Ordinal Regression Models for Continuous Scales

Maurizio Manuguerra, *Macquarie University*
Gillian Z. Heller, *Macquarie University*

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Abstract

Ordinal regression analysis is a convenient tool for analyzing ordinal response variables in the presence of covariates. In this paper we extend this methodology to the case of continuous self-rating scales such as the Visual Analog Scale (VAS) used in pain assessment, or the Linear Analog Self-Assessment (LASA) scales in quality of life studies. These scales measure subjects' perception of an intangible quantity, and cannot be handled as ratio variables because of their inherent nonlinearity. We express the likelihood in terms of a function connecting the scale with an underlying continuous latent variable and approximate this function either parametrically or non-parametrically. Then a general semi-parametric regression framework for continuous scales is developed. Two data sets have been analyzed to compare our method to the standard discrete ordinal regression model, and the parametric to the non-parametric versions of the model. The first data set uses VAS data from a study on the efficacy of low-level laser therapy in the treatment of chronic neck pain; the second comes from a study on chemotherapy treatments in advanced breast cancer and looks at the impact of different drugs on patients' quality of life. The continuous formulation of the ordinal regression model has the advantage of no loss of precision due to categorization of the scores and no arbitrary choice of the number and boundaries of categories. The semi-parametric form of the model makes it a flexible method for analysis of continuous ordinal scales.

1 Introduction

We propose regression models for outcomes which are intangible and difficult to measure on conventional scales, such as pain and quality of life. Self-rating scales are used in several disciplines to measure such outcomes. Continuous self-rating scales are referred to as Visual Analog Scales (VAS) in the pain literature and Linear Analog Self-Assessment (LASA) scales in quality of life studies. Subjects are typically given a linear scale of 100 mm and asked to put a mark where they perceive themselves. In Figure 1 an example of VAS is shown.

No
pain
$\rule{6cm}{0.4pt}$
Worst pain
imaginable

Figure 1: The Visual Analog Scale

For convenience we refer to continuous scales of this type as VAS, and to the outcome as pain. The VAS measurement is a continuous variable, discretized by the observer because of the sensitivity of the measuring instrument. Typically it is measured as a 100-point scale, and used as is, or more often with values grouped to build a discretized scale.

Historically, there has been controversy on the nature of the VAS: whether it is ratio or ordinal; linear or nonlinear. "Linear" in this context is taken to mean that differences in pain between successive increments on the VAS are constant. In a study on women with Patellofemoral Pain Syndrome (Thomeé, Grimby, Wright, and Linacre, 1995), the application of Rasch analysis to VAS measures showed the nonlinear properties of the scale. Myles, Troedel, Boquest, and Reeves (1999) searched for what regions of the VAS the scores can be considered as ratio and linear. Their results showed that the limits of these regions can include mild-to-moderate pain and, in a subsequent study (Myles and Urquhart, 2005), they extended these limits to the cases of severe acute pain (mean VAS score 84 mm). However, in a review on the use of the VAS in labor studies (Ludington and Dexter, 1998), 13% of primiparous women without analgesia report the worst pain imaginable at 3 cm cervical dilatation. If these patients receive no analgesia, their pain will certainly increase as labor progresses.

Whatever the extent of the "linear" portion in the VAS, it seems reasonable that some nonlinearity will be observed around the limits, where an higher density of signs, caused by perceptive states considered extreme or close to extreme, could be expected. The problem of non–interpretability of distances between measurements and the possibility of nonlinear behaviour, particularly at one or both

extremes of the scale, is overcome by treating VAS measurements as ordinal rather than ratio data. We therefore refer to scales of this type as continuous ordinal.

Svensson (1998) proposes rank-invariant models for the analysis of change in VAS data, treating the measurements as ordinal. They are different from the models we discuss, as they do not incorporate the effect of covariates and cannot be considered as regression models.

In Rasch analysis (see for example Fischer, 1995) this limitation is overcome, as covariates can be incorporated in the parameters of the model. The drawback is that Rasch analysis cannot deal natively with continuous scales; indeed it can be used to convert continuous recordings to a discrete scale, addressing correctly the non-linear nature of the VAS.

Finally ordinal regression models (McCullagh, 1980) are widely used for regression analysis of discrete ordinal responses Y within K ordered categories. The Y's are considered as coarse versions of an unobserved, continuous latent variable W, such that

$$Y = j \iff \alpha_{j-1} < W < \alpha_j , \qquad j = 1, \ldots, K$$

where the α_j's are the correspondence on the latent variable scale of the category boundaries on the ordinal scale and $-\infty = \alpha_0 < \alpha_1 < \cdots < \alpha_K = \infty$. Typically W is an intangible quantity such as pain, and $y = 1, 2, \ldots, K$ codes for ordinal states such as *none*, *mild*, *moderate*, *severe*. To relate the cumulative probabilities to covariates $x = (x_1, \ldots, x_p)'$ in the jth category, we write:

$$\gamma_j(x) = P(Y \leq j|x) = P(W \leq \alpha_j|x)$$

and assume that $W = -x'\beta + \varepsilon$. When ε has the standard logistic distribution having cumulative distribution function (CDF) $F(z) = P(\varepsilon \leq z) = 1/(1 + e^{-z})$, then

$$\gamma_j(x) = F(\alpha_j + x'\beta) = \frac{1}{1 + e^{-(\alpha_j + x'\beta)}} .$$

