymptotically efficient, and adaptable to machine learning models, making it suitable for complex real-world data. Through simulations, it demonstrates strong statistical properties. Applying this method to electronic health records (EHR) of ICU patients, with physician prescribing preferences as the IV, the study finds no significant benefit or harm of hydrocortisone on mortality. This approach provides reliable causal estimates despite unmeasured confounding, aiding clinical decision-making.

Lei Yan
Florida State University, Department of Statistics

TITLE:
Optimizing Quality Tolerance Limits Monitoring in Clinical Trials Through Machine Learning Methods

Summary: This paper introduces a machine learning enabled approach to facilitate real-time, automated monitoring of Quality Tolerance Limits (QTLs) in clinical trials. Unlike the traditional quality assurance process, where QTLs are evaluated based on single-source data and arbitrary defined fixed threshold, our QTL-ML framework integrates information from multiple clinical domains to predict the clinical QTL of variety types at program, study, site and patient level. Moreover, our approach is assumption-free, relying not on historical expectations but on dynamically accumulating trial data to predict quality tolerance limit risks in an automated manner. Embedded within ICH-E6 recommended risk-based monitoring principles, this innovative machine learning solution for QTL monitoring has the potential to transform sponsors' ability to protect patient safety, reduce trial duration, and lower trial costs.

Jialing Liu
University of Minnesota, Division of Biostatistics and Health Data Science

TITLE:
Variable Selection and Prediction for Longitudinal Data Using Bayesian Transfer Learning

Summary: Contemporary longitudinal data typically involve high-dimensional time-course measurements on small samples, making model estimation challenging due to variability and unstable predictions. It's natural to borrow information from additional datasets with similar covariate-outcome relations to improve inference in the target data. We propose a novel Bayesian transfer learning model for longitudinal data (BTLL) that uses mixture models to adaptively account for differences between source and target outcome parameters. This approach minimizes bias by limiting inappropriate information transfer, and simulation studies demonstrate that BTLL significantly enhances parameter precision and reduces bias in heterogeneous settings.

Siyi Liu
North Carolina State University (graduated in December, 2024)

TITLE:
Improved inference for survival heterogeneity of treatment effect leveraging trial and observational studies

Summary: This paper aims at leveraging observational studies to enhance the inference of the heterogeneity of treatment effect for time-to-event outcomes while addressing unmeasured confounding. To achieve this, a confounding function is introduced to quantify the discrepancy between observed and causal treatment effects based on measured covariates, and it facilitates the identification and construction of an integrative estimator by minimizing a penalized loss function. The proposed estimator demonstrates a promising convergence rate, asymptotic normality, and efficiency at least equal to that of the trial estimator, with its effectiveness further validated through simulations and real-world application.

With this year's competition coming to an end, we want to give a big shout-out to all the winners for their incredible achievements and hard work. Your success is truly inspirational! To everyone who participated, we appreciate your efforts and enthusiasm. Keep working on your skills and passions. We can't wait to see you shine in the years to come. Keep going, keep dreaming, and keep achieving!

UPCOMING CONFERENCES

2025 ASA Biopharmaceutical Section Regulatory-Industry Statistics Workshop

The ASA Biopharmaceutical Section Regulatory- Industry Statistics Workshop is sponsored by the ASA Biopharmaceutical Section in cooperation with the FDA Statistical Association. The conference will be held from September 24-26, 2025 in Rockville Maryland, with invited sessions co-chaired by statisticians from industry, academia, and the FDA. Short courses will be offered on the first day of the workshop. To register, please visit: *https://ww2.amstat.org/meetings/risw/2025/*

Early Registration Opens: June 11, 2025
Early Registration Closes:August 12, 2025

2025 WNAR of IBS

The WNAR 2025 will be held in Whistler, B.C., Canada from June 15-18, 2025. To register, please visit: *https://wnarofibs.wildapricot.org/wnar2025.*

JSM 2025

Joint Statistical Meetings (JSM) will be held in Nashville, Tennessee from August 2-7, 2025. It is one of the largest statistical events and the broadest, with topics ranging from statistical applications to methodology and theory to the expanding boundaries of statistics, such as analytics and data science. JSM also offers a unique opportunity for statisticians in academia, industry, and government to exchange ideas and explore opportunities for collaboration. To register, please visit: *https://ww2.amstat.org/meetings/jsm/2025/.*

Early Registration Opens: May 1, 2025
Early Registration Closes: June 3, 2025

DIA 2025

The DIA 2025 Global Annual Meeting will be held in Washington DC from June 15-19, 2025. It invites industry, regulators, governments, academics, innovators, and patients to network, problem-solve, and discuss global and local challenges facing the life sciences community. DIA 2025 will amplify different perspectives while highlighting expertise across the globe to reimagine current processes that better enhance health and well-being. To register, please visit: *https://www.diaglobal.org/en/flagship/dia-2025*.

Standard Registration Closes: May 15, 2025

13th International Conference on Multiple Comparison Procedures (MCP–2025)

The MCP-2025 will be held from August 12-15, 2025, at the Center City Campus of Temple University, Philadelphia, PA. The conference will bring together statisticians from academia, government, and industry to explore the latest advancements in multiple comparison procedures and related methodologies. To register, please visit: *https://isbiostat.org/*.

Online Registration Opens: May 15, 2025

Women in Statistics and Data Science 2025

The 2025 Women in Statistics and Data Science Conference will be held in Cincinnati, Ohio. WSDS will gather professionals and students from academia, industry, and the government working in statistics and data science. Find unique opportunities to grow your influence, your community, and your knowledge. To register, please visit: *https://ww2.amstat.org/meetings/wsds/2025/*.

