Weighted scores method for longitudinal ordinal data

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Abstract

Extending generalized estimating equations (GEE) to ordinal response data requires a conversion of the ordinal response to a vector of binary category indicators. That leads to a rather complicated association structure, and the introduction of large matrices when the number of categories and dimension of the cluster are large. To allow a richer specification of working correlation assumptions, we adopt the weighted scores method which is essentially an extension of the GEE approach, since it can also be applied to families that are not in the GLM class. The weighted scores method stems from the lack of a theoretically sound methodology for analyzing multivariate discrete data based only on moments up to second order and it is robust to dependence and nearly as efficient as maximum likelihood. There is no need to convert the ordinal response to binary indicators, thus the weight matrices have smaller dimensions and it is not necessary to guess the correlations of indicator variables for different categories. We focus on important issues that would interest the data analyst, such as choice of the structure of the correlation matrix and of explanatory variables, comparison of results obtained from our methods versus GEE, and insights provided by our method that would be missed with the GEE method. Our modelling framework is implemented in the package weightedScores within the open source statistical environment R.

Keywords: AIC/BIC; Composite likelihood; Correlation structure selection; Generalized estimating equations; Ordinal regression; Variable selection.

1 Introduction

The method of generalized estimating equations (Liang and Zeger, 1986; Zeger and Liang, 1986, GEE hereafter), which is popular in biostatistics, analyzes correlated data by assuming a generalized linear model (GLM) for the outcome variable, and a structured correlation matrix to describe the pattern of association among the repeated measurements on each subject or cluster. The associations are treated as nuisance parameters; interest focuses on the statistical inference for the regression parameters and the method is based only on moments up to second order.

Extending GEE to ordinal response data, say with \( K \) categories, requires an alteration of the general theory because the first and second moments are not defined for ordinal observations. This modification is based on a conversion of the ordinal response to a vector of \( K - 1 \) binary indicators of categories \( 1, \ldots, K - 1 \) (Lipsitz et al., 1994a; Heagerty and Zeger, 1996; Parsons et al., 2006; Touloumis et al., 2013). There are various options for choosing the binary variables and also various parts of associations which will eventually describe all of the possible outcomes for the original ordinal responses. The first part is the association between the binary variables at one time point. The second is the association of the same coded binary variables across time, and the third and final part is the association of two differently coded binary variables across time (Nooraee et al., 2014). This leads to a rather complicated association structure and the introduction of large matrices when \( K \) and \( d \) are large, where \( d \) is the dimension of a “cluster” or “panel”.

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Parsons (2013) discussed many realistic examples, where repeated ordinal data with a large number of categories are involved, e.g., clinical scoring systems such as the Oxford Hip Score (Dawson et al., 1996), and used the Warwick Arthroplasty Trial (Achten et al., 2010) data with $K = 49$ categories. Parsons (2013) described these as long ordinal scores or composite ordinal scores, that result from complex surveys. When $K$ or $d$ is large the working correlation matrix, a square matrix of dimension $d(K - 1)$, is very large, as it needs to account for correlations between the $K$-1 new binary scores at each time-point and between time-points. Matrix operations (e.g. inversion) required for parameter estimation can become very slow or even infeasible for large $K$ or $d$. For long ordinal scores, with a large number of categories, this presents a problem, as many cut-point parameters would need to be estimated with presumably poor precision and likely convergence problems that are often particularly associated with models for repeated ordinals scores (Lipsitz et al., 1994b; Parsons et al., 2006; Parsons, 2013; Touloumis et al., 2013; Nooraee et al., 2014).

Nooraee et al. (2014) made much of convergence issues with available packages for model fitting in this setting. This study used only the default options in existing softwares. This does not necessarily imply that convergence issues will still be present if the maximum number of iterations is increased. Our own take on this issue is rather different from those expressed in this latter paper. Of course quite what we mean by lack of convergence is also often not clearly defined – simply changing a starting value(s) for the association parameter(s), which is (are) often regarded as problematic, can often simply solve the issue. Hence we don’t associate lack of convergence for GEE with large matrices. However, large matrices are a problem for GEE methods, in as much as they cause model fitting algorithms to run slowly.

Furthermore, Nooraee et al. (2014) provided a comprehensive comparison of existing GEE approaches for ordinal data and revealed that different methods can lead to different estimates and identified the local odds ratio GEE approach in Touloumis et al. (2013) as the dominant among the existing GEE methods. Note in passing that each parametrization measures the correlation in a different way, e.g., using correlation coefficients, local odds ratios and global odds ratios (see Touloumis et al. (2013), and the references therein). Therefore different parametrizations would indeed lead to slightly different estimates in finite samples for the existing GEE methods but according to the GEE theory developed by Liang and Zeger (1986) all of them should produce consistent estimators of the marginal regression vector provided that the estimator of the association parameter vector is $\sqrt{N}$-consistent given the true regression parameter vector.

Nikoloulopoulos et al. (2011) developed the weighted scores method for regression models with dependent data. Similar to GEE which constructs unbiased equations weighting the residuals, the weighted scores method constructs estimating equations weighting the univariate score functions, placing the weights strategically. The novelty is the use of a discretized multivariate normal distribution as a working model to specify the weights of estimating equations based on the univariate marginal distributions of the response. Thus it can be regarded as a generalization of GEE in the sense that our method is applicable to a wider family of regression models that are not necessarily in the class of generalized linear models. For concreteness, the theory was illustrated for discrete negative binomial margins, that are not in the GLM family.

The weighted scores method stems from the lack of a theoretically sound methodology for analyzing multivariate discrete data based only on moments up to second order, and in part from recent criticism of the GEE method (Lindsey and Lambert, 1998; Chaganty and Joe, 2006; Touloumis et al., 2013). The weighted scores method is based on a plausible discretized multivariate normal (MVN) model, and the nuisance parameters are interpretable as latent correlation parameters. This avoids problems of interpretation in GEE for a working correlation matrix that in general cannot be a correlation matrix of the multivariate discrete data as the univariate means change (Chaganty and Joe, 2006; Sabo and Chaganty, 2010). Further, with the GEE methodology applied to correlated discrete responses (binary, multinomial, Poisson, etc.), the parametric space of the pairwise association parameters is likely to be restricted by the marginal model specification (Bergsma and Rudas, 2002; Chaganty and Joe, 2006). The “working correlation” used by GEE lacks a proper definition relating the work-
ing correlation matrix to the probability distribution of the response vector, leading to misapplied asymptotic theory (Crowder, 1995). With no formal definition, the working correlation, when it is not the true correlation, has no mathematical relationship to the covariance of the response vector, and in the absence of a proper underlying probability distribution assertions of consistency are invalid (law of large numbers assumes that there is an underlying probability distribution); see Lee and Nelder (2009). The weighted scores method is based on weighting the univariate score functions using a working model that is actually a proper multivariate model. Thus does not only generalize, but also overcomes the theoretical flaws associated with GEE applied to correlated discrete responses. Note that the local odds ratios GEE method in Touloumis et al. (2013) is estimating the nuisance parameter vector by maximizing an objective function (Crowder, 1995) and hence also avoids the aforementioned pitfalls in the GEE method. Their model with log odds implies an underlying bivariate Plackett (Plackett, 1965) copula (Touloumis et al., 2013, Supplementary Materials). The multivariate Plackett has not been proved to be a proper multivariate model, but Chaganty and Joe (2006) showed that the range of bivariate log odds ratios is not as constrained as bivariate correlations for multivariate binary.

The weighted scores method has the merit of robustness to mis specification of the dependence structure like in GEE, but with the additional advantage, with respect to GEE, that dependence is expressed in terms of a “real” multivariate model. Nikoloulopoulos et al. (2011) demonstrated with theoretical and simulation studies that the weighted scores method is highly efficient when compared with the “gold standard” maximum likelihood methods and robust to joint distribution assumptions. The estimating equations based on a “working” MVN copula-based model are robust if the univariate model is correct, while on the other hand ML estimates could be biased if the univariate model is correct but dependence is modelled incorrectly.