Inverting this translates to the cumulative logistic model (also called the proportional odds model) for Y:

$$\ln\left(\frac{\gamma_j(x)}{1 - \gamma_j(x)}\right) = \alpha_j + x'\beta , \qquad j = 1, \ldots, K - 1 \tag{1}$$

In the VAS and LASA scale literature, the intercepts α_j are either ignored or used to characterize differences in category "size". In agreement with the latter approach, we think that the α_js are worthy of careful modelling as they relate to an important cognitive aspect, i.e. how the perception of pain changes at different levels. This behaviour can be of particular interest around the extremes of the scale,

where steep curvature is indicative of a tendency for subjects to perceive and score their pain at the extreme.

The ordinal regression model has been developed in the last two decades in order to incorporate additive and non-linear functional forms of predictors (Hastie and Tibshirani, 1987) and spline-based smoothers of predictors (Yee and Wild, 1996). In Tutz (2003), a general framework to deal with semiparametrically structured models is given, with predictors that can contain parametric parts, additive parts with an unspecified functional form, and interactions. In particular global effects and category-specific effects are distinguished.

In the applied literature, typically continuous ordinal responses are analysed using model (1) on a discretized version of the VAS responses (for example Kelly, 2001, Jensen, Chen, and Brugger, 2003), or simply by treating the VAS measurements as continuous responses in a normal regression model (for example Schwenk, 1998). Both of these approaches are less than satisfactory: discretizing the response involves loss of information, and use of the normal regression model has obvious distributional shortcomings. More sophisticated methods have been proposed in the statistical literature. Bottai, Cai, and McKeown (2010) and Lesaffre, Rizopoulos, and Tsonaka (2007) both consider models for bounded responses, of which VAS measurements are an example. Bottai et al. apply the logistic transformation in order to overcome the difficulty inherent in formulating a model for a bounded response, and use quantile regression modelling on the transformed scores. Lesaffre et al. also apply the logistic transformation and consider models in which the transformed response has a normal distribution. In this paper we propose a generalization of the standard ordinal model (1) which leads to a semiparametric ordinal regression model for continuous scales (Section 2). In Section 3 we develop an estimation methodology based on Bayesian techniques and in Sections 4 and 5 we give two practical examples where this approach is used. We discuss the relationship between our model and the approaches of Lesaffre et al. and Bottai et al. in Section 6.

2   Regression model for continuous ordinal responses

Consider VAS measurements v which are sampled from a continuous response variable $V \in (0,1)$[1], with density $f(v)$ and CDF $\gamma(v)$. The continuous ordinal response variable V can be taken to reflect the subjective perception of an underlying continuous latent variable W defined on the real line. The dependence between V and

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[1]As was mentioned in Section 1, VAS measurements are usually expressed in the range (0,100). However, for mathematical convenience and without loss of generality, we assume in what follows that v is scaled to lie in (0,1).

W is modelled by a smooth one-to-one function $g : (0,1) \mapsto (-\infty, +\infty)$ that maps v on the VAS to $w = g(v)$ on the latent scale. This mapping is the link between the recorded perception of pain and an underlying metric. As for the standard ordinal model, covariates are modelled on the latent scale. Assuming $W = -x'\beta + \varepsilon$,

$$\gamma(v|x) = P(V \le v|x) = P(W \le g(v)|x) = F(g(v) + x'\beta) ,$$

where $F(\cdot)$ is the CDF of ε. Inverting this translates to the generic ordinal regression model for continuous observations v:

$$F^{-1}(\gamma(v|x)) = g(v) + x'\beta .$$

We assume the standard logistic distribution for ε, but other distributions, such as the normal, can be used. The cumulative logistic ordinal model for continuous response variables is:

$$\ln\left(\frac{\gamma(v|x)}{1 - \gamma(v|x)} \right) = g(v) + x'\beta . \tag{2}$$

The function $g(v)$ in model (2) is the continuous analog of the discrete intercepts α_j in model (1), and its shape is informative of the change in perception of pain at different levels (as are the α_j). The linear component $x'\beta$ may incorporate fixed and random effects. Random effects are useful not only for modelling clustered or longitudinal data, as in the examples in Sections 4 and 5, but also for modelling individual variation due to subjective perception of the pain.

