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ANALYSIS OF ORDERED CATEGORICAL DATA FROM REPEATED MEASUREMENTS ASSUMING A QUANTITATIVE LATENT VARIABLE

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Summary

The purpose of the present paper is to propose an analytical method for ordered categorical responses obtained from a repeated measurement/longitudinal experiment. The ordered categorical scale is assumed to be a manifestation of a latent quantitative variable. A linear model is assumed for location parameters of the underlying distributions. Weighted least square method is applied to parameter estimation and subsequent analysis. Two data sets are analyzed to show several aspects of analysis by the proposed model and to discuss comparative characteristics of analysis compared with earlier analysis. A mention is made for a computer software program for the proposed model.

1. Introduction

Many articles have discussed experiments in which one response variable is repeatedly observed on the same subject. Such an experiment is referred to as a repeated measures experiment and is very common in psychology, medical and social sciences. When observed variables are quantitative, analysis of variance technique such as mixed model ANOVA, split-plot ANOVA, randomized block ANOVA and multivariate ANOVA can be applied according to the design. Non-parametric methods based on ranks are also applicable. Extensive discussions and bibliographies have been given in Bryant and Gillings [4], Koch et al. [7] and Timm [13]. When the observed variables are categorical, $a \times c \times \cdots \times c$ table is obtained, where a is the number of populations and c is the number of categories. Analysis of a square or cubic table has been paied considerable attension in literature including Bishop, Fienberg and Holland [3], Koch and Reinfurt [9] and Plackett [11]. In these literature testing symmetry and marginal homogeneity is discussed.

Key words and phrases: Ordered category, repeated measurements, linear model, weighted least square, latent scale, latent distribution.

For factorial analysis of an $a \times c \times \cdots \times c$ table, Koch et al. [8] present a general methodology based on so-called GSK approach proposed by Grizzle, Starmer and Koch [6]. In case of ordered categorical data, they propose to utilize scores assigned to ordered categories and an analysis based on a linear model for mean scores. If we are interested in a special dichotomization of response categories, more extensive methods can be applied as are given in Section 3 of Koch et al. [8]. Another interesting model for a square table is given by McCullagh [10] based on marginal logistic distribution.

In the present paper another approach to analysis a $c \times \cdots \times c$ table or an $a \times c \times \cdots \times c$ table is presented based on a multivariate latent scale linear model proposed by Uesaka and Asano [14] and [17]. To fix the problem discussed in the present paper, let us give an example. In a randomized controlled clinical trial, drugs under study are randomly allocated to a number of patients, and severity of disease, symptoms and degrees of improvement are observed on the respective ordinal categorical scales at each of several successive time points. In some cases, quantitative responses are evaluated on the ordinal categorical scales. In a randomized controlled study of an antiulcer drug, the diameters of ulcer are measured at first medical examination and several time points during administration period. Table 1 shows the classification of the percentages of the diameters of ulcer at 2, 4 and 6 weeks of administration period to those of the first examination. The three classes are 0–20%, 21–50% and 51%–, which are scored 1, 2 and 3, respectively. In the study many patients missed X-ray inspection at least an observation period. When the ulcer had been sufficiently small at an observation period, the subsequent measurements were often skipped. In this case, score 1 was given. As a result 93 patients were available for the present example. The questions of interest arise as follows:

(1) Is there any difference among drugs regarding the changes of responses over time?
(2) What is the nature and extent of the differences?
(3) When do the effects of drugs become noticeable?
(4) Which drug is the most effective?

and so on.

Another example is cited from McCullagh [10], where a 3×3 table is analyzed and difference in location parameters between the two time points is estimated to test whether there exists a significant change over time. These two data sets will be analyzed by the proposed method and be compared with earlier methods of analysis.

In Section 2, the model and hypotheses are given, and the methods of estimation of parameters and testing statistical hypotheses are pre-

Table 1. Observations for each patient.

No.	Drug A_1			Drug A_2			Drug A_3		
	2w	4w	6w	2w	4w	6w	2w	4w	6w
1	2	1	1	3	3	2	3	2	2
2	2	2	1	2	1	1	1	1	1
3	2	1	1	2	1	1	3	2	1
4	3	1	1	1	1	1	3	1	1
5	2	1	1	2	1	1	3	1	1
6	2	1	1	2	1	1	2	1	1
7	3	2	1	1	1	1	3	1	1
8	2	1	1	3	1	1	1	1	1
9	3	3	3	2	2	1	3	1	1
10	3	2	1	2	1	1	3	1	1
11	3	2	1	3	1	1	2	1	1
12	3	3	2	3	1	1	2	2	1
13	2	1	1	3	3	2	3	1	1
14	2	1	1	2	1	1	3	2	1
15	3	3	2	3	1	1	3	1	1
16	2	1	1	3	2	1	1	1	1
17	3	1	3	2	1	1	1	1	1
18	3	1	1	2	1	1	3	1	1
19	3	1	1	3	2	1	1	1	1
20	3	2	2	3	2	1	2	1	1
21	3	1	1	2	1	1	2	1	1
22	3	2	1	2	1	1	3	1	1
23				3	2	1	2	1	1
24				3	1	1	3	3	1
25				2	1	1	3	1	1
26				3	1	1	2	2	1
27				3	1	1	2	2	1
28				2	1	1	2	1	1
29				3	3	2	3	2	1
30				3	2	2			
31				3	3	2			
32				3	1	1			

sented in Section 3. The Sections 4 and 5 are devoted to illustrations of analysis. In Section 6, a mention is made on computer software system for analysis of the proposed model. And the final section is to discuss other analytical methods and related topics.

2. Mathematical model and hypotheses

A random sample of n subjects is divided into I groups of sizes $n_1, n_2, \cdots, n_I$ to which I treatments $A_1, A_2, \cdots, A_I$ are randomly assigned.

