MULTIPLE IMPUTATION FOR THE COMPARISON OF TWO SCREENING TESTS IN TWO-PHASE ALZHEIMER STUDIES

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Two-phase designs are common in epidemiological studies of dementia, and especially in Alzheimer research. In the first phase, all subjects are screened using a common screening test(s), while in the second phase, only a subset of these subjects is tested using a more definitive verification assessment, i.e. golden standard test. When comparing the accuracy of two screening tests in a two-phase study of dementia, inferences are commonly made using only the verified sample. It is well documented that in that case, there is a risk for bias, called verification bias. When the two screening tests have only two values (e.g. positive and negative) and we are trying to estimate the differences in sensitivities and specificities of the tests, one is actually estimating a confidence interval for differences of binomial proportions. Notice that the two sensitivities and two specificities are both pairs of binomial proportions. Evaluating the confidence interval of the difference will determine the accuracy of the two tests. Evaluating the differences of two binomial proportions is not trivial even with complete data. It is well documented that it is a tricky task. we suggest ways to apply imputation procedures in order to correct for the verification bias. This procedure allows us to use well established complete-data methods to deal with the difficulty of the estimation of the difference of two binomial proportions in addition to deal with the incomplete data. We compare different methods of estimation, and evaluate the use of multiple imputation in this case. Our simulation results show that the use of multiple imputation is superior to other commonly used methods. We demonstrate our finding using Alzheimer data example.