Inverting and differentiating equation (2), we obtain the likelihood:

$$f(v|x) = \frac{\partial \gamma(v|x)}{\partial v} = \frac{\dot{g}(v)(e^{g(v)+x'\beta})}{(1 + e^{g(v)+x'\beta})^2} \tag{3}$$

where $\dot{g}(v) = \frac{\partial g(v)}{\partial v}$.

A more general form of this model can be obtained by introducing a set of non-parametric functions S_1 smoothing the effects of the covariates z_1, and allowing interaction terms. A case of particular interest is when a set of variables z_2 interacts with the random variable v, allowing the estimation of non-parametric functions S_2 that are v-level specific effects (analogous to the discrete case, where these were called category specific effects (Tutz, 2003)). In this case, the model can be written as:

$$\ln\left(\frac{\gamma(v|x,z,S)}{1 - \gamma(v|x,z,S)} \right) = g(v) + x^T\beta + S_1(z_1) + S_2(v,z_2)$$

with likelihood:

$$f(v|x,z,S) = \frac{\partial \gamma(v|x,z,S)}{\partial v} = \frac{(g'(v) + S_2'(v,z_2))(e^{g(v)+x^T\beta+S_1(z_1)+S_2(v,z_2)})}{(1 + e^{g(v)+x^T\beta+S_1(z_1)+S_2(v,z_2)})^2} .$$

Here a surface function $S_2(v,z_2)$ and its derivative have to be estimated.

3 Model implementation

3.1 g function

In order to complete the specification of model (2), we need to define the form of the $g(v)$ function. g has to be capable of capturing the nonlinear behaviour of the ordinal measure. Any differentiable, increasing and "flexible enough" function which maps $(0,1)$ to $(-\infty, +\infty)$ could be appropriate. This can be done using a parametric or non-parametric approach; inverse sigmoidal functions and smooth functions (for example, splines) could be appropriate choices.

3.1.1 Parametric g function

We choose g as the inverse of the generalized logistic function (Richards, 1959), which has the advantage of simplicity and mathematical tractability:

$$g_1(v) = M + \frac{1}{B} \log \left(\frac{T v^T}{1 - v^T} \right), \qquad 0 < v < 1 \tag{4}$$

where M is the offset, B is the slope and T is the symmetry of the curve. Considering that

$$\dot{g}_1(v) = \frac{T}{B} \cdot \frac{1}{v(1 - v^T)}$$

the likelihood can be written in closed form using (3). The number of parameters for model (2) with $g(v)$ as in (4), is $p + 3$. This compares favorably with $p + K - 1$ parameters for the standard ordinal regression model (1) with K categories.

3.1.2 Non-parametric g function

Many choices can be made to define the cumulative logistic ordinal regression model (2) using a smooth function for $g(v)$. In this paper we have used B-splines, as they are a convenient tool to address computational requirements. The general form can be written as

$$g_2(v) = \lambda_0 + \sum_{j=1}^{m-1+q} \lambda_j B_j(v, q), \tag{5}$$

where B_j is the j-th basis function, q is the degree of the B-spline and m is the number of knots equally spaced in the interval $[v_{min}, v_{max}]$. As $g(v)$ is an increasing

function, we need to impose monotonicity conditions on g_2 (de Boor, 1978). This is achieved by imposing a positive first derivative on $g_2(v)$:

$$\dot{g}_2(v) = \sum_{j=1}^{m-1+q} \lambda_j B'_j(v,q) = \frac{1}{h} \sum_{j=1}^{m-2+q} (\lambda_{j+1} - \lambda_j) B_j(v, q-1) > 0 \ .$$

From this equation, it is clear a sufficient condition for obtaining a monotonic $g(v)$ function is for the sequence of coefficients λ to be increasing.

To avoid overfitting of the data, the non-parametric approach has been implemented by penalizing the log-likelihood $L(v|x) = \log(f(v|x))$ by a non-negative functional J measuring the roughness of g_2. We maximize

$$L(v|x) - \lambda J(g_2)$$

where λ is the smoothing parameter, estimated using Generalized Cross Validation (GCV), and J has been chosen as the integrated squared second derivative:

$$J(g_2) = \int_{-\infty}^{+\infty} g_2''(t)^2 dt \ .$$

For details on this methodology and its application to Bayesian inference, the reader is referred to Hastie and Tibshirani (1987), Wahba (1990), Green and Silverman (1993), Ruppert, Wand, and Carroll (2003) and Hastie, Tibshirani, and Friedman (2009).

3.1.3 Scale endpoints

A problem in extending the ordinal regression model to continuous scales is that the VAS and the LASA scale are closed, i.e. they include the extremes. Besides considerations on the possibility of experiencing the worst possible pain or quality of life, there is a problem related to the acquisition of data. The patient can put the mark very close to or on the extreme of the scale. Nevertheless, data are acquired as a 100-point scale, so the ticks will be spaced at 1 mm intervals. That means that it is not possible to discriminate ticks between 99.5 and 100 mm. It is also impossible to greatly increase the number of points dividing the scale, as the mark has some thickness. From a mathematical point of view, there are two possible ways to consider boundary data. We can either consider them as equal to 0 or 100, in which case the model is not identifiable as the g function must go towards minus or plus infinity; or we can consider them as undetermined measures between 99.5 and 100 mm. This is the approach we have followed, converting values of 100 to 99.9 and values of 0 to 0.01. The fitting of the g function is then to be considered limited to the range 0.01-99.9 mm. Outside this interval, the g function is not estimated and is assumed to go towards infinity.

