

# APPLYING BOOTSTRAP IN MULTILEVEL MODELLING OF CARDIOVASCULAR DISEASE

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Interest in using multilevel modelling to analyse data with a hierarchical structure has grown in the past decade. Two assumptions are involved in such modelling: large sample size - at least 50 at the highest hierarchical level, and normal distribution of the error terms at each level of aggregation. The regression coefficients and their standard errors may show little or no bias, but variance components and their standard errors may be severely biased when these assumptions are not met. An approach to correcting bias is to bootstrap.

The Hirulog and Early Reperfusion or Occlusion (HERO-2) trial was a multi-centre, multinational trial with outcome 30-day mortality following hospital admission with acute myocardial infarction (AMI). HERO-2 makes a significant contribution to assessing risk factors in cardiovascular research. Subjects were enrolled from 46 countries. Since this number of countries is relatively small, the estimation of country level variation from generalized linear mixed models (GLMM) may be biased. For better understanding of bias in HERO-2, bootstrap methodology is available to assess the standard errors of variance components. We study both parametric and non-parametric bootstrap in multilevel models and the comparison is made with results from GLMM without bootstrap. Bootstrap at the aggregate level is also implemented. The analyses are conducted in SAS, R and MLwiN: usage of different software packages is briefly considered. Other advantages of bootstrap resampling in multilevel modelling are discussed.