A response variable X is then observed on every subject at each of K successive time points $B_1, B_2, \cdots, B_K$. Every response is classified into one of c ordered categories. Without any loss of generality, the u-th category is denoted by an integer u, $u=1,\cdots,c$. Let $\boldsymbol{X}_{ij}=(X_{ij1},\cdots, X_{ijK})'$, where X_{ijk} is the observation at B_k on the j-th subject in the i-th group, $k=1,\cdots,K$, $j=1,\cdots,n_i$, $i=1,\cdots,I$. The sample space of $\boldsymbol{X}_{ij}$ is $S=\{1,2,\cdots,c\}^K$. Let $\boldsymbol{x}=(x_1,\cdots,x_K)$ be any element of S and $N_i(\boldsymbol{x})$ be the number of observations having $\boldsymbol{X}_{ij}=\boldsymbol{x}$ in the i-th group, $i=1,\cdots,I$, respectively. Let $N_{ik}(u)$ and $N_{ikm}(u,v)$, $u,v=1,\cdots,c$, $k,m=1,\cdots,K$ $(m\neq k)$ be the univariate and bivariate marginals of $N_i(\boldsymbol{x})$, respectively. Further, let $p_{ik}(u)$ and $p_{ikm}(u,v)$ be the corresponding univariate and bivariate probabilities. Then the $\{N_i(\boldsymbol{x})\}$ have a product multinomial distribution.

Now we assume that the observed variable X is a manifestation of a latent continuous response Z basing on several unknown threshold values. Let $\boldsymbol{Z}_{ij}=(Z_{ij1},\cdots,Z_{ijK})'$, where Z_{ijk} is the latent response at B_k of the j-th subject in the i-th group, $k=1,\cdots,K$, $j=1,\cdots,n_i$, $i=1,\cdots,I$. Assume that

$$(2.1)\qquad X_{ijk}=u\,,\quad \text{for}\quad \tau_{u-1}\leqq Z_{ijk}<\tau_u\,,\quad u=1,\cdots,c\,,\ k=1,\cdots,K\,,\ j=1,\cdots,n_i\,,\ i=1,\cdots,I\,,$$

where $\tau_0=-\infty$, $\tau_c=+\infty$ and $\tau_1,\cdots,\tau_{c-1}$ are unobservable parameters to show threshold values. Now let $\boldsymbol{Z}_{ij}$, $j=1,\cdots,n_i$ be independently and identically distributed with a K-variate continuous distribution $G_i(\boldsymbol{z})=G(\boldsymbol{z}-\boldsymbol{\mu}_i)$, where $\boldsymbol{\mu}_i=(\mu_{i1},\cdots,\mu_{iK})'$ is an unknown location parameter vector, $i=1,\cdots,I$, and $G(\boldsymbol{z})$ is a K-dimensional continuous distribution function, where $G(\boldsymbol{z})$ is assumed to be interchangeable in its K variates and $F(z)$ denotes the common univariate marginal c.d.f. of $G(\boldsymbol{z})$. Then we have

$$(2.2)\qquad p_{ik}(u)=F(\tau_u-\mu_{ik})-F(\tau_{u-1}-\mu_{ik})\,,\quad u=1,\cdots,c\,,\quad k=1,\cdots,K\,,\quad i=1,\cdots,I\,.$$

A linear model for μ_{ik} is now proposed as the following expression

$$(2.3)\qquad \mu_{ik}=\sum_{j=1}^{p} w_j^{ik}\beta_j\,,\qquad k=1,\cdots,K\,,\quad i=1,\cdots,I\,,$$

where $\beta_1,\cdots,\beta_p$ are unknown parameters and w_j^{ik}'s are known constants. For notational convenience we may write $\boldsymbol{\beta}=(\beta_1,\cdots,\beta_p)'$, $\boldsymbol{\mu}=(\boldsymbol{\mu}_1',\cdots,\boldsymbol{\mu}_I')'$ and

$$\begin{bmatrix} w_1^{11},\cdots,w_p^{11} \\ w_1^{12},\cdots,w_p^{12} \end{bmatrix}$$

$$\boldsymbol{W}=\begin{bmatrix} \vdots & \vdots \\ w_1^{1K},\cdots, w_p^{1K} \\ \vdots & \vdots \\ w_1^{IK},\cdots, w_p^{IK} \end{bmatrix}. \tag{2.4}$$

Then the model defined by (2.3) is expressed as $\boldsymbol{\mu}=\boldsymbol{W\beta}$. The hypothesis of interest is represented by

$$\boldsymbol{H\beta}=\boldsymbol{h}\,, \tag{2.5}$$

where $\boldsymbol{H}$ is an $r\times p$ full rank given matrix and $\boldsymbol{h}$ is an r-dimensional given vector.

Let us consider the univariate marginal distribution $F(z)$. In what follows we assume that $F(z)$ has positive, continuous and bounded first order derivative $f(z)$ at any finite z, which is only one condition about $F(z)$. Usually a normal or logistic distribution is applied in univariate analysis, but these symmetric distributions sometimes fail to fit to data and skewed distributions have come into use. Usual candidates of the latent distributions are normal, logistic, first and second double exponential distributions, (reversed) generalized logistic and the (reversed) log-gamma distributions. For further discussion about latent distributions and latent scales, see Uesaka and Asano [15].