3.2 Predictors

The above penalized likelihood approach for B-splines has been adopted for predictors which appear in the model as smooth functions. In this case the monotonicity constraint is not required. GCV is used for estimation of the smoothing parameter.

3.3 Estimation and software

The likelihood is expressed in closed form, so maximum likelihood methodology can be used to estimate the model parameters. However, in our applications described in Sections 4 and 5, the models include random effects and model fitting involves integration of the random effects. We found it more convenient to use Bayesian methodology, performed using non-informative priors. The posterior distribution of a parameter is proportional to the product of the likelihood function and its prior distribution. Use of an non-informative prior results in the posterior distribution being proportional to the likelihood, and for large n the same estimate is achieved with ML and Bayesian estimation. Several authors (for example Huber and Train, 2001, Kuhner and Smith, 2007, Wall, 2009) have pointed out the similarity between ML and Bayesian estimates, in the contexts of choice modelling, genealogy and structural equation modelling, respectively. This suggests that the choice between ML and Bayesian estimation then becomes one of computational feasibility and convenience, rather than a philosophical choice between methodologies. In the particular case of a uniform prior distribution, the posterior distribution mode estimator is coincidental with the maximum likelihood estimator, while the mean minimizes the squared error function and the median the absolute error function. In our examples the differences between the three estimators have usually been statistically negligible; we have chosen to use the mode estimator to have results formally equivalent to the ML methodology. Model selection has been based on the Deviance Information Criteria (DIC) (see Spiegelhalter, Best, Carlin, and van der Linde, 2002).

In the next sections, these methods are applied to two data sets. In the first example, the discrete standard ordinal model is compared to the continuous model using a parametric g function. The software packages WinBUGS 1.4.3 (Lunn, Thomas, Best, and Spiegelhalter, 2000) and JAGS (Plummer, 2009a), called from R 2.8.1 (R Development Core Team, 2009) with the *R2WinBUGS* (Sturtz, Ligges, and Gelman, 2005) and *rjags* (Plummer, 2009b) libraries respectively, have been used. Estimates over several runs have been very stable, with no dependence on the chains' initial values. Burn-in periods of 4000 iterations and samples of 10000 iterations have been used to estimate the parameters.

In the second example, interest is shifted to the comparison between parametric and non-parametric versions of the *g* function. A semi-parametric model has been adopted, with the g_2 function and the nonparametric part of the predictor estimated using cubic B-splines with 30 knots. For an overview on the Bayesian perspective on penalized likelihood estimation the reader is referred to, for example, Green (1999). Estimation of the B-spline coefficients has shown some instability, given the sparsity of data for high values of the predictor (see Table 2), and long burn-in phases (30000 iterations) and samples (10000 iterations) were necessary. Bayesian confidence intervals have not reflected the instability in the convergence of the chains; for this reason we have preferred to use bootstrap methodology (see Wang and Wahba, 1995), that appears to be better for small data sets and has given more credible estimates. 200 bootstrap samples have been generated to estimate the confidence intervals and, as recommended, the method of normal intervals has been used. The analyses have been performed using the Metropolis-Hastings algorithm, implemented in R 2.8.1 using the *splines* and *MCMCpack* (Martin, Quinn, and Park, 2009) libraries.

The results and the code have been validated either using generated data sets or fitting the data with more than one package.

4 Application to pain data

In this example, we contrast the approach of analysing categorised VAS scores in the discrete standard ordinal setting, with the analysis using the continuous model with a parametric *g* function.

4.1 Chronic neck pain study

The study design has been explained in detail elsewhere (Chow, Heller, and Barnsley, 2006). Briefly, the study is a randomized, double-blind, placebo-controlled investigation on the efficacy of low-level laser therapy (LLLT) in the treatment of chronic neck pain. Ninety patients were recruited between July 2002 and May 2003 at a large suburban medical centre of 17 general practitioners in Sydney, Australia. They were 18 years of age or over, had unilateral or bilateral chronic neck pain and had never attended treatment with LLLT. Subjects were randomized to receive 14 treatments over 7 weeks, with either active or placebo laser. The primary outcome measure of the study was the VAS, marked by the patients at baseline, at the end of the course of treatment and one month after completion of the treatment

(approximately 12 weeks from baseline). After exclusion of six patients for missing recordings, we analyzed data from $n = 84$ subjects measured at the three time points.

