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Comparison of concordance correlation coefficient via variance components, generalized estimating equations and weighted approaches with model selection

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ABSTRACT

Variance components (VC) and generalized estimating equations (GEE) are two approaches for estimating concordance correlation coefficients (CCC) adjusting for covariates, and allowing dependency between replicated samples. However, under VC and GEE, a model including all potential explanatory variables may lead to biased parameter estimates. To overcome this problem, the estimation of CCC using VC and GEE approaches, as well as applying the conditional Akaike information criterion (CAIC) and the *quasi-likelihood under the independence model criterion* (QIC) measures for model selection is applied. The weighted approach which is the most efficient estimator of CCC obtained by combining the estimators from VC and GEE is also proposed. Simulation studies are conducted to compare the performance of the VC and the GEE, both with and without model-selection via CAIC and QIC, respectively, and the weighted approaches for dependent continuous data. Two applications are illustrated: an assessment of conformity between two optometric devices and an evaluation of agreement in degree of myopia for dizygotic twins. To conclude, the CAIC and QIC model-selection procedures embedded in VC and GEE approaches, respectively, can provide more satisfactory results than VC and GEE involving all possible covariates. Furthermore, the weighted approach is a reliable and stable procedure with the smallest mean square errors and nominal 95% coverage rates in estimating CCC.

1. Introduction

Measures of agreement or reproducibility are designed to assess consistency between different instruments rating measurements of interest. The most widely acceptable measures of agreement for categorical data are the kappa measures, Cohen's kappa and weighted kappa, for binary and ordinal responses, respectively (Cohen, 1960, 1968). When observations are measured on quantitative scales, the intraclass correlation coefficient (ICC), defined as the proportion of the total variance due to the between-subjects variance (Bartko, 1966; Shrout and Fleiss, 1979), is frequently used to assess the reliability of measurements. Another popular index, the concordance correlation coefficient (CCC), is used to evaluate the reproducibility between two observers by measuring the variation of the linear relationship between each pair of data from the 45° line through the origin (Lin, 1989). Two advantages of CCC are that it measures how far each observation deviates from the line fit to the data (precision) and how far this line deviates from the 45° line through the origin (accuracy) (King and

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Chinchilli, 2001a). Some extensions of CCC to categorical data produce estimates of agreement equivalent to Cohen's kappa and weighted kappa statistics (King and Chinchilli, 2001a; Fleiss and Cohen, 1973; Krippendorff, 1970; Robieson, 1999).

When covariates and subject or observer variation are considered in estimation of CCC, two research directions arise. In the first, Carrasco and Jover (2003) established the equivalence between ICC and CCC for a two-way linear mixed model (LMM) without interaction and proposed to estimate CCC through variance components (VC). Based on this rationale, the estimation of CCC via the VC approach was further extended to generalized linear mixed-effects models (GLMMs) for count data (Carrasco, 2010). The other research direction is to estimate CCC via generalized estimating equations (GEE). For this, Barnhart and Williamson (2001) proposed the GEE approach using three sets of estimating equations to model CCC between two raters for continuous readings. It was later extended to multiple observers for data without and with replications (Barnhart et al., 2002, 2005). However, one may obtain a higher agreement than a true agreement if confounding covariates are not included in a model (Carrasco and Jover, 2003). Conversely, when a model includes all potential explanatory variables, it may lead to complexity in interpretation and bias of parameter estimates. Therefore, it is essential to perform model selection when covariates are involved in estimating CCC under the VC and GEE approaches.

When competing models exist, the well-known selection information criteria such as Akaike information criterion (AIC) (Akaike, 1973) and Bayes information criterion (BIC) (Schwarz, 1978) are useful to likelihood-based model selection with the considerations of model complexity. However, when the model involves random effects, the definition of AIC is not straightforward because both the likelihood used and the number of parameters of random effects accounted for cannot be determined exclusively. For LMMs, Vaida and Blanchard (2005) proposed the conditional Akaike information criterion (CAIC) with the effective degrees of freedom treated as the number of parameters in a model. As for GEE, since there is no distribution assumed in GEE, we cannot apply AIC to perform GEE model selection directly. Thus, Pan (2001) proposed a modification to AIC based on a quasi-likelihood and a proper adjustment made for the penalty term, called the *quasi-likelihood under the independence model criterion* (QIC), in GEE models.

