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Dr. Mohammad Huque, Adjunct Professor of Biostatistics in the Jiann-Ping Hsu College of Public Health at Georgia Southern University is the lead author of “Consistency-ensured Parametric Tests for Critical Events of Composite Endpoints,” recently published in The Journal of Biopharmaceutical Statistics. Composite endpoints (CEs) are commonly used in clinical trials when clinically important events are rare or when the disease is multifaceted. However, components of a CE often differ markedly in their clinical importance. The overall treatment effect on the composite can be driven by less-important, yet more frequently occurring, components, with no effects on some clinically important components. These situations create difficulties in interpreting the results of the CE. The literature has proposed several approaches for handling these conditions, for example, by setting requirements on the results of the clinically important components. However, for a rare event, it can be difficult to draw an appropriate conclusion about its contribution to the overall result of the composite. Here, we propose combining clinically important components to jointly increase their power and to require that their findings meet a prespecified level of evidence, called the consistency criterion. With the increase in power, the study can then be designed with the objectives of establishing efficacy for the composite and/or for the subset of clinically critical components. In this regard, we introduce multiple testing strategies, which account for the consistency requirement and for the correlation between these two endpoints. We illustrate the methodology using the PROactive trial.

Dr. Huque is a Fellow of the American Statistical Association and recently retired after a long career as an applied statistician in the Center for Drug Evaluation and Research at the Food and Drug Association. The Journal of Biopharmaceutical Statistics was founded in 1991 by Dr. Karl E. Peace, who was its Editor-in-Chief for the first 10 years of its existence.
Dr. Mohammad Huque, Adjunct Professor of Biostatistics in the Jiann-Ping Hsu College of Public Health Georgia Southern University is the lead author of “Consistency Ensured Test Strategies for Supportive Evidence of Treatment Efficacy in Noninferiority Clinical Trials,” recently published in The Journal of Biopharmaceutical Statistics. Noninferiority (NI) clinical trials are designed to demonstrate that a new treatment is not unacceptably worse than an active control on a clinically meaningful endpoint. While such an endpoint can be of any type, the focus of this manuscript is on the binary-type endpoint. Examples of this endpoint can be clinical cure endpoint for patients with bacterial diseases or based on a pre-specified virological threshold for viral diseases. However, in addition to assessing such a binary endpoint for the NI comparison, the trial may also evaluate a second clinically relevant endpoint for providing additional support to the evidence of the designated primary endpoint. Specifically, if the trial is successful in demonstrating statistical significance on the first endpoint, then observing at least a positive trend in efficacy on the second endpoint may provide additional supportive evidence of efficacy. The second endpoint can be a time-to-event type endpoint, such as time-to-symptom resolution (TSR) or time to all-cause mortality for infectious disease trials, time-to-wound closure for wound healing trials, or other endpoints. We propose two consistency ensured test strategies for the two hypotheses of a trial, one associated with the binary endpoint and the other with the second endpoint, both with the objective of drawing inference regarding the efficacy of the new treatment based on findings from testing the two hypotheses. A key feature of these test strategies is that basically it does not require multiplicity adjustment of the significance levels. We conclude with general discussion of the testing methods and possible applications to unmet medical need trials.

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