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An Internet Refreshing Methodology for Testing the Relative Risks Presumption

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Description

The Cox model-which remains the first choice for analyzing time-to-event data, even for large data sets-relies on the Proportional Hazards (PH) assumption. When survival data arrive sequentially in chunks, a fast and minimally storage intensive approach to test the PH assumption is desirable. We propose an online updating approach that updates the standard test statistic as each new block of data becomes available and greatly lightens the computational burden. Under the null hypothesis of PH, the proposed statistic is shown to have the same asymptotic distribution as the standard version computed on an entire data stream with the data blocks pooled into one data set. In simulation studies, the test and its variant based on most recent data blocks maintain their sizes when the PH assumption holds and have substantial power to detect different violations of the PH assumption. We also show in simulation that our approach can be used successfully with "big data" that exceed a single computer's computational resources. The approach is illustrated with the survival analysis of patients with lymphoma cancer from the Surveillance, Epidemiology, and End Results Program. The proposed test promptly identified deviation from the PH assumption, which was not captured by the test based on the entire data. Mendelian Randomization (MR) is a type of instrumental variable (IV) analysis that uses genetic variants as IVs for a risk factor to study its causal effect on an outcome. Extensive investigations on the performance of IV analysis procedures, such as the one based on the 2-Stage Least Squares (2SLS) procedure, have been conducted under the one-sample scenario, where measures on IVs, the risk factor, and the outcome are assumed to be available for each study participant. Recent MR analysis usually is performed with data from two independent or partially overlapping genetic association studies (two-sample setting), with one providing information on the association between the IVs and the outcome, and the other on the association between the IVs and the risk factor. We investigate the performance of 2SLS in the two-sample–based MR when the IVs are weakly associated with the risk factor. We derive closed form formulas for the bias and mean squared error of the 2SLS estimate and verify them with numeric simulations under realistic circumstances.

Mendelian Randomization (MR) analysis uses genotypes as instruments to estimate the causal effect of an exposure in the presence of unobserved confounders. The existing MR methods focus on the data generated from prospective cohort studies. We develop a procedure for studying binary outcomes under a case-control design. The proposed procedure is built upon two working models commonly used for MR analyses and adopts a quasi-empirical likelihood framework to address the ascertainment bias from case-control sampling. We derive various approaches for estimating the causal effect and hypothesis testing under the empirical likelihood framework. We conduct extensive simulation studies to evaluate the proposed methods. We find that the proposed empirical likelihood estimate is less biased than the existing estimates. Among all the approaches considered, the Lagrange Multiplier (LM) test has the highest power, and the confidence intervals derived from the LM test have the most accurate coverage. We illustrate the use of our method in MR analysis of prostate cancer case-control data with vitamin D level as exposure and three single nucleotide polymorphisms as instruments.

Capture-Recapture Model

A spatial open-population capture-recapture model is described that extends both the non-spatial open-population model of Schwarz and Arnason and the spatially explicit closed-population model of Borchers and Efford. The super population of animals available for detection at some time during a study is conceived as a two-dimensional Poisson point process. Individual probabilities of birth and death follow the conventional open-population model. Movement between sampling times may be modeled with a dispersal kernel using a recursive Markovian algorithm. Observations arise from distance-dependent sampling at an array of detectors. As in the closed-population spatial model, the observed data likelihood relies on integration over the unknown animal locations; maximization of this likelihood yields estimates of the birth, death, movement, and detection parameters.

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