In this paper, we focus on estimating CCC using the VC and GEE approaches for correlated continuous data with and without choosing the best subset of covariates via the CAIC and QIC measures, respectively. In addition, we propose the weighted approach by combining the estimates of CCC from VC and GEE with consideration for the correlation between the two estimates. The rest of this paper is organized as follows. Section 2 introduces the VC and GEE approaches for dependent continuous data and the model-selection criteria CAIC in LMM and QIC in GEE. In addition, the estimation of CCC under the weighted approach is also proposed in Section 2. In Section 3, simulation studies are conducted to compare the performance of the VC and GEE approaches with and without model-selection procedure via CAIC and QIC, respectively, and the weighted approach. Two applications are illustrated in Section 4. The first example is to assess the conformity between two optometric devices with measurements on both eyes after adjusting for subject-specific covariates (Shih et al., 2001). The second application is from a study evaluating the agreement between dizygous (DZ) twin-pairs for measuring the degree of myopia (Tsai et al., 2009). Finally, in Section 5 we conclude with discussions and remarks.

2. Methods

The CCC between two variables Y_1 and Y_2 introduced by Lin (1989) is defined as

$$\rho_c = 1 - \frac{E[(Y_1 - Y_2)^2]}{E[(Y_1 - Y_2)^2 \mid Y_1 \text{ and } Y_2 \text{ are uncorrelated}]} = \frac{2\sigma_{12}}{\sigma_1^2 + \sigma_2^2 + (\mu_1 - \mu_2)^2},$$

where $\mu_1 = E(Y_1),\ \mu_2 = E(Y_2),\ \sigma_1^2 = \text{Var}(Y_1),\ \sigma_2^2 = \text{Var}(Y_2)$ and $\sigma_{12} = \text{Cov}(Y_1, Y_2)$. Note that the CCC is equivalent to the Pearson correlation coefficient ρ when $\mu_1 = \mu_2$ and $\sigma_1^2 = \sigma_2^2$. The 95% confidence interval (95% CI) for CCC can be constructed by assuming an asymptotically normal distribution for $\hat{Z}_c = \frac{1}{2}\ln\left(\frac{1+\hat{\rho}_c}{1-\hat{\rho}_c}\right)$ using the inverse hyperbolic tangent transformation (or Fisher's z transformation), where $\hat{\rho}_c$ denotes the estimator of ρ_c. Therefore, the confidence interval estimation for CCC can be made by transforming in the usual way $\hat{Z}_c \pm 1.96\sqrt{\text{Var}(\hat{Z}_c)}$, where $\text{Var}(\hat{Z}_c) = \frac{\text{Var}(\hat{\rho}_c)}{(1-\hat{\rho}_c^2)^2}$ (Lin, 1989), and then back-transforming to the original scale.

We suppose that each of the I subjects is measured K times by each of the J observers or raters. For the ith subject, the kth observed continuous reading assessed by the jth rater is denoted as y_{ijk}, where $i = 1, \ldots, I,\ j = 1, \ldots, J$ and $k = 1, \ldots, K$. The total number of observations is n, where $n = I \times J \times K$. Let $\mathbf{Y}_i = (y_{i11}, y_{i12}, \ldots, y_{i1K}, \ldots, y_{iJ1}, y_{iJ2}, \ldots, y_{iJK})^t$ be a $JK \times 1$ vector of continuous responses for the ith subject. Let $\mathbf{X}_i = (\mathbf{x}_{i11}, \mathbf{x}_{i12}, \ldots, \mathbf{x}_{i1K}, \ldots, \mathbf{x}_{iJ1}, \mathbf{x}_{iJ2}, \ldots, \mathbf{x}_{iJK})^t$ represent the $JK \times p$ covariate matrix, which may include both subject-specific and observer-specific covariates for the ith subject. Note that the covariates used for adjustment can vary across subjects, repeated measures or both of them for all subjects. In this paper, we use the VC and GEE approaches for the estimation of CCC, and the two approaches are briefly reviewed in the following subsections. However, our simulation results reveal that there exist biases in estimates of VC and GEE if the structure of repeated measures depends on covariates or/and the sample size is small. Therefore, we propose a weighted estimator that is computed as a linear combination of two estimators under the VC and GEE approaches to improve the accuracy incorporating both measures of bias and variability.