BBS Webinar

Optimizing Multiple Comparisons in Sequential and Non-Sequential Clinical Trials

Speaker: **Michael Barón**, PhD, American University, Washington DC, U.S.A.

Monday March 9th, 2026 (14:00-15:00)
VIRTUAL EVENT

Costs: Access to the webinar is free of charge, but registration is required: **Link**

Organizers: Andreas Ziegler (Cardio-CARE), Charline Mere (BMS) and Lilla Di Scala (J&J)

Target audience: Anyone who is interested in the topic of multiple testing for clinical trials and epidemiological interventional studies.

Abstract: Multiple hypothesis testing is one of central problems in modern clinical trials and medical research, where investigators often evaluate several endpoints, treatment arms, biomarkers, or interim hypotheses simultaneously. Such studies require principled statistical decisions for each individual hypothesis, rather than a single decision for a global composite null, while maintaining strict control of error rates at the study level. Similar challenges arise in other areas such as change-point detection and acceptance sampling, but clinical trials remain the primary motivation and leading application of the methodologies discussed in this talk.

Fixed-sample multiple comparison procedures are well developed and include methods such as Holm, Hommel, Benjamini–Hochberg, and Guo–Sarkar procedures for controlling the familywise error rate (FWER) or the false discovery rate (FDR). We begin

by developing sequential counterparts of these tools that are suitable for interim analyses and adaptive clinical trial designs. Proposed procedures provide simultaneous control of both Type I and Type II familywise error rates, extending the classical sequential probability ratio test from a single hypothesis to multiple hypotheses in a unified framework.

We then address the practical need to reduce expected sample size (and therefore cost, duration, and patient exposure) while preserving prespecified FWER constraints. Techniques include optimal error spending, weighted test statistics, and equalizer rules. Asymptotic optimality is established under Pitman alternatives. In settings with many endpoints or treatment comparisons, substantial efficiency gains can be achieved by controlling generalized familywise error rates, which are particularly relevant in large-scale clinical trials and biomarker studies.

By introducing asymmetry into error spending across hypotheses, we formulate and solve associated minimax optimization problems that yield more efficient and clinically meaningful testing strategies. These solutions lead to equalizer rules that minimize overall risk, cost, or required sample size, while maintaining rigorous control of familywise error rates.

Overall, the proposed methods extend classical multiple testing procedures to sequential trial settings, providing meaningful gains in efficiency without compromising statistical validity. The methodology is illustrated through a clinical case study, highlighting its relevance to real-world medical research.

Speaker background: Michael Barón is Professor at American University, where he arrived 11 years ago from the University of Texas at Dallas. He conducts research in sequential analysis, change-point problems, and Bayesian inference, with occasional applications in epidemiology, clinical trials, insurance, energy finance, and semiconductor manufacturing. This last application brought him to IBM T. J. Watson Research Center, where he was a one-year Academic Visitor. Barón is credited for extending stepwise multiple hypothesis testing methods to sequential analysis and introducing asymptotically pointwise optimal stopping rules in change-point detection. He also elaborated several classes of sequentially planned statistical procedures. These are flexible group sequential sampling schemes with dynamically determined group sizes that result in substantial time and cost saving, when the cost is nonlinear.

Barón participated in the design and analysis of several clinical trials. He authored a probability and statistics textbook for computer scientists and co-authored a series of books studying applications of statistics in sociology and marketing, classifying and

exploring lifestyles and consumer behaviors. M. Barón is a Fellow of the American Statistical Association, an Elected Member of the international Statistical Institute, and a recipient of Abraham Wald award for the best paper in Sequential Analysis.

M. Barón has a University Diploma in Mathematics from St. Petersburg State University, Russia and a Ph.D. degree in Statistics from the University of Maryland. In his turn, he graduated twelve doctoral students, all of them are happily employed, mostly at academic and research positions. During his rare free time, Barón travels and plays piano, go, bridge, and ice hockey.