

TITLE: A hybrid frequentist-Bayesian view on hypothesis testing in clinical trials borrowing external information

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ABSTRACT: When designing a novel clinical trial, some external information about the control and/or treatment effect is typically available. Taking full advantage of such information is particularly important in situations where the number of realistically recruitable patients is limited, as in, e.g., pediatric or rare disease trials. The Bayesian approach offers a natural methodological framework for information borrowing as it allows seamlessly combining existing knowledge about the parameter of interest and the information collected in the current trial via its prior-likelihood construction. A potential issue with this procedure is that external and current information may conflict, but such inconsistency may not be predictable a priori. Several robust prior choices have been proposed in the literature to limit extreme worsening of operating characteristics (OCs) in these situations, the robust mixture prior (Schmidli et al., 2014) and power prior (e.g., Ibrahim and Chen, 2000) being among the most widely adopted. However, while these approaches can limit losses, uniform gains are in general not possible without additional assumptions about the consistency between the current and external data source. One challenge in this context has therefore been how to appropriately select an approach and its tuning parameters to satisfactorily balance potential gains and losses. In this talk, we focus on hypothesis testing reviewing the connections between frequentist and Bayesian hypothesis testing in one- and two-arm trial designs. We will then highlight rationales for type I error rate inflation and provide analytical results on how frequentist robustness can be achieved in this context. We will finally show how the power function plays an important role in recently proposed Bayesian OCs, and discuss their behavior under the design and analysis prior dichotomy.

PRESENTING AUTHOR BIO: Silvia has been working as a researcher and statistical consultant at the division of Biostatistics of the German Cancer Research Center since 2017. She had previously completed a PhD in Statistics at the University of Warwick and a Master degree in Statistical Sciences at the University of Padua. Her current research focus is on Bayesian clinical trial designs and in particular on methods for robust incorporation of external information.