Adaptive borrowing of information across patient subgroups in a basket trial based on distributional discrepancy

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Abstract: Basket trials emerge as a new class of efficient approaches to evaluate a treatment in several patient subgroups simultaneously. In this paper, we develop a novel analysis methodology for early phase basket trials, which enables borrowing of information to improve decision making in a collection of subgroups. For each subgroup-specific parameter that underpins the treatment effect, a marginal predictive prior (MPP) is specified using information from the other subgroups. More specifically, it comprises a series of commensurate predictive priors (CPPs), each with a normal precision that captures the commensurability of information. We propose using a distributional discrepancy to characterise the pairwise commensurability between any two subgroups, so as to inform the choice of a spike-and-slab prior to be placed on the normal precision. This determines the degree of borrowing from an external subgroup. When there exist at least three subgroups in a basket trial, we convert the pairwise discrepancy measurements into a set of normalised weights and allocate them to the CPPs accordingly. This leads to an MPP that leverages only information from the most consistent subgroups. The MPP is then updated using the contemporary subgroup data to a robust posterior. Trial operating characteristics of the proposed methodology are evaluated through simulations motivated by a real clinical trial. Compared with alternative Bayesian analysis models, our proposal is more advantageous for (i) identifying the most consistent subgroups, and (ii) gauging the amount of information to be leveraged. Numerical results also suggest that our analysis methodology can potentially improve the precision of estimates and the statistical power for hypothesis testing.