Comparing Biomarkers as Trial Level General Surrogates

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Abstract: An intermediate response measure that accurately predicts efficacy in a new setting can reduce trial cost and time to product licensure. In this paper, we define a trial level general surrogate, which is an intermediate response that can be used to accurately predict efficacy in a new setting. Methods for evaluating general surrogates have been developed previously. Many methods in the literature use trial level intermediate responses for prediction. However, all existing methods focus on surrogate evaluation and prediction in new settings, rather than comparison of candidate general surrogates, and few formalize the use of cross validation to quantify the expected prediction error. Our proposed method uses Bayesian non-parametric modeling and cross-validation to estimate the absolute prediction error for use in evaluating and comparing candidate trial level general surrogates. Simulations show that our method performs well across a variety of scenarios. We use our method to evaluate and to compare candidate trial level general surrogates in several multi-national trials of a pentavalent rotavirus vaccine. We identify at least one immune measure that has potential value as a trial level general surrogate and use it to predict efficacy in a new trial where the clinical outcome was not measured. If time permits, we will also discuss extensions to multiple trial level general surrogates.

Professor Daniels is currently a tenured full professor in the Department of Statistics & Data Sciences and the Department of Integrative Biology (and chair of the former department) at the University of Texas at Austin. His areas of expertise are the development of methods for the analysis of longitudinal data and missing data in longitudinal studies, Bayesian causal inference, and estimation of dependence. He has held previous positions at the University of Florida, Iowa State University, and Carnegie Mellon University. He has been well funded by NIH, has written a research monograph on Bayesian methods for longitudinal data, and is currently co-editor of Biometrics.

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