3. Method of analysis

3.1 *Parameter estimation*

The model defined in the preceding section specifies only the univariate marginal probabilities. Thus the usual method of estimation such as maximum likelihood or minimum chi-square cannot be applied. However, if we define

$$q_{ik}(u)=\Pr\,(X_{ijk}\leqq u)\,, \qquad u=1,\cdots,c\,,\quad k=1,\cdots,K\,,\quad j=1,\cdots,n_i\,,\quad i=1,\cdots,I\,, \tag{3.1}$$

we have

$$q_{ik}(u)=F(\tau_u-\mu_{ik})\,, \qquad u=1,\cdots,c\,,\quad k=1,\cdots,K\,,\quad i=1,\cdots,I\,. \tag{3.2}$$

Thus we have

$$F^{-1}(q_{ik}(u))=\tau_u-\sum_{j=1}^{p} w_j^{ik}\beta_j\,, \qquad u=1,\cdots,c-1\,,\quad k=1,\cdots,K\,,\quad i=1,\cdots,I\,. \tag{3.3}$$

In other words, the model is re-expressed in terms of a linear model for functions of cell probabilities and weighted least squares method, like Bhapkar [2], Grizzle, Starmer and Koch [6], can be applied to parameter estimation. Let

$$Q_{ik}(u)=\sum_{u'=1}^{u} N_{ik}(u')/n_i\,, \qquad u=1,\cdots,c-1\,,\quad k=1,\cdots,K\,,\quad i=1,\cdots,I\,. \tag{3.4}$$

Then the covariance between $\sqrt{n_i}\,Q_{ik}(u)$ and $\sqrt{n_i}\,Q_{im}(v)$ is

$$\sigma^*_{i,km}(u,v)=\begin{cases}\sum_{u'=1}^{u}\sum_{v'=1}^{v} p_{ikm}(u',v')-q_{ik}(u)q_{im}(v)\,, & k\neq m\,,\\ q_{ik}(u_0)-q_{ik}(u)q_{im}(v)\,,\quad u_0=\min(u,v)\,, & k=m\,.\end{cases} \tag{3.5}$$

The estimate $\hat{\sigma}^*_{i,km}(u,v)$ of $\sigma^*_{i,km}(u,v)$ is obtained by substituting $p_{ikm}(u,v)$'s and $q_{ik}(u)$'s for their sample values.

In order to identify parameters, we impose a constraint on τ_u's that $\tau_1+\cdots+\tau_{c-1}=0$ in order to retain symmetric relation among τ_u's, and define $\boldsymbol{\tau}=(\tau_1,\cdots,\tau_{c-2})'$. Thus $\tau_{c-1}=-(\tau_1+\cdots+\tau_{c-2})$. Further let

$$\boldsymbol{A}_1=\mathbf{1}_K\otimes\begin{bmatrix}\boldsymbol{I}_{c-1}\\ -\mathbf{1}'_{c-1}\end{bmatrix}, \qquad \boldsymbol{A}_2=\boldsymbol{I}_K\otimes\mathbf{1}_{c-1}\,, \tag{3.6}$$

where $\boldsymbol{I}_K$ and $\boldsymbol{I}_{c-2}$ are $K\times K$ and $(c-2)\times(c-2)$ identity matrices, respectively, and $\mathbf{1}_K$, and $\mathbf{1}_{c-2}$ are the K and $(c-2)$-dimensional vectors with all elements 1, respectively. Also letting

$$\begin{aligned}&\eta_{ik}(u)=\tau_u-\mu_{ik}\,, \qquad Y_{ik}(u)=F^{-1}(Q_{ik}(u))\,,\\ &\qquad u=1,\cdots,c-1\,,\quad k=1,\cdots,K\,,\quad i=1,\cdots,I\,,\\ &\boldsymbol{\eta}_i=(\eta_{i1}(1),\cdots,\eta_{i1}(c-1),\cdots,\eta_{iK}(c-1))'\,,\\ &\boldsymbol{Y}_i=(Y_{i1}(1),\cdots,Y_{i1}(c-1),\cdots,Y_{iK}(c-1))'\,,\\ &\boldsymbol{e}_i=\boldsymbol{Y}_i-\boldsymbol{\eta}_i=(e_{i1}(1),\cdots,e_{i1}(c-1),\cdots,e_{iK}(c-1))'\,,\\ &\qquad\qquad\qquad\qquad\qquad\qquad\text{for}\quad i=1,\cdots,I\,,\end{aligned} \tag{3.7}$$

the latent scale linear model is re-expressed by a linear model for $\boldsymbol{Y}_i$, $i=1,\cdots,I$ as follows:

$$\begin{aligned}&\boldsymbol{Y}_i=\boldsymbol{\eta}_i+\boldsymbol{e}_i\,, \qquad \boldsymbol{\eta}_i=\boldsymbol{A}_1\boldsymbol{\tau}-\boldsymbol{A}_2\boldsymbol{\mu}_i\,, \qquad i=1,\cdots,I\,,\\ &\boldsymbol{\mu}=\boldsymbol{W}\boldsymbol{\beta}\,.\end{aligned} \tag{3.8}$$

The error vector $\sqrt{n_i}\,\boldsymbol{e}_i$ has the asymptotic $K(c-1)$-dimensional normal distribution with mean vector $\mathbf{0}$ and variance-covariance matrix $\boldsymbol{\Sigma}_i=$

$(\sigma_{i,km}(u, v))$, where

$$\sigma_{i,km}(u, v)=\sigma^*_{i,km}(u, v)/f(\eta_{ik}(u))f(\eta_{im}(v))\,, \qquad u, v=1,\cdots, c-1\,,\quad k, m=1,\cdots, K\,. \tag{3.9}$$

