RANDOM COMPONENT THRESHOLD MODELS

FOR

ORDERED AND DISCRETE RESPONSE DATA

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I hereby declare that this submission is my own work and that, to the best of my knowledge and belief, it contains no material previously published or written by another person nor material which to substantial extent has been accepted for the award of any other degree or diploma of a university or other institute of higher learning, except where due acknowledgement is made in the text.

(Signed) A. Saci ____________

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ABSTRACT

A general class of regression models for ordinal and ordered categorical response variables was developed by McCullagh (1980). These regression models are known as threshold models. The models supply the most appropriate technique to analyse ordinal or ordered categorical response variables as documented by a growing number of recently published papers on this topic.

However, in practice, observations are often obtained on the same subject or within a cluster. Therefore, the threshold models for such ordered or discrete data involve subject or cluster components considered to be randomly selected from some distribution.

The aim of this thesis is to develop variance component models for ordered and discrete response data based on the generalized linear mixed model (GLMM).

The GLMM approach is further extended for correlated random components. Simple expressions for the ML and REML estimators of the parameters, variance components and their information matrix are obtained. These expressions are then used in application of the GLMM to the random

component models for ordered and discrete data. In addition, the GLMM approach provides the prediction of random components that is of the particular interest in some applications.

Various random component models involving different structures of variance-covariance matrices are introduced for the ordered and discrete response data. These random component threshold models are applied to dairy produce data, arthritis clinical data, methadone program data, skin condition data, skin disorder data, respiratory disorder data, map data and to frequency data for a medical procedure data. It is shown that the GLMM approach demonstrates a great potential to analyse different ordered and discrete response data.

Moreover, it is found that threshold models are useful techniques to analyse problems where the response variable is often zero and count response data, when the number of different non-zero observations is not large, or they can be grouped into classes 0, 1, ...,M.

The performance of the GLMM approach is also studied through simulation technique for the different random component threshold models.

CONTENTS

CHAPTER ONE

INTRODUCTION

Investigation of variability in data, and relating the variability to explanatory or regression variables, has been a longstanding problem. There are two important types of modelling used to study this phenomenon. A traditional, useful and more applied type of modelling uses fixed effect models which have been extensively investigated since 1806. These models relate a response variable to explanatory or regression variables with coefficients the same (fixed) for all responses. Sometimes, however, the model also contains components considered to be randomly selected from some distribution and these are called random components. Interest is in predicting random components, or estimating the variance of the those random components in addition to the fixed regression parameters. This family of models is called mixed models. They also have a long history, but have only received special attention in the last few decades. Applications of these models vary with the types of the response variables.

Estimation and inference techniques have been developed for normally distributed response variables but are less easy to apply to discrete response variables. This thesis is concerned specifically with the fitting of mixed models when the response variable is discrete. Possible values of the response fall into an ordinal scale which may be coded into a discrete variable with values representing the ordinal outcomes.

A particular discrete response variable is the polytomous random variable. McCullagh and Nelder (1989) have summarised different situations which result in such polytomous responses. This family of discrete random variables includes the binary response variable as a special case where the responses have two categories, yes/no or 0/1. One specific polytomous random variable is called the ordinal or ordered categorical response. Some ordinal responses arise from grouping an underlying continuous random variable.

1.1 THRESHOLD MODELS

McCullagh (1980) developed a general class of regression models for ordinal and ordered categorical response variables. These regression models are known as threshold models. The models supply the most appropriate technique to analyse ordinal or ordered categorical response variables as documented by a growing number of recently published papers on this topic.

The threshold model may be based on an unobservable underlying continuous response variable of a specified distribution type, the observed ordinal response variable being formed by taking contiguous intervals of the continuous scale, with cut-points (threshold parameters) unknown. The response variable changes as it moves from one interval to another. Although, for the threshold models it is not necessary to postulate the existence of an unobservable underlying continuous response variable, never-the-less, the threshold models are best interpreted in that way.

In practice, ordinal data are presented in two forms; ordinal where observations are ordinal values; frequency data where observations are the frequency of categories levels. Two examples of the first type are now described briefly. In a dairy produce example, the response variable is the coded time it takes until gas production occurs in the sample, with observation 0,1,2 indicating that gas production occurs >48hr, >24hr and ≤48hr, ≤24hr respectively. In the another example, the status of each patient is recorded according to a five point ordinal response scale (0=terrible, 1=poor, 2=fair, 3=good, 4=excellent) at each of four visits during the time period of observation. This illustrates repeated measures data with each observation being an ordered response.

An example for frequency data is the annual frequency of use of different medical procedures recorded for each county in Washington State (Table 8 in appendix B). Although number of uses made of the medical procedure is recorded for each person in the county, it is more appropriate to simply count the number of people who make zero use, number who use once and so on. Hence the data is recorded as frequency data. It is different in that the total number of people in each county is taken to be known.

In the threshold models of McCullagh (1980), the observations were taken to be independent. However, in the above examples, the observations may be correlated and there may be considerable variation between subjects or counties. Moreover, the prediction of random components for the threshold models has also its own special interest. Consequently, the extension of the threshold models (McCullagh 1980) to include random components is of considerable interest.

1.2 THE RESEARCH

The aim of this thesis is to develop variance component models for ordered and discrete response data. This involves the extension of McCullagh's (1980) work to include random components with associated variance components for ordinal and ordered categorical response variables. Various models involving different structures of variance-covariance matrices are introduced for ordinal and ordered categorical response variables. The extension is given in general and then it is simplified for four common threshold models in applications.

The approach to estimation is the generalized linear mixed model (GLMM) of McGilchrist (1994). The GLMM tries to unify the relationship between best linear unbiased predictor (BLUP) or penalized likelihood (PL) Henderson (1959, 1963, 1973, 1975) with maximum likelihood (ML) and residual maximum likelihood (REML) for discrete and continuous response variables. For normal error models, the interrelationship between BLUP (PL) with ML and REML was developed in Harville (1977) and investigated further in Thompson (1980), Kackar and Harville (1984), Fellner (1986, 1987) and Speed (1991).

McGilchrist (1994) has described the variance component threshold models as an application of the GLMM. The thesis uses the GLMM to develop ML and REML estimation equations of the parameters and variance components for the various threshold models on ordered and discrete response data. The inferences are based on the asymptotic distributions of the estimators.

1.3 OVERVIEW

Chapters 2 and 3 review different approaches to the variance components models for continuous and discrete response variables respectively. The general approach GLMM is further extended by introducing a correlation parameter into the variance-covariance matrix in chapter 4. It is shown how the BLUP or PL estimation equations can be used to obtain approximate maximum likelihood (ML) and residual maximum likelihood (REML) estimates of variance components including the correlation parameter. Those BLUP or PL estimation equations are also used to derive information matrices for the ML and REML estimators.

An extension of McCullagh's (1980) approach is provided in chapter 5. Four threshold models, in which the response variable is related to regression variables with fixed coefficients as well as random components, are fitted to ordinal response variables. Estimates of the parameters, variance components and their approximate variance-covariances are given by three methods, BLUP, ML and REML. The procedures are applied to a problem arising in the testing of dairy produce in New Zealand, and to arthritis clinical data.

In chapter 6, random component threshold models are used to analyse data from a methadone program, shown in Table 3 in appendix B. The data set are provided by the Kirketon Road Centre (KRC), a primary health care centre in Sydney, Australia. For the methadone program, the response variables are related to subject characteristics and treatment program. However, in some cases subjects cohabit so that a further factor is a household effect which is included in the model as a random effect.

For each of threshold models given in chapter 5, chapter 7 defines two longitudinal threshold models. Three different structures of modelling linear predictors are given for those longitudinal threshold models. The estimates of the parameters are used to predict a profile over time by extending Anderson and Philips (1981) and Albert and Anderson (1981) to include random components in the linear predictor. Both ML and REML estimates are derived and applied to skin condition data (Table 4 in appendix B), skin disorder data (Table 5 in appendix B) and respiratory disorder data (Table 6 in appendix B).

Chapter 8 generalises the models in chapter 7 by allowing the random components for the same subject to be correlated. The ML and REML estimation equations of the correlation parameter are developed for constant correlation and AR(1), two correlation structures for random components. Both exchangeable (constant correlation) and AR(1) are used in analysing the respiratory disorder data (Table 6 in appendix B) and map data (Table 7 in appendix B).

In the chapters 5-8, the approaches are based on the ordinal response variables. Chapter 9 presents an approach to the analysis of data recorded in a frequency table. For example, frequency of use different medical procedures are recorded for each adult person in Washington State. Results are given county by county and the county effect is taken to be random. For this data there is a high probability of a zero response which becomes a modelling problem. Estimation procedures are set out in terms of composite link functions. The ML and REML estimation equations are developed for a general structure of variance-covariance matrix of the random components. Three possible forms of the variance-covariance matrix for the county random effect are presented.

Chapter 10 demonstrates a simulation study. For each of the threshold models given in chapter 5, observations are generated under the three different random component structures; one component, two components and AR(1). In the one component structure, the random components are distributed as normal with zero mean and constant variance. Two random components vectors are assumed to be independent in the two components structure. The random components are given a first order autoregressive process in the AR(1) structure. In this chapter, the simulation results are provided for both ML and REML methods for all combinations of the parameters.

Chapter 11 discusses the results for the threshold models. Some results in matrix algebra are provided in appendix A. Appendix B gives the data sets that are used in applications of the different random components threshold models in different chapters. Appendix C gives some the programs that have been written in DYALOG APL version 7.1 to carry out the computations of the thesis.

1.4 COMMENTS

1 In chapter 5-9, some of the ordinal data sets are commenced at zero and some at one. Without loss of generality, the threshold models and estimation results are given for ordinal data sets that coding begins at zero.

2 During preparation of this thesis four papers have been submitted for different journals. Two of them have been accepted for publication and other two are in process. Chapters 5 and 6 are an extension of the accepted papers.

CHAPTER TWO

LITERATURE REVIEW OF COMPONENTS OF VARIANCE IN CONTINUOUS MODELS

2.1 INTRODUCTION

Statisticians have introduced two important types of models to study the dependence of a response variable upon explanatory or regression variables. A traditional, useful and more applied type of modelling is called a fixed effect model, which focuses on the variation that is caused by factors that are in the sample. This model has been extensively investigated since Legendre (1806). The other type of modelling is known as a mixed model. It also has a long history, but has received special interest only in the last few decades. The neglect was partly due to the heavy computational burden in the estimation methods. Developments in computing hardware, software and estimation methods have brought much attention to the mixed model.

The aim of this chapter is to give a brief discussion of the development of variance components, for detailed review of this issue please see Searle, Casella and McCullagh (1992). The following sections attempt to outline some of the basic work on the variance component theory that is fundamental to the development of Generalized Linear Mixed Model (GLMM) approaches. The relevant works are; best linear unbiased predictor (BLUP), maximum likelihood and residual maximum likelihood methods.

2.2 MIXED MODELS

Most of the statistical models that are applied to data sets can be considered as special cases of a general mixed model

2.2.1 $\mathbf{y} = \mathbf{X}\boldsymbol{\beta} + \mathbf{Z}\mathbf{u} + \mathbf{e}$

where $\mathbf{y}$ is a n×1 vector of observations, $\boldsymbol{\beta}$ is a p×1 vector of unknown regression parameters with known n×p design matrix $\mathbf{X}$, incidence matrix $\mathbf{Z}$ corresponding to random component $\mathbf{u}$. Moreover, $\mathbf{u}$ can be partitioned into q subvectors

2.2.2 $\mathbf{u} = [\mathbf{u}_1', \mathbf{u}_2', \ldots, \mathbf{u}_q']'$

where $\mathbf{u}_j$ is a $v_j \times 1$ vector of random components with incidence matrix $\mathbf{Z}_j$. The matrix $\mathbf{Z}$ is partitioned conformably to the partition of $\mathbf{u}$ as $\mathbf{Z} = [\mathbf{Z}_1, \mathbf{Z}_2, \ldots \mathbf{Z}_q]$. Furthermore, it is assumed that

2.2.3 $E(\mathbf{u}_j) = 0$, for j=1,2,...q, and $E(\mathbf{e}) = 0$

$E(\mathbf{y}) = \mathbf{X}\boldsymbol{\beta}$, and $E(\mathbf{y}|\mathbf{u}) = \mathbf{Z}\boldsymbol{\beta} + \mathbf{Z}\mathbf{u} = \mathbf{X}\boldsymbol{\beta} + \sum_{j=1}^{q} \mathbf{Z}_j \mathbf{u}_j$,

$\mathrm{Var}(\mathbf{u}_j) = \sigma_j^2 \mathbf{A}_j(\rho)$, for j=1,2,3...q, $\mathrm{Cov}(\mathbf{y}, \mathbf{u}_j) = \sigma_j^2 \mathbf{Z}_j \mathbf{A}_j$

$\mathrm{Cov}(\mathbf{u}_j, \mathbf{u}_{j'}) = 0$, for $j \neq j' = 1,2,3 \ldots q$, $\mathrm{Cov}(\mathbf{u}_j, \mathbf{e}) = 0$,

$\mathrm{Var}(\mathbf{e}) = \sigma^2 \mathbf{D}$, $\mathrm{Var}(\mathbf{y}) = \mathbf{V} = \sigma^2 \mathbf{D} + \mathbf{Z}(\mathrm{var}(\mathbf{u}))\mathbf{Z}' = \mathbf{V}$,

where $\rho = (\rho_1, \rho_2, \ldots \rho_s)'$, and $\mathrm{var}(\mathbf{u})$ is a block diagonal matrix, with the blocks being matrices $\sigma_j^2 \mathbf{A}_j(\rho)$, for j=1,2,3...,q.

