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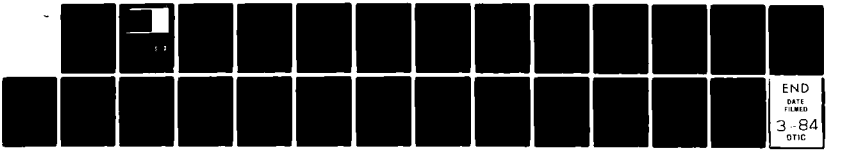

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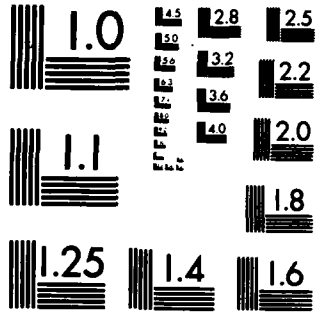

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COMPARISON OF THE DICHOTOMOUS AND POLYCHOTOMOUS QUANTAL RESPONSE MODELS

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ABSTRACT

A class of polychotomous quantal response models is defined, including the dichotomous response model. As an application of the Missing Information Principle, it is shown that the Fisher information for the common parameters in the more elaborate model is greater. For the logistic curve and several design schemes, the above result is supported in a numerical study. For estimating the common parameters of the dichotomous-response and trichotomous-response models and the percentiles of the common tolerance curve, an extensive simulation study shows that in general the latter model gives more accurate estimates than the former one. The situations in which such gains are substantial are identified.

AMS (MOS) Subject Classifications: 62K99, 62N05, 62B15

Key Words: Dichotomous quantal response, Polychotomous quantal response, Fisher information, Missing information principle, LD50, Logistic curve

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SIGNIFICANCE AND EXPLANATION

A dichotomous quantal-response model is commonly used to relate the response probability to the underlying stimulus variable. The percentiles of the quantal response curve are often used as measures of the quality of the test item. Sometimes it is practically feasible to classify the responses into three (or more) ordered categories, say, animal alive, moribund, or dead. A basic issue is whether any (or how much) gain in statistical efficiency can be realized from this more elaborate classification of the response. We give a positive answer both theoretically and empirically, and identify the situations in which such gains are substantial.

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COMPARISON OF THE DICHOTOMOUS AND POLYCHOTOMOUS QUANTAL RESPONSE MODELS

Siu-Keung Tse and C. F. Jeff Wu

1. Introduction

In quantal response model, the observed response is impossible to measure quantitatively but instead is a nominal variable which usually takes on two possible outcomes, response or non-response. This model is characterized by assuming a tolerance distribution F for every subject in the population. Thus, if stress level x is applied to a test subject, then the response y is a random variable taking value 1 with probability $F(x)$ and 0 with probability $1 - F(x)$. This model is common to many areas of research. In engineering the stress levels may be the pounds force applied to equipments or the temperature increases in a system. Then the number of brittle failures or unsuccessful performances can be recorded. In material testing, glass containers are submitted to a drop height test, the response is "broken" or "not broken". In drug testing, if the houseflies are exposed to a particular insecticide, the number of houseflies that are either dead or alive can be observed.

Usually, the tolerance distribution assumes the form of a probit or logistic model. Some other models include the angular distribution model, the rectangular model, etc. Finney (1978) compared the various models and concluded that they are indistinguishable between response rates 0.05 and 0.95. Thus, in our numerical and simulation study, we use the logistic function for the tolerance curve but the theoretical results hold more generally.

However, in the examples mentioned above, there may be more refined classifications of the responses. For example, a response can further be classified according to the varying degrees of damage or moribundity besides the two definite responses. Aitchison and Silvey (1957), Ashford (1959) examined the problem based on the maximum likelihood

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2. Comparison of Informations in Large Samples

2.1. Polychotomous Quantal Response Model

Assume that k groups consisting of $N_1, N_2, \ldots, N_k$ subjects are tested with stimulus levels $x_1, x_2, \ldots, x_k$ respectively. Out of the N_i subjects being tested at level x_i, the possible ordered outcomes of the test are $O_1, O_2, \ldots, O_s$. In the housefly example, for $s = 3$, O_1 = dead, O_2 = moribund, O_3 = alive. For $s > 3$, the O_i's represent decreasing degrees of moribundity as i increases. For consistency, the first outcome represents dead and the last alive. For simplicity and clarity, we use this housefly example to describe the model.

For level x_i, let $r_{i1}, \ldots, r_{is}$ be the numbers of subjects with outcomes $O_1, \ldots, O_s$ respectively, i.e. $N_i = r_{i1} + r_{i2} + \cdots + r_{is}$. The observed proportions of outcomes are $p_{ij} = r_{ij}/N_i$, $j = 1,2,\ldots,s$, $i = 1,2,\ldots,k$. Assume the outcome O_j has a tolerance distribution function of the form $F(x,\beta,\alpha_j)$ where F satisfies:

i) The first and second partial derivatives of F exist and are not identically zero,

ii) $F(x,\beta,\alpha)$ is a strictly monotone function of α.

Note that β is restricted to be constant for all the tolerance distributions. Therefore, with assumption (ii), the tolerance curves would not cross each other so that the probability of each outcome O_j is well-defined. Gurland, Lee and Dahm (1961) pointed out this fact. For instance, the logit and probit models satisfy (i) and (ii).