Early Registration Opens: June 30, 2025

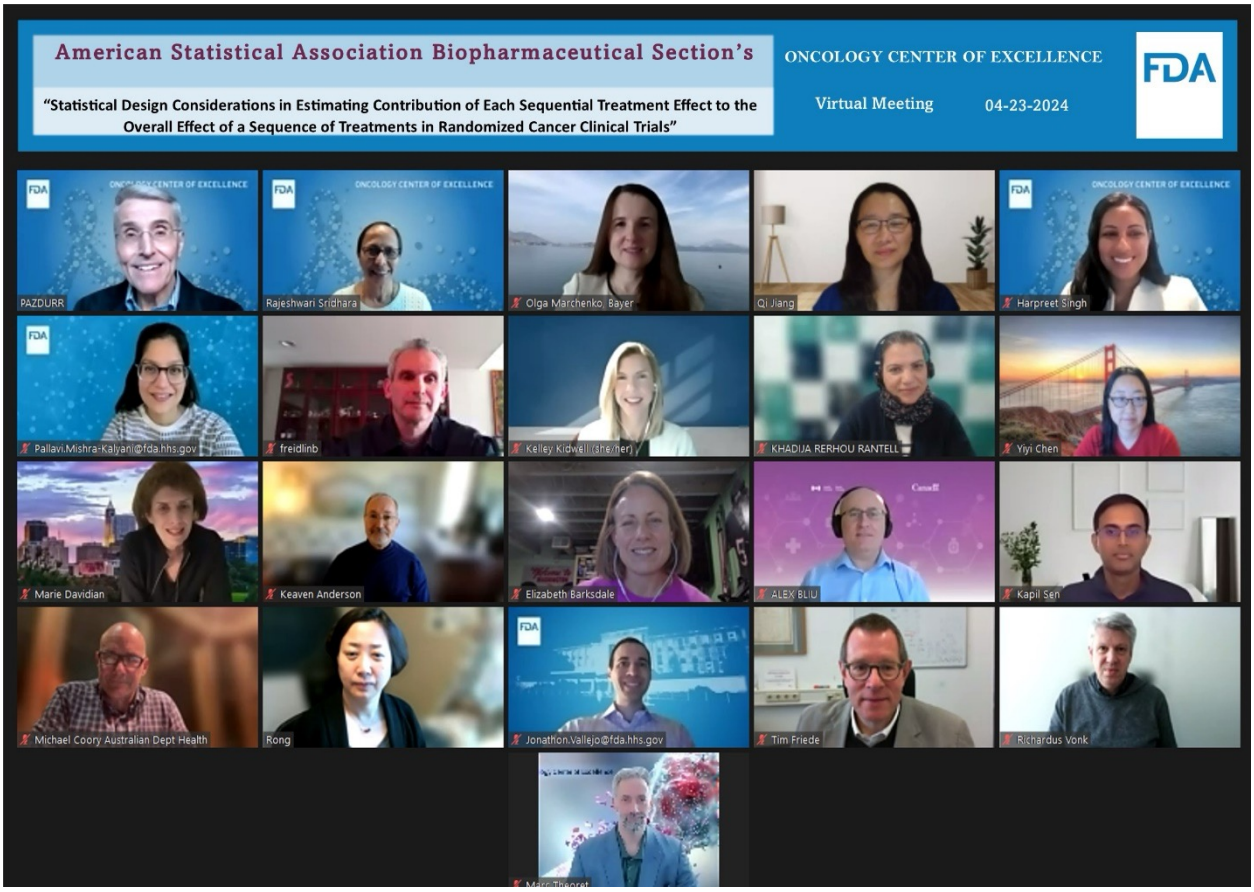
SUMMARY OF ASA BIOP SECTION'S VIRTUAL DISCUSSION WITH REGULATORS ON STATISTICAL DESIGN CONSIDERATIONS IN ESTIMATING CONTRIBUTION OF EACH SEQUENTIAL TREATMENT EFFECT TO THE OVERALL EFFECT OF A SEQUENCE OF TREATMENTS IN RANDOMIZED CANCER CLINICAL TRIALS

Rajeshwari Sridhara (FDA), Olga Marchenko (Bayer), Qi Jiang (Pfizer), Elizabeth Barksdale (LUNGevity Foundation), Yiyi Chen (Pfizer), Marc Theoret (FDA)

On April 23rd, 2024, the American Statistical Association (ASA) Biopharmaceutical Section (BIOP) and LUNGevity Foundation hosted a virtual forum to discuss Statistical Design Considerations in Estimating Contribution of Each Sequential Treatment Effect to the Overall Effect of a Sequence of Treatments in Randomized Cancer Clinical Trials. This forum was part of a series conducted under the guidance of the U.S. FDA Oncology Center of Excellence's Project SignifiCanT (Statistics in Cancer Trials). The goal of Project SignifiCanT is to advance cancer drug development through collaboration and engagement among various stakeholders in the design and analysis of cancer clinical trials. The discussion was organized jointly by the ASA BIOP Statistical Methods in Oncology Scientific Working Group, the FDA Oncology Center of Excellence (OCE), and LUNGevity Foundation.

Anti-cancer therapies, or regimens, increasingly comprise sequences of treatments, such as (1) neoadjuvant therapy, surgery, and adjuvant treatment in early-stage solid tumors; or (2) induction therapy, consolidation (with or without hematopoietic stem cell transplant), and maintenance therapy in some hematological malignancies. In clinical trials evaluating sequential treatments, patients are typically randomized at the start and the treatment effect is assessed as a treatment policy encompassing all sequential treatments without re-randomization. However, this approach does not enable evaluation of the contribution of each phase of the sequence to the overall combined effect. Re-randomization at initiation of each phase can help assess their contribution to treatment effect, but may add complexity to the trial design, conduct, and analyses due to the diminishing number of eligible patients for subsequent randomizations. Recent advances in innovative clinical trial designs, such as Sequential Multi-arm Randomized Trials (SMART), allow for evaluation of a sequence of treatments and are currently being used in oncologic and non-oncologic diseases. This open forum discussion among multi-disciplinary experts examined the potential use of SMART and other innovative clinical trial designs to better understand the contribution of each phase of sequential treatments to the overall treatment effect in cancer trials.