Model selection is an important issue in longitudinal data analysis, since when conducting a GEE analysis, it is essential to carefully model the correlation parameters, in order to avoid a substantive loss in efficiency in the estimation of the regression parameters (Albert and McShane, 1995; Crowder, 1995; Wang and Carey, 2003; Shults et al., 2009). Nikoloulopoulos (2016) has proposed the CL1 information criteria as an intermediate step for correlation structure and variable selection in the weighted scores method. The proposed criteria have the similar attractive property with QIC (Pan, 2001) of allowing covariate selection and working correlation structure selection using the same model selection criteria. It has been demonstrated that outperform QIC and several other existing approaches in the GEE literature for model selection. The main reason is that they are being likelihood-based (Varin et al., 2011).

In this paper we modify the general theory in Nikoloulopoulos et al. (2011) and Nikoloulopoulos (2016) for longitudinal ordinal response data. To sum up the advantages of the proposed method over existing approaches in GEE for ordinal regression are (a) the avoidance of large matrices when \( K \) or \( d \) are large (since there is no need to create a set of binary variables), (b) a proper definition relating the working discretized MVN model to the probability distribution of the response vector, (c) a latent correlation matrix for the ordinal outcomes induced by the MVN latent variables, and (d) analogues of the AIC and the BIC for variable and correlation structure selection, namely the CL1AIC and CL1BIC, can be derived. Hence the weighted scores method for repeated ordinal responses on the one hand can allow for a richer specification of the correlation assumptions and on the other hand a correct specification in both the correlation and mean function (covariate) modelling.

The remainder of the paper proceeds as follows. Section 2 provides the theory of the weighted scores method for ordinal regression with dependent data. Section 3 derives the CL1 information criteria in the context of longitudinal data analysis with an ordinal margin. Section 4 describes the simulation studies we perform to gauge the efficiency and robustness of the weighted scores and GEE method, and to assess the performance of the CL1 information criteria for longitudinal ordinal data. We discuss an application example in Section 5 and conclude with some discussion in Section 6, followed by a brief section with the software details.
2 The weighted scores estimating equations

The main idea of weighted scores method is to write out the score equations for independent data within clusters or panels, and then generalize to estimating equations by inserting weight matrices between the matrix of covariates and the vector of scores for regression and non-regression parameters. The general theory (Nikoloulopoulos et al., 2011) is modified here for ordinal regression models.

For ease of exposition, let \( d \) be the dimension of a “cluster” or “panel” and \( n \) the number of clusters. The theory can be extended to varying cluster sizes. Let \( p \) be the number of covariates, that is, the dimension of a covariate vector \( x \). Let \( Z \sim \mathcal{F} \) be a latent variable, such that \( Y = y \) if \( \alpha_{y-1} + x^T \beta \leq Z \leq \alpha_y + x^T \beta \), \( y = 1, \ldots, K \), where \( K \) is the number of categories of \( Y \) (without loss of generality, we assume \( \alpha_0 = -\infty \) and \( \alpha_K = \infty \)), and \( \beta \) is the \( p \)-dimensional regression vector. From this definition, the response \( Y \) is assumed to have density

\[
 f_1(y; \nu, \gamma) = \mathcal{F}(\alpha_y + \nu) - \mathcal{F}(\alpha_{y-1} + \nu),
\]

where \( \nu = x^T \beta \) is a function of \( x \) and the \( p \)-dimensional regression vector \( \beta \), and \( \gamma = (\alpha_1, \ldots, \alpha_{K-1}) \) is the \( q \)-dimensional vector of the univariate cutpoints (\( q = K - 1 \)). Note that \( \mathcal{F} \) normal leads to the probit model and \( \mathcal{F} \) logistic leads to the cumulative logit model for ordinal response.

Suppose that the data are \( (y_{ij}, x_{ij}) \), \( j = 1, \ldots, d \), \( i = 1, \ldots, n \), where \( i \) is an index for individuals or clusters, \( j \) is an index for the repeated measurements or within cluster measurements. The univariate marginal model for \( Y_{ij} \) is \( f_1(y_{ij}; \nu_{ij}, \gamma) \) where \( \nu_{ij} = x_{ij}^T \beta \) and \( \gamma \) of dimension \( q \) be the vector of univariate cutpoints. Here we consider univariate parameters that are common to different margins, i.e., common regression parameters \( \beta \) and cut-points \( \gamma \) for different univariate margins. The theory can be extended for the case the univariate parameters are not common to the different margins. If for each \( i \), \( Y_{i1}, \ldots, Y_{id} \) are independent, then the log-likelihood is

\[
 L_1 = \sum_{i=1}^n \sum_{j=1}^d \log f_1(y_{ij}; \nu_{ij}, \gamma) = \sum_{i=1}^n \sum_{j=1}^d \ell_1(\nu_{ij}, \gamma, y_{ij}),
\]

where \( \ell_1(\cdot) = \log f_1(\cdot) \). The score equations for \( \beta \) and \( \gamma \) are

\[
 \frac{\partial L_1}{\partial \beta} = \sum_{i=1}^n \sum_{j=1}^d \left( x_{ij} 0 \right) \frac{\partial f_1(\nu_{ij}, \gamma, y_{ij})}{\partial \nu_{ij}} = \sum_{i=1}^n \sum_{j=1}^d \left( x_{ij} I_q \right) \frac{\partial \ell_{1ij}(\gamma_{ij}, y_{ij})}{\partial \gamma_{ij}} = 0, \tag{1}
\]

where \( \gamma_{ij} = (\alpha_1 + \nu_{ij}, \ldots, \alpha_{K-1} + \nu_{ij}) = (\gamma_{ij1}, \ldots, \gamma_{ij,K-1}) \), \( \ell_{1ij}(\cdot) = \log f_{1ij}(\cdot) \), \( f_{1ij}(\gamma_{ij}, y) = \mathcal{F}(\gamma_{ijy}) - \mathcal{F}(\gamma_{ij,y-1}) \), and \( I_q \) is an identity matrix of dimension \( q \). Let \( X_{ij}^T = \left( x_{ij}^T I_q \right) \) and \( s_{ij}^{(1)}(a) = \frac{\partial f_{1ij}(\gamma_{ij}, y_{ij})}{\partial \gamma_{ij}} \) where \( a^T = (\beta^T, \gamma^T) \) is the column vector of all \( r + q \) univariate parameters. The score equations (1) can be written as

\[
 g_1 = g_1(a) = \frac{\partial L_1}{\partial a} = \sum_{i=1}^n \sum_{j=1}^d X_{ij}^T s_{ij}^{(1)}(a) = \sum_{i=1}^n X_{i}^T s_{i}^{(1)}(a) = 0, \tag{2}
\]

where \( X_i^T = (X_{i1}^T, \ldots, X_{id}^T) \) and \( s_{i}^{(1)}(a) = (s_{i1}^{(1)}(a), \ldots, s_{id}^{(1)}(a)) \). The vectors \( s_{ij}^{(1)}(a) \) and \( s_{i}^{(1)}(a) \) have dimensions \( q \) and \( dq \) respectively. The dimensions of \( X_{ij} \) and \( X_i \) are \( q \times r \) and \( dq \times r \) respectively.

For estimation of \( a \), when \( Y_{i1}, \ldots, Y_{id} \) are dependent and a multivariate model is not used, an approach is to use a “working model” for the purpose of getting the weight matrices, which might be near optimal for the “true joint distribution”. We select a “working model” based on the discretized MVN distribution as this allows a wide range of dependence. The discretized MVN (or the multivariate normal copula with discrete margins) model has the following cumulative distribution function (cdf):

\[
 F(y_1, \ldots, y_d) = \Phi_d \left( \Phi^{-1}[F_1(y_1; \nu_1, \gamma)], \ldots, \Phi^{-1}[F_1(y_d; \nu_d, \gamma)]; R \right),
\]
where $\Phi_d$ denotes the standard MVN distribution function with correlation matrix $R = (\rho_{jk} : 1 \leq j < k \leq d)$, $\Phi$ is cdf of the univariate standard normal, and $F_1(y; \nu, \gamma) = F(\alpha + \nu)$ is the univariate cdf for $Y$. The MVN copula inherits the dependence structure of the MVN distribution, but lacks a closed form cdf; this means likelihood inference might be difficult as $d$-dimensional integration is required for the multivariate probabilities ($d > 3$); see e.g., Nikoloulopoulos and Karlis (2009). However, in our case as the weight matrices will depend on the covariances of the scores, only the bivariate marginal probabilities of $Y_{ij}$ and $Y_{ik}, j \neq k$ will be needed for estimation.