Denoting the sample estimate of $\sigma_{i,km}(u, v)$ by $\hat{\sigma}_{i,km}(u, v)$, let $\boldsymbol{V}_i=(\hat{\sigma}_{i,km}(u, v))$, and $\boldsymbol{V}$ be the block diagonal matrix of $(n/n_1)\boldsymbol{V}_1,\cdots,(n/n_I)\boldsymbol{V}_I$, and let $\boldsymbol{Y}=(\boldsymbol{Y}_1',\cdots,\boldsymbol{Y}_I')'$, $\boldsymbol{e}=(\boldsymbol{e}_1',\cdots,\boldsymbol{e}_I')'$, and

$$\boldsymbol{A}=\begin{bmatrix} \boldsymbol{A}_1 & -\boldsymbol{A}_2 & & \\ \vdots & & \ddots & \boldsymbol{0} \\ \vdots & & \boldsymbol{0} & \ddots \\ \boldsymbol{A}_1 & & & -\boldsymbol{A}_2 \end{bmatrix}.$$

Then the full linear equation for the model is simply written as

$$\boldsymbol{Y}=\boldsymbol{A}\begin{pmatrix}\boldsymbol{\tau}\\ \boldsymbol{\mu}\end{pmatrix}+\boldsymbol{e}\,. \tag{3.10}$$

Applying the method of weighted least squares with empirical weight matrix $\boldsymbol{V}^{-1}$, we obtain estimates of $\boldsymbol{\tau}$ and $\boldsymbol{\mu}$;

$$\begin{pmatrix}\tilde{\boldsymbol{\tau}}\\ \tilde{\boldsymbol{\mu}}\end{pmatrix}=(\boldsymbol{A}'\boldsymbol{V}^{-1}\boldsymbol{A})^{-1}\boldsymbol{A}'\boldsymbol{V}^{-1}\boldsymbol{Y}\,. \tag{3.11}$$

The simultaneous estimates of $\boldsymbol{\tau}$ and $\boldsymbol{\beta}$ are

$$\begin{pmatrix}\hat{\boldsymbol{\tau}}\\ \hat{\boldsymbol{\beta}}\end{pmatrix}=\boldsymbol{V}^*\boldsymbol{W}^{*\prime}(\boldsymbol{A}'\boldsymbol{V}^{-1}\boldsymbol{A})\begin{pmatrix}\tilde{\boldsymbol{\tau}}\\ \tilde{\boldsymbol{\mu}}\end{pmatrix}, \tag{3.12}$$

where

$$\boldsymbol{W}^*=\begin{bmatrix}\boldsymbol{I}_{c-2} & \boldsymbol{0}\\ \boldsymbol{0} & \boldsymbol{W}\end{bmatrix}, \tag{3.13}$$

and

$$\boldsymbol{V}^*=[(\boldsymbol{A}\boldsymbol{W}^*)'\boldsymbol{V}^{-1}(\boldsymbol{A}\boldsymbol{W}^*)]^{-1}\,. \tag{3.14}$$

3.2 *Some properties of estimators and testing statistical hypotheses*

Now let us consider some asymptotic properties of weighted least squares estimators of $\boldsymbol{\tau}$ and $\boldsymbol{\beta}$, and of test statistics for some statistical hypotheses. Main results are direct consequences of theorems on the method of weighted least squares by Bhapkar [2]. In what follows we assume that $n_1,\cdots, n_I$ tend to infinity under the condition that

$$\lim_{n\to\infty} n_i/n=\lambda_i>0\,, \qquad i=1,\cdots, I\,. \tag{3.15}$$

Let $\boldsymbol{\Sigma}$ be the block diagonal matrix of $(1/\lambda_1)\boldsymbol{\Sigma}_1,\cdots,(1/\lambda_I)\boldsymbol{\Sigma}_I$, which is the limit of $\boldsymbol{V}$ as n_i's tend to infinity. Further let

$$\Sigma^*=[(AW^*)'\Sigma^{-1}(AW^*)]^{-1}. \tag{3.16}$$

Then we obtain the following properties.

(1) When n tends to infinity under the condition (3.15), $\sqrt{n}(\hat{\tau}-\tau)$ and $\sqrt{n}(\hat{\beta}-\beta)$ belong asymptotically to a joint normal distribution $N(0, \Sigma^*)$.

The predicted value of η is given by $\hat{\eta}=AW^*(\hat{\tau}', \hat{\beta}')'$ under the model specified by (2.3) and (2.4), and $\sqrt{n}(\hat{\eta}-\eta)$ is approximately distributed in the multivariate normal distribution with mean 0 and variance-covariance matrix

$$\Sigma(\hat{\eta})=(AW^*)\Sigma^*(AW^*)'. \tag{3.17}$$

The estimate $V(\hat{\eta})$ of $\Sigma(\hat{\eta})$ is obtained by replacing Σ^* by V^* in (3.17). This distribution of $\hat{\eta}$ is singular when $c\geqq 3$. The residual vector is given by $Y-\hat{\eta}$ and its variance-covariance matrix is estimated by $n^{-1}(V-V(\hat{\eta}))$. This covariance matrix is of rank $IK(c-1)-(p+c-2)$. The residual sum of squares is given by

$$SS(\hat{\tau}, \hat{\beta})=n(Y-\hat{\eta})'V^{-1}(Y-\hat{\eta}). \tag{3.18}$$

The goodness-of-fit of the model (3.8) is evaluated by $SS(\hat{\tau}, \hat{\beta})$ for the model, that is, the following proposition holds.

(2) When the model defined by (2.3) and (2.4) is true, as n_i's tend to infinity under the condition of (3.16), $SS(\hat{\tau}, \hat{\beta})$ has an asymptotic chi-square distribution with $IK(c-1)-(p+c-2)$ degrees of freedom.