Without loss of generality, we assume $\alpha_1 < \alpha_2 < \cdots < \alpha_{s-1}$. Therefore

$$P_{ij} = P\{x_i > \text{tolerance level for } O_j\}$$
$$= F(x_i,\beta,\alpha_j) \qquad j = 1,2,\ldots,s-1 .$$

Hence
$$P\{\text{outcome is } O_1\} = P_{i1}$$
$$P\{\text{outcome is } O_j\} = P_{ij} - P_{i,j-1} \qquad j = 2,\ldots,s-1$$
$$P\{\text{outcome is } O_s\} = 1 - P_{i,s-1} .$$

The parameters in these models are $\beta,\alpha_1,\alpha_2,\ldots,\alpha_{s-1}$. Our main interest is to estimate the percentiles of the tolerance function.

Define the ED_p or LD_p to be the level x_p such that on the average $100p$ percent of the test subjects will die at this dose level. Then, we have

$$p = F(x_p,\beta,\alpha_1) .$$

Therefore, the estimation of ED_p depends only on the parameters β,α_1. The log-likelihood function of this model takes the form

$$\log L_s = \sum_{i=1}^{k} \{r_{i1}\log P_{i1} + r_{i2}\log(P_{i2} - P_{i1}) + \cdots +$$

$$(N_i - r_{i1} - \cdots - r_{i,s-1})\log(1 - P_{i,s-1})\} .$$

Denote $\underset{\sim}{\theta} = (\beta,\alpha_1,\alpha_2,\ldots,\alpha_{s-1})^T$. The Fisher information matrix is $J_s = (J_{ij}(s))$, $1 \le i,j \le s$ where

$$J_{ij}(s) = E\left(\frac{\partial \log L_s}{\partial \theta_i}\right)\left(\frac{\partial \log L_s}{\partial \theta_j}\right) = -E\left(\frac{\partial^2 \log L_s}{\partial \theta_i \partial \theta_j}\right) .$$

Under some regularity conditions on $F(x,\beta,\alpha)$, the matrix J_s is well-defined and is positive definite. Furthermore, the asymptotic distribuiton of the MLE of $\underset{\sim}{\theta}$ is $N(\underset{\sim}{\theta},J_s^{-1})$, i.e. the asymptotic covariance matrix is the inverse of the Fisher information matrix. Therefore, the Fisher information matrix is a measure of the size of the asymptotic confidence ellipsoid.

One can partition J_s into $\begin{bmatrix} J_{11}^{(m)} & J_{12}^{(m)} \\ J_{21}^{(m)} & J_{22}^{(m)} \end{bmatrix}$ for any $m = 1,2,\ldots,s$,

where $J_{11}^{(m)}$ is an $m \times m$ matrix, $J_{22}^{(m)}$ an $(s - m) \times (s - m)$ matrix. In particular,

$$J_{11}^{(2)} = E\left(\frac{\partial \log L_s}{\partial \beta}, \frac{\partial \log L_s}{\partial \alpha_1}\right)^T \left(\frac{\partial \log L_s}{\partial \beta}, \frac{\partial \log L_s}{\partial \alpha_1}\right) , \tag{1}$$

$$J_{22}^{(2)} = E\left[\frac{-\partial^2 \log L_s}{\partial \alpha_i \partial \alpha_j}\right]_{2 \le i,j \le s-1} , \tag{2}$$

$$J_{12}^{(2)} = J_{21}^{(2)T} = E\begin{bmatrix} \frac{-\partial^2 \log L_s}{\partial\beta\partial\alpha_2} & \frac{-\partial^2 \log L_s}{\partial\beta\partial\alpha_3} & \cdots & \frac{-\partial^2 \log L_s}{\partial\beta\partial\alpha_{s-1}} \\ \frac{-\partial^2 \log L_s}{\partial\alpha_1\partial\alpha_2} & \frac{-\partial^2 \log L_s}{\partial\alpha_1\partial\alpha_3} & \cdots & \frac{-\partial^2 \log L_s}{\partial\alpha_1\partial\alpha_{s-1}} \end{bmatrix} . \tag{3}$$

Then the Fisher information matrix corresponding to (β,α_1) is $J_{11}^{(2)} - J_{12}^{(2)}J_{22}^{(2)^{-1}}J_{21}^{(2)}$.

2.2. Dichotomous Quantal Response Model

If only two outcomes are recorded, either dead or alive, then this model is equivalent to combining the outcomes $O_2,O_3,\ldots,O_s$ into one class, namely, the total number of subjects that are not dead.

With the notations of §1, the proportions are $p_{i1} = r_{i1}/N_i$ dead, and $1 - p_{i1} = (N_i - r_{i1})/N_i$ not dead. Similarly,

$$E(p_{i1}) = P_{i1} = P\{x_i > \text{tolerance level for } O_1\}$$
$$= F(x_i,\beta,\alpha_1) .$$

The Fisher information matrix for (β,α_1) under this model is

$$J_2 = E\begin{bmatrix} \frac{-\partial^2 \log L_2}{\partial\beta^2} & \frac{-\partial^2 \log L_2}{\partial\beta\partial\alpha_1} \\ \frac{-\partial^2 \log L_2}{\partial\beta\partial\alpha_1} & \frac{-\partial^2 \log L_2}{\partial\alpha_1^2} \end{bmatrix} . \tag{4}$$

2.3. Comparison of the Fisher Information Matrices

In a $(s + 1)$-response model, the numbers of subjects with outcomes $O_1,O_2,\ldots,O_{s+1}$ at level x_i are $r_{i1},r_{i2},\ldots,r_{i,s+1}$ respectively. Let $R_i = (N_i,r_{i1},\ldots,r_{i,s+1})$, $i = 1,2,\ldots,k$ be the vectors of responses for the polychotomous response model. If the outcomes O_s,O_{s+1} are collapsed into one class, then the number of response subjects in this combined category is the sum of the corresponding r_{ij}'s. Equivalently, O_s and O_{s+1} can be viewed *as missing* data with only the total $O_s + O_{s+1}$ available. Therefore,

the information available in the latter s-response model can be summarized by the vectors $R_i' = (N_i, r_{i1}, \ldots, r_{is} + r_{i,s+1})$, $i = 1,2,\ldots,k$, i.e. each R_i' is a function of R_i.