The estimating equations based on a “working” discretized MVN, take the form:

$$g_1^* = g_1^*(a) = \sum_{i=1}^{n} X_i^T W_{i,\text{working}}^{-1} s_i^{(1)}(a) = 0, \quad (3)$$

where $W_{i,\text{working}}^{-1} = \Delta_i^{(1)}(\tilde{a}) |\Omega_i^{(1)}(\tilde{a}, \tilde{R})|^{-1}$ is based on the covariance matrix $\Omega_i^{(1)}(\tilde{a}, \tilde{R})$ of $s_i^{(1)}(a)$ computed from the fitted discretized MVN model with estimated parameters $\tilde{a}$ and $\tilde{R}$ and the symmetric $dq \times dq$ matrix

$$\Delta_i^{(1)} = \text{diag}(\Delta_{i1}^{(1)}, \ldots, \Delta_{id}^{(1)}) \quad \text{with} \quad \Delta_{ij} = -E \left( \frac{\partial^2 f(y_{ij}, y_{ik}; \nu_{ij}, \nu_{ik}, \gamma, \rho_{jk})}{\partial \nu_{ij} \partial \nu_{ik}} \right) .$$

As bivariate normal cdf calculations are needed for the calculation of $\Omega_i^{(1)}(\tilde{a}, \tilde{R})$ (different ones for different clusters), a good approximation that can be quickly computed is important. We used the approximation given by Johnson and Kotz (1972).

The estimated parameters $\tilde{a}$ and $\tilde{R}$ of the working discretized MVN model can be easily obtained in a two-step approach, namely the CL1 method in Zhao and Joe (2005). Estimated $\tilde{a}$ and $\tilde{R}$ are obtained by solving the CL1 univariate and bivariate composite score functions, respectively. The former are the same with the independent estimating equations (2), while the latter are given below:

$$g_2 = \sum_{i=1}^{n} s_i^{(2)}(\tilde{a}, R) = 0,$$

where $s_i^{(2)}(a, R) = \frac{\partial}{\partial R} \sum_{i < k} \log f_2(Y_{ij} = y_{ij}; Y_{ik} = y_{ik}, \gamma, \rho_{jk})$ with $f_2(\cdot)$ the bivariate marginal probability of $Y_{ij}$ and $Y_{ik}$, viz.

$$f_2(y_{ij}, y_{ik}; \nu_{ij}, \nu_{ik}, \gamma, \rho_{jk}) = \int \Phi^{-1}[F_1(y_{ij}; \nu_{ij}, \gamma)] \int \Phi^{-1}[F_1(y_{ik}; \nu_{ik}, \gamma)] \phi_2(z_j, z_k; \rho_{jk}) dz_j dz_k;$$

$\phi_2(\cdot; \rho)$ denotes the standard bivariate normal density with correlation $\rho$.

If the $W_{i,\text{working}}$ are assumed fixed for the second stage of solving the weighted scores estimating equations (3), then the asymptotic covariance matrix of the solution $\tilde{a}$ is

$$V_1^* = (-H_{g_1^*})^{-1} J_{g_1^*} (-H_{g_1^*})^{-1}$$

with

$$-H_{g_1^*} = \sum_{i=1}^{n} X_i^T W_{i,\text{working}}^{-1} \Delta_i^{(1)} X_i, \quad J_{g_1^*} = \sum_{i=1}^{n} X_i^T W_{i,\text{working}}^{-1} \Omega_i^{(1)}(W_{i,\text{working}}^{-1})^T X_i,$$

where $\Omega_i^{(1)}$ is the “true covariance matrix” of $s_i^{(1)}(a)$. The $\Omega_i^{(1)}$ can be estimated by $s_i^{(1)}(\tilde{a})s_i^{(1)\top}(\tilde{a})$. This estimate is similar to what is done in the “sandwich” covariance estimator in GEE.

### 3 CL1 information criteria

The CL1 method in Zhao and Joe (2005) is used to estimate conveniently the univariate and latent correlation parameters of the discretized MVN model in order to compute the working weight matrices and then solve the weighted score equations (3). Herein, we also call the CL1 information criteria, for correlation structure and variable selection in the weighted scores estimating equations. This section provides the form of the CL1
information criteria, proposed by Nikoloulopoulos (2016) for longitudinal binary and count data, in the context of longitudinal ordinal data.

The CL1 versions of AIC and BIC criteria are defined as:

\[
\text{CL1AIC} = -2L_2 + 2\text{tr}\left( J_g H_g^{-1} \right);
\]
\[
\text{CL1BIC} = -2L_2 + \log(n)\text{tr}\left( J_g H_g^{-1} \right),
\]
where \( L_2 = \sum_{i=1}^{n} \sum_{j<k} \log f_2(y_{ij}, y_{ik}; \nu_{ij}, \nu_{ik}, \gamma, \rho_{jk}) \) is the bivariate CL1 log-likelihood, \( J_g \) is the covariance or variability matrix, and \( H_g \) is the sensitivity or Hessian matrix of the CL1 estimating equations \( g = (g_1, g_2)^\top \).

The covariance matrix \( J_g \) of the composite score functions \( g \) is given as below

\[
J_g = \text{Cov}(g) = \begin{pmatrix}
\text{Cov}(g_1)
\text{Cov}(g_1, g_2)
\text{Cov}(g_2)
\text{Cov}(g_2, g_1)
\end{pmatrix}
= \frac{1}{n} \sum_i \begin{pmatrix}
X_i^\top \Omega_i^{(1)} X_i
X_i^\top \Omega_i^{(2,1)} X_i
X_i^\top \Omega_i^{(1,2)}
\end{pmatrix},
\]

where

\[
\begin{pmatrix}
\Omega_i^{(1)}
\Omega_i^{(1,2)}
\Omega_i^{(2,1)}
\Omega_i^{(2)}
\end{pmatrix} = \begin{pmatrix}
\text{Cov}(s_i^{(1)}(\mathbf{a}))
\text{Cov}(s_i^{(2)}(\mathbf{a}, \mathbf{R}), s_i^{(1)}(\mathbf{a}))
\text{Cov}(s_i^{(1)}(\mathbf{a}), s_i^{(2)}(\mathbf{a}, \mathbf{R}))
\end{pmatrix}.
\]

To define the Hessian matrix of the CL1 estimating equations, first set \( \theta = (\mathbf{a}, \mathbf{R})^\top \), then

\[-H_g = E\left( \frac{\partial g}{\partial \theta} \right) = \begin{pmatrix}
E\left( \frac{\partial g_1}{\partial \mathbf{a}} \right)
E\left( \frac{\partial g_1}{\partial \mathbf{R}} \right)
\end{pmatrix} = \begin{pmatrix}
-H_{g_{1,1}} & 0
-H_{g_{2,1}} & -H_{g_{2,2}}
\end{pmatrix},
\]

where \( -H_{g_{1,1}} = \frac{1}{n} \sum_i X_i^\top \Delta_i^{(1)} X_i \), \( -H_{g_{2,1}} = \frac{1}{n} \sum_i \Delta_i^{(2,1)} X_i \), and \( -H_{g_{2,2}} = \frac{1}{n} \sum_i \Delta_i^{(2,2)} \). The forms of \( \Delta_i^{(1)}, \Delta_i^{(2,1)}, \Delta_i^{(2,2)} \) are given in an Appendix.

Summing up, to evaluate the CL1 information criteria involves the computation of matrices described above; their dimensions are given in Table 1. The computations involve the trivariate and four-variate margins along with their derivatives; technical details are shown in the Appendix.