The speakers/panelists* for the discussion included members of the BIOP Statistical Methods in Oncology Scientific Working Group representing pharmaceutical companies; representatives from international regulatory agencies (Food and Drug Administration (FDA), Health Canada (HC), Medicines and Healthcare products Regulatory Agency (MHRA), and Therapeutic Goods Administration (TGA)); clinicians; academicians; and expert statisticians. In addition, over 100 participants attended the virtual meeting, including representatives from other international regulatory agencies (Brazilian Health Regulatory Agency (ANVISA), Health Sciences Authority (HAS), European Medicines Agency (EMA), Singapore; Ministry of Health, Israel; Pharmaceuticals and Medical Devices Agency (PMDA), Japan). The discussions were moderated by the BIOP Statistical Methods in Oncology Scientific Working Group co-chairs, Dr. Olga Marchenko from Bayer and



Dr. Qi Jiang from Pfizer; Dr. Elizabeth Barksdale from LUNGevity Foundation; and Dr. Rajeshwari Sridhara, consultant from OCE, FDA.

In the introductory presentation, the OCE leadership discussed two examples of planned sequential treatments in oncology trials. The first was a trial for Rituxan in diffuse large B cell lymphoma (DLBCL), where patients were randomized to standard of care in the first phase, and responders from both arms were re-randomized to receive either Rituxan or placebo in the second phase. In the second example, patients with resectable non-small cell lung cancer (NSCLC) were randomized to platinum-based chemotherapy with or without an immune checkpoint inhibitor (ICI) prior to surgery. After surgery, patients in the experimental arm (i.e., chemotherapy plus ICI) continued to receive the immune checkpoint inhibitor for up to one year while those on the control arm received placebo. The concern highlighted by these examples is whether all treatments in a sequence are necessary to achieve the overall treatment effect, and how best to design or analyze trials to address this question

The speaker, from academia, provided an overview of the SMART approach: utilizing a multi-stage randomized design that allows for the evaluation of treatment effects of sequential treatments and their components, and leads to the development of dynamic treatment regimens (DTRs). These trials are helpful when there may be delayed, prescriptive, or sample selection effects. SMARTs involve at least two randomizations of all trial participants at critical decision points and provide robust evidence for effective DTRs: evidence-based guidelines for clinical practice that account for ongoing treatment decisions based on factors such as progress, side effects, and patient preferences. The speaker also discussed design and analysis of SMART, including sample size considerations, the use of SMART-specific methods like inverse probability of treatment weighting, and the availability of resources and workshops for those interested in learning more about SMART.

The key points raised in the panel discussion following the presentation were:

- The FDA expressed concerns about potential overtreatment in perioperative trials, especially for early-stage cancer patients, and iterated that exploration of innovative designs to evaluate the contribution of each phase of a sequence to the overall treatment effect is important. SMART designs can efficiently evaluate treatment sequences by comparing treatment regimens, but potential efficiency gains should be

weighed against feasibility burdens, such as patient anxiety, data management challenges, and varying dropout rates.

- Companies are increasingly recognizing the importance of demonstrating the efficacy of each treatment in a sequence. However, using surrogate endpoints, such as pathological complete response (pCR), for re-randomization in SMART designs can be challenging due to their questionable predictive value for ultimate endpoints like overall survival (OS) and event-free survival (EFS), making it difficult to draw definitive conclusions about the efficacy of individual treatment components.

- Alternative designs, such as factorial design, four-arm trials, or three-arm trials comparing control, neoadjuvant only, and neoadjuvant plus adjuvant arms, could provide insights into the contribution of adjuvant therapy to the total treatment effect.

- SMART designs typically involve a single consent at the beginning, which can include the potential for multiple randomizations and can be reassuring for patients; they do not inherently introduce additional bias compared to other trial designs, but they are not commonly proposed by sponsors.

- SMART approach will not be appropriate in all situations. Trial design must take into account the main objective(s) of the development program, potential for dropout, and other operational challenges (e.g., number of sites, sample size, etc.).

This forum provided an opportunity to have open scientific discussion among a diverse multidisciplinary stakeholder group – clinicians, epidemiologists, and statisticians from academia and pharmaceutical companies, patient advocates, and international regulators-focused on emerging statistical issues in cancer drug development. This collaborative forum highlighted the promise of SMART designs to improve patient outcomes, while recognizing the logistical and analytical complexities with such designs.

Acknowledgement: Authors thank Joan Todd (FDA) and Syed Shah (FDA) for technical support.

*** Speakers/ Panelists:**

Dr. Keaven Anderson (Merck), Dr. Elizabeth Barksdale (LUNGevity Foundation), Dr. Alex Bliu (Health Canada), Dr. Michael Coory (TGA, AU), Prof. Marie Davidian (North Carolina State University), Dr. Boris Freidlin (National Cancer Institute), Prof. Tim Friede (University Medical Center Göttingen), Dr. Qi Jiang (Pfizer), Prof. Kelley M. Kidwell (University of Michigan), Dr. Rong Liu (Regeneron), Dr. Olga Marchenko (Bayer), Dr. Pallavi Mishra-Kalya (FDA), Dr. Richard Pazdur (FDA), Dr. Khadija Rantell (MHRA, UK), Dr. Kapil Sen (BMS), Dr. Harpreet Singh (FDA), Dr. Rajeshwari Sridhara (FDA), Dr. Marc Theoret (FDA), Dr. Jonathon Vallejo (FDA), Dr. Xian Zhou (AstraZeneca)

SUMMARY OF ASA BIOP SECTION'S VIRTUAL DISCUSSION WITH REGULATORS ON TRIAL CONSIDERATIONS IN INDOLENT CANCERS WITH OVERALL SURVIVAL AS A SAFETY ENDPOINT

