Marburg University

RESEARCH SEMINAR

Flexible Modeling of Biomarker Ratios with Correlated Components

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PD Dr. Moritz Berger
Head of Core Facility Biostatistics
Central Institute of Mental Health Mannheim

Abstract:

A frequent objective in observational studies is to model the ratio of two non-negative components. It's of major relevance in biomedical research, where biomarker ratios are used for early diagnoses of specific diseases. Examples include, among others, the low-density lipoprotein (LDL)/high-density lipoprotein (HDL) cholesterol ratio in cardiovascular research, the GEFC/REFC ratio in ophthalmic research as well as the CD4/CD8 ratio of T helper cells in infectiology. In such studies, the focus typically is not only on the characterization of the marginal ratio distribution, but also on modeling this distribution as a function of covariates.

When setting up a regression model that relates the ratio outcome to covariates, two strategies are in common use. The first one assumes that the ratio outcome follows a normal distribution after transformation; the second one assumes gamma distributed components, thereby accounting for the positivity of the component values and the skewness of their distributions. We consider both approaches for modeling ratio outcomes and embed them into a distributional regression framework that allows us to relate all distributional parameters to a set of covariates. These are more flexible than classical regression approaches (which focus on the mean ratio only), as they enable to derive the conditional probability density function as well as quantities of interest (like the median or quantiles) as functions of covariates. We consider (i) Gaussian models with log-transformed outcome and Box-Cox-transformed outcome, and (ii) gamma distribution-based models, where the joint distribution of the two components is defined by either Kibble's bivariate gamma distribution (‘extended GB2 model’) or Frank's copula (‘FCGAM model’). While the extended GB2 model is tailored to the case of positively correlated components, the FCGAM model allows for positive or negative correlation between the two components. We evaluate and compare these four approaches in an analysis of data from dementia research, where cerebrospinal fluid biomarkers are used for early diagnoses of Alzheimer’s disease.

Institute for Medical Biometry and Statistics (IMBS)
Philipps University Marburg
Hans-Meerwein-Straße 6
35043 Marburg

imbs@uni-marburg.de

IMBS seminar room
Room 04B11