**Table 1: The dimensions of various matrices involved in the calculation of CL1 information criteria.** Note that \( t = p + \left( \frac{d}{2} \right) + q \) and \( r = p + q \).

| Matrix | \( \mathbf{J}_g \) | \( \mathbf{J}_g^{(1)} \) | \( \mathbf{J}_g^{(1,2)} \) | \( \mathbf{J}_g^{(2)} \) | \( \Omega_i^{(1)} \) | \( \Omega_i^{(1,2)} \) | \( \Omega_i^{(2,1)} \) | \( \Omega_i^{(2)} \) |
|--------|----------------|----------------|----------------|----------------|-------------|-------------|-------------|-------------|
| Dimensions | \( t \times t \) | \( r \times r \) | \( r \times \left( \frac{d}{2} \right) \) | \( \left( \frac{d}{2} \right) \times r \) | \( dq \times dq \) | \( dq \times \left( \frac{d}{2} \right) \) | \( dq \times dq \) | \( dq \times \left( \frac{d}{2} \right) \) |

| Matrix | \( \mathbf{H}_g \) | \( \mathbf{H}^{(1)} \) | \( \mathbf{H}^{(1,2)} \) | \( \mathbf{H}^{(2)} \) | \( \Delta_i^{(1)} \) | \( \Delta_i^{(1,2)} \) | \( \Delta_i^{(2,1)} \) | \( \Delta_i^{(2)} \) |
|--------|----------------|----------------|----------------|----------------|-------------|-------------|-------------|-------------|
| Dimensions | \( t \times t \) | \( r \times r \) | \( r \times \left( \frac{d}{2} \right) \) | \( \left( \frac{d}{2} \right) \times r \) | \( dq \times dq \) | \( dq \times \left( \frac{d}{2} \right) \) | \( dq \times dq \) | \( dq \times \left( \frac{d}{2} \right) \) |

### 4 Simulations

In order to study the robustness and efficiency of the weighted scores method for longitudinal ordinal responses, we will use various multivariate copula models as true models. We will compare the weighted scores method with the ‘gold standard’ maximum likelihood and also include in the comparison the local odds ratio GEE approach in Touloumis et al. (2013) as the current state of the art of the various GEE approaches for ordinal regression (Nooraee et al., 2014). This GEE approach avoids the theoretical problems (see Section 1) by using a local odds ratios parametrization to describe the association pattern within subjects. We also assess the performance of the CL1 information criteria proposed by Nikoloulopoulos (2016) for longitudinal ordinal response data. Before that, the first subsection provides some background on copula models that might be suitable for clustered and longitudinal ordinal data.
4.1 Relevant background for copula models

A copula is a multivariate cdf with uniform $U(0, 1)$ margins (Joe, 1997, 2014; Nelsen, 2006). If $G$ is a $d$-variate cdf with univariate margins $G_1, \ldots, G_d$, then Sklar’s (1959) theorem implies that there is a copula $C$ such that

$$G(y_1, \ldots, y_d) = C(G_1(y_1), \ldots, G_d(y_d)).$$

Copulas enable you to break the model building process into two separate steps:

1. Choice of arbitrary marginal distributions $G_1(y_1), \ldots, G_d(y_d)$;
2. Choice of an arbitrary copula function $C$ (dependence structure).

If one assumes a different copula, then a different multivariate distribution is constructed. The copula is unique if $G_1, \ldots, G_d$ are continuous, but not if some of the $G_j$ have discrete components. If $G$ is continuous and $(Y_1, \ldots, Y_d) \sim G$, then the unique copula is the distribution of $(U_1, \ldots, U_d) = (G_1(Y_1), \ldots, G_d(Y_d))$ leading to

$$C(u_1, \ldots, u_d) = G(G_1^{-1}(u_1), \ldots, G_d^{-1}(u_d)), \quad 0 \leq u_j \leq 1, \ j = 1, \ldots, d,$$

where $G^{-1}_j$ are inverse cdfs. In particular, if $T_d(\cdot; \nu, R)$ is the MVT cdf with correlation matrix $R = (\rho_{jk} : 1 \leq j < k \leq d)$ and $\nu$ degrees of freedom, and $T(\cdot; \nu)$ is the univariate Student t cdf with $\nu$ degrees of freedom, then the MVT copula is

$$C(u_1, \ldots, u_d) = T_d\left(T^{-1}_d(u_1; \nu), \ldots, T^{-1}_d(u_d; \nu); \nu, R\right).$$

For ordinal (discrete) random vectors, multivariate probabilities of the form $\pi_d(y) = \Pr(Y_1 = y_1, \ldots, Y_d = y_d)$ involve $2^d$ finite differences of the joint cdf. Therefore likelihood inference for discrete data is straightforward for copulas with a computationally feasible form of the cdf. Archimedean (Joe, 1997) and mixtures of max-id (Joe and Hu, 1996) parametric family of copulas have closed form cdfs but have less range of dependence compared with the MVN or MVT copulas. However they provide enough structure to study the efficiency of the weighted scores method using the discretized MVN as a “working model”. For example, the Archimedean copula is suitable for positive dependent clustered data with exchangeable dependence, while the mixture of max-id copula is suitable for more general positive dependence, including dependence that is decreasing with lag as in longitudinal data. More importantly, these copulas have different dependence properties than the “working” MVN copula. For example they provide reflection asymmetric tail dependence, while the MVN copula provides tail independence (Joe, 1997, 2014). Hence they are suitable to study the robustness to dependence of the weighted scores method. These parametric families of copulas are briefly defined below:

- **Multivariate Archimedean copulas** have the form

  $$C(u_1, \ldots, u_d; \theta) = \phi\left(\sum_{j=1}^{d} \phi^{-1}(u_j; \theta) ; \theta\right),$$

  where $\phi(u; \theta)$ is the Laplace transform of a univariate family of distributions of positive random variables indexed by the parameter $\theta$, such that $\phi(:, \theta)$ and its inverse has closed form (Joe, 1997).

- **Mixture of max-id copulas** (Joe and Hu, 1996) have the form

  $$C(u_1, \ldots, u_d; \theta, \theta_{jk} : 1 \leq j < k \leq d) = \phi\left(\sum_{j<k} \log C^{(m)}_{jk}(e^{-p_j\phi^{-1}(u_j; \theta)}, e^{-p_k\phi^{-1}(u_k; \theta)}; \theta_{jk}) ; \theta\right); \ p_j = (d-1)^{-1}, \ j = 1, \ldots, d.$$
Since the mixing operation introduces dependence this new copula has a dependence structure that comes from the form of the max-id copula \( C_{jk}^{(m)}(\cdot; \theta_{jk}) \) and the form of Laplace transform \( \phi(\cdot; \theta) \). Another interesting interpretation is that the Laplace transform \( \phi \) introduces the smallest dependence between random variables (exchangeable dependence), while the copulas \( C_{jk}^{(m)} \) add some pairwise dependence.

To this end, we consider a multivariate ordinal regression setting in which the \( d \geq 2 \) dependent ordinal variables \( Y_1, \ldots, Y_d \) are observed together with a vector \( x \in \mathbb{R}^p \) of explanatory variables. If \( C(\cdot) \) is any parametric family of copulas and \( F_1(y_j, \nu_j, \gamma) \) is the parametric model for the \( j \)th univariate ordinal variable then

\[
C\left( F_1(y_1, \nu_1, \gamma), \ldots, F_1(y_d, \nu_d, \gamma) \right)
\]

is a multivariate parametric model with univariate margins \( F_1(y_1, \nu_1, \gamma), \ldots, F_1(y_d, \nu_d, \gamma) \). For copula models, the response vector \( Y = (Y_1, \ldots, Y_d) \) can be discrete (Nikoloulopoulos, 2013; Nikoloulopoulos and Joe, 2015b). The only assumption we make is that the margins of the joint distribution \( \mathcal{G} \) are identical, that is, \( G_1 = \ldots = G_d = F_1 = \mathcal{F} \). \( \mathcal{F} \) normal leads to the probit model and \( \mathcal{F} \) logistic leads to the cumulative logit model for ordinal response. The theory of the weighted scores method is not robust to margin misspecification, but it extends to any univariate regression method. For instance, Nikoloulopoulos et al. (2011) used discrete negative binomial margins (that are not in the GLM family) and Nikoloulopoulos (2016) used GLM (Bernoulli and Poisson) margins.

### 4.2 Small sample efficiency of the weighted scores

We randomly generate \( B = 10^4 \) samples of size \( n = 50, 100, 300 \) from the the above copula models with exchangeable and unstructured dependence. Note that AR(1)-like dependence is not used here since the local odds ratio GEE method in Touloumis et al. (2013) does not include this structure. For exchangeable dependence structure, the Gumbel copula in the Archimedean class with Laplace transform \( \phi_G(t; \theta) = \exp(-t^{1/\theta}) \) was used as the “true model”. For unstructured dependence, the mixture of max-id copula with Laplace transform \( \phi_G(\cdot; \theta) \) and the bivariate Gumbel copula for the \( C_{jk}^{(m)}(\cdot; \theta_{jk}) \) was used as the “true model”. For simulation from Archimedean and mixture of max-id copulas we have used the algorithms in Joe (2014, pp. 272–274).