4.2 Discrete response variable

To assess the suitability of the cumulative logistic ordinal model for continuous responses, we have compared it with the discrete standard ordinal model. In order to analyze the data set in the discrete framework, we divided the VAS scores into nine equally-spaced classes. Within-subject correlation is modelled using a random effect for subject. The model for subject i at time t and VAS category j is:

$$\log \frac{\gamma_{ijt}}{1 - \gamma_{ijt}} = \alpha_j + x_i \beta_t + b_i \qquad i = 1,\ldots,n; \ j = 1,\ldots,8; \ t = 1,2,3 \ , \qquad (6)$$

where $\gamma_{ijt} = P(Y_{it} \leq j | x_i, t)$, b_i are the individual effects sampled from $N(0, \sigma^2)$ and x_i is an indicator variable for active laser. The parameters $\beta_1, \beta_2, \beta_3$ give the effect of the laser treatment at the three time points. The time main effect has not been included in the model as it has been found to be non-significant. In principle, other covariates may be incorporated in the model. None of the available covariates (age, sex, type of injury, laterality) was found to be significant in any of the analyses.

The results (Table 1) show a bias between the treated and placebo groups prior to treatment described by β_1, and a significant effect of laser on pain relief after the treatment (β_2) and one month later (β_3), with an attenuation of the positive effect. Note that, since e^{β_t} is the effect of laser on the odds of scoring $Y \leq j$, at time t, positive β_t signifies *lower* VAS scores due to laser, i.e. pain relief. The individual effects (b) are sampled from a normal distribution with significant standard deviation $\sigma \approx 3$, signifying a persistent subject effect. It is particularly important to incorporate this effect because of the individual and subjective nature of the measurements.

4.3 Continuous response variable

Analogous to the discrete case, for continuous response variables the model is:

$$\log \frac{\gamma_{it}}{1 - \gamma_{it}} = g(v_{it}) + x_i \beta_t + b_i$$

where v_{it} are the scaled VAS scores and the term $g(v_{it})$ is approximated using formula (4).

The model parameters β are consistent with those of the discrete model, with slightly lower standard errors. The model has the advantage of no loss of information due to categorization of the VAS scores and no arbitrary choice of the number and boundaries of the categories.

The estimated g function, shown in Figure 2, can be seen to have a different slope, but possibly similar symmetry, to the intercepts α_j estimated in the discrete standard ordinal regression model. This is the consequence of the finite number of categories K used in the discrete case. Increasing K has the effect of shifting the estimated α_j to better agree with the continuous case, while decreasing K shifts the intercepts in the opposite direction. (These results have been computed but are not shown.) Note that we are unable to use the DIC for comparison of the discrete and continuous models, as the likelihoods for the discrete and continuous cases are not comparable.

	Discrete $K = 9$			Continuous (parametric g function)		
	Mode	95% CI		Mode	95% CI	
β_1	-2.26	-3.31	-1.19	-1.90	-2.78	-0.95
β_2	1.73	0.77	2.77	1.74	0.86	2.68
β_3	1.06	0.08	1.98	1.01	0.19	1.96
σ	2.95	2.33	3.81	2.74	2.20	3.41
M	-	-	-	0.63	-0.29	1.49
T	-	-	-	0.85	0.49	1.18
B	-	-	-	0.43	0.35	0.54

Table 1: Chronic neck pain study: parameter estimates.

5   Application to quality of life data

5.1   Chemotherapy treatments in advanced breast cancer study

In this example, we compare the parametric and non-parametric approaches to approximate the g function, and demonstrate the use of a smooth term for one of the covariates.

Metastatic breast cancer is the most common cause of cancer death and the greatest cause of cancer morbidity among Australian women. The ANZ 0001 trial, conducted by the ANZ Breast Cancer Trials Group, is an unblinded, multi-centre, randomised trial with three chemotherapy treatment arms ($n = 292$ patients

