

Subgroup Identification using Covariate Adjusted Interaction Trees

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We consider the problem of identifying sub-groups of participants in a clinical trial that have enhanced treatment effect. Recursive partitioning methods that recursively partition the covariate space based on some measure of between groups treatment effect difference are popular for such sub-group identification. The most commonly used recursive partitioning method, the classification and regression tree algorithm, first creates a large tree by recursively partitioning the covariate space using some splitting criteria and then selects the final tree from all subtrees of the large tree. In the context of subgroup identification, calculation of the splitting criteria and the evaluation measure used for final tree selection rely on comparing differences in means between the treatment and control arm. When covariates are prognostic for the outcome, covariate adjusted estimators have the ability to improve efficiency compared to using differences in means between the treatment and control group. We discuss properties and final sample performance of two covariate adjusted estimators that can be used to both make splitting decisions and for final tree selection.