Sometimes, matrix var(**u**) is given in terms of ratio of σ_j^2 to σ^2, i.e., if $\sigma_j^2 / \sigma^2 = \varphi_j$ and var(u)=$\sigma^2 \mathbf{A}$, then matrix **A** is given as

$$2.2.4 \quad \mathbf{A} = \begin{bmatrix} \varphi_1 \mathbf{A}_1(\rho) & & & & \\ & \varphi_2 \mathbf{A}_2(\rho) & & & \\ & & \cdot & & \\ & & & \cdot & \\ & & & & \varphi_q \mathbf{A}_q(\rho) \end{bmatrix}.$$

From 2.2.3 and 2.2.4, we have

2.2.5 $\mathrm{Var}(\mathbf{y}) = \sigma^2(\mathbf{D} + \mathbf{ZAZ}) = \sigma^2 \Sigma$, $\mathbf{D} + \mathbf{ZAZ} = \Sigma$.

The σ^2 and elements in the vectors ρ and φ are called **variance components.** The resulting models are known as **variance component models.**

The appearance of such models has a similar history to the fixed effect model that Legendre (1806) and Gauss (1809) discussed for the first time in books on astronomical problems. Airy (1861) wrote down the model of 2.2.1 as

2.2.5 $y_{ik} = \mu + u_k + e_{ik}$, for i=1,2,3,...a and k=1,2,3...n_i, $n = \sum_{i=1}^{a} n_i$ with

2.2.6 $\mathrm{Var}(u_k) = \sigma_u^2$, $\mathrm{Var}(e_{ik}) = \sigma^2$, $\mathrm{Var}(y_{ik}) = \sigma_u^2 + \sigma^2$.

Chauvenet (1863) applied model 2.2.1 without writing down model equations. It is not well known that astronomers, long before statisticians, also formulated variance components models (Scheffe 1956).

2.3 ANOVA

Sir Ronald Fisher (1918) introduced the terms "Variance" and "Analysis of Variance" (ANOVA). He also (1925) proposed equations that later became the central idea for estimating variance components.

Tippett (1931) proposed ANOVA methods for one-way and two-way classification. Sampling design was introduced by Yates and Zacopanay (1935). Other important works are Daniels (1939), Winsor and Clark (1940) on the ANOVA methods. Ganguli (1941) extended Winsor and Clark's discussion to the multi-way and nested classification. Crump (1946, 1947) used ANOVA methods to estimate variance components in random effect models for balanced data. He derived the distributional properties of estimated variance components by applying the following criteria for balanced data.

If components in the random effect models follow the normal distribution, then any mean square in an ANOVA table, say ms, with f degree of freedom are distributed as

2.3.1 $E(ms)f^{-1}\chi^2_f$.

In addition, for any estimated variance components, say

2.3.2 $\hat{\sigma}^2 = a_1 ms_1 + \ldots + a_k ms_k$,

where ms_j (j=1,2,...k) is a mean square based on f_j degree of freedom, has sampling variance ,

2.3.3 $Var(\hat{\sigma}^2) = 2a_1^2[E(ms_1)]^2 f_1^{-1} + \ldots + 2a_k^2[E(ms_k)]^2 f_k^{-1}$.

Daniels (1939) suggested to replace f_j by f_j+2 in 2.3.3.

Eisenhart (1947) gave a comprehensive description of two types of models, the fixed effect models (type I) and random effect models (type II), see Scheffe (1956), Anderson (1978), Searle (1988) and Searle, McCullagh and Casella (1992). Crump (1951) gave maximum likelihood estimators of variance components by replacing negative values with zero in the ANOVA methods for the type II models of Eisenhart.

The major work for the unbalanced models was done by Henderson (1953). He introduced three types of methods for estimating variance components. In method I, he applied ANOVA methods to estimate variance components. He adjusted for fixed effects in a mixed model, then he employed ANOVA methods for the adjusted model, in the method II. Method III uses reduction in sum of squares. This method is called the fitting constants method. Herbach (1959) used the maximum likelihood principle to estimate variance components. Thompson (1962) proposed the restricted (residual) maximum likelihood method. Searle (1956) introduced variance components in terms of matrix format. Mahamumula (1963) extended Searle's (1956) work to the unbalanced three-way classification.

There are also some other methods of dealing with variance components. For example, the Bayesian method, was introduced by Hill (1965, 1967) for balanced models. The most important work using Bayesian methods is Gnot and Kleffe (1983) for unbalanced models. Rao (1971a, 1971b, 1979) introduced a general method called MINQUE (minimum norm quadratic unbiased estimation) method into the variance components literature.

Maximum likelihood (ML) and residual maximum likelihood (REML) are two frequently used methods with variance components.

We will go through the development of one of the important approaches that is very useful for deriving ML and REML estimates of variance components. The approach is Best Linear Unbiased Predictor (BLUP). It might have been mentioned that the ML and REML approaches to variance components would be taken in sections 2.5-2.7.

2.4 BEST LINEAR UNBIASED PREDICTION (BLUP)

In a series papers Henderson (1948, 1949, 1959, 1963, 1973, 1975) developed the BLUP method. It became a powerful and widely used procedure in animal breeding to evaluate genetic trends of animals for traits measured not only on the continuous scale, but also on a categorical scale. Robinson (1990) argued that the term BLUP was applied by Goldberger (1962) for first time and Henderson started using the acronym BLUP in (1973). However, it was Henderson in (1948, 1949) who discussed the deficiency of classical least square methods. Henderson et al (1959) proposed a solution to this problem by using a discussion given in Henderson (1950). Henderson introduced a predicted value of $\mathbf{u}$ as a linear function of $\mathbf{y}$. He continued discussion on the prediction by including predicting or estimating a linear function of fixed effects and random effects in 1973. He proposed the BLUP method to predict and estimate random effects and fixed effects in cases where the assumption of random sampling is seldom valid.

Suppose that we have a set of observations say $\mathbf{y}$, where $\mathbf{y}$ is defined in the model 2.2. The matrix $\mathbf{Z}$ is known and random effect $\mathbf{u}$ has the same distribution structure as the model 2.2. Then the BLUP method is designed to handle the prediction of $\mathbf{u}_j$ when second moments of the joint distribution of $\mathbf{y}$ and $\mathbf{u}_j$ are known. Henderson (1963) in an attempt to predict $\mathbf{u}_j$, used a prediction of a linear combination of random effect $\mathbf{u}_j$ and fixed effect β. Let us define an unobservable random vector ζ_j, which is jointly distributed with $\mathbf{y}$ as

2.4.1 $\zeta_j = \mathbf{B}_j\beta + \mathbf{u}_j$, for j=1,2,...q.

Both means of ζ_j and $\mathbf{y}$ are given in terms of the unknown parameter vector β.

Theorem 2.4.1:

1. $E(\zeta_j) = \alpha_j$, for j=1,2,...,q where $\alpha_j = \mathbf{B}_j\beta$
2. $Var(\zeta_j) = \sigma^2\varphi_j\mathbf{A}_j$
3. $Cov(\zeta_j, \zeta'_{j'}) = 0$, for $j \neq j'$=1,2,...,q
4. $Cov(\zeta_j, \mathbf{e}') = 0$ for j=1,2,...,q
5. $Cov(\mathbf{y}, \zeta'_j) = \sigma^2 \varphi_j\mathbf{A}_j\mathbf{Z}'_j = \mathbf{C}_j$, for j= 1,2,...,q.

Proof:

1. $E(\zeta_j) = E(\mathbf{B}_j\beta + \mathbf{u}_j) = \mathbf{B}_j\beta + E(\mathbf{u}_j) = \mathbf{B}_j\beta = \alpha_j$, using $E(\mathbf{u}_j) = 0$.
2. Since $\mathbf{B}_j$ is a fixed value, we have $Var(\mathbf{B}_j\beta) = 0$ and $Cov(\mathbf{B}_j\beta,\ \mathbf{u}_j) = 0$. Therefore, $Var(\zeta_j) = Var(\mathbf{B}_j\beta + \mathbf{u}_j) = Var(\mathbf{u}_j) = \sigma^2\varphi_j\mathbf{A}_j$.

3 $\text{Cov}(\zeta_j,\zeta_{j'}) = \text{Cov}(\mathbf{B}_j\beta,(\mathbf{B}_{j'}\beta)') + \text{Cov}(\mathbf{B}_j\beta,\mathbf{u}'_{j'}) + \text{Cov}(\mathbf{u}_j,(\mathbf{B}_{j'}\beta)') +$

$\text{Cov}(\mathbf{u}_j,\mathbf{u}'_{j'}) = 0+0+0+\text{Cov}(\mathbf{u}_j,\mathbf{u}'_{j'}) = \text{Cov}(\mathbf{u}_j,\mathbf{u}'_{j'})$,

since $\mathbf{u}_j$ and $\mathbf{u}'_j$ are independent, therefore

$$\text{Cov}(\zeta_j,\zeta'_{j'}) = \text{Cov}(\mathbf{u}_j,\mathbf{u}'_{j'}) = 0.$$

4 $\text{Cov}(\zeta_j,\mathbf{e}') = \text{Cov}(\mathbf{B}_j\beta,\mathbf{e}') + \text{Cov}(\mathbf{u}_j,\mathbf{e}') = \text{Cov}(\mathbf{u}_j,\mathbf{e}')$

the $\mathbf{u}_j$ and $\mathbf{e}$ are independent, thus

$$\text{Cov}(\zeta_j,\mathbf{e}') = \text{Cov}(\mathbf{u}_j,\mathbf{e}') = 0.$$

5 $\text{Cov}(\mathbf{y},\zeta'_j) = \text{Cov}(\mathbf{X}\beta,(\mathbf{B}_{j'}\beta)') + \text{Cov}(\mathbf{X}\beta,\mathbf{u}'_j) + \text{Cov}(\mathbf{Zu},(\mathbf{B}_j\beta)') +$

$\text{Cov}(\mathbf{Zu},\mathbf{u}'_j) + \text{Cov}(\mathbf{e},(\mathbf{B}_j\beta)') + \text{Cov}(\mathbf{e},\mathbf{u}'_j)$

$= 0+0+0+0+0+\text{Cov}(\mathbf{Zu},\mathbf{u}'_{j'}) = \text{Cov}((\sum_{j=1}^{q}\mathbf{Z}_j\mathbf{u}_j),\mathbf{u}'_j)$

from independence of $\mathbf{u}_j$ and $\mathbf{u}_{j'}$ for $j\neq j'=1,2,\ldots,q$ we have

$$\text{Cov}(\mathbf{y},\zeta'_j) = \text{Cov}(\mathbf{Z}_j\mathbf{u}_j,\mathbf{u}'_j) = \sigma^2\varphi_j\mathbf{A}_j\mathbf{Z}'_j,$$

by this the proof of the theorem 2.4.1 is completed.

Following Henderson (1963), if ζ_{jh} is the h^{th} element of the vector ζ_j, then $\tilde{\zeta}_{jh}$, the predicted value of ζ_{jh}, should be linear function of $\mathbf{y}$, i.e.,

2.4.2 $\tilde{\zeta}_{jh} = \Delta'_{jh}\mathbf{y} + \nabla_{jh}$, where Δ_{jh} and ∇_{jh} are vector and scalar respectively.