with complete quality of life measurements) concluded in 2005 (Stockler, Sourjina, Grimison, Gebski, Byrne, Harvey, Francis, Nowak, Hazel, Forbes, and Group, 2007) . Health-related quality of life is assessed at each chemotherapy treatment cycle, from randomization until disease progression, when treatment is interrupted. The treatments Intermittent Capecitabine (IC) and Continuous Capecitabine (CC) are compared with the standard combination treatment CMF, each with its own protocol. There is no maximum duration of treatment, but it is interrupted on disease progression, or when patient intolerance or unacceptable toxicity are recorded.
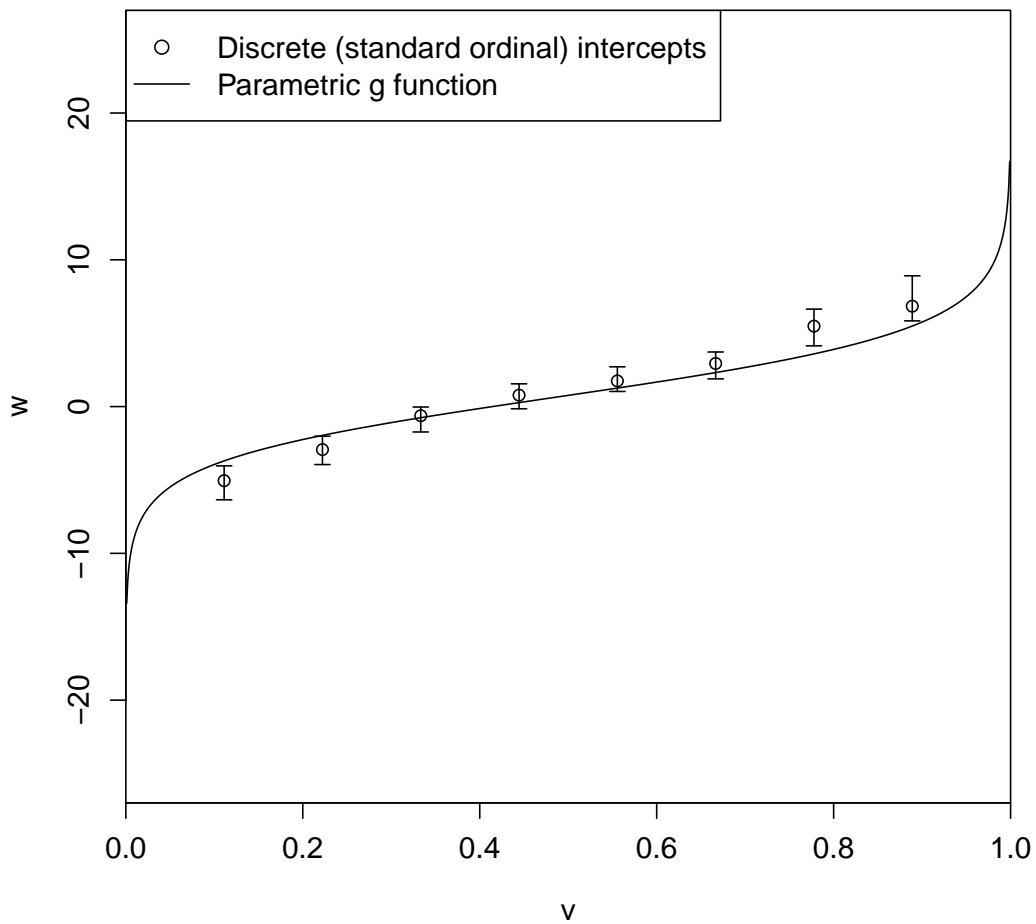

Figure 2: Intercepts and *g* function of the discrete and continuous models evaluated in the chronic neck pain study.

The study aims to verify which treatment has a better impact on quality of life, and in particular how this impact changes over chemotherapy cycle. Various aspects of quality of life are assessed using LASA scales. The number of remaining patients in selected cycles, by treatment arm, are shown in Table 2. Note that no patients on standard CMF treatment progressed beyond cycle 20, and for the other two treatments the data are sparse beyond this point.

We used the overall quality of life LASA scale as dependent variable. Among the several covariates available, we have selected ECOG score, oestrogen level, age, body surface area (BSA) and chemotherapy cycle number. BSA, ECOG score and oestrogen were found to be not signficant and have been excluded from the final model.

	Treatment		
Cycle	IC	CC	CMF
0	97	94	101
5	65	63	57
10	37	37	10
15	22	21	3
20	12	11	2
25	7	6	0
45	1	3	0
60	0	1	0

Table 2: Remaining subjects at different cycle numbers.

5.2 Model

The model for the overall quality of life v_{ij} for patient i at chemotherapy cycle j is:

$$\log \frac{\gamma_{ij}}{1 - \gamma_{ij}} = g(v_{ij}) + x_i\beta + s(j) + b_i$$

where x_i is the age of patient i (not standardized), $s(j)$ is a smooth term that depends on cycle number j and b_i are random effects sampled from $N(0, \sigma^2)$. We compare the parametric and non-parametric approaches for $g(v_{ij})$, using the inverse generalized logistic function (4) and B-splines (5), respectively. B-splines are used for estimation of $s(j)$.

5.3   Results

Table 3 compares the parameters estimated with the parametric and non-parametric approaches. The two methods show similar results for β and σ, with a significant worsening of quality of life with increasing age. The β coefficients have the same interpretation as those from the cumulative logistic model (1). In the table, the 95% percentile confidence intervals are estimated using bootstrap methods as already discussed. In terms of DIC, the non-parametrically formulated model has an advantage over the parametric approach.

In Figure 3 the parametric and non-parametric estimates of the g function are shown. The accordance is good over the range of the scale, except in the region of worst quality of life (right side of the scale), where fewer subjects have marked their perception. The fact that the non-parametric model has obtained a better fit (smaller DIC) of the data is probably due to a lack of flexibility of the parametric curve at this extreme of the scale.