The above reformulation paves the way for proving the following theorem by hitchhiking the general result of the Missing Information Principle (Orchard and Woodbury, 1972). This theorem states that the Fisher information matrix associated with the first s parameters, namely, $\beta, \alpha_1, \ldots, \alpha_{s-1}$ in the $(s+1)$-response model is always greater than or equal to the Fisher information matrix for parameters $\beta, \alpha_1, \ldots, \alpha_{s-1}$ in the s-response model. The second model is obtained by combining the last two outcomes of the first model into one group.

Theorem 1: $J_{11}^{(s+1)} - J_{12}^{(s+1)} J_{22}^{(s+1)^{-1}} J_{21}^{(s+1)} \geq J_s$ for $s \geq 2$. In fact,

$$J_{11}^{(s+1)} - J_{12}^{(s+1)} J_{22}^{(s+1)^{-1}} J_{21}^{(s+1)} - J_s = \begin{bmatrix} \Delta_{11} & 0 & \cdots & \Delta_{21} \\ 0 & 0 & & 0 \\ \cdot & \cdot & & \cdot \\ \cdot & \cdot & & \cdot \\ \cdot & \cdot & & \cdot \\ \Delta_{21} & 0 & \cdots & \Delta_{22} \end{bmatrix} - \frac{1}{\Delta_{33}} \begin{bmatrix} \Delta_{31} \\ 0 \\ \cdot \\ \cdot \\ \cdot \\ \Delta_{32} \end{bmatrix} [\Delta_{31}, 0, \ldots, \Delta_{32}]$$

where

$$\Delta_{11} = E\left(\frac{-\partial^2 \log L_{s+1}}{\partial \beta^2}\right) - E\left(\frac{-\partial^2 \log L_s}{\partial \beta^2}\right)$$

$$= \sum_{i=1}^{k} N_i \left[\frac{-1}{1 - P_{i,s-1}} \left(\frac{\partial P_{i,s-1}}{\partial \beta}\right)^2 + \frac{1}{P_{is} - P_{i,s-1}} \left(\frac{\partial P_{is}}{\partial \beta} - \frac{\partial P_{i,s-1}}{\partial \beta}\right)^2 + \frac{1}{1 - P_{is}} \left(\frac{\partial P_{is}}{\partial \beta}\right)^2\right],$$

$$\Delta_{21} = E\left(\frac{-\partial^2 \log L_{s+1}}{\partial \beta \partial \alpha_{s-1}}\right) - E\left(\frac{-\partial^2 \log L_s}{\partial \beta \partial \alpha_{s-1}}\right)$$

$$= \sum_{i=1}^{k} N_i \left[\frac{1 - P_{is}}{(1 - P_{i,s-1})(P_{is} - P_{i,s-1})} \frac{\partial P_{i,s-1}}{\partial \beta} - \frac{1}{P_{is} - P_{i,s-1}} \frac{\partial P_{i,s}}{\partial \beta}\right] \frac{\partial P_{i,s-1}}{\partial \alpha_{s-1}},$$

$$\Delta_{22} = E\left(\frac{-\partial^2 \log L_{s+1}}{\partial \alpha_{s-1}^2}\right) - E\left(\frac{-\partial^2 \log L_s}{\partial \alpha_{s-1}^2}\right)$$

$$= \sum_{i=1}^{k} N_i \left[\frac{1 - P_{is}}{(1 - P_{i,s-1})(P_{is} - P_{i,s-1})}\right] \left(\frac{\partial P_{i,s-1}}{\partial \alpha_{s-1}}\right)^2,$$

$$\Delta_{31} = E\left(\frac{-\partial^2 \log L_{s+1}}{\partial\beta\partial\alpha_s}\right)$$

$$= \sum_{i=1}^{k} N_i \left[\frac{1 - P_{i,s-1}}{(P_{is} - P_{i,s-1})(1 - P_{is})} \frac{\partial P_{is}}{\partial\beta} - \frac{1}{P_{is} - P_{i,s-1}} \frac{\partial P_{i,s-1}}{\partial\beta}\right] \frac{\partial P_{is}}{\partial\alpha_s},$$

$$\Delta_{32} = E\left(\frac{-\partial^2 \log L_{s+1}}{\partial\alpha_s \partial\alpha_{s-1}}\right) = \sum_{i=1}^{k} \left[\frac{-N_i}{(P_{is} - P_{i,s-1})} \frac{\partial P_{is}}{\partial\alpha_s} \frac{\partial P_{i,s-1}}{\partial\alpha_{s-1}}\right],$$

$$\Delta_{33} = E\left(\frac{-\partial^2 \log L_{s+1}}{\partial\alpha_s^2}\right) = \sum_{i=1}^{k} N_i \frac{1 - P_{i,s-1}}{(P_{is} - P_{i,s-1})(1 - P_{is})} \left(\frac{\partial P_{is}}{\partial\alpha_s}\right)^2.$$

The proof is given in the Appendix.

By a similar argument, we can show that more information is gained by having a more refined classification of other ordered responses. Therefore, although there are additional parameters to be estimated in the augmented model, there is still an information gain as a result of refining the classification of the response.

In particular, the next result compares the Fisher information matrix associated with the parameters (β,α_1) of any polychotomous response model with that of the corresponding dichotomous response model.