The unbiasedness and minimum mean square in the class of linear prediction are two ~~other~~ properties of the BLUP method. So

2.4.3 $E(\tilde{\zeta}_{jh}) = E(\zeta_{jh})$ i.e, $\tilde{\zeta}_{jh}$ is an unbiased predictor for ζ_{jh} and

2.4.4 $E(\tilde{\zeta}_{jh}-\zeta_{jh})^2$ should be mininimized.

From theorem 2.4.1 and 2.4.3, 2.4.4, we have, 2.4.5 $E(\tilde{\zeta}_{jh})=\Delta'_{jh}\mathbf{E}(\mathbf{y})+\nabla_{jh}=\Delta'_{jh}\mathbf{X}\beta+\nabla_{jh}=E(\zeta_{jh})=\mathbf{B}'_{jh}\beta$

where the $\mathbf{B}'_{jh}$ is the h^{th} row of the matrix $\mathbf{B}_j$.

For ∇_{jh} not dependent on the β, the relation 2.4.5 holds if

2.4.6 $\Delta'_{jh}\mathbf{X}\beta=\mathbf{B}'_{jh}\beta$, which implies ∇_{jh}=0.

For $\mathbf{C}_{jh}=\mathrm{Cov}(\mathbf{y},\zeta_{jh})$, the problem of predicting ζ_{jh} reduces to a minimization of a function say $F(\Delta_{jh})$ with respect to the Δ_{jh} with a constraint $G(\Delta_{jh})=0$ given in 2.4.6. Therefore, the problem is

2.4.7 Minimise $F(\Delta_{jh})=[\Delta'_{jh}\Sigma\Delta_{jh}+\mathrm{var}(\zeta_{jh})-2\Delta'_{jh}\mathbf{C}_{jh}]$

subject to: $\Delta'_{jh}\mathbf{X}=\mathbf{B}'_{jh}$

The problem 2.4.7 can be solved by introducing a vector 2λ of Lagrange multipliers. So we find the derivatives of

2.4.8 $F_0(\Delta_{jh},\lambda)=[\Delta'_{jh}\Sigma\Delta_{jh}+\mathrm{var}(\zeta_{jh})-2\Delta'_{jh}\mathbf{C}_{jh}+2(\Delta'_{jh}\mathbf{x}-\mathbf{B}'_{jh})\lambda]$.

Differentiating 2.4.8 with respect to Δ_{jh} and λ yields

2.4.9 $\Sigma\Delta_{jh}-\mathbf{C}_{jh}+\mathbf{X}\lambda=0$

2.4.10 $\mathbf{X}'\Delta_{jh}=\mathbf{B}_{jh}$ or in the matrix format these two equations is given by

2.4.11 $$\begin{bmatrix}\Sigma & \mathbf{X}\\ \mathbf{X}' & 0\end{bmatrix}\begin{bmatrix}\Delta_{jh}\\ \lambda\end{bmatrix}=\begin{bmatrix}\mathbf{C}_{jh}\\ \mathbf{B}_{jh}\end{bmatrix}.$$

A generalized inverse of the matrix of coefficients 2.4.11 is given by using Searle (1982) (p-261-262) as

2.4.12 $$\begin{bmatrix}\Sigma^{-1} & 0\\ 0 & 0\end{bmatrix}+\begin{bmatrix}-\Sigma^{-1}\mathbf{X}\\ \mathbf{I}\end{bmatrix}(-\mathbf{X}'\Sigma^{-1}\mathbf{X})^{-}\begin{bmatrix}-\mathbf{X}'\Sigma^{-1} & \mathbf{I}\end{bmatrix}.$$

Therefore, using 2.4.9 , the Δ_{jh} is given by,

2.4.13 $$\Delta_{jh}=\Sigma^{-1}\mathbf{C}_{jh}+\Sigma^{-1}\mathbf{X}(\mathbf{X}'\Sigma^{-1}\mathbf{X})^{-}(\mathbf{B}_{jh}-\mathbf{X}'\Sigma^{-1}\mathbf{C}_{jh}).$$

Replacing 2.4.13 into the equation 2.4.2 yields,

2.4.14 $$\tilde{\zeta}_{jh}=[\Sigma^{-1}\mathbf{C}_{jh}+\Sigma^{-1}\mathbf{X}(\mathbf{X}'\Sigma^{-1}\mathbf{X})^{-}(\mathbf{B}_{jh}-\mathbf{X}'\Sigma^{-1}\mathbf{C}_{jh})]'\mathrm{y}$$
$$=\mathbf{B}'_{jh}(\mathbf{X}'\Sigma^{-1}\mathbf{X})^{-}\mathbf{X}'\Sigma^{-1}\mathbf{y}+\mathbf{C}'_{jh}\Sigma^{-1}[\mathbf{y}-\mathbf{X}(\mathbf{X}'\Sigma^{-1}\mathbf{X})^{-}\mathbf{X}'\Sigma^{-1}\mathbf{y}].$$

We may replace $\mathbf{X}\hat{\beta}=\mathbf{X}(\mathbf{X}'\Sigma^{-1}\mathbf{X})^{-}\mathbf{X}'\Sigma^{-1}\mathbf{y}$ in the equation 2.4.14 and obtain,

2.4.15 $$\tilde{\zeta}_{jh}=\mathbf{B}'_{jh}\hat{\beta}+\mathbf{C}'_{jh}\Sigma^{-1}(\mathbf{y}-\mathbf{X}\hat{\beta})=\hat{\alpha}_{jh}.$$

where $\hat{\beta}$ is the Aitken's generalized least square (GLS) estimator of the β. Then the BLUP of $\mathbf{u}_{jh}$ is obtained by taking $\mathbf{B}_{jh}$ equal to zero in 2.4.15

2.4.16 $$\tilde{\mathbf{u}}_{jh}=\mathbf{C}'_{jh}\Sigma^{-1}(\mathbf{y}-\mathbf{X}\hat{\beta}).$$

Equation 2.4.16 gives

2.4.17 $$\tilde{\mathbf{u}}_{j}=\mathbf{C}_{j}\Sigma^{-1}(\mathbf{y}-\mathbf{x}\hat{\beta}),\text{ giving }\tilde{\mathbf{u}}=\mathbf{C}\,\Sigma^{-1}(\mathbf{y}-\mathbf{X}\hat{\beta}),$$

2.4.18 $$\tilde{\zeta}_{j}=\mathbf{B}_{j}\hat{\beta}+\mathbf{C}_{j}\Sigma^{-1}(\mathbf{y}-\mathbf{X}\hat{\beta}),\text{ giving, }\tilde{\zeta}=\mathbf{B}\hat{\beta}+\mathbf{C}\Sigma^{-1}(\mathbf{y}-\mathbf{X}\hat{\beta}).$$

Henderson (1963) developed equation 2.4.17, and he also (1973) introduced equation 2.4.18 to predict a linear combination of fixed effect, say β, and random effect $\mathbf{u}$.

2.4.1 SOME CHARACTERISTICS OF THE BLUP

The BLUP method also carries some other properties as follows.

1 Henderson (1963) showed that under certain assumptions (including normality) the BLUP estimators of $\mathbf{u}$ maximise the probability of correct ranking of $\mathbf{u}$. An extension of this is given by Portnoy (1982).

2 The conditional expected value of $\mathbf{u}$ for given $\mathbf{y}$ is the BLUP estimate of $\mathbf{u}$ under the normality assumptions. See Henderson (1963).

3 In the class of linear predictors, BLUP estimators maximise the correlation between the predictor $\tilde{\mathbf{u}}$, and predictant $\mathbf{u}$.

4 Henderson (1973) extended the BLUP to predict $\mathbf{k}'\boldsymbol{\beta}+\mathbf{m}'\mathbf{u}$ by $\mathbf{k}'\tilde{\boldsymbol{\beta}}+\mathbf{m}'\tilde{\mathbf{u}}$, where $\tilde{\boldsymbol{\beta}}$ and $\tilde{\mathbf{u}}$ are BLUP estimators of $\boldsymbol{\beta}$ and $\mathbf{u}$.

2.4.2 HENDERSON MIXED MODELS EQUATIONS (MME)

It is clear that the BLUP method can hold if the covariance between observable random variable $\mathbf{y}$ with non observable random variable $\mathbf{u}$ is known, but equation 2.4.17 involves the inverse of the variance-covariance matrix of y which is potentially large in many applications.

An alternative way to get BLUP estimators was introduced by Henderson (1950). The approach estimates $\boldsymbol{\beta}$ and predicts $\mathbf{u}$ simultaneously. These are values of $\boldsymbol{\beta}$ and $\mathbf{u}$ that maximise the logarithm of the joint density function of $\mathbf{y}$ and $\mathbf{u}$, denoted by l. The function l can be written as

2.4.2.1 $\quad l = l_1 + l_2 \quad$ where

2.4.2.2 $l_1 = -(1/2)[\text{const.} + n\ln\sigma^2 + |\mathbf{D}| + \sigma^{-2}(\mathbf{y} - \mathbf{X}\beta - \mathbf{Z}\mathbf{u})'\mathbf{D}^{-1}(\mathbf{y} - \mathbf{X}\beta - \mathbf{Z}\mathbf{u})]$

2.4.2.3 $l_2 = -(1/2)[\text{const.} + v\ln\sigma^{-2} + \ln|\mathbf{A}| + \sigma^{-2}\mathbf{u}\mathbf{A}^{-1}\mathbf{u}]$,

where $v = \sum_{j=1}^{q} v_j$ and v_j is the dimension of random vector $\mathbf{u}_j$ for j=1,2,...q. Equating to zero the derivatives of 2.4.2.1 with respect to the β and $\mathbf{u}$ yields equations

2.4.2.4 $$\begin{bmatrix} \mathbf{X}'\mathbf{D}^{-1}\mathbf{X} & \mathbf{X}'\mathbf{D}^{-1}\mathbf{Z} \\ \mathbf{Z}'\mathbf{D}^{-1}\mathbf{X} & \mathbf{Z}'\mathbf{D}^{-1}\mathbf{Z} + \mathbf{A}^{-1} \end{bmatrix} \begin{bmatrix} \tilde{\beta} \\ \tilde{\mathbf{u}} \end{bmatrix} = \begin{bmatrix} \mathbf{X}'\mathbf{D}^{-1}\mathbf{y} \\ \mathbf{Z}'\mathbf{D}^{-1}\mathbf{y} \end{bmatrix}.$$

These are called the Mixed Models Equations (MME). Let $\mathbf{V}$ be the matrix coefficient in 2.4.2.4 and non-singular. Then using lemma 1 in appendix A, it can be easily proved that

2.4.2.5 $$\mathbf{V}^{-1} = \begin{bmatrix} \mathbf{V}_{11} & \mathbf{V}_{12} \\ \mathbf{V}'_{12} & \mathbf{V}_{22} \end{bmatrix}^{-1} = \mathbf{B} = \begin{bmatrix} 0 & 0 \\ 0 & \mathbf{V}_{22}^{-1} \end{bmatrix} + \begin{bmatrix} \mathbf{I} \\ -\mathbf{V}_{22}^{-1}\mathbf{V}'_{12} \end{bmatrix} \mathbf{G} [\mathbf{I} \quad -\mathbf{V}_{12}\mathbf{V}_{22}^{-1}]$$

where

2.4.2.6 $$\mathbf{G} = [\mathbf{V}_{11} - \mathbf{V}_{12}\mathbf{V}_{22}^{-1}\mathbf{V}'_{12}]^{-1}, \text{ and } \mathbf{B} = \begin{bmatrix} \mathbf{B}_{11} & \mathbf{B}_{12} \\ \mathbf{B}'_{12} & \mathbf{B}_{22} \end{bmatrix} = \begin{bmatrix} \cdot & \cdot \\ \cdot & \mathbf{T} \end{bmatrix}.$$

The submatrices in the matrix $\mathbf{V}$ are

2.4.2.7 $$\mathbf{V}_{11} = \mathbf{X}'\mathbf{D}^{-1}\mathbf{X},\ \mathbf{V}_{12} = \mathbf{X}'\mathbf{D}^{-1}\mathbf{Z}, \text{ and } \mathbf{V}_{22} = \mathbf{Z}'\mathbf{D}^{-1}\mathbf{Z} + \mathbf{A}^{-1}.$$

The corresponding submatrices in the matrix $\mathbf{B}$ are,

2.4.2.8 $$\mathbf{B}_{11} = [\mathbf{X}'\mathbf{D}^{-1}\mathbf{X} - \mathbf{X}'\mathbf{D}^{-1}\mathbf{Z}\mathbf{T}^*\mathbf{Z}'\mathbf{D}^{-1}\mathbf{X}]^{-1} = (\mathbf{X}'\Sigma^{-1}\mathbf{X})^{-1},$$

2.4.2.9 $$\mathbf{B}_{22} = \mathbf{T}^* + \mathbf{T}^*\mathbf{Z}'\mathbf{D}^{-1}\mathbf{X}\mathbf{B}_{11}\mathbf{X}'\mathbf{D}^{-1}\mathbf{Z}\mathbf{T}^*, \text{ and } \mathbf{B}_{12} = -\mathbf{B}_{11}\mathbf{X}'\mathbf{D}^{-1}\mathbf{Z}\mathbf{T}^*.$$

where $\mathbf{T}^* = (\mathbf{A}^{-1} + \mathbf{Z}'\mathbf{D}\mathbf{Z})^{-1}$.