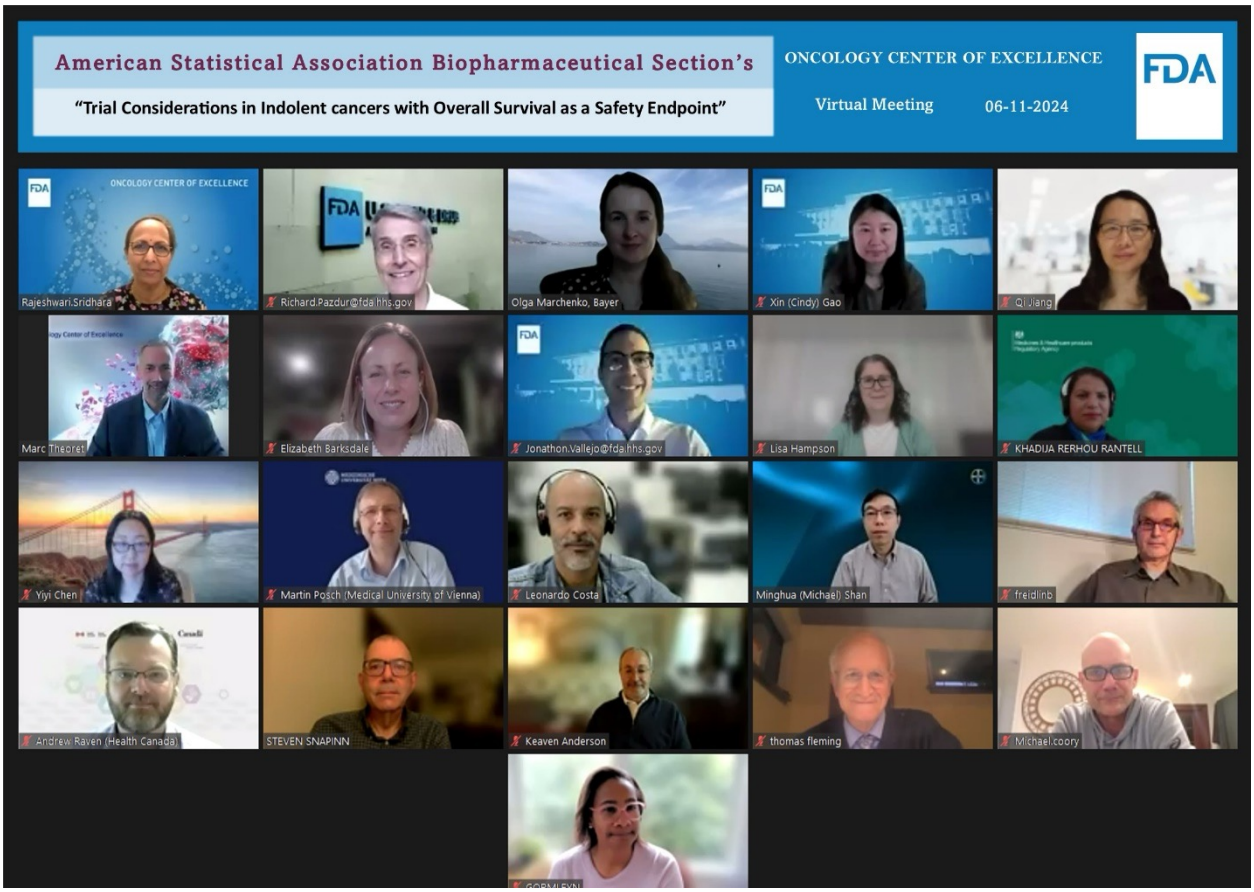
Rajeshwari Sridhara (FDA), Olga Marchenko (Bayer), Qi Jiang (Pfizer), Elizabeth Barksdale (LUNGevity Foundation), Yiyi Chen (Pfizer), Marc Theoret (FDA)

On June 11, 2024, the American Statistical Association (ASA) Biopharmaceutical Section (BIOP) and LUNGevity Foundation hosted a virtual forum to discuss Trial Considerations in Indolent Cancers with Overall Survival as a Safety Endpoint. This forum was part of a series conducted under the guidance of the U.S. FDA Oncology Center of Excellence's Project SignifiCanT (Statistics in Cancer Trials) and the third discussion on Overall Survival (OS) considerations in indolent cancer trials. The goal of Project SignifiCanT is to advance cancer drug development through collaboration and engagement among various stakeholders in the design and analysis of cancer clinical trials. The discussion was organized jointly by the ASA BIOP Statistical Methods in Oncology Scientific Working Group, the FDA Oncology Center of Excellence (OCE), and LUNGevity Foundation.

Progression-free Survival (PFS) is generally considered the primary endpoint for regulatory decision-making in indolent or chronic cancers. In randomized clinical trials for these conditions, OS is commonly evaluated as a secondary efficacy endpoint. However, due to the long course of such chronic diseases, a limited number of OS events are typically observed at the time of PFS analysis. Therefore, when assessing the benefit-risk profile of a treatment, it is crucial to evaluate OS as a safety endpoint to ensure there is no detrimental effect on survival. This open forum discussion among multi-disciplinary experts explored design considerations for randomized trials that incorporate OS as a safety endpoint, as is often done for indolent cancers.

The speakers/panelists* for the discussion included members of the BIOP Statistical Methods in Oncology Scientific Working Group representing pharmaceutical companies, representatives from international regulatory agencies (Food and Drug Administration (FDA), Health Canada (HC), Medicines and Healthcare products Regulatory Agency (MHRA), Therapeutic Goods Administration (TGA), and Brazilian Health Regulatory Agency (ANVIS)), clinicians, academicians, and expert statisticians. In addition, over 100 participants attended the virtual meeting, including representatives from other international regulatory agencies (Health Sciences Authority (HAS), European Medicines Agency (EMA), Singapore; Ministry of Health, Israel; Pharmaceuticals and Medical Devices Agency (PMDA), Japan). The discussions were moderated by the BIOP Statistical Methods in Oncology Scientific Working Group co-chairs, Dr. Olga Marchenko from Bayer and Dr. Qi Jiang from Pfizer; Dr. Elizabeth Barksdale from LUNGevity Foundation; and Dr. Rajeshwari Sridhara, consultant from OCE, FDA.

In the introductory presentation, OCE leadership discussed the challenges and considerations surrounding OS as an endpoint in clinical trials for indolent or chronic cancers. In these cancers, where patients often survive for 5-10 years or more, using OS as a primary endpoint is impractical due to time constraints. Instead, PFS or disease-free survival (DFS) are commonly used as primary efficacy endpoints. Recent discussions, including the Oncologic Drugs Advisory Committee (ODAC) meeting in April 2022 and subsequent panels, raised concerns about potential detrimental effects on OS in some trials and emphasized the need for pre-planned OS interim analysis at the time of final PFS analysis, with pre-set criteria for detrimental OS effect. Questions posed to panelists from academia, industry, and regulatory bodies included the following: Is it rea-



sonable to evaluate OS as a safety endpoint in indolent cancers? And, if so, what are the critical considerations, minimum data requirements, and potential challenges in establishing detrimental effect criteria?

