

BIOSTATISTICS SEMINAR

Survival Analysis using a 5-STAR Approach in Randomized Clinical Trials



Devan V. Mehrotra,
PhD
Vice President,
Biostatistics,
at Merck Research
Laboratories (MRL)

Randomized clinical trials are often designed to assess whether a test treatment prolongs survival relative to a control treatment. Increased patient heterogeneity, while desirable for generalizability of results, can weaken the ability of common statistical approaches to detect treatment differences, potentially hampering the regulatory approval of safe and efficacious therapies. A novel solution to this problem is proposed. A list of baseline covariates that have the potential to be prognostic for survival under either treatment is pre-specified in the analysis plan. At the analysis stage, using observed survival times but blinded to patient-level treatment assignment, 'noise' covariates are removed with elastic net Cox regression. The shortened covariate list is subsequently used by a conditional inference tree algorithm to segment the heterogeneous trial population into subpopulations of prognostically homogeneous patients (risk strata). After patient-level treatment unblinding, a treatment comparison is done within each formed risk stratum and stratum-level results are combined for overall statistical inference. The impressive power-boosting performance of our proposed 5-step stratified testing and amalgamation routine (5-STAR), relative to that of the logrank test and other common approaches that do not leverage inherently structured patient heterogeneity, is illustrated using a hypothetical and three real datasets along with simulation results. In addition, the importance of reporting stratum-level comparative treatment effects is highlighted as a potential enabler of personalized medicine. An R package is available for implementation.

Devan V. Mehrotra and Rachel Marceau West, Biostatistics and Research Decision Sciences, Merck & Co., Inc.

Thursday January 21, 2021

Pls. Note New Time 3:30 pm - 4:30 pm

Zoom meeting: Please also find a link in the email invite, with the password.
<https://uncsph.zoom.us/j/95116832073?pwd=TnV4QUtGLzMwaFRBTlRsd2xmTjVMQQT09>



UNC
GILLINGS SCHOOL OF
GLOBAL PUBLIC HEALTH