From the above, $\tilde{\beta}$ and $\tilde{\mathbf{u}}$ are

2.4.2.10 $$\tilde{\beta} = [\mathbf{B}_{11}\mathbf{X}' + \mathbf{B}_{12}\mathbf{Z}']\mathbf{D}^{-1}\mathbf{y}$$

$$=\mathbf{B}_{11}\mathbf{X}'[\mathbf{D}^{-1}-\mathbf{D}^{-1}\mathbf{T}^{*}\mathbf{Z}'\mathbf{D}^{-1}]\mathbf{y}$$, by using equations in 2.4.2.9

$$=\mathbf{B}_{11}\mathbf{X}'\Sigma^{-1}\mathbf{y}=(\mathbf{X}'\Sigma^{-1}\mathbf{X})^{-}\mathbf{X}'\Sigma^{-1}\mathbf{y}$$ and

2.4.2.11 $$\tilde{\mathbf{u}}=[\mathbf{B}_{12}'\mathbf{X}'+\mathbf{B}_{22}\mathbf{Z}']\mathbf{D}^{-1}\mathbf{y}$$

$$=\mathbf{B}_{21}\mathbf{X}'([\mathbf{I}-\mathbf{D}^{-1}\mathbf{Z}\mathbf{T}^{*}\mathbf{Z}']+\mathbf{T}^{*}\mathbf{Z}')\mathbf{D}^{-1}\mathbf{y}$$, by using equation in 2.4.2.9

$$=\mathbf{B}_{21}\mathbf{X}'\Sigma^{-1}\mathbf{y}+\mathbf{T}^{*}\mathbf{Z}'\mathbf{D}^{-1}\mathbf{y}=-\mathbf{T}^{*}\mathbf{Z}'\mathbf{D}^{-1}\mathbf{X}(\mathbf{X}'\mathbf{D}^{-1}\mathbf{X})^{-}\mathbf{X}'\Sigma^{-1}\mathbf{y}+\mathbf{T}^{*}\mathbf{Z}'\mathbf{D}^{-1}\mathbf{y}$$

$$=\mathbf{T}^{*}\mathbf{Z}'\mathbf{D}^{-1}[\mathbf{y}-\mathbf{X}\tilde{\beta}]=\mathbf{A}\mathbf{Z}'\Sigma^{-1}[\mathbf{y}-\mathbf{X}\tilde{\beta}].$$

Henderson (1959) proved that $\tilde{\beta}$ in the 2.4.2.10 is identical to the GLS $\hat{\beta}$. He (1963) also proved that predicted value given in 2.4.2.11 is identical to those in 2.4.17.

2.4.3 DISTRIBUTIONAL PROPERTIES OF $\tilde{\mathbf{u}}$ AND $\tilde{\beta}$

The proceeding developments are based on the theorem 2 of appendix A.

Theorem 2.4.3.1 :

1. $\mathrm{Var}(\mathbf{k}'\tilde{\beta})=\sigma^2\mathbf{k}'\mathbf{B}_{11}\mathbf{k}$,
2. $\mathrm{Cov}(\mathbf{k}'\tilde{\beta},\tilde{\mathbf{u}}')=0$,
3. $\mathrm{Cov}(\mathbf{k}'\tilde{\beta},\mathbf{u}')=-\sigma^2\mathbf{k}'\mathbf{B}_{12}$,
4. $\mathrm{Cov}(\mathbf{k}'\tilde{\beta},\tilde{\mathbf{u}}'-\mathbf{u}')=\sigma^2\mathbf{k}'\mathbf{B}_{12}$,
5. $\mathrm{Var}(\tilde{\mathbf{u}})=\sigma^2(\mathbf{A}-\mathbf{B}_{22})$,
6. $\mathrm{Cov}(\tilde{\mathbf{u}},\mathbf{u}')=\mathrm{Var}(\tilde{\mathbf{u}})$,
7. $\mathrm{Var}(\tilde{\mathbf{u}}-\mathbf{u})=\sigma^2\mathbf{B}_{22}$,
8. $\mathrm{Var}(\mathbf{k}'\tilde{\beta}+\mathbf{m}'\tilde{\mathbf{u}}-\mathbf{k}'\beta+\mathbf{m}'\mathbf{u})=\sigma^2[\mathbf{k}',\ \mathbf{m}']\begin{bmatrix}\mathbf{B}_{11} & \mathbf{B}_{12}\\ \mathbf{B}_{21} & \mathbf{B}_{22}\end{bmatrix}\begin{bmatrix}\mathbf{k}\\ \mathbf{m}\end{bmatrix}$,

9 $$\mathrm{Var}((\tilde{\mathbf{u}}',\mathbf{u}'))' = \sigma^2\begin{bmatrix}\mathbf{A}-\mathbf{B}_{22} & \mathbf{A}-\mathbf{B}_{22}\\ \mathbf{A}-\mathbf{B}_{22} & \mathbf{A}\end{bmatrix}.$$

Proof:

1 $$\mathrm{Var}(\tilde{\beta}) = [\mathbf{B}_{11}\mathbf{X}' + \mathbf{B}_{12}\mathbf{Z}']\mathbf{D}^{-1}\sigma^2[\mathbf{D}+\mathbf{Z}'\mathbf{A}\mathbf{Z}]\mathbf{D}^{-1}[\mathbf{B}_{11}\mathbf{X}' + \mathbf{B}_{12}\mathbf{Z}']'$$

$$= \mathbf{B}_{11}\mathbf{X}'[\mathbf{I}-\mathbf{D}^{-1}\mathbf{Z}\mathbf{T}^{*}\mathbf{Z}']\mathbf{D}^{-1}\sigma^2[\mathbf{D}+\mathbf{Z}'\mathbf{A}\mathbf{Z}]\mathbf{D}^{-1}[\mathbf{I}-\mathbf{Z}\mathbf{T}^{*}\mathbf{Z}'\mathbf{D}^{-1}]\mathbf{X}\mathbf{B}_{11}$$

$$= \mathbf{B}_{11}\mathbf{X}'[\mathbf{D}^{-1}-\mathbf{D}^{-1}\mathbf{Z}\mathbf{T}^{*}\mathbf{Z}'\mathbf{D}^{-1}]\sigma^2[\mathbf{D}+\mathbf{Z}'\mathbf{A}\mathbf{Z}][\mathbf{D}^{-1}-\mathbf{D}^{-1}\mathbf{Z}\mathbf{T}^{*}\mathbf{Z}'\mathbf{D}^{-1}]\mathbf{X}\mathbf{B}_{11}$$

$$= \sigma^2\mathbf{B}_{11}\mathbf{X}'\Sigma^{-1}\Sigma\Sigma^{-1}\mathbf{X}\mathbf{B}_{11} = \sigma^2\,\mathbf{B}_{11}.$$

Thus, $\mathrm{Var}(\mathbf{k}'\tilde{\beta}) = \sigma^2\mathbf{k}'\mathbf{B}_{11}\mathbf{k}$.

2 $$\mathrm{Cov}(\tilde{\beta},\tilde{\mathbf{u}}') =$$

$$= \mathbf{B}_{11}\mathbf{X}'[\mathbf{I}-\mathbf{D}^{-1}\mathbf{Z}\mathbf{T}^{*}\mathbf{Z}']\mathbf{D}^{-1}\sigma^2[\mathbf{D}+\mathbf{Z}'\mathbf{A}\mathbf{Z}]\mathbf{D}^{-1}([\mathbf{I}-\mathbf{Z}\mathbf{T}^{*}\mathbf{Z}'\mathbf{D}^{-1}]\mathbf{X}\mathbf{B}_{12}+\mathbf{Z}\mathbf{T}^{*})$$

$$= \sigma^2\mathbf{B}_{11}\mathbf{X}'([\mathbf{D}^{-1}-\mathbf{D}^{-1}\mathbf{Z}\mathbf{T}^{*}\mathbf{Z}'\mathbf{D}^{-1}]\mathbf{X}\mathbf{B}_{12}+\mathbf{Z}\mathbf{T}^{*})$$

$$= \sigma^2(\mathbf{B}_{11}\mathbf{X}'\Sigma^{-1}\mathbf{X}\mathbf{B}_{12}+\mathbf{B}_{11}\mathbf{X}'\mathbf{D}^{-1}\mathbf{Z}\mathbf{T}^{*}) = \sigma^2(-\mathbf{B}_{11}\mathbf{X}'\mathbf{D}^{-1}\mathbf{Z}\mathbf{T}^{*}+\mathbf{B}_{11}\mathbf{X}'\mathbf{D}^{-1}\mathbf{Z}\mathbf{T}^{*})$$

$$=0.$$

Therefore, $\mathrm{Cov}(\mathbf{k}'\tilde{\beta},\tilde{\mathbf{u}}'\mathbf{m}) = 0.$

3 $$\mathrm{Cov}(\tilde{\beta},\mathbf{u}') = \mathbf{B}_{11}\mathbf{X}'[\mathbf{D}^{-1}-\mathbf{D}^{-1}\mathbf{Z}\mathbf{T}^{*}\mathbf{Z}'\mathbf{D}^{-1}]\mathrm{cov}(\mathbf{y},\mathbf{u}')$$

$$= \mathbf{B}_{11}\mathbf{X}'[\mathbf{D}^{-1}-\mathbf{D}^{-1}\mathbf{Z}\mathbf{T}^{*}\mathbf{Z}'\mathbf{D}^{-1}]\mathrm{cov}(\mathbf{X}\beta+\mathbf{Z}\mathbf{u}+\mathbf{e},\mathbf{u}')$$

$$= \sigma^2\mathbf{B}_{11}\mathbf{X}'[\mathbf{D}^{-1}-\mathbf{D}^{-1}\mathbf{Z}\mathbf{T}^{*}\mathbf{Z}'\mathbf{D}^{-1}]\mathbf{Z}\mathbf{A}$$

$= \sigma^2\,\mathbf{B}_{11}\mathbf{X}'\Sigma^{-1}\mathbf{Z}\mathbf{A}$, and using $\mathbf{X}'\Sigma^{-1}\mathbf{Z} = \mathbf{X}'\mathbf{D}^{-1}\mathbf{Z}\mathbf{T}^{*}\mathbf{A}^{-1}$, gives

$= \sigma^2\,\mathbf{B}_{11}\mathbf{X}'\mathbf{D}^{-1}\mathbf{Z}\mathbf{T}^{*}\mathbf{A}^{-1}\mathbf{A} =- \sigma^2\,\mathbf{B}_{12}$, so $\mathrm{Cov}(\mathbf{k}'\tilde{\beta},\mathbf{u}') = -\sigma^2\mathbf{k}'\mathbf{B}_{12}$.

4 $$\mathrm{Cov}(\tilde{\beta},\tilde{\mathbf{u}}'-\mathbf{u}') = \mathbf{Q}\,\mathrm{cov}(\tilde{\beta},\tilde{\mathbf{u}}')\mathbf{P}' - \mathbf{B}_{11}\mathbf{X}'[\mathbf{D}^{-1}-\mathbf{D}^{-1}\mathbf{Z}\mathbf{T}^{*}\mathbf{Z}'\mathbf{D}^{-1}]\mathrm{cov}(\mathbf{y},\mathbf{u}')$$

$=0-- \sigma^2\,\mathbf{B}_{12} = \sigma^2\,\mathbf{B}_{12}$, giving $\mathrm{Cov}(\mathbf{k}'\tilde{\beta},\tilde{\mathbf{u}}'-\mathbf{u}') = \sigma^2\mathbf{k}'\mathbf{B}_{12}$

where $\mathbf{Q}$ and $\mathbf{P}$ are known matrices.

