Performance of binary markers for censored failure time outcome: nonparametric approach based on proportions

Nonparametric analysis of sensitivity and specificity of markers used to detect the presence of disease at the same time of marker measurement is based on simple proportions on a classification matrix in both case-control and cohort designs.

If the disease status is subject to verification bias, i.e. it is unknown for some statistical units, weighting or imputation techniques can be used relying on the estimation of the probability of being case or control, and on the probability of being verified or not verified. This enables to asjust the classification matrix resorting again to simple proportions to estimate classification probabilities.

When the marker aims at detecting the future development of disease within a time window, instead of the presence of disease at the same time of test administration, in a cohort study, inference becomes more complex because of censoring.

A fully nonparametric solution based on smoothed estimation of the joint survival function of time to disease and the marker was proposed, where bootstraap is recommended for asympotics. Semiparametric approaches have also been developed.

Here we consider the occurrence of censoring as a particular source of verification bias on the time to development of disease. Full and partial imputation of the disease status by Kaplan-Meier estimation of survival functions conditional on the marker value, and inverse probability of censoring weighting are used to obtain a censored adjusted classification matrix. Classification probabilities are then estimated by proportions which are proved to be equivalent to those obtained by the aforementioned nonparametric approach.

Our approach enables to derive asymptotic variance of sensibility and specificity and their covariance, using the delta method on logit transformations. The performance of the confidence interval for single sensibility and specificity, and the joint confidence interval for the two are investigated via simulation.

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