The speaker, from industry, introduced a noninferiority approach to ensure that new treatments do not have an unacceptably detrimental effect on OS, acknowledging the challenges of limited OS data in cancers with typically long survival times (Fleming et al, 2024). The method uses clinically informed parameters, such as hazard ratios for unacceptable detriment (HR null) and plausible benefit (HR alt), and the number of deaths feasible to accrue in a reasonable time to set thresholds at interim and final analyses. These thresholds help balance the risks of both false negative and false positive errors, while recognizing the need for decision-making under high uncertainty. The guidelines are flexible, allowing for tailoring to specific indications and disease settings. By providing a structured framework, this approach aims to facilitate transparent discussions between stakeholders about acceptable risk trade-offs in drug development for indolent cancers. An R package, monitOS (*https://cran.r-project.org/web/packages/monitOS/index.html*), is publicly available for implementing the guidelines.

The key points raised in the panel discussion following the presentation were:

- OS remains a critical endpoint for evaluating both efficacy and safety, even when it is not the primary endpoint.

- Like previously set guidelines for monitoring safety in diabetes clinical trials, Fleming et al proposed monitoring guidelines balancing false positive and negative error rates; unlike group sequential guidelines, these are not anticipated to prompt trial termination.

- Results presented by industry suggest that it is not possible to have a procedure that protects against OS detrimental effect without rejecting a large proportion of treatments.

- Pre-specifying OS thresholds and criteria for ruling out harm is essential for interpreting early OS data; this will require prospective discussions between sponsors and regulators.

- Alternative statistical methods, such as repeated confidence intervals, restricted mean survival time (RMST) test, or Bayesian methods, may be useful in certain scenarios.

- The challenge of achieving targeted death events in a relevant timeframe (e.g., 5 years) needs to be anticipated and addressed with appropriate methods.

- Comprehensive OS analysis should incorporate safety considerations (e.g., dose modifications, toxicities) and quality of life measures. The willingness to accept safety risks may depend on disease severity and available treatment options, with less tolerance for risk in indolent cancers.

- Capturing exposure to effective agents, including subsequent therapies, is important for understanding OS effects.

- Designs with control arm crossover to the experimental agent (that is not approved in the subsequent line) confound OS safety signal.

- To capture the relevant OS safety signal in the population of interest, trials should be restricted to countries with comparable standard of care.

- Interpretability of OS analyses rely on longer term data integrity. Long-term follow-up is crucial for detecting OS detriments in indolent cancers.

This forum provided an opportunity to have open scientific discussion among a diverse multidisciplinary stakeholder group – clinicians, epidemiologists, and statisticians from academia, pharmaceutical companies, patient advocates, and international regulators- focused on emerging statistical issues in cancer drug development.

Acknowledgement: Authors thank Joan Todd (FDA) and Syed Shah (FDA) for technical support.

*** Speakers/ Panelists:**

Dr. Keaven Anderson (Merck), Dr. Elizabeth Barksdale (LUNGevity Foundation), Dr. Michael Coory (TGA, AU), Dr. Leonardo Costa (ANVIS, BR), Prof. Thomas Fleming (University of Washington), Dr. Boris Freidlin (National Cancer Institute), Prof. Tim Friede (University Medical Center Göttingen), Dr. Xin (Cindy) Gao (FDA), Dr. Nicole Gormley (FDA), Dr. Lisa Hampson (Novartis), Dr. Qi Jiang (Pfizer), Dr. Olga Marchenko (Bayer), Dr. Richard Pazdur (FDA), Prof. Martin Posch (Center for Medical Statistics, Informatics, and Intelligent Systems at the Medical University of Vienna), Dr. Khadija Rantell (MHRA, UK), Mr. Andrew Raven (Health Canada), Dr. Minghua (Michael) Shan (Bayer), Dr. Steve Snapinn (Independent Consultant), Dr. Rajeshwari Sridhara (FDA), Dr. Marc Theoret (FDA), Dr. Jonathon Vallejo (FDA)

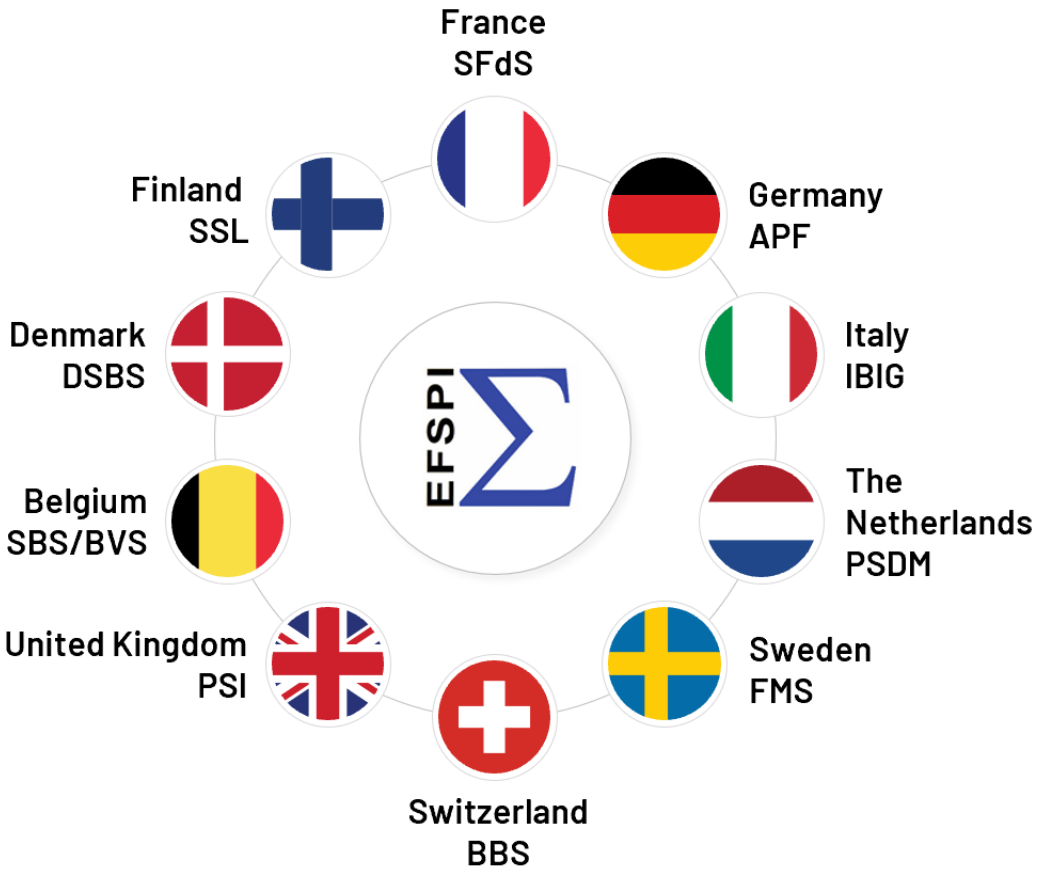
Reference:

Fleming, T. R., Hampson, L. V., Bharani, B.-D., Bretz, F., Chakravartty, A., Coroller, T., Koukouli, E., Wittes, J., Yateman, N. and Zumber, E. (2024), 'Monitoring overall survival in pivotal trials in indolent cancers', *Statistics in Biopharmaceutical Research* . doi: 10.1080/19466315.2024.2365648.

THE EVOLVING ROLE OF STATISTICIANS IN THE PHARMACEUTICAL INDUSTRY: EFSPI'S CONTRIBUTION TO EXCELLENCE

Justine Rochon (Boehringer Ingelheim) on behalf of EFSPI

The pharmaceutical industry is witnessing a transformative era where statistical innovation and artificial intelligence are reshaping the landscape of drug development, including not only regulatory science but also health technology assessment. In this context, the European Federation of Statisticians in the Pharmaceutical Industry (EFSPI) plays a pivotal role. Founded in 1992, EFSPI serves as a non-profit umbrella organization for ten national statistical associations, representing approximately 4,000 professionals across Europe.



EFSPI's Mission and Vision

EFSPI's mission is to uphold professional standards and enhance the stature of the statistical profession within the European pharmaceutical industry. By providing collective expert input on statistical matters to national and international authorities, EFSPI ensures that the voice of statisticians is heard in crucial discussions and considered in policy making. The organization also fosters the exchange of information and harmonization of statistical practices among its member groups.

A Brief History

The federation's journey began in 1990, with the official launch following in 1992. Over the years, EFSPI has grown to include 10 member groups from different

European countries. Each member organization has two representatives in EFSPI's Council. The organization has maintained its focus on professional standards and collaboration through regular council meetings and the establishment of special working and interest groups to tackle industry-specific scientific and leadership challenges.

Engaging with the Community

EFSPI's commitment to the community is evident through its various initiatives. For example, the European Special Interest Groups (ESIGs) play a crucial role in connecting professionals across disciplines and fostering collaboration on joint topics of interest. For more information, please visit *https://efspi.org/EFSPI/SIGS/EFSPI/Special_Interest_Groups/SIGS.aspx*.

Another example is the Statistics Leaders Forum, which was established in 2010 and brings together senior leaders to address strategic challenges and share leadership developments within the industry. This year's 16th annual Statistics Leaders Meeting will take place from 12th to 13th May 2025, in Copenhagen, Denmark.

Lastly, in September 2023, EFSPI launched the Statistical Methodology Leaders Group to connect statistical methodology leaders across Europe. This initiative focuses on sharing best practices, developing and deploying new statistical methods, and implementing statistical innovation within organizations. It aims to anticipate future trends, drive innovation, manage stakeholder relationships, and inspire talent seeking non-traditional career paths. The group fosters collaboration and critical strategic thinking in statistical methodology through regular meetings and interactions with key stakeholders. For more details, please visit *https://efspieurope.github.io/efspi/methods/methods_intro.html*.

EFSPI's Annual Flagship Event

EFSPI's flagship event is the Regulatory Statistics Workshop, which has become a key platform for dialogue between the pharmaceutical industry, regulatory agencies, health technology assessment bodies, and academia. The workshop emphasizes collaboration and focuses on open dialogue on statistical and regulatory decision science. The next workshop is scheduled for the 10th to 12th of September 2025 at the Biozentrum in Basel, Switzerland, and it promises to uphold the tradition of excellence established by previous events. This year is particularly special as we celebrate the 10th anniversary of the workshop! We warmly invite all participants, whether joining in person or online, to be part of this landmark celebration. This event is not just an opportunity to reflect on the past decade's achievements but also a time to look forward with optimism to the future collaborations, interactions, and advancements that will shape our field.

For more information and to access materials from previous workshops, please visit the workshop website at *https://efspieurope.github.io/workshop/next.html*.

Embracing the Future

Looking ahead, EFSPI is focusing on business continuity, strengthening its strategic partnerships, enhancing its branding and visibility, and transforming into a federation that makes a difference today and into the future. Initiatives like the EFSPI Scientific and Training Academy, the NextGen movement, and engagement with key stakeholders such as the European Medicines Agency (EMA), the European Federation of Pharmaceutical Industries and Associations (EFPIA), and the American Statistical Association (ASA) are evidence of this forward-thinking approach.

With regards to EMA, just recently, EFSPI made contributions to the ACT EU Workshop on ICH E6 R3 at EMA in Amsterdam, which focused on the revised guidelines for Good Clinical Practice (GCP). EFSPI's involvement in this workshop underscores its commitment to ensuring that statisticians remain at the forefront of industry standards and practices. For those interested in exploring the workshop materials, including video recordings and slides, please visit the event page *https://www.ema.europa.eu/en/events/act-eu-workshop-ich-e6-r3-principles-annex-1*.

EFSPI actively participates in an industry focus group for future EU electronic submissions, known as the clinical data submission pilot. This EMA-led initiative, which includes an advisory industry group, aims to enhance data value in submissions. The focus group, with EFSPI holding three seats including the chair, works closely with EFPIA. The ongoing initiative has recently released an interim report which is available at *https://www.gmp-compliance.org/gmp-news/interim-report-on-emas-clinical-study-data-proof-of-concept-pilot*.