5 $$\mathrm{Var}(\tilde{\mathbf{u}}) = [\mathbf{B}_{12}'\mathbf{X}' + \mathbf{B}_{22}\mathbf{Z}']\mathbf{D}^{-1}\sigma^2[\mathbf{D}+\mathbf{Z}'\mathbf{A}\mathbf{Z}]\mathbf{D}^{-1}[\mathbf{B}_{12}'\mathbf{X}' + \mathbf{B}_{22}\mathbf{Z}']'$$

$$=\sigma^2(B'_{12}X'[D^{-1}-D^{-1}ZT^*Z'D^{-1}]+T^*Z'D^{-1})\Sigma([D^{-1}-D^{-1}ZT^*Z'D^{-1}]XB_{12}+D^{-1}ZT^*)$$

$$=\sigma^2(B'_{12}X'\Sigma^{-1}+T^*Z'D^{-1})\Sigma(\Sigma^{-1}XB_{12}+D^{-1}ZT^*)$$

$$=\sigma^2(B'_{12}X'\Sigma^{-1}XB_{12}+T^*Z'D^{-1}XB_{12}+B'_{12}X'D^{-1}ZT^*+T^*Z'D^{-1}\Sigma D^{-1}ZT^*)$$

$$=\sigma^2(-B'_{12}X'D^{-1}ZT^*+T^*Z'D^{-1}XB_{12}+B'_{12}X'D^{-1}ZT^*+T^*Z'D^{-1}\Sigma D^{-1}ZT^*)$$

$$=\sigma^2(T^*Z'D^{-1}XB_{12}+T^*Z'D^{-1}\Sigma D^{-1}ZT^*)=\sigma^2(T^*-B_{22}+A-T^*)$$

$$=\sigma^2(A-B_{22})$$

Thus, $\mathrm{Var}(\tilde{u})=\sigma^2(A-B_{22})$.

6 $\quad \mathrm{Cov}(\tilde{u},u')=[B'_{12}X'+B_{22}Z']D^{-1}\mathrm{cov}(y,u')$

$$=\sigma^2(B'_{12}X'[D^{-1}-D^{-1}ZT^*Z'D^{-1}]+T^*Z'D^{-1})ZA$$

$$=\sigma^2(B'_{12}X'\Sigma^{-1}ZA+T^*Z'D^{-1}ZA)$$

$$=\sigma^2(B'_{12}X'\Sigma^{-1}ZA+A-T^*)$$

$$=\sigma^2(B'_{12}X'D^{-1}ZT^*+A-T^*)$$

$$=\sigma^2(T^*-B_{22}+A-T^*)=\sigma^2(A-B_{22})=\mathrm{Var}(\tilde{u})$$

therefore, $\mathrm{Cov}(\tilde{u},u')=\mathrm{Var}(\tilde{u})$.

7 $\quad \mathrm{Var}(\tilde{u}-u)=\mathrm{Var}([B'_{12}X'+B_{22}Z']D^{-1}y-u)=$

$$[B'_{12}X'+B_{22}Z'][D+ZAZ'][B'_{12}X'+B_{22}Z']'+\mathrm{Var}(u)-2[B'_{12}X'+B_{22}Z']\mathrm{Cov}(y,u')$$

$$=\sigma^2(A-B_{22}+A-2(A-B_{22}))=\sigma^2B_{22}$$

therefore, $\mathrm{Var}(\tilde{u}-u)=\sigma^2B_{22}$.

8 $\quad \mathrm{Var}(k'\tilde{\beta}+m'\tilde{u}-k'\beta+m'u)$

$$=k'\mathrm{Var}(\tilde{\beta})k+m'\mathrm{Var}(\tilde{u})m+k'\mathrm{Var}(\beta)k+m'\mathrm{Var}(u)m+$$

$$2k'\mathrm{Cov}(\tilde{\beta},\tilde{u}')m-2k'\mathrm{Cov}(\tilde{\beta},\beta')k+2k'\mathrm{Cov}(\tilde{\beta},u')m-$$

$$2m'\mathrm{Cov}(\tilde{u},\beta')k-2m'\mathrm{Cov}(\tilde{u},u')m+2k'\mathrm{Cov}(\tilde{\beta},u')m$$

$$=\sigma^2(k'B_{11}k+2k'B_{12}m+m'B_{22}m)$$

$$=\sigma^2[k',\ m']\begin{bmatrix}B_{11} & B_{12}\\ B_{21} & B_{22}\end{bmatrix}\begin{bmatrix}k\\ m\end{bmatrix}$$ which is the left handside of 8.

Result 9 follows from 5 and 6.

2.4.4 NORMALITY

Application of the BLUP method with all the properties given in the previous section can hold without assuming normality for the joint distribution of the $\mathbf{u}$ and $\mathbf{y}$. Nevertheless, that assumption contains certain properties that are based on properties of the normal distribution given in theorem 2 of appendix A.

Theorem 2.4.4.1:

1 The $\tilde{\beta}$ and $\tilde{\mathbf{u}}$ are identical to the corresponding maximum likelihood estimators derived under normal theory assumptions and given variance-covariance matrix of $\mathbf{y}$ denoted by $\sigma^2 \Sigma$.

2 $E(\mathbf{u}|\tilde{\mathbf{u}}) = \tilde{\mathbf{u}}$

3 $\text{Var}(\mathbf{u}|\tilde{\mathbf{u}}) = \text{Var}(\mathbf{u}) - \text{Var}(\tilde{\mathbf{u}})$.

The proof is given in Searle et al (1992) (page 273).

Thompson (1979) argued that the Henderson (1975) is hard to understand and made some modification to the Henderson approach. A generalization of the Henderson BLUP approach is Harville (1976). Goldberger (1962), in an attempt to predict a single drawing of the regressand given the vector of regressors noted that the prediction disturbance is correlated with the sample disturbance. He used the BLUP method to give a prediction. Bulmer (1980) proposed a two stage BLUP method. Gianola and Goffinet (1982) showed that the two stage method of Bulmer is equivalent to Henderson's BLUP. Robinson (1990) has reviewed BLUP. Searle, Casella and McCullagh (1992) have discussed BLUP methods in more detail.

The developments in these sections is concerned with estimation and prediction assuming that the variance components are known. Perhaps, in practice, we may encounter a problem in which neither first nor second moments are known. Of course we never really know parameter values, but we may have good prior estimates of them.

There are three methods under Henderson's name to estimate variance components. These were the most frequently used methods up to 1970. Subsequently the estimation of components of variance relied more heavily on the maximum likelihood and residual maximum likelihood methods.

Henderson (1975) showed that estimates and predictions are biased by substituting estimated values of variance covariances into selection models. Kackar and Harville (1981) proved that two-stage method (first estimate variance components, then use these to estimate and predict fixed parameters and random components) gives unbiased estimators and predictors provided the distribution of the data vector is symmetric about its expected value and provided the variance component estimators are translation invariant and are even functions of the data vector. They showed that the ML, REML and ANOVA estimators involve those properties. They also (1984) argued that by replacing true values of variance components with estimates, the estimators are BLUP but the mean squared errors increase in size. They proposed a general approximation to the mean squared errors. Harville (1985) extended this approximation generally.

2.5 MAXIMUM LIKELIHOOD (ML)

The difficulty with the established methods discussed in the previous section was partly the impetus for a continued search into other methods. The most frequently applied method to estimate the variance components is maximum likelihood (ML). This is partly because the ML method has a number of well-known features, some of which are mentioned by Harville (1977). The ML method requires that a distribution be attributed to the random component in a mixed model. It is often confined to the normal distribution on continuous data. The general mixed model we consider is the same as that given in the section 2.2 with the following additional properties.

For observation vector $\mathbf{y}$ from a mixed model given in the section 2.2, the log-likelihood function is given by,

2.5.1 $l = -1/2[\text{cont.} + \ln|\mathbf{V}| + (\mathbf{y}-\mathbf{X}\beta)'\mathbf{V}^{-1}(\mathbf{y}-\mathbf{X}\beta)]$.

Maximum likelihood estimates for the β, σ^2, ρ, and σ_j^2 are those that maximise the log-likelihood l. Differentiation of the l with respect to β, σ^2, σ_j^2 and ρ, gives

2.5.2 $\partial l / \partial\beta = \sigma^{-2}[\mathbf{X}'\mathbf{V}^{-1}(\mathbf{y}-\mathbf{X}\beta)]$,

2.5.3 $\partial l / \partial\sigma^2 = -(1/2)[\text{tr}(\mathbf{V}^{-1}\partial\mathbf{V}/\partial\sigma^2) - (\mathbf{y}-\mathbf{X}\beta)'\mathbf{V}^{-1}\partial\mathbf{V}/\partial\sigma^2\mathbf{V}^{-1}(\mathbf{y}-\mathbf{X}\beta)]$,

2.5.4 $\partial l / \partial\sigma_j^2 = -(1/2)[\text{tr}(\mathbf{V}^{-1}\mathbf{Z}_j\mathbf{A}_j\mathbf{Z}_j') - (\mathbf{y}-\mathbf{X}\beta)'\mathbf{V}^{-1}\mathbf{Z}_j\mathbf{A}_j\mathbf{Z}'\mathbf{V}^{-1}(\mathbf{y}-\mathbf{X}\beta)]$, 2.5.5

$$\partial l / \partial \rho_s = -(1/2)[\mathrm{tr}(\mathbf{V}^{-1}\mathbf{Z}\partial \mathbf{A} / \partial \rho_s \mathbf{Z}') - (\mathbf{y} - \mathbf{Z}\beta)'\mathbf{V}^{-1}\mathbf{Z}\partial \mathbf{A} / \partial \rho_s \mathbf{Z}'\mathbf{V}^{-1}(\mathbf{y} - \mathbf{X}\beta)].$$

Equating 2.5.2, 2.5.3, 2.5.4, and 2.5.5 to zero yields the ML estimators. However, the resulting equations for 2.5.3, 2.5.4, and 2.5.5 are nonlinear and have to be solved numerically for a general variance-covariance matrix $\mathbf{V}$.

Fisher (1925) introduced the ML method. Crump (1949, 1951) and Herbach (1959) give an important discussion of this method. The computational and some other problems were the reasons for this neglect of the ML method until 1967. Hartley and Rao (1967) proposed a solution to some of those problems and brought greater attention to this important method.

Hartley and Rao (1967) introduced simultaneous estimation equations for variance components and obtained ML estimates by some numerical techniques. They formulated variance-covariance matrix of $\mathbf{y}$ in terms φ_js the ratios of σ_j^2s to the σ^2. Their likelihood or log of likelihood function is based on the matrix $\mathbf{H}$ given by

2.5.6 $\mathbf{V} = \sigma^2\mathbf{H} = \sigma^2[\mathbf{I} + \mathbf{ZAZ}']$

where the $\mathbf{A}$ is a block diagonal matrix of blocks $\varphi_j\mathbf{I}$ as the jth diagonal block and $\mathbf{I}$ is an identity matrix of the corresponding dimension. Using 2.5.6 in the derivatives 2.5.2, 2.5.3 and 2.5.4 gives

2.5.7 $\mathbf{X}'\mathbf{H}^{-1}\mathbf{y} = \mathbf{X}'\mathbf{H}^{-1}\mathbf{X}\hat{\beta}$,

2.5.8 $\sigma^2 n = (\mathbf{y} - \mathbf{X}\beta)'\mathbf{H}^{-1}(\mathbf{y} - \mathbf{X}\beta)$

2.5.9 $\mathrm{tr}(\mathbf{H}^{-1}\mathbf{Z}_j\mathbf{Z}_j') = \sigma^{-2}(\mathbf{y} - \mathbf{X}\beta)'\mathbf{H}^{-1}\mathbf{Z}_j\mathbf{Z}_j'\mathbf{H}^{-1}(\mathbf{y} - \mathbf{X}\beta)$.

The derivative with respect to ρ is zero since 2.5.6 does not depend on the parameter ρ. The ML estimators of β and σ^2 can be easily derived from 2.5.7 and 2.5.8. The ML estimation equation of φ_j is given by

2.5.10 $\quad f(\varphi_j)=0.$

It can be solved by

2.5.11 $\quad \varphi_j = \varphi_{j0} - f(\varphi_{j0})f^{-1}(\varphi_{j0})$, for j=1,2,3,...q.

Hartley and Rao (1967) also introduced an alternative estimation equation by applying the joint likelihood of **y** and $\mathbf{u}_j$ for some j and then obtaining likelihood L as the marginal of **y** by integrating over $\mathbf{u}_j$.