On the other hand, the two models have given similar results for the dependence of the overall quality of life on cycle number. In Figure 4, the result obtained by the non-parametric model is shown. The CC treatment has a clear advantage over IC in terms of quality of life, while it is not possible to give clear indications on the standard CMF treatment. Confidence intervals for the functions are wide because of the sparsity of data for high cycle numbers, see Table 2. This aspect of the data presented a challenge for stability of the computation.

6   Discussion

We provide a regression framework for a response variable that is a recorded perception of an underlying latent variable which is difficult to observe or measure. The model is an extension of the cumulative logistic ordinal regression model for discrete ordinal responses and incorporates both parametric and non-parametric covariate terms, as well as random effects. The recorded perception is mapped to the latent variable using either a parametric or non-parametric function.

A commonly used approach for VAS reponses is to categorize them, and analyze them as discrete ordinal responses. Our model obviates the need for this aggregation of information. We have shown that the results obtained are consistent with those from the discrete variable analyses, with more precise estimates. Some differences have been observed in the intercepts, as shown in Figure 2. This is due to the low sensitivity of the discrete model: when few categories are used as in this case, the behaviour of α cannot be observed accurately around the extremes, where the major non-linearities can be observed. In contrast, the continuous formulation

of the model gives the same weight to the whole VAS, and the higher sensitivity around the limits makes the slope of the curve different from the discrete case.
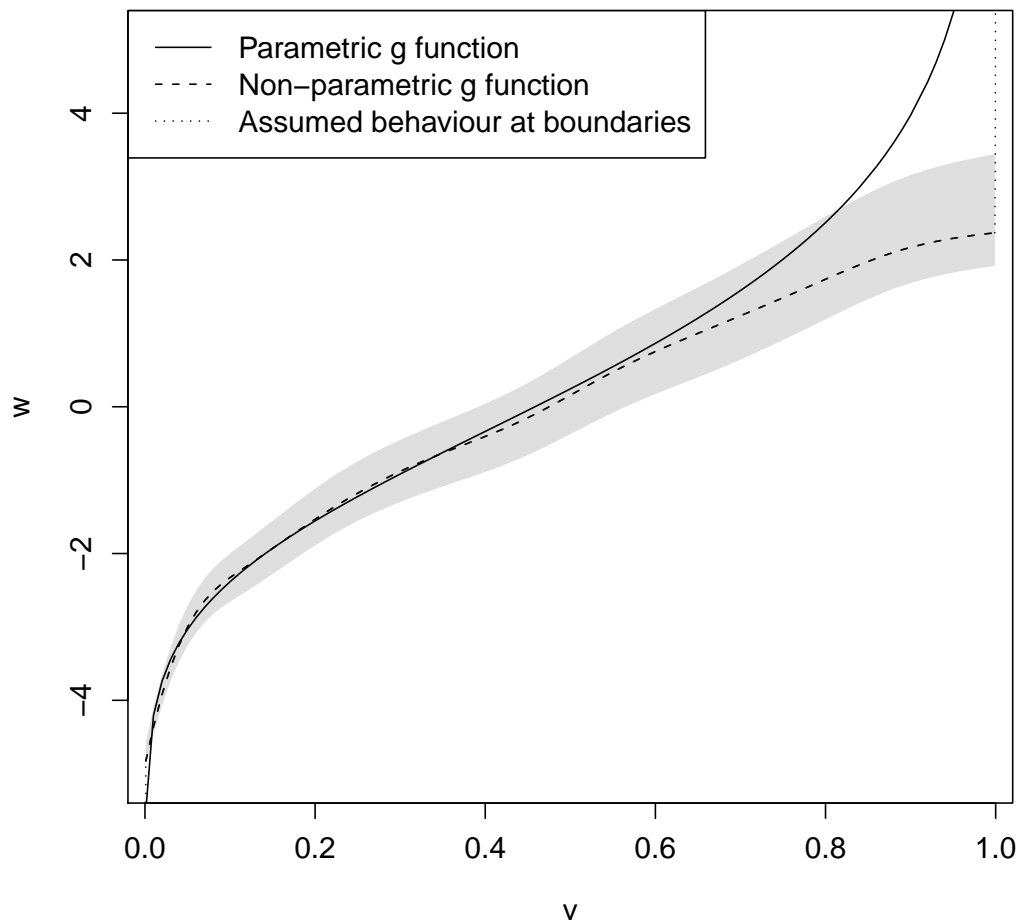

Figure 3: Parametric and non-parametric estimates of the *g* function. The 95% percentile confidence intervals are obtained with bootstrap methods.

