Joint Modelling of Hierarchically Clustered Binary Data with Crossed Random Effects: An Application to Diabetic Retinopathy Data

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Abstract

Clustered binary data are ubiquitous in many diagnostic studies in medicine and health. This is true in situations where the same group of readers evaluates the presence or absence of certain diseases on binocular organs. Note the complex correlation structure in the data: in addition to the correlation induced by the binocular nature of data one other source of correlation is present. Since readers rely on same patients' result, their diagnoses are potentially correlated. The later correlation can be accounted by incorporating reader-specific and patient-specific random effects. These random effects are crossed rather than nested. Hence, the evaluation of full likelihood is cumbersome since the integral suffers from the curse of dimensionality and integral increases with the number of patients and readers. In this study, a likelihood-based method of estimating disease-specific sensitivities and specificities via generalized linear mixed models with copula to capture the binocular correlation is proposed. To overcome the computational complexities in the likelihood, pairwise likelihood approach is adopted. An underlying latent t- distribution is assumed for binary observations; this is robust to the conventional probit and logistic regression models. Data from a study on diabetic retinopathy are analyzed to illustrate the methodology.

Keywords: Copula, Crossed Random Effects, Pairwise Likelihood, Reader-Based Diagnostic Studies