The implementation of the Hartley and Rao (1967) approach involves taking the inverse of the H matrix that has a dimension as large as the number of observations. Hemmerle and Hartley (1973) introduced a **W** transformation to reduce the computational problem in yielding ML estimates for mixed ANOVA models. They obtained estimates of β and σ^2 for given φ_j, and then used those to perform a numerical solution for φ_j. Jennrich and Sampson (1976) applied Newton-Raphson and score numerical methods to obtain simultaneous estimates of fixed effects and variance components in the mixed ANOVA models. An efficient Cholesky type algorithm to perform transformation **W** was developed in Hemmerle and Lorens (1976).

2.5.1 ASYMPTOTIC VARIANCE-COVARIANCE

One of the advantages that the ML method carries is the ability to obtain large-sample asymptotic variance-covariance of the ML estimators. The asymptotic variance-covariance matrix for the ML estimators is the inverse of the information matrix. The information matrix is given by

$$2.5.1.1 \quad \mathbf{I}_{ML} = -E\begin{bmatrix} l_{\beta\beta'} & l_{\beta\sigma^2} & l_{\beta\varphi'} & l_{\beta\rho'} \\ l'_{\beta\sigma^2} & l_{\sigma^2\sigma^2} & l_{\sigma^2\varphi'} & l_{\sigma\rho'} \\ l'_{\beta\varphi'} & l'_{\sigma^2\varphi'} & l_{\varphi\varphi'} & l_{\varphi\rho'} \\ l'_{\beta\rho'} & l'_{\sigma\rho'} & l'_{\varphi\rho'} & l_{\rho\rho'} \end{bmatrix}$$

where the elements are second order derivatives of l with respect to appropriate parameters.

Hartley and Rao (1967) derived the limiting properties of the ML estimators of β and ratio's φ_js as both number of individuals (n) and number of random effects (v_j) become infinitely large (j=1,2,...q) simultaneously in such a way that the number of observations falling into any particular level of any random effect stays below some universal constant. Searle (1970) extended Hartley and Rao (1967) by including more variance component parameters. Miller (1973) argued that the latter restriction greatly limits the applicability of the Hartley and Rao results. He (1977) generalised Hartley and Rao (1967) further.

2.6 RESIDUAL MAXIMUM LIKELIHOOD (REML)

One criticism to the ML method of estimating variance components is that it does not take account of the reduction in degrees of freedom due to estimation of fixed effects in estimating variance components. Residual maximum likelihood (REML) method was established to cover this weakness of the ML method. In some balanced models, REML estimators are identical to those given by the ANOVA with well known properties of unbiasedness and minimum variances. As it is often defined, the REML method derives estimated variance components from the following log-likelihood function, l′,

2.6.1 $l' = -1/2[\text{cont.} + (n-p)\ln\sigma^2 + \ln|\mathbf{K\Sigma K}| + \sigma^{-2}\mathbf{y}'\mathbf{K}(\mathbf{K\Sigma K})^{-}\mathbf{Ky}]$,

where $\mathbf{K} = \mathbf{D}^{-1} - \mathbf{D}^{-1}\mathbf{X}(\mathbf{X}'\mathbf{D}^{-1}\mathbf{X})^{-}\mathbf{X}'\mathbf{D}^{-1}$ is a symmetric matrix and $\mathbf{X}'\mathbf{KX} = 0$ implies $\mathrm{KX} = 0$.

Differentiating 2.6.1 with respect to σ^2, φ_j, ρ_s yields

2.6.2 $\partial l'/\partial\sigma^2 = -1/2[\sigma^{-2}(n-p) - \sigma^{-4}\mathbf{y}'\mathbf{K}(\mathbf{K\Sigma K})^{-}\mathbf{Ky}]$,

2.6.3 $\partial l'/\partial\varphi_j =$

$-1/2[\mathrm{tr}((\mathbf{K\Sigma K})^{-}\mathbf{K}(\partial\Sigma/\partial\varphi_j)\mathbf{K}) - \sigma^{-2}\mathbf{y}'\mathbf{K}(\mathbf{K\Sigma K})^{-}\mathbf{K}(\partial\Sigma/\partial\varphi_j)\mathbf{K}(\mathbf{K\Sigma K})^{-}\mathbf{Ky}]$

2.6.4 $\partial l'/\partial\rho_s =$

$= -1/2[\mathrm{tr}((\mathbf{K\Sigma K})^{-}\mathbf{K}(\partial\Sigma/\partial\rho_s)\mathbf{K}) - \sigma^{-2}\mathbf{y}'\mathbf{K}(\mathbf{K\Sigma K})^{-}\mathbf{K}(\partial\Sigma/\partial\rho_s)\mathbf{K}(\mathbf{K\Sigma K})^{-}\mathbf{Ky}]$

Equating 2.6.2-2.6.4 to zero yields REML estimation equations of σ^2, φ_j, ρ_s which have to be solved by some numerical techniques. The asymptotic variance-covariance of the REML estimators of σ^2, φ_j, ρ_s is inverse of the information matrix $\mathbf{I}_{\text{REML}}$, viz.,

2.6.5 $$\mathbf{I}_{\text{REML}} = -E\begin{bmatrix} l'_{\sigma^2\sigma^2} & l'_{\sigma^2\varphi} & l'_{\sigma^2\rho} \\ . & l'_{\varphi\varphi} & l'_{\varphi\rho} \\ . & . & l'_{\rho\rho} \end{bmatrix}$$

where elements inside the information matrix are second derivatives of l′ with respect to component parameters.

The REML method dated back to Anderson and Bancroft (1952). In an attempt to derive a non-negative value of variance components, Thompson (1962) used the REML method. Patterson and Thompson (1971) described this method in the Hartley and Rao's (1967) way for simple mixed models. A generalization of Patterson and Thompson's (1971) was derived by Corbiel and Searle (1976).

2.7 FROM BLUP TO ML AND REML

Implementation of the ML and REML methods in previous sections involve evaluating first and second order derivatives of the corresponding log-likelihood functions to obtain ML and REML estimators and their approximate variance-covariance matrices. However, except for some special mixed models, computational problems arise in application of the ML and REML methods. Harville (1977) gave some solution to the computational problems of the ML and REML methods by introducing a link between section 2.4 (BLUP) and sections 2.5, 2.6. He used BLUP equations to set up iterative procedures in calculating ML and REML estimators of variance components and their asymptotic variance-covariance matrices for ANOVA mixed model. He stated that the establishment of the numerical methods might be improved by making the log-likelihood function more quadratic. Harville (1977) also argued that the REML method is a method that is marginally sufficient for variance components in the sense given by Sprott (1975). Fellner (1986, 1987) discussed Harville's (1977) method for some special models. The method was reviewed in more detail by Thompson (1981). The derivation of the link between BLUP, ML and REML will be discussed further in chapter 4.

2.8 NONLINEAR MODELS

There are also some problems concerned with a continuous random variable y related to fixed and random effects by a respecified nonlinear function f. Sheiner and Beal (1985) discussed a least square approach to the non linear random effect models. They have taken a linearization of the nonlinear function f(.) about 0. A Bayesian approach was proposed on random models by Racine-Poon (1985). Lindstrom and Bates (1990) have derived ML and REML estimates of variance components by linearizing f(.) about the current estimated values of random effects. Vonesh and Carter (1992) have also linearized about current estimated values of random effects, and used a four stage generalized least square. Gumpertz and Pantula (1992) have employed the linearization and discussed ML and REML methods. An extension of Sheiner and Beal (1985) is given in Solomon and Cox (1992). Wolfinger (1993) has discussed Laplace's approximation technique.

CHAPTER THREE

LITERATURE REVIEW OF COMPONENT VARIANCE IN DISCRETE RESPONSE VARIABLES

3.1 INTRODUCTION

The preceding chapter has addressed various forms of variance component estimation in continuous random variables, topics that have been extensively investigated. Success in developing estimation and inference techniques is partly due to the existence of a well known normal distribution for these families of random variables. Roughly speaking, in the most cases, continuous response data is analysed by relating the means of various normal distributions to underlying factors, and an idea behind the estimating of variance components is to obtain more reliable inferences about means.

Although estimation and inference techniques in discrete response variables are not comparable with continuous cases, the analysis of discrete data has a long history dating back to 1662. In 1662, John Graunt collected the frequencies of death from several causes, as well as frequencies of birth and he concluded that more male than female children were born.

Estimation and inference techniques are not easy to apply to regression problems with discrete response variables. Also the range of analysis associated with discrete data is very wide. For example, in a cross-classification table, one may focus on the estimation and inferences techniques about association between row and columns, whereas others may wish to estimate and make inference about odds ratios or relative risk.

For the many problems, the focus is on the probability of a certain event (P). The estimation and inference of P becomes more difficult when it is modelled in terms of some covariates. Yet more problems arise when models on the P involve not only covariates but also terms corresponding to random components.

In this chapter, we review the estimation and inferences techniques in discrete response variables.

3.2 WEIGHTED LEAST SQUARE (WLS)

While log-linear models were used for estimation and inferences in cross-classifications, several alternative approaches were also applied to this class of response variable. Kullback and Ku (1968) and Ireland et al (1969) investigated the procedure for minimum discrimination information estimation to estimate and make inference about multinomial probabilities. Neyman (1949) derived best asymptotic normal (BAN) estimates of cell probabilities by minimising the usual Pearson chi-square statistic (X_P^2). He introduced a modified chi-square by replacing the expected value in the dominator of the usual chi-square with the observed value. He also described an alternative way to minimise the modified chi-square (X_N^2) by imposing constraint functions on cell probabilities. He used first order approximation for constraint functions and proved that the resultant estimates are BAN. This last approach of the problem of minimising X_N^2 has potential as a theoretical base for some later approaches.

Berkson (1968) applied constraints to minimise logit X^2 to the problem of Grizzle (1961). Yet another important application of constraints on cell probabilities is Grizzle et al (1969). They introduced a general class of weighted least squares (WLS) estimate and inference approach to analyse categorical response variables. The approach has the advantage that one can utilise the same algorithm as that used for the analysis of the linear models with normally distributed errors, and it permits great latitude in choosing models. It also unifies some previous approaches into one framework.

Briefly, let i(i=1,2,3,...I) refer to factors and j(j=1,2,3,...r) indicates the jth category, then n_{ij} denotes frequency of the ith factor and jth category in cross-classification of factors with categories. Assume that the vector $\mathbf{n}_i' = (n_{i1}, n_{i2}, n_{i3}, \ldots, n_{ir})$ follows the multinomial distribution with components of $n_{i.} = \sum_{j=1}^{r} n_{ij}$ and $\pi_i' = (\pi_{i1}, \pi_{i2}, \pi_{i3}, \ldots, \pi_{ir})$. Let $\mathbf{P}_i$ be the observed value for the π_i and $\mathbf{P} = [P_1', P_2', P_3', \ldots, P_I']'$. The estimated variance-covariance matrix of $\mathbf{P}$ is a block diagonal matrix with blocks

3.2.1 $$V(\mathbf{P}_i) = n_{i.}^{-1}[\mathbf{D}_{Pi} - \mathbf{P}_i\mathbf{P}_i']$$

where $\mathbf{D}_{Pi}$ is a diagonal matrix of elements vector $\mathbf{P}_i$. For any function F=$\mathbf{X}\beta$ of the $\mathbf{P}$ that has partial derivatives up to second degree with respect to p, the sample variance-covariance matrix of F, by applying δ method, is

3.2.2 $$\mathbf{S}=\mathbf{H}V(\mathbf{P})\mathbf{H}' \quad \text{where } \mathbf{H} = \frac{\partial \mathbf{F}}{\partial \mathbf{P}}.$$

The WLS method tries to find an estimator for β say $\hat{\beta}$ that minimises the quadratic form

3.2.4 $$(\hat{\mathbf{F}} - \hat{\beta})'\mathbf{S}^{-1}(\hat{\mathbf{F}} - \hat{\beta}).$$

Koch and Reinfurt (1971) extended WLS to split-plot experiments and Koch et al (1972) applied the WLS to incomplete response data. Two approaches to estimation and inference for ordered categorical response by using WLS were given by Williams and Grizzle (1972). Koch et al (1977) generalised the paper by Koch and Reinfurt (1971) to repeated measurement. In studying longitudinal clinical trials with missing responses, Standish et al (1978) gave some discussion on the WLS approach. Stanek III and Diehl (1988) applied the WLS method to develop a growth curve model for binary response. In developing estimation and inference for longitudinal polytomous response, Miller et al (1993) have discussed the connection between WLS and GEE and have suggested the need for further study. Application of the WLS approach to repeated categorical measurements with outcomes subject to non-response is in Lipsitz et al (1994).