For the parametric approximation of the *g* function, our choice of the inverse of the generalized logit function was based on its simplicity and flexibility. However, our method is not limited to this choice and the inverse of any sigmoid function may be used, as appropriate for the data set at hand. Use of a non-parametric *g* function eliminates the need for a choice of function, at the expense of several degrees of freedom. In the case of a sparse data set, there will be obvious advantages to a judicious choice of parametric *g* function over the non-parametric approach.
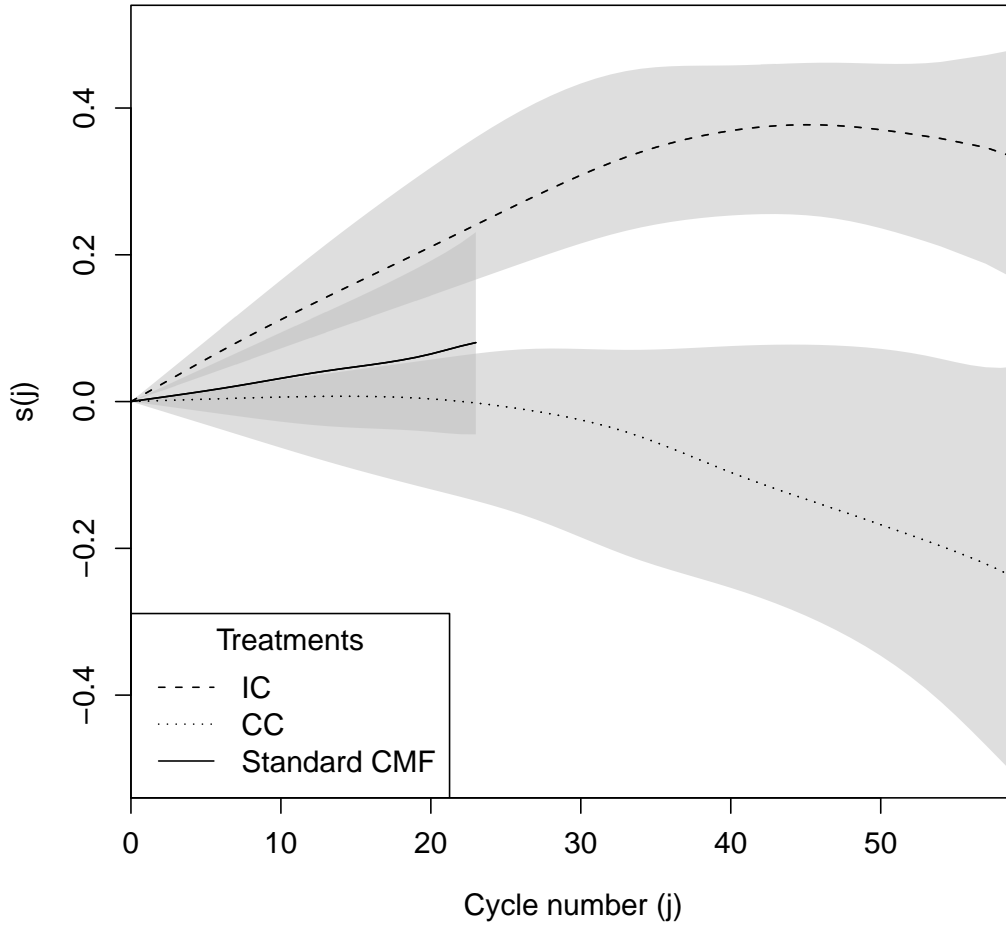
Figure 4: Dependence of the overall quality of life on chemotherapy cycle number with 95% percentile CI obtained with bootstrap methods. Higher values correspond to worse quality of life.

Our approach is more general than those of Lesaffre et al. (2007) and Bottai et al. (2010). In both of these, the application of the logistic transformation to the scores assumes an underlying symmetry in the mapping of the observed score to the latent variable. In the cases of both pain and quality of life, it is unlikely that behaviour at the two extremes of the scale is symmetric, and this is borne out by the asymmetric nature of the estimates of the *g* function in our two applications. Our approach is flexible, allowing either a parametric transformation which has flexibility in its shape, such as the generalized logistic transformation with three parameters governing the curve's location, symmetry and slope; or a smooth func-

tion with no constraints on its shape besides monotonicity. Having mapped the scores to the latent scale, the chosen regression model depends on distributional

	Parametric g function			Non-parametric g function		
	Mode	95% CI		Mode	95% CI	
β	0.014	0.009	0.021	0.022	0.019	0.023
σ	0.204	0.192	0.232	0.174	0.158	0.193
Deviance	-1652.7			-2260.8		
Effective no of parameters	3.4			14.0		
DIC	-1647.9			-2244.3		

Table 3: Chemotherapy impact on quality of life in advanced breast cancer patients: parameter estimates. Modes of posterior samples and 95% bootstrap confidence intervals are given.

assumptions made on the latent variable. Lesaffre et al. (2007) assume normality, and Bottai et al. (2010) make no distributional assumptions and use quantile regression. Our approach allows any distributional assumption, although we have found the logistic distribution convenient because of the resulting similarity of the model with proportional hazards ordinal regression.

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