The statistic $SS(\hat{\tau}, \hat{\beta})$ of the goodness-of-fit suggests the validity of combined specification of marginal probabilities as given by (2.3) and (2.4). Alternatively, the validity of the model can be assessed in two steps. The first is directed to the validity of the assumption for marginal distribution. The statistic for goodness-of-fit is given by

$$SS(\tilde{\tau}, \tilde{\mu})=n\left(Y-A\begin{pmatrix}\tilde{\tau}\\ \tilde{\mu}\end{pmatrix}\right)'V^{-1}\left(Y-A\begin{pmatrix}\tilde{\tau}\\ \tilde{\mu}\end{pmatrix}\right). \tag{3.19}$$

When the model (2.3) is true, the statistic has asymptotic chi-square distribution with $(IK-1)(c-2)$ degrees of freedom. The second step is for the structure of μ defined by (2.4). When our assumptions for the marginal distributions are true and the model $\mu=W\beta$ holds,

$$SS(\hat{\beta}|\tilde{\mu})=n(\tilde{\mu}-W\hat{\beta})'V(\tilde{\mu})^{-1}(\tilde{\mu}-W\hat{\beta}) \tag{3.20}$$

has asymptotic chi-square distribution with $IK-p$ degrees of freedom, where $V(\tilde{\mu})$ is the estimated variance-covariance matrix of $\Sigma(\tilde{\mu})$. Thus we can test the adequacy of the model $\mu=W\beta$ by referring $SS(\hat{\beta}|\tilde{\mu})$ to chi-square distribution with $IK-p$ degrees of freedom. It is noted

that $SS(\hat{\tau}, \hat{\beta}) = SS(\tilde{\tau}, \tilde{\mu}) + SS(\hat{\beta}|\tilde{\mu})$.

Now let us consider testing a linear hypothesis $H_0: H\beta = h$. The chi-squared test statistic is given by

$$X^2 = n(H\hat{\beta} - h)'[HV(\hat{\beta})H']^{-1}(H\hat{\beta} - h), \tag{3.21}$$

where $V(\hat{\beta})$ is the estimated covariance matrix of $\sqrt{n}\hat{\beta}$ and is given as a submatrix composed of the last $p \times p$ elements of V^*. From (1), we have

(3) When our model is true and H_0 holds, X^2 defined by (3.21) has asymptotic chi-square distribution with r degrees of freedom.

3.3 *Adjustment for zero frequencies*

When there are zeros in $N_{ikm}(u, v)$'s, $F^{-1}(Q_{ik}(u))$'s happen to be unbounded, or V_i sometimes becomes singular. The singular covariance matrix is obtained when, for example, $N_{ikm}(1, 1) > 0$ and $N_{ikm}(u, v) = 0$ for $u = 1$, $v > 1$ and $u > 1$, $v = 1$. In order to avoid such a difficulty, some adjustments for $\{Q_{ikm}(u, v)\}$ and $\{P_{ik}(u)\}$ are required. The usual suggestion is to add some small numbers to the frequencies. For example, one may employ $N_{ik}(u) + 1/c$ and $N_{ikm}(u, v) + 1/c^2$ instead of $N_{ik}(u)$ and $N_{ikm}(u, v)$ and replace n_i by $n_i + 1$. The asymptotic results stated in the subsection 3.2 remain valid under such adjustments.

3.4 *Asymptotic power of the test under local alternatives*

Let us consider a Pitman type sequence of alternatives such as

$$\mu^{(n)} = W(\beta^{(0)} + \xi/\sqrt{n}), \tag{3.22}$$

where n is the total sample size and $\mu^{(n)}$ is the location vector. $\beta^{(0)}$ and ξ are unknown p-dimensional constant vectors, such that $H\beta^{(0)} = 0$ and $H\xi \neq 0$, where H is an $r \times p$ known matrix of rank r. Let $\Sigma^{*(0)}$ be the asymptotic covariance matrix of $\sqrt{n}(\hat{\tau}', \hat{\beta}')'$ for infinitely large n. Let $\Sigma^{*(0)}(\beta)$ be the submatrix of $\Sigma^{*(0)}$ composed of the last $p \times p$ elements. Then we can state that the chi-squared statistic for testing the linear hypothesis $H\beta = 0$ has asymptotic noncentral chi-square distribution with r degrees of freedom and the noncentrality parameter

$$\gamma^2 = (H\xi)'[H\Sigma^{*(0)}(\beta)H']^{-1}(H\xi). \tag{3.23}$$

4. Analysis of the data in Table 1

4.1 *Analysis by the present model*

In a randomized controlled study, usually drugs are assigned to patients according to double blined method and restricted random permuted blocks of several patients. Although the present study was

conducted in this manner, we neglect the aspect of this particular randomization scheme and the patients are treated as if they constituted random samples of respective sizes. Because the original randomization is meaningless due to drop-outs of many patients from measurements and the block size is too small.

It is often assumed that the size of an organ has a log-normal distribution. If the logarithmic transformations of the sizes of ulcer on the same subject jointly have a multivariate normal distribution, the ratio of the sizes is also log-normal. Thus it may be reasonable to assume the latent distribution to be normal. Table 2 shows cross classifications of observations in Table 1. Since there are several empty rows and columns, adjustment for zero frequency was done following the rule given in subsection 3.3. The matrices A_1 and A_2 are

$$A_1=\begin{bmatrix} 1 \\ -1 \\ 1 \\ -1 \\ 1 \\ -1 \end{bmatrix} \quad \text{and} \quad A_2=\begin{bmatrix} 1 & 0 & 0 \\ 1 & 0 & 0 \\ 0 & 1 & 0 \\ 0 & 1 & 0 \\ 0 & 0 & 1 \\ 0 & 0 & 1 \end{bmatrix}.$$

The estimates of population mean vectors for the drugs and threshold τ_1 are obtained by using $W=I_9$. Table 3 shows these estimates and their estimated standard deviations. Changes of mean values over time are shown in Figure 1. The chi-squared value for goodness-of-fit of the normal linear model is 7.372 with 8 degrees of freedom. The drug A_1 has been conjectured to have little effect on ulcer. The drug A_3 is mixture of A_1 and A_2 and has been expected to be most effective and

Table 2. Two-way cross-classification of the data in Table 1.

