April 5, 2020

Dear Editor,

Please find the attached manuscript entitled "Analyzing Basket Trials under Multisource Exchangeability Assumptions," which we would like to be considered for publication in the R Journal.

Basket designs are prospective clinical trials that are devised with the hypothesis that the presence of selected molecular features determine a patient's subsequent response to a particular "targeted" treatment strategy. Basket trials are designed to enroll multiple clinical subpopulations to which it is assumed that the therapy in question offers beneficial efficacy in the presence of the targeted molecular profile. The treatment, however, may not offer acceptable efficacy to all subpopulations enrolled. Moreover, for rare disease settings, such as oncology wherein these trials have become popular, marginal measures of statistical evidence are difficult to interpret for sparsely enrolled subpopulations. Consequently, basket trials pose challenges to the traditional paradigm for trial design, which assumes inter-patient exchangeability.

The R-package **basket** facilitates the analysis of basket trials by implementing multi-source exchangeability models. By evaluating all possible pairwise exchangeability relationships, this hierarchical modeling framework facilitates Bayesian posterior shrinkage among a collection of discrete and pre-specified subpopulations. Analysis functions are provided to implement posterior inference of the response rates and all possible exchangeability relationships between subpopulations. In addition, the package can identify "poolable" subsets of and report their response characteristics. The functionality of the package is demonstrated using data from an oncology study with subpopulations defined by tumor histology.

We believe this manuscript will be of interest readers in the area of clinical trials. This package and the accompanying paper the culmination of several years of research and clinical trial analysis experience. Despite this the interface has been designed to be simple to use with informative outputs appropriate for intermediate R users with intermediate clinical trial knowledge.

Regards,

Michael Kane

School of Public Health, Biostatistics Department

Yale University,

New Haven, CT

michael.kane@yale.edu