Dahshu IDSWG Oncology Working Group

NEWSLETTER

January 1, 2024
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Notes from the Chairs

We are pleased to present the first edition of our Oncology Working Group's Newsletter covering comprehensive compilation of insights, trends, and analyses that shed light on the evolving landscape of statistics in oncology.

Our working group, which is a part of Dahshu's Innovative Designs Scientific Working Group (IDSWG), focuses on statistical methods in oncology clinical trials, with the objectives to develop, explore, promote, and implement innovative clinical trial (DEPICT) designs in cancer drug clinical development.

The Dahshu IDSWG Oncology Working Group Newsletter is our new initiative to share information to the working group members including our achievements and key community news. Our WG members are also allowed to share to other colleagues if found the information useful. We would like to thank Dr. Haijun Ma and Dr. Fengyu Zhao for leading the newsletter initiative. In biopharmaceutical industry, innovation is the foundation. Besides the traditional statistical innovations in trial designs, AI/ML has become increasingly important in multiple fronts of drug development. We are grateful that Dr. Haoda Fu delivers us a KOL message in AI/ML applications. The rest of the newsletter includes highlights of the WG accomplishments, upcoming statistical conferences, FDA new drug approvals in cancer, and statistical bytes (statistical terms explained in layman English). Together, we believe in the power of collective action to drive evidence-based practices, advance informed decision-making, and ultimately make a difference in the lives of individuals affected by cancer.

Reach out to us if you want to participate in the working group, we are always looking out for talented and passionate volunteers (https://oncotrialdesign.github.io/join/). Amidst the challenges and conflicts that persist worldwide, we extend our heartfelt wishes for a peaceful and rejuvenating holiday season for you and your loved ones.

Dr. Philip He and Dr. Laura Fernandes
Co-chairs

Dr. Philip He

Dr. Laura Fernandez

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Taskforce Leads

Seamless development: Philip He & Yingwen Dong
Master protocols: Freda Cooner & Cindy Lu
RWD/RWE: Binbing Yu & Haijun Ma
Dose optimization: Pat Mitchell

Multiple Sessions Organized

- *"Statistical Considerations in Basket Trial Design"*, Toronto, Canada, JSM 2023
- *"Seamless Late-Stage Development in Oncology – the Past Decade in Practice"*, Toronto, Canada, JSM 2023
- *"Getting the Dose Right - FDA's Project Optimus in Practice"*, Rockville MD, Regulatory-Industry Statistics Workshop (RISW) 2023

Submitted Public Comments on FDA Draft Guidance Documents

- "Clinical Trial Considerations to Support Accelerated Approval of Oncology Therapeutics"
- "Considerations for the Design and Conduct of Externally Controlled Trials for Drug and Biological Products"
- "Decentralized Clinical Trials for Drugs, Biological Products, and Devices"
- "Optimizing the Dosage of Human Prescription Drugs and Biological Products for the Treatment of Oncologic Diseases"

Submitted Multiple Manuscripts and More are coming ...

Upcoming Conferences

- 2024 ASA Conference on Statistical Practice (CSP), Feb. 27-29, 2024
- ENAR 2024 Spring Meeting, March 10-13, 2024
- Pharmaceutical Data Science (PharmaDS) Conference 2024, March 18-19, 2024
- Duke-Industry Statistics Symposium (DISS2024), April 3–5, 2024
- The 7th Stat4Onc Annual Symposium, May 8-11, 2024
- 2024 Symposium on Data Science & Statistics, June 4–7, 2024
- 2024 WNAR/IMS/Graybill Annual Meeting, June 9-12, 2024

KOL Message: AI and Machine Learning for Drug Discovery and Development

By Haoda Fu, Ph.D. †

The fields of artificial intelligence and machine learning (AI/ML) have progressed significantly over the past decade, and we are now beginning to see their impact on drug discovery and development. This presents unique opportunities and challenges for statisticians to play a leading role as data scientists in the era of AI/ML.

In the past few years, we have observed several impactful examples of AI/ML applications in drug discovery and development. In drug discovery, AlphaFold 2 became a handy tool for understanding protein targets in 2020, and diffusion models generated promising protein binders with picomolar binding affinity without further experimental optimization in 2022. In the clinical space, digital biomarkers have augmented clinical endpoints and provided objective measurements in areas such as pain, dementia, and insomnia. This totality of evidence has facilitated better key phase III decision-making, thereby improving clinical technical success. ChatGPT and large language models attracted significant attention in 2023, showing great promise in clinical development areas such as regulatory document queries, event adjudication, and speeding up clinical report generation. They also play a role in Phase IV, including new indications and line extensions.