3.3 ASSOCIATION MODELS

As soon as the data is arranged in a table, the measure of association is one of the important questions that have been addressed in the statistical literature. Kendall et al (1961) and Edwards (1963) defined various functions for the measure of association. While the association is between two or more variables, it is required to integrate a bivariate distribution in simple cases or multivariate in some applications.

Plackett (1965) and Gumbel (1960, 1961) introduced Plackett and exponential bivariate distributions respectively. These families of distributions have been used occasionally when the approach needs to calculate integrals of bivariate distributions.

Bhapker and Koch (1968) investigated interaction in multidimensional cross-classifications for various possible combination structures. Symmetry and marginal symmetry in a multidimensional table were studied by minimum discrimination estimation procedure in Ireland et al (1969). Ashford and Sowden (1970) presented an extension of the probit model and used correlation in bivariate normal underlying distribution as an association between bivariate discrete responses. A logistic model that allows for the inclusion of an associated occurrence between two responses is in Mantel and Brown (1973).

Goodman (1979) introduced different association models for contingency tables with ordered categories. He modelled association in terms of the odds-ratios in 2×2 subtables built from adjacent rows and adjacent columns. Plackett's class of bivariate distributions was used for analysing the pattern of association in cross-classifications with ordered categories in Wahrendorf (1980). Goodman (1981) generalised the association models in Goodman (1979). He compared the association model approach with the canonical correlation method for estimating and testing in cross-classification with ordered categories. Association models were used to derive an estimate for the correlation parameter in the underlying bivariate normal distribution in Goodman (1981). He showed the association models approach more closely the bivariate normal than Plackett's does.

A test was proposed for dependence in multivariate probit models by Kiefer (1982). Dale (1984) compared local and global association in cross-classification with ordered categories. The relationship between the latent class and canonical models as two approaches for cross-classification with ordered categories, was studied by Gilula (1984).

Anderson and Pemberton (1985) extended Pearson (1904) and Tallis (1962) to multivariate responses and derived estimates of the cut-points from the one-way marginal distribution. They obtained an estimate of the correlation matrix by polychoric correlation coefficients from cross-classification. In 1985 and 1991, Goodman gave two comprehensive lectures for analysing cross-classification with and without ordered categories. Lesaffre and Molenberghs (1991) have described another application of multivariate probit models. Best et al (1994) have compared two approaches for the estimation of the correlation parameter in an underlying bivariate normal distribution. The cut-points (threshold parameters) have been estimated by fitting marginal distributions and then maximisation of the log-likelihood function with respect to the correlation parameter. In the second approach, they have used the polychoric correlation method to obtain an estimate of correlation.

Dale (1986) proposed a family of bivariate distributions for cross-classified with ordered categories responses. Both association and threshold parameters were modelled in terms of covariates. Estimates of parameters were obtained by the maximum likelihood procedure. Dale models have been extended to multivariate data by Molenberghs and Lesaffre (1994). Kenward et al (1994) have also discussed a generalisation of Dale's models. They have applied two approaches to estimation, the GEE and ML.

Carey and Diggle (1993) have proposed alternating logistic regressions to overcome computational problems that proved difficult in the application of GEE approach to estimation of parameters in both mean and association coefficients simultaneously. The approach has been used in modelling binary time series response with serial odds ratios in Fitzmaurice and Lipsitz (1995).

3.4 RESAMPLING AND BOOTSTRAP APPROACHES

Geman and Geman (1984) described a general algorithm for computing the marginal distributions from full conditional distributions of components in joint distributions. This general algorithm is called the Gibbs sampler technique. In 1990, Gelfand and Smith gave a comparison between the Gibbs sampler and two other sampling-based approaches for computing marginal distributions. They have applied Gibbs sampler and the other two sampling-based approaches to linear variance components models.

Zeger and Karim (1991) have introduced a cluster random effect to the GLM and used the Gibbs sampling approach to calculate the marginal distribution. The Gibbs sampling technique have been applied to the analysis of binary and polychomous response variables by Albert and Chib (1993).

Bootstrap: The other inference technique for ordinal or more general discrete response variables is the bootstrap approach. The bootstrap technique was introduced by Efron (1979). It has enjoyed wide application. Efron (1979) also discussed an application of boostrap in regression models. It was followed by Freedman (1981), Weber (1984) and Shao (1988).

Moulton and Zeger (1989) described bootstrap to analysing repeated measures on GML's.

3.5 GENERALISED LINEAR MIXED MODELS (GLMM)

In chapter 2, we reviewed variance component models for continuous response variables. The linear models (LM) have a major part in modelling variance component for continuous random variables. In LM, a vector of n observations, $\mathbf{y}$ is modelled by

3.5.1 $$\mathbf{y} = \boldsymbol{\mu} + \mathbf{e} = \mathbf{X}\boldsymbol{\beta} + \mathbf{e},$$

where $\mathbf{e}$ is a vector of random errors with zero expectation and covariance matrix $\mathbf{R}$. The matrix $\mathbf{X}$ comprises all regression variables and the design matrix corresponding to the fixed effects, $\boldsymbol{\beta}$ is a vector including regression coefficients and fixed effects.

Two popular estimation and inference methods are least squares (LS) and maximum likelihood (ML). The LS is based on certain assumptions, eg equal variances, independence; the ML assumes that $\mathbf{e}$ in 3.5.1 follows a normal distribution.

Certain attempts have been made to extend the domain of application of the methods LS and ML to discrete random variables by relaxing some those assumptions. The Probit model was introduced by Bliss and Fisher (1935) and discussed extensively in Finney (1947, 1952). Berkson (1955) estimated parameters by ML methods. The pioneer of logistic regression was D. R. Cox. He introduced logistic regression with wide applications. Cox (1966) described the link between logistic regression and discriminant analysis. Later in 1970, he discussed the analysis of binary data in general in a book (*The Analysis of Binary Data*). Cox and Snell (1972) investigated models on binary response variables in more detail. Cox (1972) introduced a general method that became basic for developing regression in survival analysis.

In 1972, Nelder and Wedderburn extend the LM and gave a unified method for fitting models to continuous and discrete random variables. The approach was called Generalised Linear Models (GLM). Estimation and inference in the GLM are based on the likelihood approach. GLM assumes that the dependent random variable belongs to the exponential family distribution and the linear predictor is related to the mean of the dependent variable by a known link function g(.). In terms of model equations, the GML can be written as

3.5.2 $$\eta = g(\mu) = \mathbf{X}\beta, \ E(\mathbf{y}) = \mu, \ h(.) = g^{-1}(.)$$

where **y** is an observation vector such that the components of **y** have independent exponentional distributions.

Wedderburn (1974) generalised the GLM to problems where there was insufficient information to build up a likelihood function. He introduced estimation equations that satisfied the properties in common with a log-likelihood function. The proposed estimation approach was called quasi-likelihood. This approach is described in more detail in Chapter 9 of McCullagh and Nelder(1989).

The likelihood function sometimes involves additional parameters that are not of interest and are termed nuisance parameters. One way to estimate such nuisance parameters is to use the partial likelihood method in Cox (1975) which defines a likelihood function based on the important parameters.

Prentice (1976) defined a class of models that he called a generalisation of probit and logit models. The proposed model is:

3.5.3 $$f(\omega) = \exp(\omega \mathbf{m}_1)(1-\exp(\omega))^{-(m_1+m_2)} \Big| (\beta(m_1, m_2))^{-1}$$

where β represents the beta function. The function yields four density functions, normal, logistic, extreme minimal and extreme maximal by varying parameters m_1 and m_2 respectively.

Wedderburn (1976) discussed the existence and uniqueness of the maximum likelihood estimates of the GLM based on the normal, Poisson, binomial and gamma distributions. Modelling of repeated binary data appeared in Korn and Whittemore (1979). Pregibon (1980) proposed an approach to test the adequancy of link functions in the GLM.

McCullagh (1980) developed a general class of regression models for ordinal data by introducing an unobservable continuous random variable of a specified distribution type. Observations in the ordinal categories occur as the unobservable variable takes values in different intervals separated by cut-points. Cut-points were assumed as nuisance parameters by McCullagh (1984). Snapinn and Small (1986) proposed a modified test procedure different from the usual likelihood-ratio test in ordinal regression models. Anderson (1984) responded to McCullagh (1980) and introduced a stereotype ordered regression model. Anderson and Philips (1981) applied McCullagh (1980) and showed how it could be used in discrimination.

The performance of the GLM is based on a one-to-one relationship between observation and link function. The introduction of the composite link function by Thompson and Baker (1981) allows an association of more than one link function with each observation. This greatly extends the scope of the GLM.

A parameterization of log-likelihood was suggested by Burridge (1981) to obtain a concave log-likelihood for regression models in grouped data. Silvapulle (1981) gave necessary and sufficient conditions for the existence of maximum likelihood estimators of the linear regression parameter in binomial response models. Albert and Anderson (1984) also investigated the same topic as Silvapulle (1981). The GLM was extended to nonlinear regression by Jorgensen (1983).

A further generalisation of the GLM needs to incorporate terms corresponding to random components into the linear predictor η. By introducing $\mathbf{u}$ as the vector of random components with zero as mean and $\mathbf{A}$ as variance-covariance matrix, a generalisation of the GLM can be formulated as

3.5.4 $\mu = h(\eta) + \mathbf{e}$,

3..5.5 $\eta = g(\mu) = \mathbf{X}\beta + \mathbf{Z}\mathbf{u}, \; E(\mathbf{y}) = \mu, \; h(.) = g^{-1}(.)$

where $\mathbf{Z}$ is incidence matrix for $\mathbf{u}$.

Let $f(\mathbf{u};\mathbf{A})$ be the density function of $\mathbf{u}$ for given components in matrix $\mathbf{A}$ and $f(\mathbf{y};\beta|\mathbf{u})$ be the probability function of $\mathbf{y}$ condition on fixed $\mathbf{u}$. The marginal likelihood of the observation vector $\mathbf{y}$ has an important role in estimating $\mathbf{u}$ and β. The likelihood is given by

3.5.6 $$L(.) = \int f(\mathbf{y};\beta|\mathbf{u}) f(\mathbf{u};\mathbf{A}) d\mathbf{u}.$$

To obtain 3.5.6, we need to integrate out the random effect $\mathbf{u}$, but except for a few special cases, that cannot be achieved analytically. Different techniques, some of them analytic and some numerical have been given to solve 3.5.6 .

Williams (1982) and Breslow (1984) discussed this issue in the context of extra-binomial and extra-Poisson variation respectively. Harville and Mee (1984) assumed a standard normal distribution for $\mathbf{u}$ and developed a model like 3.5.6 for ordered categorical response. The approach has elements in common with the BLUP of Henderson (1975). They simultaneously estimated threshold parameters θ, fixed effect β and predicted $\mathbf{u}$ by the mixed model equation (MME) of Henderson (1975). They also derived estimation equations for variance components similar to REML by using a Bayes-like approach. Gianola and Foulley (1983) estimated threshold parameters θ, fixed effect β and predicted $\mathbf{u}$ in a similar way to Harville and Mee for known variance components. The Stiratelli et al (1984) approach to the serial binary response is analogous to the mixed model of Laird and Ware (1982). They applied the maximum likelihood method and approximated the posterior variances by asymptotic variances, implemented by means of the EM algorithm. A numerical integration technique along with the application of EM algorithm was applied by Anderson and Aitkin (1985). Zeger et al (1985) discussed a marginal logistic model for binary serial response. They assumed in the working model that each series was a stationary Markov chain of order one. The Markov model was also discussed by Muenz et al (1985).

An alternative to Harville and Mee (1984) was proposed by Gilmour et al (1985) for analysis of binary response. They maximised the likelihood function with respect to fixed effects, took expectation over random components and predicted values for random components obtained from the equations that were solved. From those equations, they derived an estimation equation for variance components. They called Harville and Mee (1984) the 'joint maximisation' methods, and the new approach 'expectation' methods.