Theorem 2: Consider the Fisher information matrix J_s of an s-response model and partition J_s into $J_s = \begin{bmatrix} J_{11}^{(2)} & J_{12}^{(2)} \\ J_{21}^{(2)} & J_{22}^{(2)} \end{bmatrix}$ where $J_{11}^{(2)}$ is the 2×2 upper-left sub-matrix. Then $J_{11}^{(2)} - J_{12}^{(2)} J_{22}^{(2)^{-1}} J_{21}^{(2)} \geq J_2$ for any $s \geq 3$.

The proof is given in the appendix.

This theorem states that the Fisher information matrix associated with the parameters (β,α_1) in the polychotomous model is always greater than or equal to the Fisher information matrix for the corresponding dichotomous response model. From this result, it is concluded that more information is gained in using the polychotomous response model for

estimating the ED_p, or any smooth function of (β,α_1) over the dichotomous response model in large samples.

2.4. Evaluation of the Fisher Information Matrices

In this section, we perform a small sample comparison of the Fisher information matrices. In particular, we assume the underlying tolerance distribution function is logistic and $s = 3$, i.e. O_1 = dead, O_2 = moribund, O_3 = alive. Therefore P_{i1} = probability of dead $= 1/[1 + \exp(-\beta x_i - \alpha_1)]$, P_{i2} = probability of dead or moribund $= 1/(1 + \exp(-\beta x_i - \alpha_2))$, $\alpha_2 > \alpha_1$.

Three different design patterns are chosen. Scheme I chooses the 10, 40, 60, 90 percentiles of the standard logistic curve $(\beta = 1, \alpha_1 = 0)$ as design points. Scheme II chooses the 5, 40, 60, 95 percentiles while the 5, 45, 55, 95 percentiles are used in Scheme III. Note that these levels are symmetric and the probability of moribund would be affected solely by α_2. Therefore, different values of α_2 will change the relationship between the two tolerance curves. Various numbers of observations are allocated to each percentile. The design configurations vary from the balanced to the unbalanced, either skewed to the left or right.

The criterion for comparing the two measurement procedures is the volumes of the corresponding confidence ellipsoids of the parameter estimates for a specified confidence coefficient. The volume of the confidence ellipsoid depends on the determinant of the corresponding asymptotic covariance matrix. Therefore, such a comparison reduces to the comparison of the generalized variances of the asymptotic multivariate normal distribution involved. Thus, the ratio of the determinants of the corresponding asymptotic covariance matrices, or equivalently, the inverses of the Fisher information matrices based on different models gives a numerical measure of the asymptotic relative efficiency. In Table 1, we computed the ratio of the determinants of the Fisher information matrices corresponding to (β,α_1) under the two models. The formulae are given by (1), (2), (3), (4) in Sections 2.1 and 2.2.

Table 1: Ratio of the Determinants of the Fisher Information Matrices for the 3-Response and 2-Response Model ($\beta = 1$, $\alpha_1 = 0$)

Design Scheme		$\alpha_2 = 0.1$	$\alpha_2 = 0.5$	$\alpha_2 = 1.0$	$\alpha_2 = 1.5$	$\alpha_2 = 2.0$	$\alpha_2 = 3.0$	$\alpha_2 = 4.0$
(15,5,5,15)	I	1.04	1.18	1.29	1.32	1.28	1.15	1.06
	II	1.04	1.22	1.41	1.50	1.48	1.28	1.12
	III	1.05	1.23	1.43	1.53	1.50	1.29	1.12
(10,10,10,10)	I	1.04	1.19	1.36	1.44	1.43	1.27	1.12
	II	1.04	1.24	1.49	1.70	1.79	1.57	1.27
	III	1.05	1.25	1.53	1.77	1.87	1.62	1.29
(15,15,5,5)	I	1.04	1.21	1.39	1.48	1.47	1.29	1.13
	II	1.05	1.29	1.61	1.85	1.93	1.65	1.30
	III	1.06	1.32	1.67	1.94	2.01	1.67	1.31
(5,5,15,15)	I	1.04	1.18	1.33	1.43	1.44	1.29	1.14
	II	1.03	1.18	1.39	1.58	1.69	1.56	1.28
	III	1.03	1.17	1.38	1.58	1.70	1.58	1.29
(5,15,15,5)	I	1.04	1.19	1.37	1.50	1.54	1.39	1.19
	II	1.04	1.23	1.49	1.76	1.96	1.90	1.49
	III	1.05	1.25	1.57	1.92	2.18	2.11	1.60

Note: (15,5,5,15) I means that 15,5,5,15 observations are respectively assigned to the four levels of design scheme I.

The two tolerance curves are related in the following manners:

i) If α_2 is close to α_1, then the two curves are close to each other, i.e. the probability $P_{i2} - P_{i1}$ of being moribund is small and most of the subjects observed are either dead or alive.

ii) Similarly, if α_2 is too large, the curve corresponding to $O_1 + O_2$ is close to 1, i.e. the probability $1 - P_{i2}$ of being alive is small and the subjects observed are mostly dead or moribund.

In either case, one of the classes O_2, O_3 has few subjects. Therefore, it is not worth spending additional labor in refining the response $O_2 + O_3$ into O_2 and O_3. Thus, the gain in using the trichotomous response model in these cases would not be very significant. As we can see from the table, the ratio increases as α_2 increases to 2.0 and then decreases. In fact, when α_2 is sufficiently large, the corresponding ratio of the determinants of the information matrices is close to 1. These facts can be seen by observing that the likelihood equations are the same by letting $\alpha_2 \to \alpha_1$ or $\alpha_2 \to \infty$.