Another example is EFSPI's recent letter, which expresses our support for efforts to advance open-source collaboration in statistical engineering and clinical reporting. We believe that cross-company collaborations, such as openstatsware (*https://www.openstatsware.org/*) and pharmaverse (*https://pharmaverse.org/*), offer unique opportunities to harmonize methodologies, standardize practices, and create accessible platforms for innovation in statistical analysis.

Conclusion

EFSPI's role in the pharmaceutical industry has become increasingly vital as it champions scientific excellence and adapts to the changing environment. Through the application of critical thinking and statistical knowledge, EFSPI not only aids existing professionals but also plays a pivotal role in developing future leaders and drug developers with a strong emphasis on statistics. As the industry evolves, EFSPI emerges as a pillar of knowledge, fostering collaboration and driving statistical innovation.

For more information on EFSPI's activities and resources, including previous workshops and webinars, please visit our website at *www.efspi.org* and follow EFSPI on LinkedIn (*https://www.linkedin.com/company/efspi/*).

RECAP: 2025 BIOSTATISTICS SYMPOSIUM OF SOUTHERN CALIFORNIA (BSSC)

Nicole (Xiaoyun) Li (BeOne Medicines), Larry Shen (Pharmapace, Inc.), Gajanan Bhat (TORL BioTherapeutics), Lindsay Younis (Children's Oncology Group), Thomas Lin, Jihao Zhou (BlossomHill Therapeutics, Inc.), Olga Korosteleva (California State University, Long Beach), Cathy Cai (Pharmapace, Inc.)

Highlights

- **2025 Biostatistics Symposium of Southern California (BSSC)** is the inaugural symposium and a landmark event that brought together **250 participants, 28 sponsors,** and a powerful lineup of speakers, panelists, and presenters.
- **Keynotes & Presentations:** The symposium featured eight keynote speakers and panelists representing diverse roles in life science development, all centered around the theme: *"Transforming Life Sciences through Data Analytics, Innovation & Collaboration."* A total of 56 invited presentations were delivered across three distinct tracks—**Clinical and Statistics, Data Science and Analytics, and Academic Research**—alongside 16 poster presentations from students and postdoctoral researchers. A dedicated panel discussion on career opportunities for graduates further enriched the program. Together, these sessions highlighted cutting-edge research and fostered meaningful collaboration between industry and academia, while also empowering the next generation of biostatisticians.
- **Community Engagement and Impact:** The symposium was a collaborative effort supported by three ASA chapters in Southern California: the Orange County and Long Beach Chapter, the San Diego Chapter, and the Southern California Chapter. This joint initiative fostered a unified biostatistics community across the region, expanding engagement beyond individual chapters. It also strengthened interdisciplinary connections among industry leaders, academic institutions, nonprofit organizations, students, and early-career professionals, promoting collaboration and advancing the field of biostatistics

The inaugural Biostatistics Symposium of Southern California (BSSC) took place on February 21–22, 2025, at the Renaissance Newport Beach Hotel in Newport Beach, CA.

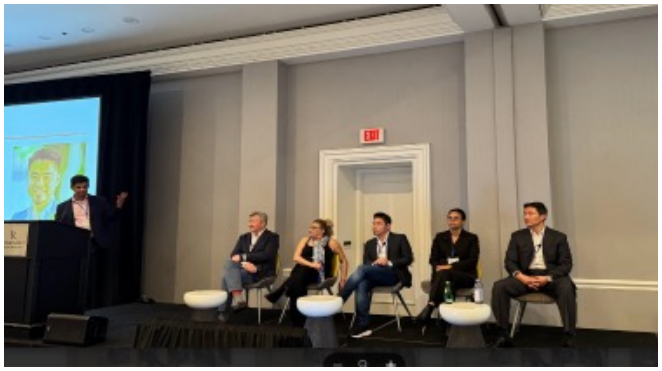
This two-day statistics symposium with the theme "Transforming Life Sciences through Data Analytics, Innovation & Collaboration" made a significant milestone with 250 attendees.

The morning of Day 1 featured three insightful keynote presentations:

Dr. Susan Abushakra, Chief Medical Officer at Alzheon, presented on the *Development of New Medicines for Alzheimer's Disease.* She shared the scientific journey behind advancing treatments for Alzheimer's, highlighting the challenges, emerging opportunities, and the essential collaboration between clinicians and statisticians in driving innovation.

Dr. Joycelynne Palmer, Ph.D., Director of the Division of Biostatistics at City of Hope National Medical Center, presented on *The Changing Landscape of Early-Phase Cell and Immunotherapy Clinical Trials in Oncology*. She provided an in-depth overview of evolving approaches in early-phase oncology trials and offered valuable insights into how statisticians can play a pivotal role in shaping drug development strategies.

Following the keynote speaker session, BSSC Director Dr. Gajanan Bhat led an engaging Q&A and panel discussion on Technological Advancements and Productivity in Drug/Device Development. The session featured a distinguished panel of experts, including Dr. Susan Abushakra, Dr. Peter Chang, Allen Keel, Dr. Joycelynne Palmer, and Adrian Hsing, with Dr. Bhat serving as the moderator.



Allen Keel, Senior Director of Innovation & Advanced Technology at Edwards Lifesciences, presented on *Needs-Driven Innovation: What Drives New Product Categories.* He shared real-world examples of how identifying unmet needs can lead to the creation of entirely new product categories in the medical device industry, highlighting the critical intersection of innovation, collaboration, and patient-focused design.

In the afternoon, the symposium broke into three well-attended parallel tracks: *Clinical and Statistics, Data Science and Analytics,* and *Academic Research.* Each track featured a series of insightful invited presentations, sparking lively discussions and knowledge sharing among attendees.

The first day of the symposium concluded with a beautiful reception held in the courtyard of the Renaissance Hotel, set against the backdrop of a stunning sunset. Guests enjoyed delicious food, lively music, and great company, making for a perfect end to an inspiring and productive day.

The morning of Day 2 of the symposium kicked off with three compelling keynote speakers.