We use \( d = 3, K = 5 \) ordinal categories (equally weighted) and ordinal probit regression. For the covariates and regression parameters, we use a combination of a time-stationary and a time-varying design, i.e., include covariates that are typically constant over time, and correlated over time. More specifically, we chose \( p = 4, x_{ij} = (x_{1ij}, x_{2ij}, x_{3ij}, x_{4ij}) \) with \( x_{1i} \in \{0, 1\} \) a group variable, \( x_{2ij} \) an i.i.d. from a \( d \)-variate Gumbel copula with standard uniform margins and \( d \times d \) Kendall’s tau association matrix with off-diagonal elements equal to 0.5, \( x_{3ij} = x_{1ij} \times x_{2ij} \), and \( x_{4ij} \) a uniform random variable in the interval \([-1, 1] \); \( \beta_1 = -\beta_2 = -\beta_3 = -0.5, \beta_4 = 0 \). By considering the noise variable \( x_{4i} \) we aim to check the Type I error rate for inference on \( H_0 : \beta_4 = 0 \) (see e.g., Larrabee et al., 2014) based on the weighted scores, local odds ratios GEE and ML methods.

Table 2 contains the parameter values, the bias, standard deviations (SD) and root mean square errors (RMSE) of the maximum likelihood (ML), weighted scores (WS) and GEE estimates, along with the average of their theoretical SDs (\( \sqrt{V} \)). The theoretical variance of the ML estimate is obtained via the gradients and the Hessian computed numerically during the maximization process. The GEE estimates and their theoretical variance are calculated with the function \texttt{ordLORgeeR} in the R package \texttt{multgee} (Touloumis, 2015). For the local odds ratios GEE approach we use the ‘uniform’ and the ‘category exchangeability’ structure for the exchangeable and unstructured case, respectively, as suggested by Touloumis et al. (2013). From the results, we can see that the weighted scores and the local odds ratio GEE method are robust to dependence and nearly as efficient as maximum likelihood for fully specified copula models.
Table 2: Small sample of sizes $n = 50, 100, 300$ simulations ($10^4$ replications) and resultant biases, root mean square errors (RMSE), and standard deviations (SD), along with average theoretical SDs ($\sqrt{n}$) scaled by $n$, for the maximum likelihood of the regression parameters for the trivariate Gumbel copula (exchangeable) or the mixture of max-id copula with Laplace transform $\varphi_\tau$ and the bivariate Gumbel copula for the $C_{jk}^{(m)}(\cdot; \theta_{jk})$ (unstructured) model and ordinal probit regression, and the weighted scores (WS) and GEE with exchangeable or unstructured correlation matrix.

|        | $\beta_1 = -0.5$ |         | $\beta_2 = 0.5$ |         | $\beta_3 = 0.5$ |         | $\beta_4 = 0$ |         |
|--------|------------------|---------|-----------------|---------|-----------------|---------|--------------|---------|
|        | WS GEE ML        | WS GEE ML | WS GEE ML       | WS GEE ML | WS GEE ML       | WS GEE ML | WS GEE ML    | WS GEE ML |
| Exch   | $n = 50$         | $\theta = 3$ | $n = 100$       | $n = 300$ | $\theta = 5$   | $n = 100$ | $\theta = 1.2$ | $\theta = 1.2$ |
| $\theta = 3$ | Bias            | SD      | RMSE            | $\sqrt{V}$ | Bias            | SD      | RMSE            | $\sqrt{V}$ |
| $n = 50$ | -1.29 -0.73 -0.94 | 1.53 0.70 0.88 | 1.59 0.83 1.01 | -0.03 -0.04 -0.02 | | | | |
| $n = SD$ | 20.88 20.43 19.37 | 20.24 19.59 18.46 | 28.99 28.10 26.51 | 4.22 4.17 3.89 | | | | |
| $n = 100$ | 20.92 20.44 19.39 | 20.29 19.60 18.48 | 29.03 28.11 26.53 | 4.22 4.17 3.90 | | | | |
| $n = SD$ | 19.71 19.29 18.77 | 18.63 18.10 17.79 | 26.70 25.98 25.63 | 4.16 4.09 3.91 | | | | |
| $n = RMSE$ | 19.71 19.29 18.77 | 18.63 18.10 17.79 | 26.70 25.98 25.63 | 4.16 4.09 3.91 | | | | |
| $n = 300$ | 28.23 28.26 26.55 | 27.06 26.75 24.99 | 38.76 38.39 35.85 | 5.79 5.79 5.42 | | | | |
| $n = SD$ | 27.32 27.14 25.97 | 25.64 25.43 24.35 | 36.75 36.53 35.03 | 5.68 5.68 5.34 | | | | |
| $n = RMSE$ | 27.32 27.14 25.97 | 25.64 25.43 24.35 | 36.75 36.53 35.03 | 5.68 5.68 5.34 | | | | |
| $n = 50$ | 46.78 46.85 44.40 | 43.59 43.74 41.29 | 62.65 62.95 59.46 | 6.94 6.97 6.09 | | | | |
| $n = SD$ | 47.09 47.33 44.39 | 44.69 44.89 41.94 | 63.70 64.11 59.82 | 6.94 6.97 6.09 | | | | |
| $n = RMSE$ | 47.10 47.33 44.39 | 44.73 44.91 41.97 | 63.71 64.11 59.82 | 6.94 6.97 6.09 | | | | |
| $n = 100$ | 47.09 47.33 44.39 | 44.73 44.91 41.97 | 63.71 64.11 59.82 | 6.94 6.97 6.09 | | | | |
| $n = SD$ | 42.82 43.68 41.84 | 39.33 38.89 35.25 | 48.77 48.52 46.27 | 6.92 6.98 6.57 | | | | |
| $n = RMSE$ | 43.85 43.68 41.84 | 39.33 38.89 35.25 | 48.77 48.52 46.27 | 6.92 6.98 6.57 | | | | |
| $n = 300$ | 47.35 47.07 41.50 | 43.35 43.17 32.06 | 48.06 47.65 46.13 | 6.87 6.90 6.54 | | | | |
| $n = SD$ | 43.85 43.68 41.84 | 39.33 38.89 35.25 | 48.77 48.52 46.27 | 6.92 6.98 6.57 | | | | |
| $n = RMSE$ | 43.35 43.07 41.50 | 39.33 38.89 35.25 | 48.06 47.65 46.13 | 6.87 6.90 6.54 | | | | |
Table 3: Empirical Type I error rates for inference on $H_0: \beta_4 = 0$ based on the weighted scores, local odds ratios GEE and ML methods.

|       | $\alpha = 0.01$          |        | $\alpha = 0.05$        |        | $\alpha = 0.1$         |        |
|-------|--------------------------|--------|------------------------|--------|------------------------|--------|
|       | WS | GEE | ML | WS | GEE | ML | WS | GEE | ML | WS | GEE | ML |
| Exch, $\theta = 3$ | n = 50 | 0.014 | 0.014 | 0.008 | 0.060 | 0.063 | 0.048 | 0.112 | 0.114 | 0.097 |
|       | n = 100 | 0.013 | 0.013 | 0.010 | 0.057 | 0.056 | 0.053 | 0.114 | 0.112 | 0.105 |
|       | n = 300 | 0.011 | 0.011 | 0.010 | 0.050 | 0.050 | 0.051 | 0.101 | 0.101 | 0.099 |
| Exch, $\theta = 5$ | n = 50 | 0.015 | 0.019 | 0.008 | 0.059 | 0.068 | 0.049 | 0.113 | 0.120 | 0.102 |
|       | n = 100 | 0.013 | 0.013 | 0.011 | 0.053 | 0.060 | 0.050 | 0.106 | 0.110 | 0.099 |
|       | n = 300 | 0.012 | 0.012 | 0.010 | 0.054 | 0.053 | 0.051 | 0.105 | 0.107 | 0.102 |
| Unstr | n = 50 | 0.020 | 0.015 | 0.024 | 0.072 | 0.060 | 0.068 | 0.132 | 0.117 | 0.121 |
|       | n = 100 | 0.012 | 0.011 | 0.014 | 0.056 | 0.050 | 0.056 | 0.111 | 0.102 | 0.110 |
|       | n = 300 | 0.010 | 0.009 | 0.009 | 0.050 | 0.049 | 0.051 | 0.101 | 0.099 | 0.105 |

For unstructured dependence the true copula parameters are $\{\theta, \theta_{12}, \theta_{13}, \theta_{23}\} = \{1.2, 1.5, 1.1, 2.7\}$.