The percentage gains shown in the table are at least 5% with most of them more than 15%, some up to 100%. This gives an asymptotic justification for choosing the 3-response model to estimate the parameters. We have also computed the ratio of the determinants of the Fisher information matrices for other design schemes. They exhibit the same pattern, and are therefore omitted.

In the above comparison we use the determinant of the Fisher information matrix as a convenient summary criterion. A practical question is to what extent does this criterion reflect the performance of estimates of different parameters in the finite sample situations? It can only be answered by Monte Carlo simulation. Such results, reported in the next section, support the general conclusion of this section that the use of the 3-response model gives rise to improvement in efficiency of estimates.

3. A Simulation Study

The experimenters are often interested in the estimation of the percentiles of the tolerance distribution associated with death. In the housefly example, we may be interested in estimating the dose level x_p such that 100p% of the houseflies are killed. In this section, we will present an extensive simulation study to compare the trichotomous response and dichotomous response models for estimating β, α_1, ED10, ED30, ED50, ED70, ED90 under different design schemes. The Fisher information in §2 is an asymptotic measure while Table 2 presents simulation results for sample size 40. The latter results provide a more realistic indication of the performance of these estimates in small samples under the two models.

Again, we assume the underlying tolerance distribution $F(x,\beta,\alpha)$ is logistic. Therefore, the $100p^{th}$ percentile of the distribution function corresponding to death is given by

$$x_p = -[\alpha_1 + \log(1 - p)/p]/\beta \ . \tag{5}$$

The MLE of x_p is then obtained by substituting $\hat{\alpha}_1,\hat{\beta}$, the MLE of α_1,β into (5). The MLE $\hat{\alpha}_1,\hat{\beta}$ of α,β are found by using the iterative Newton-Raphson method.

The design schemes are the same as those considered in Table 1. For each of the design scheme considered, we generated 1000 random samples. The method of maximum likelihood is used in estimating the parameters. The results are summarized in Table 2. The MSE is computed. The true values of the parameters are $\alpha_1 = 0.0$, $\beta = 1.0$. By (5), we have ED10 = -2.1972, ED30 = -0.8473, ED50 = 0.0, ED70 = 0.8473 and ED90 = 2.1972. Therefore, if $\hat{\alpha}_1,\hat{\beta}$ are the MLE of α_1,β, then the MLE of ED_p is given by $\widehat{ED}_p = [-\hat{\alpha}_1 + ED_p]/\hat{\beta}$. Note that the MLE $\hat{\alpha}_1$, $\widehat{ED50}$ of α_1 and ED50 may not take the same value although $\alpha_1 = ED50 = 0$.

Table 2: Comparison of MSE of the MLE of Parameters α_1, β and the Percentiles in Standard Logistic Model with 1000 Simulation Samples ($\alpha_1 = 0$, $\beta = 1$)

Design Scheme		Parameter	3-Response Model							2-Response Model
			0.1	0.5	1.0	1.5	2.0	3.0	4.0	
(15,5,5,15)	I		0.26	0.26	0.24	0.23	0.25	0.26	0.27	0.33
	II	α_1	0.33	0.35	0.32	0.31	0.31	0.34	0.34	0.54
	III		0.33	0.33	0.31	0.31	0.31	0.33	0.34	0.33
	I		0.15	0.15	0.11	0.10	0.11	0.15	0.18	0.64
	II	β	0.28	0.24	0.19	0.14	0.13	0.20	0.25	1.58
	III		0.38	0.36	0.29	0.20	0.19	0.37	0.53	0.83
	I		0.65	0.62	0.52	0.51	0.53	0.64	0.72	0.74
	II	ED10	0.68	0.63	0.53	0.51	0.51	0.61	0.69	0.75
	III		0.73	0.65	0.55	0.52	0.51	0.63	0.72	0.79
	I		0.26	0.25	0.22	0.22	0.23	0.26	0.28	0.28
	II	ED30	0.30	0.29	0.26	0.26	0.26	0.29	0.31	0.31
	III		0.31	0.29	0.26	0.26	0.27	0.30	0.31	0.31
	I		0.20	0.20	0.19	0.18	0.19	0.20	0.20	0.19
	II	ED50	0.24	0.24	0.22	0.23	0.23	0.24	0.24	0.24
	III		0.24	0.24	0.22	0.23	0.24	0.24	0.24	0.24
	I		0.28	0.28	0.27	0.25	0.26	0.26	0.27	0.27
	II	ED70	0.30	0.30	0.29	0.29	0.29	0.30	0.30	0.30
	III		0.31	0.31	0.29	0.30	0.30	0.31	0.31	0.31
	I		0.70	0.69	0.63	0.58	0.59	0.65	0.70	0.72
	II	ED90	0.67	0.66	0.62	0.59	0.59	0.63	0.66	0.71
	III		0.71	0.68	0.63	0.62	0.61	0.67	0.72	0.78