Drug	Pair of weeks	2w-4w			2w-6w			4w-6w		
	Category	1	2	3	1	2	3	1	2	3
A_1	1	0	0	0	0	0	0	12	0	1
	2	8	1	0	9	0	0	5	1	0
	3	5	5	3	8	3	2	0	2	1
A_2	1	2	0	0	2	0	0	22	0	0
	2	12	1	0	13	0	0	5	1	0
	3	8	5	4	12	5	0	0	4	0
A_3	1	5	0	0	5	0	0	21	0	0
	2	6	3	0	9	0	0	6	1	0
	3	10	4	1	14	1	0	1	0	0

Table 3. Estimates of mean values and its estimated standard deviations based on normal distribution.

Drug		2nd week	4th week	6th week
A_1	Mean	0.784	−0.461	−0.967
	sd	0.267	0.288	0.264
A_2	Mean	0.623	−0.813	−1.448
	sd	0.207	0.211	0.261
A_3	Mean	0.488	−1.039	−2.047
	sd	0.214	0.236	0.377

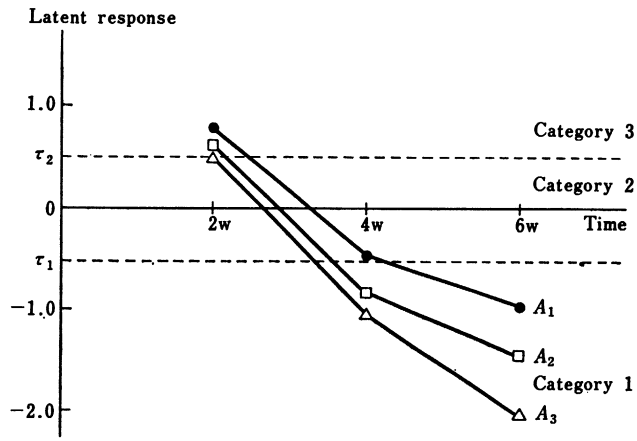

Fig. 1. Changes of mean values of latent responses for three drugs.

that the effect is largely due to A_2. Thus our interest is in the differences between A_1 and A_3, and A_2 and A_3. It is also known that ulcer tends to cure, if life environment of the patient would be improved. Taking these into consideration, let us redefine parameters as follows;

β_1 is overall mean,
β_2 is the mean difference between A_1 and A_3,
β_3 is the mean difference between A_2 and A_3,
β_4 and β_5 are linear and quadratic trends over time points averaged over the drugs, respectively,
β_6 and β_8 are linear and quadratic trends over time points for the differences between A_1 and A_2, respectively,
β_7 and β_9 are linear and quadratic trends over time points for the differences between A_1 and A_3, respectively.

Thus we take $\boldsymbol{W}$ as

$$W=\begin{bmatrix} 1 & 1 & 0 & 1 & 1 & 1 & 0 & 1 & 0 \\ 1 & 1 & 0 & 0 & -2 & 0 & 0 & -2 & 0 \\ 1 & 1 & 0 & -1 & 1 & -1 & 0 & 1 & 0 \\ 1 & 0 & 1 & 1 & 1 & 0 & 1 & 0 & 1 \\ 1 & 0 & 1 & 0 & -2 & 0 & 0 & 0 & -2 \\ 1 & 0 & 1 & -1 & 1 & 0 & -1 & 0 & 1 \\ 1 & 0 & 0 & 1 & 1 & 0 & 0 & 0 & 0 \\ 1 & 0 & 0 & 0 & -2 & 0 & 0 & 0 & 0 \\ 1 & 0 & 0 & -1 & 1 & 0 & 0 & 0 & 0 \end{bmatrix}.$$

The estimate of β_j and its estimated standard deviation for $j=1,\cdots,p$ are as follows:

$$\hat{\beta}_1=-0.866 \quad (0.191) \qquad \hat{\beta}_2=0.651 \quad (0.274) \qquad \hat{\beta}_3=0.302 \quad (0.262)$$

$$\hat{\beta}_4=1.268 \quad (0.211) \qquad \hat{\beta}_5=0.086 \quad (0.086) \qquad \hat{\beta}_6=-0.392 \quad (0.252)$$

$$\hat{\beta}_7=-0.232 \quad (0.246) \qquad \hat{\beta}_8=0.037 \quad (0.109) \qquad \hat{\beta}_9=0.047 \quad (0.098)$$

Tests of significance of factor effects are performed by using appropriate $\boldsymbol{H}$ matrices in (2.5). The results are given in Table 4. The interaction effects between drugs and times are negligible. The main effect of time is highly significant, and is mainly due to linear trend. The significance probability of main effect of drugs is a little greater than 0.05. However the difference between A_1 and A_3 is 0.651 with estimated standard deviation 0.274, and is significantly different from zero at 5% level of significance as was expected.

Table 4. Table for analysis of chi-squares.

Factor	Degrees of freedom	Chi-squared value
Main effect of Drugs (A)	2	5.640
A_1-A_3	1	5.639
A_2-A_3	1	1.490
Main effect of Time (T)	2	43.562
Linear	1	36.128
Quadratic	1	0.997
Interaction effect	4	2.514

4.2 *Differences of results from different latent distributions*

Now let us examine effects of different latent distributions. Dis-

tributions to be examined are those given in Section 2. However, since the generalized logistic family and reversed generalized logistic family are very similar to reversed log-gamma family and log-gamma family, respectively, and the former families are much easier to treat with, the (reversed) log-gamma family is not examined. Table 5 shows goodness-of-fit of the models of the four one-parameter distributions. Curves of the goodness-of-fit statistics of the generalized and the reversed generalized logistic distributions are plotted in Figure 2. When ν, the shape parameter, tends to infinity, generalized logistic distribution approaches to the first double exponential distribution and also

Table 5. Goodness-of-fit statistics of the four distributions.

