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Bootstrap Bias-reduction in Genetic Association Analysis of Time-to-event Outcomes

While it is necessary to control the false-positive error rate in genome-wide studies, selection of genetic markers (SNPs) with small association p-values introduces optimistic bias into parameter estimates. Motivated by an investigation of complications in diabetes, we extend a bootstrap-resampling method for quantitative/binary traits to analyse time to nephropathy under a proportional hazards model. We evaluate relative and absolute bias via simulations. For SNPs with low to moderate power, bootstrap estimates are closer to the truth than uncorrected estimates, but the method tends to over-correct when power is high. Among false positives, however, bias-reduction shrinks estimates appropriately toward the null.