(10,10,10,10) I		0.18	0.18	0.17	0.17	0.17	0.17	0.18	0.19
II	α_1	0.21	0.22	0.20	0.19	0.19	0.20	0.20	0.21
III		0.19	0.21	0.20	0.19	0.19	0.19	0.20	0.20
I		0.21	0.21	0.14	0.11	0.13	0.17	0.23	0.28
II	β	0.38	0.38	0.23	0.14	0.14	0.21	0.31	0.44
III		0.84	0.59	0.47	0.23	0.20	0.39	0.63	1.18
I		0.96	0.81	0.62	0.63	0.64	0.76	0.86	0.99
II	ED10	0.78	0.71	0.59	0.57	0.49	0.62	0.68	0.87
III		0.86	0.75	0.64	0.52	0.55	0.60	0.74	0.99
I		0.28	0.25	0.21	0.22	0.22	0.24	0.26	0.29
II	ED30	0.26	0.24	0.22	0.22	0.20	0.23	0.24	0.27
III		0.25	0.24	0.22	0.20	0.21	0.22	0.24	0.28
I		0.17	0.15	0.15	0.16	0.15	0.16	0.16	0.16
II	ED50	0.17	0.17	0.16	0.16	0.16	0.17	0.17	0.17
III		0.15	0.16	0.16	0.16	0.16	0.16	0.16	0.16
I		0.29	0.26	0.24	0.23	0.23	0.26	0.27	0.28
II	ED70	0.27	0.26	0.24	0.23	0.24	0.24	0.25	0.26
III		0.28	0.26	0.25	0.24	0.25	0.25	0.27	0.28
I		0.99	0.83	0.70	0.66	0.67	0.80	0.88	0.97
II	ED90	0.81	0.76	0.65	0.60	0.59	0.65	0.71	0.84
III		0.94	0.79	0.72	0.63	0.64	0.70	0.81	0.99

(15,15,5,5)	I		0.19	0.19	0.20	0.19	0.20	0.20	0.20	0.39
	II	α_1	0.22	0.22	0.22	0.22	0.22	0.22	0.21	0.76
	III		0.22	0.21	0.21	0.21	0.21	0.21	0.21	0.85
	I		0.23	0.19	0.16	0.13	0.14	0.16	0.27	1.72
	II	β	0.37	0.29	0.20	0.15	0.12	0.15	0.30	1.64
	III		0.83	0.57	0.36	0.22	0.16	0.35	0.70	4.88
	I		0.80	0.61	0.47	0.44	0.47	0.58	0.72	0.92
	II	ED10	0.61	0.53	0.43	0.40	0.41	0.45	0.56	0.72
	III		0.77	0.59	0.46	0.41	0.41	0.49	0.65	0.92
	I		0.18	0.18	0.16	0.17	0.17	0.19	0.19	0.21
	II	ED30	0.20	0.20	0.18	0.19	0.19	0.19	0.20	0.21
	III		0.22	0.21	0.19	0.19	0.19	0.20	0.21	0.24
	I		0.24	0.21	0.20	0.19	0.19	0.18	0.21	0.23
	II	ED50	0.21	0.21	0.20	0.20	0.20	0.20	0.19	0.20
	III		0.20	0.20	0.19	0.20	0.20	0.19	0.19	0.20
	I		0.64	0.46	0.41	0.36	0.36	0.37	0.50	0.63
	II	ED70	0.41	0.37	0.34	0.33	0.33	0.33	0.36	0.40
	III		0.43	0.37	0.33	0.32	0.33	0.33	0.36	0.43
	I		1.98	1.33	1.12	0.94	0.94	1.06	1.51	2.02
	II	ED90	1.14	0.97	0.84	0.78	0.77	0.80	0.98	1.20
	III		1.30	1.01	0.84	0.75	0.78	0.85	1.04	1.42

(5,5,15,15) I	α_1	0.20	0.19	0.19	0.18	0.19	0.20	0.19	0.22
II		0.22	0.23	0.21	0.21	0.20	0.20	0.20	0.21
III		0.20	0.22	0.20	0.20	0.19	0.19	0.20	0.21
I	β	0.22	0.20	0.19	0.14	0.14	0.18	0.23	0.25
II		0.39	0.40	0.34	0.22	0.20	0.24	0.31	0.35
III		0.74	0.72	0.51	0.35	0.37	0.47	0.61	1.14
I	ED10	1.74	2.77	3.60	2.52	3.71	3.93	3.89	4.41
II		1.04	1.12	0.91	0.80	0.75	0.88	0.95	1.15
III		1.12	1.14	0.93	0.79	0.75	0.85	0.98	1.29
I	ED30	0.54	0.89	1.15	0.81	1.19	1.24	1.24	1.38
II		0.35	0.38	0.32	0.30	0.28	0.32	0.33	0.39
III		0.35	0.37	0.32	0.28	0.27	0.29	0.33	0.39
I	ED50	0.21	0.31	0.38	0.29	0.39	0.40	0.40	0.43
II		0.18	0.19	0.17	0.17	0.17	0.18	0.18	0.19
III		0.17	0.18	0.17	0.17	0.16	0.17	0.18	0.18
I	ED70	0.21	0.19	0.21	0.20	0.20	0.21	0.19	0.22
II		0.20	0.20	0.19	0.19	0.20	0.20	0.19	0.21
III		0.22	0.22	0.21	0.21	0.21	0.21	0.22	0.23
I	ED90	0.86	0.94	1.17	0.93	1.16	1.27	1.16	1.40
II		0.63	0.65	0.56	0.53	0.54	0.57	0.59	0.67
III		0.77	0.77	0.65	0.62	0.61	0.63	0.67	0.87