	Latent distribution			
	Normal	First DE	Logistic	Second DE
Total group	7.372	4.846	6.284	11.817
A_1	3.301	0.993	2.459	3.699
A_2	3.480	1.297	3.228	5.689
A_3	0.591	2.555	0.598	2.432

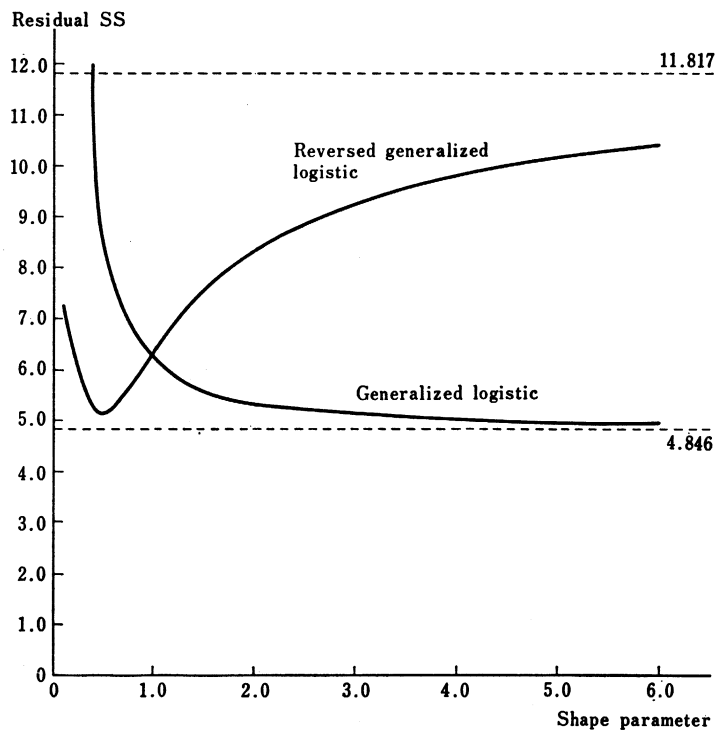

Fig. 2. Changes of residual SS in generalized logistic and reversed generalized logistic distributions.

the reversed generalized logistic one does to the second double exponential distribution. Thus in the former family the minimum value of the goodness-of-fit statistic might be attained by the first double exponential distribution. In the latter family the minimum value 5.101 was attained at $\nu=0.50$. The smallest value of the goodness-of-fit statistic obtained was 4.846, which was given by the first double exponential distribution. The largest value, 11.817, was given by the second double exponential distribution, which is the reflection of the first double exponential distribution in a vertical line. From these results, the second double exponential distribution seems to be inappropriate, although the goodness-of-fit statistic does not indicate inadequacy.

Next let us examine differences of the test statistics of the factor effects among the latent distributions. Table 6 shows the test statistics of the factor effects based on each of the four distributions. Chi-square values for testing main effects of drugs and time are considerably different among the four distributions, and the order of magnitude of the statistics is not consistent with those of the goodness-of-fit statistics. Fortunately, in the present data, we reach the same conclusion.

Table 6. Test statistics for linear hypotheses about factor effects.

	Latent distribution			
	Normal	First DE	Logistic	Second DE
Drugs	5.640	5.949	4.160	4.359
A_1-A_3	5.639	5.813	4.155	4.341
A_2-A_3	1.490	1.808	1.189	1.029
Time	43.562	31.115	35.574	39.665
Linear	36.128	20.195	26.209	38.513
Interaction	2.514	2.959	2.655	2.223
All factors	100.303	89.019	77.093	81.323

5. Analysis of coalface worker's data

McCullagh [10] analyzed a 4×4 table obtained by classifying 82 coalface workers according to the degrees of pneumoconiosis evaluated twice, the interval being 2.5 years. The scale $\{1, 2, 3, 4\}$ indicates increasing severity of the disease. McCullagh assumes that X_{ik}, the rating of the severity at the k-th time on the i-th individual, is obtained as

$$X_{ik}=u\,, \qquad \text{if} \quad \tau_{u-1}\leqq Z_{ik}<\tau_u\,,$$

and

$$Z_{ik}=U_i+\mu_k+Y_{ik}\,, \qquad k=1,2\,, \quad i=1,\cdots,n\,,$$

where $\{Y_{ik}\}$ are independently and identically distributed in the standard logistic distribution. He also assumes that U_i is a nuisance parameter, and developes a conditional argument for estimation of $\Delta=(\mu_1-\mu_2)$. The method does not provide any estimate of τ_u and testing goodness-of-fit of the model. In the present method, $(U_i+Y_{i1},\ U_i+Y_{i2})$, $i=1,\cdots,n$ are assumed to be independently and identically distributed in an interchangeable bivariate distribution. Four distributional models of the marginals of the bivariate distribution were examined. Adjustment for cell frequencies given in Section 3 was also applied. Table 7 shows the goodness-of-fit statistics, estimated parameters, their standard deviations and correlation coefficient and test statistics for the hypothesis that there is no progression of the disease, that is, Δ is zero. Among the latent distributions, no substantial difference is observed in goodness-of-fit statistics as well as the test statistics for the null hypothesis about Δ. To see the effects of the adjustment of cell frequencies, same information as that in Table 7 is given in Table 8. This shows that the adjustment gives rather conservative results.

