A Novel Information Borrowing Approach for Evaluating Response in Pediatric Basket Trials with Limited Sample Sizes

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Background: Basket trials are seeing increased use to assess safety and efficacy of novel treatments targeting rare cancer mutations which occur in many tumour histologies. Bayesian hierarchical modelling (BHM) approaches have been proposed to account for potential cross-histology heterogeneity in responses and allow for partial pooling of information across histologies based on the degree of heterogeneity. Additionally, Bayesian borrowing approaches have precedent for supplementing limited sample sizes in pediatric trials using data from adult populations. Due to generally limited sample sizes in pediatric single-arm basket trials, there is potential benefit for methods accounting for both cross-histology heterogeneity in outcomes and allowing for information borrowing from adult basket trials when estimating response rates.

Methods: We construct a 3-level BHM which models (i) heterogeneity in response across histologies, (ii) heterogeneity in relative pediatric vs. adult response across histologies, and (iii) heterogeneity in mean response between pediatric and adult populations. Heterogeneity parameters for levels (i) and (ii) of the model are learned from the data. The heterogeneity parameter for level (iii) is generally not estimable and requires imposition of a strong prior. Consequently, the primary function of level (iii) of the model is to allow for bias correction and flexible down-weighting of the adult data for probabilistic sensitivity analysis (PSA).

Results: The performance of the model will be demonstrated using simulated data. Credible intervals by histology will be compared between a no-pooling and 3-level BHM approach. Additionally, impacts of several adult data down-weighting and bias correction PSA scenarios will also be demonstrated.

Conclusion: Extremely small sample sizes in many pediatric basket trials presents a significant challenge for evaluating response rates—especially for individual tumour histologies. Our method provides a potential solution to this challenge by allowing for borrowing of information both across histologies and from adult basket trials.