(5,15,15,5)	I		0.14	0.15	0.14	0.14	0.14	0.14	0.14	0.15
	II	α_1	0.15	0.15	0.15	0.15	0.15	0.15	0.15	0.16
	III		0.14	0.14	0.15	0.15	0.14	0.14	0.14	0.15
	I		0.32	0.26	0.25	0.21	0.19	0.19	0.29	0.39
	II	β	0.43	0.34	0.33	0.26	0.24	0.21	0.29	0.47
	III		1.00	0.92	0.82	0.58	0.48	0.38	0.76	1.42
	I		2.79	3.58	2.84	2.47	3.18	2.73	2.60	5.29
	II	ED10	1.23	0.99	0.87	0.80	0.75	0.86	0.99	1.25
	III		1.35	1.19	1.03	0.92	0.81	0.98	1.12	1.38
	I		0.57	0.83	0.67	0.60	0.76	0.63	0.60	1.20
	II	ED30	0.30	0.26	0.24	0.23	0.22	0.24	0.26	0.31
	III		0.30	0.29	0.26	0.24	0.22	0.24	0.26	0.32
	I		0.21	0.20	0.20	0.19	0.20	0.19	0.18	0.25
	II	ED50	0.15	0.15	0.14	0.15	0.15	0.15	0.15	0.15
	III		0.13	0.14	0.14	0.15	0.16	0.17	0.15	0.14
	I		0.65	0.42	0.43	0.37	0.38	0.42	0.42	0.55
	II	ED70	0.33	0.30	0.27	0.27	0.29	0.29	0.31	0.32
	III		0.34	0.31	0.30	0.31	0.34	0.39	0.38	0.32
	I		3.00	2.53	2.24	1.89	2.22	2.18	2.13	3.58
	II	ED90	1.30	1.09	0.96	0.90	0.92	1.00	1.13	1.26
	III		1.45	1.25	1.15	1.09	1.12	1.35	1.44	1.36

Summary of Table 2:

1. For nearly all the design schemes considered, the estimates of the parameters (β, α_1) from the trichotomous response model have smaller MSE than those from the dichotomous response model. The reduction is about 50% in the best case. Therefore, even for small sample sizes, the results of §2 still hold. This gives an empirical support of those results.

2. Similar to the performance of the Fisher information matrix discussed in §2, the MSE of the parameter estimates $\hat{\beta}$ and $\hat{\alpha}_1$ are minimized at $\alpha_2 = 1.5$ or 2. But, the MSE increases when α_2 is too large or small. Therefore, the trichotomous response model is useful only if the two curves corresponding to O_1 and $O_1 + O_2$ are not too close to each other, or if the curve corresponding to $O_1 + O_2$ is not too close to 1. See the explanation after Table 1.

3. The simulation study shows that there is a significant improvement in estimating β by using the trichotomous response model while the gain is not so significant in estimating α_1. This can be explained by observing that the slope parameter β is common to the two curves in the 3-response model and can be estimated efficiently by "borrowing strength" from data in all categories.

4. For the estimation of the extreme percentiles, ED10 or ED90, there is large reduction in MSE by using the 3-response model instead of the 2-response model. On the other hand, the reduction is not so remarkable for the median ED50. A heuristic justification is given as follows.

Since $x_p = [\log \frac{p}{1-p} - \alpha_1]/\beta$,

$$\operatorname{var}(\hat{x}_p) = \left(\frac{\partial x_p}{\partial \alpha_1}, \frac{\partial x_p}{\partial \beta}\right) \begin{pmatrix} \operatorname{var}(\hat{\alpha}_1) & \operatorname{cov}(\hat{\alpha}_1, \hat{\beta}) \\ \operatorname{cov}(\hat{\alpha}_1, \hat{\beta}) & \operatorname{var}(\hat{\beta}) \end{pmatrix} \begin{pmatrix} \frac{\partial x_p}{\partial \alpha_1} \\ \frac{\partial x_p}{\partial \beta} \end{pmatrix}$$

where $$\frac{\partial x_p}{\partial \alpha_1} = \frac{-1}{\beta} \qquad \frac{\partial x_p}{\partial \beta} = \frac{-1}{\beta^2} [\log \frac{p}{1-p} - \alpha_1] .$$

Therefore, when $p = 0.5$, $\alpha_1 = 0$, $\beta = 1$ implies $\frac{\partial x_{0.5}}{\partial \beta} = 0$ and

$$\text{var}(\hat{x}_{0.5}) = \text{var}(\hat{\alpha}_1) .$$

As pointed out in 3) the estimation of α_1 and equivalently of $x_{0.5}$ does not benefit much from the second tolerance curve in the 3-response model.

5. When α_2 is too large or small, i.e $\alpha_2 = 0.1$ or 4, the MSE from the trichotomous response model may produce slightly larger MSE than those from the dichotomous response model. However, the differences in all cases are less than 5%. This may be due to the sampling fluctuation in the Monte Carlo simulation.

6. For the estimation of low (high) percentiles, the designs that are skew to the right (left), i.e. allocating more subjects at the low (high) dose levels, perform better than the others. The MSE associated with the extreme percentiles ED10 and ED90, are higher than those of ED30, ED50, ED70. This illustrates the fact that the estimates of these extreme percentiles are very unstable. In particular, the V-shaped design (i.e. more observations on the extreme) gives the smallest MSE for these extreme percentiles while those associated with the A-shaped design (i.e. fewer observations on the extremes) are the largest. However, the balanced design gives overall good performance in estimating the percentiles.

4. Conclusion

Generally, our main concern is with the estimation of the percentiles. The simulation study shows that in most cases considered, the MSE of $\hat{ED}_p$ from the trichotomous response model is less than that of the dichotomous response model. Although the decrease is negligible in some cases, the majority of them are from 5% to 10%, some up to 20%. Therefore, it is worthwhile to use the trichotomous response model if the classification of outcomes can be defined clearly and implemented easily. Especially, if one is interested in estimating the extreme percentiles and the test subjects are expensive, it would be very costly to use a relatively large sample size in order to have reliable estimates. The use of the trichotomous response model is a viable alternative for providing better estimates of these extreme percentiles. Therefore it should be seriously considered in practice.

Appendix

Proof of Theorem 1:

Define $\underset{\sim}{\theta} = (\beta, \alpha_1, \ldots, \alpha_s)$, $\underset{\sim}{R} = (R_1, R_2, \ldots, R_k)$, $\underset{\sim}{R}' = (R_1', R_2', \ldots, R_k')$ and let $J(\underset{\sim}{\theta}|\underset{\sim}{R})$, $J(\underset{\sim}{\theta}|\underset{\sim}{R}')$ be the Fisher information matrices associated with the vectors $\underset{\sim}{R}, \underset{\sim}{R}'$ respectively, i.e. information from the (s + 1)-response and s-response model.