Furthermore, Table 3 contains the observed level of the bilateral test for three common nominal levels for inference on $H_0: \beta_4 = 0$ based on the weighted scores, local odds ratios GEE and ML methods. The observed levels are close to nominal levels and hence demonstrate that the tests from all the competing approaches are reliable.

Finally in order to study the relative performance of the weighted scores over the local odds ratios GEE method as the dimension $d$ or the number of categories increase we randomly generated $B = 20$ samples of size $n = 100$ from the Gumbel copula model with exchangeable dependence for $d, K \in \{10, 15, 20, 25\}$. The link function, model parameters and covariates are set as before. The simulations were carried out on an Intel(R) Xeon(R) CPU X5650 2.67GHz.

Table 4 summarizes the computing times (averaged over 20 replications) in seconds. Clearly the local odds ratios GEE approach requires a much higher computing time for large $d$ or $K$. Note in passing that for large $d$ or $K$, memory up to 60GB was required for the local odds ratios GEE approach. Hence it is demonstrated that large matrices are a problem for GEE methods, in as much as they cause model fitting algorithms to run slowly. Note in passing that for larger (than the ones in Table 4) values of $K$ or $d$ the local odds ratio GEE implementation (Touloumis, 2015) is infeasible.

4.3 Model selection criteria

We perform simulation studies to examine the reliability of using CL1AIC and CL1BIC to choose the correct model for longitudinal ordinal data. In Subsection 4.3.1 we assess the performance of CL1AIC, CL1BIC in correlation structure selection, and in Subsection 4.3.2 we investigate the performance of CL1AIC, CL1BIC in variable selection. For exchangeable, AR(1), and unstructured dependence, the Gumbel copula, the mixture of max-id copula with Laplace transform $\phi_G(\cdot; \theta)$ and the bivariate Gumbel copula for the $C_{jk}^{(m)}(\cdot; \theta_{jk})$, and the MVT copula were used as the “true models”, respectively.

4.3.1 Correlation structure selection

We randomly generate $B = 10^3$ samples of size $n = 50, 100, 300$ with $d = 3$ and ordinal probit regression with $p = 3$, $x_{ij} = (1, x_{1ij}, j - 1)^T$ where $x_{1ij}$ are taken as Bernoulli random variables with probability of success $1/2$, and $\beta_0 = 0.25 = -\beta_1 = -\beta_2$.

In Table 5, we present the number of times that different working correlation structures are chosen over 1000 simulation runs under each true correlation structure. If the true correlation structure is exchangeable or AR(1), CL1BIC is better than CL1AIC. If the true correlation structure is unstructured, CL1AIC performs extremely well, especially for a small sample size, which is typical of medical studies. The difference between the correct
Table 4: Computing times (averaged over 20 replications) in seconds of the weighted scores (WS) over the local odds ratios GEE approach.

| d   | K  | θ | time(WS) | time(GEE) | time(GEE)/time(WS) |
|-----|----|---|----------|-----------|--------------------|
| 10  | 10 | 3 | 88.1     | 35.3      | 0.4                |
|     | 5  |   | 95.4     | 69.7      | 0.7                |
| 10  | 15 | 3 | 184.2    | 126.7     | 0.7                |
|     | 5  |   | 193.9    | 182.2     | 0.9                |
| 10  | 20 | 3 | 363.2    | 444.9     | 1.2                |
|     | 5  |   | 422.8    | 640.0     | 1.5                |
| 10  | 25 | 3 | 760.8    | 1559.4    | 2.0                |
|     | 5  |   | 716.1    | 1490.9    | 2.1                |
| 15  | 10 | 3 | 208.4    | 254.1     | 1.2                |
|     | 5  |   | 219.6    | 388.2     | 1.8                |
| 15  | 15 | 3 | 350.4    | 1267.6    | 3.6                |
|     | 5  |   | 371.1    | 1566.2    | 4.2                |
| 15  | 20 | 3 | 636.8    | 6057.0    | 9.5                |
|     | 5  |   | 706.1    | 6738.5    | 9.5                |
| 15  | 25 | 5 | 1524.1   | 23221.8   | 15.2               |
|     | 3  |   | 1380.5   | 25139.2   | 18.2               |
| 20  | 10 | 3 | 334.4    | 1289.0    | 3.9                |
|     | 5  |   | 360.7    | 1646.5    | 4.6                |
| 20  | 15 | 3 | 562.4    | 8165.8    | 14.5               |
|     | 5  |   | 602.9    | 9196.7    | 15.3               |
| 20  | 20 | 3 | 1287.1   | 48270.2   | 37.5               |
|     | 5  |   | 1268.0   | 50030.8   | 39.5               |
| 20  | 25 | 3 | 2131.3   | 153707.2  | 72.1               |
|     | 5  |   | 2243.1   | 138304.0  | 61.7               |

identification rate of CL1AIC and that of CL1BIC becomes small when the sample size increases to 100 or 300. The CL1AIC tends to choose the unstructured correlation structure more often than CL1BIC does, since AIC is more likely to result in an overparametrized model than BIC in parametric settings (Chen and Lazar, 2012).

4.3.2 Variable selection

We randomly generate $B = 10^3$ samples of size $n = 50, 100, 300$ with $d = 3$ and ordinal probit regression with $p = 5, x_{ij} = (1, x_{1ij}, j - 1, x_{3ij}, x_{4ij})^T$ where $x_{1ij}, \beta_0, \beta_1, \beta_2$ are as before, $x_{3ij}, x_{4ij}$ are independent uniform random variables in the interval $[-1, 1]$ (and independent of $x_{1ij}$), and $\beta_3 = \beta_4 = 0$. We consider the same candidate models, with various subsets of covariates, and include all the aforementioned parametric correlation structures as true correlation structures. The subsets of covariates that we consider are the following:

- $x_1 = (1, x_{1ij})^T$.
- $x_{12} = (1, x_{1ij}, j - 1)^T$ (the true regression model).
- $x_{123} = (1, x_{1ij}, j - 1, x_{3ij})^T$.
- $x_{1234} = (1, x_{1ij}, j - 1, x_{3ij}, x_{4ij})^T$.

In Table 5, we present the number of times that different subsets of covariates are chosen over 1000 simulation runs under each true correlation structure. For all the true correlation structures, CL1BIC performs better than CL1AIC, and its performance increases as the sample size increases.
ordinal regression (W are and Lipsitz, 1986; Lipsitz et al., 1994a; T ouloumis et al., 2013). The data were taken
from a randomized clinical trial designed to evaluate the ef fectiveness of the treatment Auranofin versus a
placebo therapy for the treatment of rheumatoid arthritis. The repeated ordinal response is the self-assessment
of arthritis, classified on a five-level ordinal scale (1 = poo r, . . . , 5 = very good). Patients (n=303) were
randomized into one of the two treatment groups after baseli ne self-assessment followed during five months
during treatment resulting in a maximum of 3 measurements per subject (unequal cluster size s). The covariates are time, baseline-assessment, age in years at baseline, sex and treatment. W e treat time and baseline-assessment as categorical variables
and we will prefer CL1BIC since one can easily distinguish betwe en the various structures, as their difference in
magnitude is large. This is not the case for the CL1AIC, where the differences are rather small. This was
also the finding in our simulation studies, where it has been revealed that CL1AIC is more prone to select the
unstructured case. Further, ordinal logistic regression is slightly better than ordinal probit regression.

5 The rheumatoid arthritis data

We illustrate the weighted scores method by re-analysing the rheumatoid arthritis data-set (Bombardier et al.,
1986). These data have previously been used as an example for other methodological papers on GEE for
ordinal regression (Ware and Lipsitz, 1986; Lipsitz et al., 1994a; Touloumis et al., 2013). The data were taken
from a randomized clinical trial designed to evaluate the effectiveness of the treatment Auranofin versus a
placebo therapy for the treatment of rheumatoid arthritis. The repeated ordinal response is the self-assessment
of arthritis, classified on a five-level ordinal scale (1 = poor, . . . , 5 = very good). Patients (n=303) were
randomized into one of the two treatment groups after baseline self-assessment followed during five months
during treatment resulting in a maximum of 3 measurements per subject (unequal cluster sizes). The covariates are time, baseline-assessment, age in years at baseline, sex and treatment. W e treat time and baseline-assessment as categorical variables
following Touloumis et al. (2013). However, instead of testing for differences to the reference category we
look at differences between adjacent categories (see, e.g., Tutz and Gertheiss, 2016). To this end we followed
the coding scheme for ordinal independent variables in Walter et al. (1987).