The explosion of AI/ML provides unique opportunities and challenges for statisticians. Over the past century, the field of statistics has evolved with the emergence of new data types. As time-to-event data emerged in the 1950s, Kaplan-Meier curves and various statistical models, including the Cox model, were developed. Later, statisticians also played a leading role in handling longitudinal data and high-dimensional genetics data. The types of data exploded in the 21st century, with images, audio, video, and web pages all considered data. The emergence of these new data types has outpaced the development of new statistical methods, with various deep learning-based solutions developed outside the field of statistics. As statisticians, we need to embrace this exciting AI/ML era and continue to focus on the social impact of developing methods.

We have also observed a key trend in recent AI/ML, which I call the shift from technology to science. Here are two examples. In the past, data augmentation was often used to improve training accuracy for deep learning. With objects in higher dimensions, such as 3D molecules or robotics, brute-force rotation/translation data augmentation does not work well. In the past couple of years, theoretical approaches leveraging symmetries and introducing Lie group machinery have significantly improved efficiency by more than 500-fold. Another example is generative AI; in recent years, stable diffusion models have become popular generation methods. Recently, these models have been placed under a rigorous stochastic diffusion equation framework, enabling much more efficient generation and better understanding of various theoretical properties. With accumulated empirical evidence in the field of AI/ML over the past two decades, it might be a good time now for a better understanding of these methods. I believe our statisticians will play important roles here.

"As statisticians, we need to embrace this exciting AI/ML era and continue to focus on the social impact of developing methods."

† About the author: Dr. Haoda Fu is the enterprise lead for AI/ML at Eli Lilly and Company. He is a Fellow of the American Statistical Association and a Fellow of the Institute of Mathematical Statistics. He has been actively involved in AI/ML method development, with more than 100 peer-reviewed publications.

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Biostat Bytes

NDA/BLA Oncology Approvals in 2023

Click the links to access to the FDA's official review materials.

nirogacestat
11/27/2023 desmoid tumors

capivasertib
11/16/2023 Breast cancer

repotrectnib
11/15/2023 non-small cell lung cancer

fruquintnib
11/8/2023 metastatic colorectal cancer

toripalimbab-tpzi
10/27/2023 nasopharyngeal carcinom

motixafortide
9/8/2023 Myeloma

elranatamab-bcmm
8/14/2023 Myeloma

talquetamab-tgvs
8/9/2023 Myeloma

quizartinib
7/20/2023 Myeloma

glofitamab-gxbm
6/15/2023 lymphoma

flotufolastat F-18 GALLIUM
5/25/23 prostate cancer

epcoritamab-bysp
5/19/23 lymphoma

retifanlimab-dlwr
3/22/23 Merkel cell carcinoma

elacestrant
1/27/23 metastatic breast cancer

pirtobrutinib
1/27/23 lymphoma

What is Hazard Ratio (HR)?

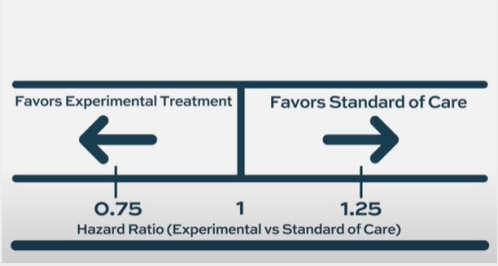
By Philip He, Ph.D. †

HR is a measure commonly used in time-to-event analysis, e.g., progression free survival (PFS) and overall survival (OS), to compare an experimental treatment and a control treatment in clinical trials.

The hazard ratio is basically the ratio of the hazard rates in the experimental group versus the control group. The hazard rate represents the risk of having the event. A hazard ratio of 1 indicates no difference in the hazard rates between the two groups. A hazard ratio less than 1 suggests a lower hazard in the experimental group, in other words, beneficial compared to the control treatment.

HR is often estimated from a Cox proportional hazards model which assumes the HR is a fixed number irrespective of time. This is a strong assumption but convenient for description of treatment benefit compared to the control group.

For example, in a clinical trial (Cortés et al. (2022)) comparing PFS in trastuzumab deruxtecan versus trastuzumab emtansine for breast cancer, a hazard ratio of 0.28 would imply a 72% reduction in the hazard of progression or death in the trastuzumab deruxtecan treatment compared to the trastuzumab emtansine treatment.



†Daiichi Sankyo Inc.

Reference: Cortés J et al. (2022) Trastuzumab Deruxtecan versus Trastuzumab Emtansine for Breast Cancer. DOI: 10.1056/NEJMoa2115022