By the result of the general Missing Information Principle (Orchard and Woodbury, 1972), we have

$$J(\underset{\sim}{\theta}|\underset{\sim}{R}) = J(\underset{\sim}{\theta}|\underset{\sim}{R}') + J(\underset{\sim}{\theta}, \underset{\sim}{R}'|\underset{\sim}{R}) \qquad (A)$$

and $J(\underset{\sim}{\theta}; \underset{\sim}{R}'|\underset{\sim}{R}) \geq 0$, which is the information lost from combining O_s and O_{s+1} into one category. In particular, $J(\underset{\sim}{\theta}|\underset{\sim}{R})$ is the expectation of the symmetric matrix

$$\begin{pmatrix} \frac{-\partial^2 \log L_{s+1}}{\partial \beta^2} & \cdots & \\ \frac{-\partial^2 \log L_{s+1}}{\partial \beta \partial \alpha_1} & \frac{-\partial^2 \log L_{s+1}}{\partial \alpha_1^2} & \\ \vdots & \vdots & \ddots \\ \frac{-\partial^2 \log L_{s+1}}{\partial \beta \partial \alpha_s} & & \frac{-\partial^2 \log L_{s+1}}{\partial \alpha_s^2} \end{pmatrix} = \begin{pmatrix} J_{11}^{(s+1)} & J_{12}^{(s+1)} \\ J_{21}^{(s+1)} & J_{22}^{(s+1)} \end{pmatrix}$$

and $J(\underset{\sim}{\theta}|\underset{\sim}{R}')$ is obtained by replacing the last row and column of the above matrix by zero, i.e.,

$$J(\underset{\sim}{\theta}, \underset{\sim}{R}') = \begin{pmatrix} J_s & \underset{\sim}{0} \\ \underset{\sim}{0} & \underset{\sim}{0} \end{pmatrix}.$$

Since by (A), we have $J(\underset{\sim}{\theta}|\underset{\sim}{R}) \geq J(\underset{\sim}{\theta}|\underset{\sim}{R}')$, which is equivalent to

$$\begin{pmatrix} J_{11}^{(s+1)} - J_s & J_{12}^{(s+1)} \\ J_{21}^{(s+1)} & J_{22}^{(s+1)} \end{pmatrix} \geq 0$$

which in turn implies $(J_{11}^{(s+1)} - J_s) - J_{12}^{(s+1)} J_{22}^{(s+1)^{-1}} J_{21}^{(s+1)} \geq 0$, thus proving Theorem 1.

The formulae for Δ_{ij} are easily obtained from computing $E\left(\frac{-\partial^2 \log L_{s+1}}{\partial\theta_i \partial\theta_j}\right)$ and $E\left(\frac{-\partial^2 \log L_s}{\partial\theta_i \partial\theta_j}\right)$.

Proof of Theorem 2:

Since

$$J(\underset{\sim}{\theta}|\underset{\sim}{R}') = E\begin{pmatrix} \frac{-\partial^2 \log L_2}{\partial\beta^2} & \frac{-\partial^2 \log L_2}{\partial\beta\partial\alpha_1} & 0 & \cdots & 0 \\ \frac{-\partial^2 \log L_2}{\partial\beta\partial\alpha_1} & \frac{-\partial^2 \log L_2}{\partial\alpha_1^2} & 0 & \cdots & 0 \\ 0 & 0 & \cdot & & \cdot \\ \cdot & \cdot & \cdot & & \cdot \\ \cdot & \cdot & \cdot & & \cdot \\ \cdot & \cdot & \cdot & & \cdot \\ 0 & 0 & \cdot & & 0 \end{pmatrix}.$$

The result follows by applying an argument similar to the above.

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A class of polychotomous quantal response models is defined, including the dichotomous response model. As an application of the Missing Information Principle, it is shown that the Fisher information for the common parameters in the more elaborate model is greater. For the logistic curve and several design schemes, the above result is supported in a numerical study. For estimating the common parameters of the dichotomous-response and trichotomous-response models and the percentiles of the common tolerance curve, an extensive simulation study shows that in general the latter model gives more accurate estimates than the former one. The situations in which such gains are substantial are identified.

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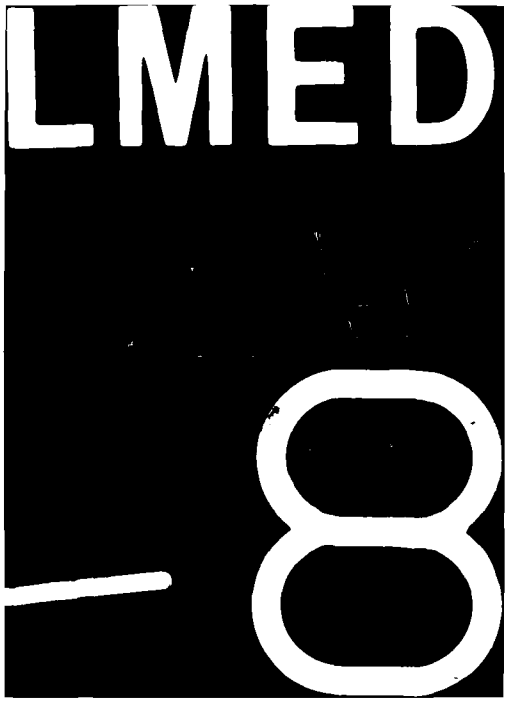
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