To select the appropriate correlation structure, we use the proposed model selection criteria in the weighted
scores estimating equations, based on the full model with all covariates (Table 6, correlation structure selection).
Further, both logit and probit links are used for the ordinal regressions. According to CL1AIC the correct
correlation structure is the unstructured, while according to the CL1BIC, it is exchangeable. In this example
we will prefer CL1BIC since one can easily distinguish between the various structures, as their difference in
magnitude is large. This is not the case for the CL1AIC, where the differences are rather small. This was
also the finding in our simulation studies, where it has been revealed that CL1AIC is more prone to select the
unstructured case. Further, ordinal logistic regression is slightly better than ordinal probit regression.

Table 5: Frequencies of the correlation structure and the set of the variables identified using CL1AIC and CL1BIC from
1000 simulation runs in each setting. The first column indicates the true correlation structure; the numbers of correct choices by each
criterion are bold faced.
Under the preferred exchangeable structure, we fit different models with different subsets of covariates, and find that the model with time, baseline-assessment, treatment and age, has the smallest CLAIC and CLBIC. Note that in Touloumis et al. (2013) age (and sex) have been not considered at all.

Table 6: The values of the different criteria for correlation structure selection at the full model and variable selection for the exchangeable structure for the arthritis data. The smallest value of each criterion is boldfaced.

| Link          | Probit          | Logit          |
|---------------|-----------------|----------------|
|               | CLAIC | CLBIC | CLAIC | CLBIC |
| Exchangeable  | 4280.92 | 4357.81 | 4275.09 | 4351.41 |
| AR(1)         | 4298.97 | 4374.26 | 4292.42 | 4367.20 |
| Unstructured  | **4279.97** | 4362.37 | **4273.87** | 4355.72 |

Table 6: The values of the different criteria for correlation structure selection at the full model and variable selection for the exchangeable structure for the arthritis data. The smallest value of each criterion is boldfaced.

Table 7: Weighted scores and GEE estimates (Est.), along with their standard errors (SE) under the optimal correlation structure and set of covariates for the arthritis data.

|          | Weighted scores | GEE          |
|----------|-----------------|--------------|
|          | Est.  | se   | Z    | p-value | Est.  | se   | Z    | p-value |
| α1       | -2.050 | 0.638 | -3.215 | 0.001   | -2.081 | 0.637 | -3.268 | 0.001   |
| α2       | 0.058  | 0.607 | 0.096  | 0.924   | 0.028  | 0.606 | 0.046  | 0.963   |
| α3       | 2.021  | 0.612 | 3.305  | 0.001   | 1.994  | 0.610 | 3.268  | 0.001   |
| α4       | 4.329  | 0.653 | 6.634  | < 0.001 | 4.307  | 0.650 | 6.625  | < 0.001 |
| I(time = 2, 3) | -0.007 | 0.121 | -0.059 | 0.953   | 0.003  | 0.122 | 0.021  | 0.984   |
| I(time = 3)   | -0.370 | 0.113 | -3.267 | 0.001   | -0.365 | 0.113 | -3.220 | 0.001   |
| I(time = 5)   | -0.511 | 0.168 | -3.037 | 0.002   | -0.507 | 0.168 | -3.023 | 0.003   |
| I(baseline = 2, 3, 4, 5) | -0.620 | 0.380 | -1.631 | 0.103   | -0.650 | 0.380 | -1.710 | 0.087   |
| I(baseline = 3, 4, 5) | -0.567 | 0.226 | -2.510 | 0.012   | -0.548 | 0.227 | -2.418 | 0.016   |
| I(baseline = 4, 5) | -1.369 | 0.236 | -5.790 | < 0.001 | -1.395 | 0.236 | -5.921 | < 0.001 |
| I(baseline = 5) | -1.417 | 0.403 | -3.519 | < 0.001 | -1.389 | 0.406 | -3.424 | 0.001   |
| age        | 0.013  | 0.008 | 1.656  | 0.098   | 0.014  | 0.008 | 1.736  | 0.083   |

Our analysis shows that the estimates of all the parameters and their corresponding standard errors obtained
from the weighted scores method are nearly the same as those obtained from the local odds ratios GEE approach. In fact, the columns of \( p \)-values for the two methods agree very closely and the same factors are found to be significant and insignificant. Our study has also revealed that age is of marginal statistical significance.

This example also shows that if the correlation structure and the variables in the mean function modelling are correctly specified, then there is no loss in efficiency in GEE. In fact, if a ‘time exchangeability’ or a homogenous Goodman’s row and column effects (‘RC’) structure is assumed in the local odds ratios GEE approach (Touloumis et al., 2013; Touloumis, 2015) the age effect is statistically insignificant (results are not shown here); see also Nikoloulopoulos (2016) for another concrete example for longitudinal binary (special case of ordinal). Hence, an advantage of our method is the variable/correlation structure selection, which is well-grounded in likelihood theory, and cannot be used in GEE methods, which are based on moments with no defined likelihood.

6 Discussion

In this article, we have introduced ordinal logistic and probit regression in the weighted scores method for regression with dependent data. Our method of combining the univariate scores for ordinal regression is theoretically sound, and gives estimates of regression parameters that are efficient and robust to dependence. The theory extends to any univariate regression method (such as multinomial probit), applied to dependent data, such as repeated measure multinomial (categorical non-ordinal).

Comparing our method with GEE for ordinal regression, we have shown that GEE are generally efficient for inference for the regression parameters if the variable selection in the mean function modelling and the working correlation structure are correctly specified. Composite likelihood information criteria for both correlation structure and variable selection have been proposed to achieve this. However, our working MVN copula model is a proper multivariate model, and the correlations can be interpreted as latent or polychoric (Olsson, 1979) correlations; this is not the case for the GEE estimated correlation parameters, which can also sometimes violate the Fréchet bounds of the feasible range of the correlation (Chaganty and Joe, 2006).

We would also like to stress that our method can allow any latent correlation structure and is not restricted to an exchangeable or unstructured one. For example, SAS software only offers the independence working assumption as the only option to fit ordinal GEEs or the dominant of the GEE methods in Touloumis et al. (2013) does not allow an AR(1)-like association structure.

Last but not least, the weighted scores method overcomes computational issues (matrix operations required for GEE estimation are very slow or even infeasible for large \( K \) and \( d \)) that occur in the existing GEE approaches/implementations for ordinal longitudinal data.

Software

R functions to implement the weighted scores method and the CL1 information criteria for longitudinal ordinal data have been implemented in the package \texttt{weightedScores} (Nikoloulopoulos and Joe, 2015a) within the open source statistical environment \texttt{R} (R Core Team, 2015).