Now let us compare our results with those in McCullagh [10]. He gives two estimates of Δ; $\hat{\Delta}=1.45$ (sd=0.53) and $\Delta^*=1.503$ (sd=0.53). Test statistics for the null hypothesis that $\Delta=0$ are, thus, 2.7 and 2.8. On the other hand, the estimates of Δ and their standard deviations

Table 7. Results of fitting four latent distributions to the coaleface workers data with adjustment.

Statistic	Latent distribution			
	Normal	Logistic	First DE	Second DE
Residual SS	0.886	0.916	1.263	1.031
$\hat{\mu}_1$	−0.895	−1.495	−1.592	−0.506
	(0.140)	(0.252)	(0.226)	(0.119)
$\hat{\mu}_2$	−0.604	−1.005	−1.197	−0.236
	(0.128)	(0.222)	(0.189)	(0.122)
Corr $(\hat{\mu}_1, \hat{\mu}_2)$	0.773	0.789	0.816	0.755
$\hat{\Delta}$	0.292	0.491	0.395	0.269
sd	(0.091)	(0.155)	(0.130)	(0.084)
ratio	3.212	3.158	3.151	3.202
$\hat{\tau}_1$	−0.462	−0.791	−0.675	−0.423
	(0.066)	(0.121)	(0.109)	(0.061)
$\hat{\tau}_2$	−0.090	−0.184	−0.186	−0.056
	(0.055)	(0.099)	(0.090)	(0.047)
Corr $(\hat{\tau}_1, \hat{\tau}_2)$	0.174	0.299	0.398	0.006

Table 8. Results of fitting four latent distributions to the coaleface workers data without adjustment.

Statistic	Latent distribution			
	Normal	Logistic	First DE	Second DE
Residual SS	0.918	0.965	1.350	1.085
$\hat{\mu}_1$	−0.909	−1.521	−1.615	−0.516
	(0.141)	(0.256)	(0.230)	(0.119)
$\hat{\mu}_2$	−0.612	−1.016	−1.203	−0.248
	(0.129)	(0.223)	(0.191)	(0.121)
Corr $(\hat{\mu}_1, \hat{\mu}_2)$	0.811	0.824	0.844	0.803
$\hat{\Delta}$	0.297	0.505	0.412	0.268
sd	(0.084)	(0.146)	(0.123)	(0.075)
ratio	3.553	3.470	3.345	3.554
$\hat{\tau}_1$	−0.461	−0.790	−0.673	−0.420
	(0.068)	(0.124)	(0.113)	(0.062)
$\hat{\tau}_2$	−0.092	−0.186	−0.187	−0.057
	(0.055)	(0.101)	(0.092)	(0.047)
Corr $(\hat{\tau}_1, \hat{\tau}_2)$	0.198	0.323	0.417	0.018

obtained from our model based on the logistic distribution and analysis with and without adjustment are 0.491, sd=0.155 (ratio=3.158) and 0.503, sd=0.149 (ratio=3.470), respectively. Thus our method gives more convincing evidence for the progression of the disease than McCullagh's method.

Further, McCullagh [10] gives results of analysis based on exponential and normal distributions which use only the information in the marginals. The estimates of Δ are equal to those in the present analysis based on the respective latent distribution. However, the standard deviations of the estimates are much larger than those of the present analysis.

6. On computer software

A computer program for the method proposed in the present paper was written by one of the authors and has been implemented to the **NISAN** system developed by Asano et al. [1]. The command is ANOCM and is for the multivariate latent scale linear model discussed by Uesaka and Asano [17]. ANOCM permits an interactive analysis. Details are given by Uesaka and Asano [16].

7. Discussion

Analysis of ordered categorical data from repeated measurement/longitudinal studies is very important in medical, social and psychological researches. Usual analysis may be conventional parametric analysis of variance using pre-assigned scores, such as split-plot ANOVA, mixed model ANOVA, multivariate ANOVA for general linear hypotheses about mean scores. However, these are not valid because of violation of the conditions about covariance structure. There are a few articles which discuss the analysis of repeated measurement/longitudinal experiments on ordered categorical responses. Koch et al. [7] discussed various aspects of repeated measurements and suggested to use Wilcoxon type rank analysis of variance. They also suggested not to apply the rank method to subjective ratings such as improvement of a disease. Koch et al. [8] and Koch and Reinfurt [9] proposed a linear model for mean scores based on pre-assigned scores and to analyze by the method of weighted least squares. This approach avoids the invalidity involved in conventional parametric analysis. The pre-assigned scores can produce cumulative probability up to a specific category. These approaches do not assume any latent continuous scale, and are directed to comparisons of summary measures such as mean scores, cumulative probabilities, response ratio to a specific set of categories, etc. Also it does not assume any model for the response structures. The summary measure should be selected in advance of analysis, and there is no statistical way to assess the validity of the measure. When the within-subject factor is ordinal, multivariate rank test can be applied for testing hypotheses about regression coefficients (see Ghosh, Grizzle and Sen [5]).

On the other hand, our approach gives parametric model for univariate marginal probabilities, scale values of the categories, predicted values of the category probabilities as well as summary measures of factor effects. This additional information is provided by imposing the more stringent conditions on the nature of response variables. Our approach can be applied to subjective rating scales assuming the unidimensionality of the latent psychological continuum and theory of subjective measurement developed by Thurstone and others (see Thurstone [12]).

Furthermore, we can assess the validity of the latent scale, that is, the latent distributional model. The criterion of selecting the latent distribution may be

i) physical meaning and interpretability,
ii) goodness-of-fit,
iii) to attain simple structure.

When the model gives poor fit, possible reasons are ; unequal correlations between variables, heteroscedasticity among variables and/or populations, differences in criteria for categorical judgement among variables and/or populations, unequal latent distributions between variables and/or populations, etc. Thus we can get deep insight into the response structure.

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