Dr. Bill Rote, Senior Vice President of Research & Development at Travere Therapeutics, who delivered an insightful presentation on GLP-1 Agonists. He took the audience through the fascinating journey of these groundbreaking therapies, highlighting their rapid development and transformative impact on the treatment of chronic conditions.

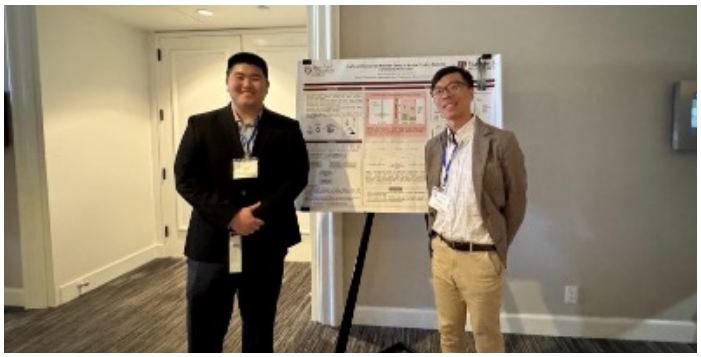
Dr. David Zhang, Chief Strategy Officer at Abivax, took the stage next with his keynote on "Pursuing a Broader Role as a Statistician." He shared his personal career journey, highlighting how he evolved beyond the traditional role of a statistician to take on broader strategic responsibilities in the biopharmaceutical industry.

Dr. Ronald L. Wasserstein, Executive Director of ASA, gave an engaging presentation on moving beyond $p<0.05$. He discussed the long-standing issues with using statistical significance as a measure of scientific worth and why he advocates for its end. With humor and clarity, he explained the challenges of making this shift and the benefits of adopting alternative approaches in science and statistics.

The rest of Day 2 featured presentations across the three parallel tracks, culminating in the Student/Postdoc Poster Competition in Biostatistics. The competition showcased exceptional talent from across Southern California. Sixteen posters were displayed at the event, prepared by undergraduate, master's, and Ph.D. students representing the University of California, Los Angeles; California State University, San Bernardino; University of Southern California; University of California, Santa Barbara; University of California, San Diego; Chapman University; and University of California, Riverside.

Top honors went to **Ami Sheth** (University of California, Los Angeles, Ph.D.) for Best Visualization with their project on "Sparse Bayesian Multidimensional Scaling(s)," **Josephine Kaminaga** (University of California, Santa Barbara, BS) for Best Statistical Analysis with "The Geometry of Survival: Variable Selection in Radius-Specific Cox Models," and **Srisai Saavarni Chilukuri** (University of California, Riverside, BS) for Best Insight with "Neuropsychiatric Symptoms Across Levels of Cognition in Alzheimer's Disease in Down Syndrome Alzheimer's Disease and Late-Life Sporadic Alzheimer's Disease."

Honorable Mentions recognized **Anthony Gutierrez** and **Liam Daly** (California State University, San Bernardino), **Daniel Rud** (University of Southern California), **Emily Tian** (University of California, Santa Barbara), **Kevin Li** (University of California, San Diego/Stanford University), **Philip Yeung** (University of California, San Diego/University of Kansas), and **Yudi Mu** (University of California, Riverside) for their outstanding contributions.



Awards were presented during the lunch break on the second day of the symposium, followed by a poster presentation session. The event celebrated the next generation of biostatisticians and data scientists and was very well received by all participants.

For the full event agenda, visit the BSSC website: *biostatsymposium.org*

The Organizing Committee of BSSC 2025 played a crucial role in organizing the symposium and made it possible. The leaders of the Organizing Committee included Chair of the Organizing Committee, **Larry Shen,** PhD, pStat; Co-Chairs of Clinical and Statistics Committee, **Xinping Cui** and **Jin Zhou**, co-chairs of Data Science and Analytics Committee, **Weining Shen** and **Wei Cheng**; Co-chairs of Academic Committee, **Esra Kurum** and **Eric Kawaguchi**; Co-chairs for Facilities Support Committee, **Xingyu Gao** and **Kim Phan;** Co-chair for Registration Committee, **Lindsay Younis** and **Francis Lai**; Co-chairs for Budget Committee, **Pamela Hsu** and **Nicole Li;** Co-chair of Sponsorship and Outreach Committee, **Larry Shen** and **Gajanan Bhat.**

Last, we deeply appreciate our generous sponsors. We had a total of 28 sponsors that made the event a great success! Our **Diamond and Founding Sponsors-- Pharmapace, Inc. and Q2BI**, were invaluable to the event's success. Our **Gold Sponsors -- Abbvie, Edwards Life Sciences, SAS, Travere, ASA Orange County and Long Beach Chapter,** and **ClinChoice,** made tremendous contribution to the symposium. We also acknowledge our Silver Sponsors --- **Clin-Data Insight, Redbock, the Lotus Group, BeiGene, Amgen, and Alector, Silver-Bronze sponsors --- ASA and ASA BIOP section; Bronze Sponsors ---UCLA Biostatistics Department, UC Riverside, Phastar, Precision for Medicine, Emanate Biostats, Neurocrine Biosciences, UC San Diego, ASA San Diego Chapter, Clymb Clinical, Acadia, BBSW, and ASA Southern California Chapter.**

BSSC 2025 is the inaugural symposium in Southern California. The largest biostatistics event in Southern California was a great success and we look forward to continuing this landmark event annually moving forward. Thank you again for your continued support and for making the event successful.

Diamond

Pharmapace, Inc. · Q2BI

Gold

abbvie · ClinChoice · Edwards Lifesciences · OCLBASA · SAS · TRAVERE THERAPEUTICS

Silver

alector · AMGEN · BeiGene · CLINDATA INSIGHT · THE LOTUS GROUP · REDBOCK An NES Fircroft Company

Silver-Bronze

ASA · ASA Biopharmaceutical Section

Bronze

ACADIA · ASA San Diego Chapter · BSW · CLYME CLINICAL · Emanate BIOSTATS · NEUROCRINE BIOSCIENCES · phastar · PRECISION for medicine · UCLA Biostatistics · UC RIVERSIDE · UC San Diego