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Appendix

For \( d = 4 \) the matrices involved in the calculation of the sensitivity matrix \( \mathbf{H}_g \) of the CL1 estimating functions take the form:

\[
-\mathbf{H}_{g1} = \mathbf{X}^T \mathbf{E} \begin{pmatrix}
\frac{\partial s_{i,j}^{(1)}(a)}{\partial \gamma_{1}} & 0 & 0 & 0 \\
0 & \frac{\partial s_{i,j}^{(1)}(a)}{\partial \gamma_{2}} & 0 & 0 \\
0 & 0 & \frac{\partial s_{i,j}^{(1)}(a)}{\partial \gamma_{3}} & 0 \\
0 & 0 & 0 & \frac{\partial s_{i,j}^{(1)}(a)}{\partial \gamma_{4}} \\
\end{pmatrix} \mathbf{X}_i;
\]

\[
-\mathbf{H}_{g2,1} = \mathbf{E} \begin{pmatrix}
\frac{\partial s_{i,j}^{(2)}(a,p_{12})}{\partial \gamma_{1}} & \frac{\partial s_{i,j}^{(2)}(a,p_{12})}{\partial \gamma_{2}} & 0 & 0 \\
\frac{\partial s_{i,j}^{(2)}(a,p_{13})}{\partial \gamma_{1}} & \frac{\partial s_{i,j}^{(2)}(a,p_{13})}{\partial \gamma_{2}} & 0 & 0 \\
\frac{\partial s_{i,j}^{(2)}(a,p_{14})}{\partial \gamma_{1}} & \frac{\partial s_{i,j}^{(2)}(a,p_{14})}{\partial \gamma_{2}} & 0 & 0 \\
0 & 0 & \frac{\partial s_{i,j}^{(2)}(a,p_{23})}{\partial \gamma_{3}} & \frac{\partial s_{i,j}^{(2)}(a,p_{23})}{\partial \gamma_{4}} \\
0 & 0 & 0 & \frac{\partial s_{i,j}^{(2)}(a,p_{24})}{\partial \gamma_{3}} \\
0 & 0 & 0 & 0 \\
0 & 0 & 0 & 0 \\
\end{pmatrix} \mathbf{X}_i;
\]

\[
-\mathbf{H}_{g2} = \mathbf{E} \begin{pmatrix}
\frac{\partial s_{i,j}^{(2)}(a,p_{12})}{\partial p_{12}} & 0 & 0 & 0 \\
0 & \frac{\partial s_{i,j}^{(2)}(a,p_{13})}{\partial p_{13}} & 0 & 0 \\
0 & 0 & \frac{\partial s_{i,j}^{(2)}(a,p_{14})}{\partial p_{14}} & 0 \\
0 & 0 & 0 & \frac{\partial s_{i,j}^{(2)}(a,p_{23})}{\partial p_{23}} \\
0 & 0 & 0 & 0 \\
0 & 0 & 0 & 0 \\
0 & 0 & 0 & 0 \\
\end{pmatrix}.
\]

The elements of these matrices are calculated as below:

\[
-E \left( \frac{\partial s_{i,j}(a,p_{jk})}{\partial p_{jk}} \right) = -E \left( \frac{\partial^2 \log f_2(y_{ij}, y_{ik}, \gamma, \rho_{jk})}{\partial^2 p_{jk}} \right) = E \left( \frac{\partial \log f_2(y_{ij}, y_{ik}, \gamma, \rho_{jk})}{\partial p_{jk}} \left( \frac{\partial \log f_2(y_{ij}, y_{ik}, \gamma, \rho_{jk})}{\partial p_{jk}} \right)^2 \right),
\]

where

\[
\frac{\partial \log f_2(y_{ij}, y_{ik}, \gamma, \rho_{jk})}{\partial p_{jk}} = \frac{\partial f_2(y_{ij}, y_{ik}, \gamma, \rho_{jk})}{\partial p_{jk}} / f_2(y_{ij}, y_{ik}, \gamma, \rho_{jk});
\]

\[
-E \left( \frac{\partial s_{i,j}(a,p_{jk})}{\partial a} \right) = -E \left( \frac{\partial^2 \log f_2(y_{ij}, y_{ik}, \gamma, \rho_{jk})}{\partial a \partial p_{jk}} \right) = E \left( \frac{\partial \log f_2(y_{ij}, y_{ik}, \gamma, \rho_{jk})}{\partial a} \frac{\partial \log f_2(y_{ij}, y_{ik}, \gamma, \rho_{jk})}{\partial p_{jk}} \right),
\]

where

\[
\frac{\partial \log f_2(y_{ij}, y_{ik}, \gamma, \rho_{jk})}{\partial a} = \frac{\partial f_2(y_{ij}, y_{ik}, \gamma, \rho_{jk})}{\partial a} / f_2(y_{ij}, y_{ik}, \gamma, \rho_{jk}),
\]

\[
\frac{\partial f_2(y_{ij}, y_{ik}, \gamma, \rho_{jk})}{\partial a} \frac{\partial f_2(y_{ij}, y_{ik}, \gamma, \rho_{jk})}{\partial p_{jk}} = \frac{\partial f_2(y_{ij}, y_{ik}, \gamma, \rho_{jk})}{\partial a} \frac{\partial f_2(y_{ij}, y_{ik}, \gamma, \rho_{jk})}{\partial p_{jk}}
\]

\[
+ \frac{\partial f_2(y_{ij}, y_{ik}, \gamma, \rho_{jk})}{\partial a} X_{i,j} + \frac{\partial f_2(y_{ij}, y_{ik}, \gamma, \rho_{jk})}{\partial p_{jk}} X_{i,k},
\]

\[
\frac{\partial f_2(y_{ij}, y_{ik}, \gamma, \rho_{jk})}{\partial a} \frac{\partial f_2(y_{ij}, y_{ik}, \gamma, \rho_{jk})}{\partial p_{jk}} = \frac{\partial f_2(y_{ij}, y_{ik}, \gamma, \rho_{jk})}{\partial a} \frac{\partial f_2(y_{ij}, y_{ik}, \gamma, \rho_{jk})}{\partial p_{jk}}
\]

\[
+ \frac{\partial f_2(y_{ij}, y_{ik}, \gamma, \rho_{jk})}{\partial a} \frac{\partial f_2(y_{ij}, y_{ik}, \gamma, \rho_{jk})}{\partial p_{jk}} X_{i,j}
\]

\[
+ \frac{\partial f_2(y_{ij}, y_{ik}, \gamma, \rho_{jk})}{\partial a} \frac{\partial f_2(y_{ij}, y_{ik}, \gamma, \rho_{jk})}{\partial p_{jk}} X_{i,k},
\]

\[
\frac{\partial f_2(y_{ij}, y_{ik}, \gamma, \rho_{jk})}{\partial a} \frac{\partial f_2(y_{ij}, y_{ik}, \gamma, \rho_{jk})}{\partial p_{jk}} = \frac{\partial f_2(y_{ij}, y_{ik}, \gamma, \rho_{jk})}{\partial a} \frac{\partial f_2(y_{ij}, y_{ik}, \gamma, \rho_{jk})}{\partial p_{jk}}
\]

\[
+ \frac{\partial f_2(y_{ij}, y_{ik}, \gamma, \rho_{jk})}{\partial a} \frac{\partial f_2(y_{ij}, y_{ik}, \gamma, \rho_{jk})}{\partial p_{jk}} X_{i,j}
\]

\[
+ \frac{\partial f_2(y_{ij}, y_{ik}, \gamma, \rho_{jk})}{\partial a} \frac{\partial f_2(y_{ij}, y_{ik}, \gamma, \rho_{jk})}{\partial p_{jk}} X_{i,k}.
\]
\[
\frac{\partial \Phi^{-1}(F_{ij}(y;\gamma_{ij}))}{\partial \gamma_{ij}} = \sum_{i} \frac{\partial f_{1}(y;\gamma_{ij})}{\partial \gamma_{ij}} / \phi\left(\Phi^{-1}(F_{ij}(y;\gamma_{ij}))\right), \quad \text{where} \quad \frac{\partial 1}{\partial \gamma_{ij}} = f_{1}(y;\gamma_{ij}) \frac{\partial 1}{\partial \gamma_{ij}}.
\]

At the above formulas
\[
f_{2ijk}(y_{ij}, y_{ik}; \gamma_{ij}, \gamma_{ik}, \rho_{jk}) = \int \Phi^{-1}(F_{ijk}(y_{ij};\gamma_{ij})) \int \Phi^{-1}(F_{ijk}(y_{ik};\gamma_{ik})) \phi_{2}(z_{j}, z_{d}; \rho_{jk}) dz_{j} dz_{k},
\]
where

\[
F_{ijk}(y;\gamma_{ij}) = \mathcal{F}(\gamma_{ij}y).
\]

The derivatives \( \frac{\partial f_{1}(y;\gamma_{ij})}{\partial \rho_{jk}} \) and \( \frac{\partial f_{2ijk}(y_{ij}, y_{ik}; \gamma_{ij}, \gamma_{ik}, \rho_{jk})}{\partial \Phi^{-1}(F_{ijk}(y_{ij};\gamma_{ij}))} \) are computed with the R functions \text{exchmvn}.\text{deriv}.\text{rho} \text{ and } \text{exchmvn}.\text{deriv}.\text{margin}, \text{respectively, in the R package mprobit} (Joe, 1995; Joe et al., 2011).

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