An extension of the coin package for comparing interventions assigned by dynamic allocation

Johannes Hüsing*

Restricted randomisation or algorithm-based allocation procedures enjoy some popularity among clinical researchers, promising a lower variance of the treatment effect estimate and balanced subgroups for exploratory analysis. They have met criticism because classical asymptotics don't hold and the argument for a random distribution may be less soundly based. This has led to a statement of mistrust in the form of a guideline issued by pharmaceutical regulators.

Permutation tests give rise to analysis strategies which incorporate the allocation strategy in order to generate more realistic null distributions. The plethora of published allocation algorithms calls for a common framework which can be used regardless of the algorithm employed. The package `coin` currently offers complete randomisation and balanced block randomisation as alternative procedures.

An extension of `coin` is introduced which allows users to consistently write new allocation procedures. The interface of the coin extension is defined so that algorithms can be used to be used both in treatment allocation service programs and in the reallocation procedure. Following this requirement, algorithms should be formulated in an incremental way, returning only the next allocation instead of the whole vector.

Algorithms should accept as parameters all previously allocated treatments and the common distribution of all factors the allocation decision is based on. It is passed as a data frame which contains all factors and the treatments. Treatment is null for the last observation, which is subject to the current allocation. The completed data frame is returned.

The interface to coin is confined to the `ApproxNullDistribution` method. Two additional arguments, `algorithm` (defaulting to "full permutation") and `shuffle` (sampling from alternative accrual sequences, defaulting to "identity") are passed. an engine is started which applies the (incrementally formulated) algorithm sequentially to the set of patients, ie. the (possibly shuffled) `x` slot of the `IndependenceTestStatistic` object.

It is hoped that the introduction of a common interface may encourage the use of dynamic allocation methods, and increase the acceptance for the results gained from appropriate analyses of data obtained this way.

*Koordinierungszentrum für Klinische Studien, Universität Heidelberg