Liang and Zeger (1986) prescribed a general technique to estimate and make inferences about longitudinal continuous or discrete response models for data in the GLM framework. In 1986, Zeger and Liang generalised Liang and Zeger (1986) by relaxing dependence of the marginal distribution on the exponential family. The approach was called generalised estimation equations (GEE). An extension of the GEE approach to estimate parameters, additional to the mean parameters in the variance-covariance matrix for correlated binary response was given by Prentice (1988). Subsequently, Zhao and Prentice (1990) defined a class of quadratic exponential models for correlated binary response. Lipsitz et al (1991) modified Prentice (1988) and applied odds ratios to model association between repeated measures for the binary response. Prentice and Zhao (1991) derived a second set of estimating equations to obtain estimates of the components in the correlation matrix for a general multivariate response including continuous and discrete responses. Liang et al (1992) developed the GEE approach for mutltivariate categorical responses and they called the GEE of Liang et al (1986) and Zhao et al (1990) GEE1 and GEE2 respectively. Fitzmaurice and Laird (1993) reformulated Zhao and Prentice (1990) to incorporate higher-order associations for binary response.

Stram et al (1988) developed a method similar to the GEE but did not assume a parametric model for the dependence among repeated measurements. The idea was extended by applying quasi-likelihod in Wei and Stram (1988). Ware et al (1988) investigated two general types of statistical methods (marginal and transitional) for the analysis of repeated observations of categorical variables. Zeger et al (1988) discussed the subject-specific and population-averaged models. They approximated first and second marginal moments and then applied GEE approach to get consistent estimates. A quasi-likelihood approach to regression with time series data was developed in Zeger and Qaqish (1988). Solomon (1989) proposed models for repeated measurements of blood pressure. Jansen has applied the composite link function of Thompson and Baker (1981) to extra variation in ordinal models (1990), nested models (1992) and proportions (1993).

A class of random effect models for binary data has been introduced by treating the random effect (**u** in 3.5.6) as having a log-gamma distribution and using log-log as link function in Conaway (1990). Goldstein (1991) generalised multilevel models of Goldstein (1986, 1989) to the discrete response variables.

McGilchrist and his colleagues in a series of attempts (McGilchrist and Aisbett 1991a,b, McGilchrist and Zhaorong 1990, 1992 and Zhaorong et al 1992) have proposed a method of estimation that resembles best linear unbiased prediction (BLUP). The approach avoids numerical integration, however, the BLUP estimates are asymptotically biased.

A generalisation of the Rasch 1961 model has been developed for repeated ordered categorical data by Agresti and Lang (1993).

In the above approaches, the three components ($\boldsymbol{\beta}$, $\mathbf{u}$, $\mathbf{A}$) have not been of main interest simultaneously in the mixed model 3.5.5 and 3.5.6 or they have been investigated in special applications. For example, the GEE approach does not need to estimate the random effect $\mathbf{u}$.

Recently several attempts have been made to estimate $\boldsymbol{\beta}$, $\mathbf{A}$ and predict the value for $\mathbf{u}$. The generalised linear mixed model (GLMM) covers those above approaches that aim to estimate and make inference about three components $\boldsymbol{\beta}$, $\mathbf{u}$ and $\mathbf{A}$ at same time.

The introduction of mixed model equations (MME) by Henderson (1959) gives a flexible way to set up an iterative procedure for evaluating maximum likelihood (ML) and residual maximum likelihood (REML) estimates of variance components and their information matrices. Harville (1976) extended the MME approach and he (1977) applied the MME to estimate variance components in ANOVA mixed models. It was extended to nonlinear mixed models by Lindstrom and Bates (1990).

This interrelationship between MME and ML and REML has also played an important role in developing some of the approaches for non-Gaussian response variables.

For a mixed model that is defined by 3.5.4, 3.5.5 and 3.5.6, Schall (1991) has linearised the link function for response variables that belong to the exponential family distribution. Wolfinger (1993) has developed an alternative approach to Linstrom and Bates (1990) by applying Laplace's approximation. He has sketched how the approach can be modified to a non-Gaussian response variable. A pseudo-likelihood approach is given by Wolfinger and O'Connell (1993). Breslow and Clayton (1993) have developed two estimation methods, penalised quasi-likelihood (PQL) and marginal quasi-likelihood (MQL) for GMMLS. In the PQL, they have applied Laplace's method for approximate integrals and replaced the deviance by the Pearson residuals. In the MQL, they have followed Goldstein (1991) and Zeger et al (1988). McGilchrist (1994) has presented a general estimation procedure by making a quadratic approximation to the likelihood in the region of the maximum. Solomon and Cox (1992) have approximated the likelihood function by Laplace's method using an expansion about vanishing random effects.

Waclawiw and Liang (1993) have extended the Stein-type estimating equations of Liang and Waclawiw (1990) to the GLMMs. The four stage estimation procedure of Vonesh and Carter (1992) has been generalised by Davidian and Giltinan (1993).

Ten Have and Uttal (1994) have investigated subject-specific and population-averaged continuation ratio logit models for multiple discrete time survival profiles. Estimation equations are obtained by numerical quadrature techniques for mixed multi level models on ordinal data in Hedeker and Gibbons (1994). Crouchley (1995) has discussed mixed models for ordered categorical data, and assumed that the random component follows a Hougaard (1986) family distribution.

CHAPTER FOUR

GENERALIZED LINEAR MIXED MODELS

4.1 INTRODUCTION

Chapter 2 has summarised some of the contributions to the field of variance component models for normal error models. Material reviewed in that chapter suggests that the maximum likelihood (ML) method is one important estimation method used to derive an estimate for the random component. However, ML estimates of variance components are negatively biased. The residual maximum likelihood (REML) was developed to reduce bias of ML estimators for random component (Patterson and Thompson 1971). Harville (1977) introduced some solutions to the computational problems in calculating ML and REML estimators. He used BLUP estimation and prediction equations to derive ML and REML estimators and their information matrices. This approach was also followed in Fellner (1986, 1987) Thompson (1980), Kackar et al (1984) and Speed (1991).

Chapter 3 has discussed the generalized linear model (GLM) of Nelder and Wedderburn (1972) as one of the important techniques in analysing data. In that chapter the GLM models that include random components in addition to regression parameters have been called a generalization of the GLM. This family of models is called the generalised linear mixed model (GLMM). In a particular GLMM the random component is taken to be normally distributed with zero mean. This class of GLMM (from now on just GLMM) uses the penalised likelihood (PL) (or BLUP) estimation equations to obtain ML and REML estimators. Some notable contributors to the GLMM are McGilchrist and Aisbett (1991), Schall (1991), Solomon and Cox (1992), Wolfinger (1993), Wolfinger and O'Connell (1993), Breslow and Clayton (1993), McGilchrist (1994) and Engel and Keen (1994).

Some of the applications of McGilchrist (1994) are McGilchrist and Zhaorong (1990) to multicentre clinical trials, Zhaorong, Matawie and McGilchrist (1992) to discordance data, McGilchrist and Aisbett (1991), McGilchrist (1993) to survival analysis and Zhaorong et al (1992), Saei and McGilchrist (1995, 1996a,b) and Saei, Ward and McGilchrist (1996) to ordinal response data (threshold models).

This chapter gives more detail of the derivations of the GLMM by introducing more variance component parameters into the variance-covariance matrix of random components **A** in McGilchrist (1994). Subsequent sections derive estimators and their approximate variance-covariance matrix for new variance components (ρ) and other parameters in general. The last section describes the GLMM for ordinal response data, in particular, it extends the flexible ordinal regression model of McCullagh (1980).

The estimation approach uses best linear unbiased estimation equations to obtain maximum likelihood (ML) and residual maximum likelihood estimators and their asymptotic variance.

4.2 BEST LINEAR UNBIASED PREDICTION (BLUP)

For an observed vector $\mathbf{y}$ from a normal distribution, the mixed linear model is

4.2.1 $\mathbf{y} = \boldsymbol{\eta} + \mathbf{e}\ ,\quad \boldsymbol{\eta} = \mathbf{X}\boldsymbol{\beta} + \mathbf{Z}\mathbf{u}\ ,$

where $\mathbf{e}$ is a random error vector distributed as $N(0, \sigma^2\mathbf{D})$ and $\mathbf{D}$ is a known matrix. The $\mathbf{X}$ is a $n\times p$ matrix of regression variables with regression parameters $\boldsymbol{\beta}$ and $\mathbf{Z}$ is an incidence matrix corresponding to random component $\mathbf{u}$. The random component $\mathbf{u}$ and incidence matrix $\mathbf{Z}$ may be partitioned conformally

4.2.2 $\mathbf{u} = [\mathbf{u}_1', \mathbf{u}_2', \ldots, \mathbf{u}_q']'\ ,\quad \mathbf{Z} = [\mathbf{Z}_1, \mathbf{Z}_2, \ldots, \mathbf{Z}_q]$

where $\mathbf{u}_j$ are independent random components and distributed as $N(0,\ \sigma_j^2\mathbf{A}_j(\rho))$. **The ρ is a vector of dimension S and it does not depend on j in thesis.**

The logarithm of the joint density function of $\mathbf{y}$ and $\mathbf{u}$ is the sum of two components l_1 and l_2. The l_1 and l_2 are log-likelihood function of $\mathbf{y}$ for fixed value of $\mathbf{u}$ and logarithm of the probability density function of $\mathbf{u}$ respectively. They are given by equations 4.2.3 and 4.2.4.

4.2.3 $l_1 = -(1/2)[n\ln 2\pi\sigma^2 + |\mathbf{D}| + \sigma^{-2}(\mathbf{y} - \mathbf{X}\boldsymbol{\beta} - \mathbf{Z}\mathbf{u})'\mathbf{D}^{-1}(\mathbf{y} - \mathbf{X}\boldsymbol{\beta} - \mathbf{Z}\mathbf{u})]$

4.2.4 $l_2 = -(1/2)\sum_{j=1}^{q}[v_j \ln \pi\sigma_j^2 + \ln|\mathbf{A}_j| + \sigma_j^{-2}\mathbf{u}_j\mathbf{A}_j^{-1}\mathbf{u}_j]$

where v_j is the dimension of $\mathbf{u}_j$. The values of the parameter $\boldsymbol{\beta}$ and random components $\mathbf{u}$ that maximise $l_1 + l_2$ are best linear unbiased estimate of β and best linear unbiased predictor of $\mathbf{u}$ for given values of variance components φ and ρ. Differentiating $l_1 + l_2$ with respect to β and $\mathbf{u}$ and equating to zero yields mixed models equations (Henderson 1959), viz.

$$4.2.5 \qquad \begin{bmatrix} \mathbf{X'D^{-1}X} & \mathbf{X'D^{-1}Z} \\ \mathbf{Z'D^{-1}X} & \mathbf{Z'D^{-1}Z + A^{-1}} \end{bmatrix} \begin{bmatrix} \tilde{\beta} \\ \tilde{\mathbf{u}} \end{bmatrix} = \begin{bmatrix} \mathbf{X'D^{-1}y} \\ \mathbf{Z'D^{-1}y} \end{bmatrix}.$$

For given variance components σ_j^2, σ^2 and ρ, best linear unbiased estimator $\tilde{\beta}$ and BLUP $\tilde{\mathbf{u}}$ are

4.2.6 $\tilde{\beta} = \mathbf{B_{11}X'[D^{-1} - D^{-1}T^{*}Z'D^{-1}]y}$, by using equations 2.4.2.9 in chapter 2

$$= \mathbf{(X'[D^{-1} - D^{-1}T^{*}Z'D^{-1}]X)^{-}X'[D^{-1} - D^{-1}T^{*}Z'D^{-1}]y}$$

$$= \mathbf{(X'\Sigma^{-1}X)^{-}X'\Sigma^{-1}y}$$

and

4.2.7 $\tilde{\mathbf{u}} = \mathbf{[B'_{12}X' + B_{22}Z']D^{-1}y}$

$= \mathbf{B_{21}X'([I - D^{-1}ZT^{*}Z'] + T^{*}Z')D^{-1}y}$, by using equation 2.4.2.9 in chapter 2

$$= \mathbf{B_{21}X'\Sigma^{-1}y + T^{*}Z'D^{-1}y = -T^{*}Z'D^{-1}X(X'D^{-1}X)^{-}X'\Sigma^{-1}y + T^{*}Z'D^{-1}y}$$

$= \mathbf{T^{*}Z'D^{-1}[y - X\tilde{\beta}] = AZ'\Sigma^{-1}[y - X\tilde{\beta}]}$ or

$$= \mathbf{(Z'KZ + A^{-1})^{-}Z'Ky}$$

where $\mathbf{T^{*}} = \mathbf{(A^{-1} + Z'D^{-1}Z)^{-1}}$, matrices $\mathbf{B_{11}}$, $\mathbf{B_{12}}$, $\mathbf{B_{22}}$ are given by 2.4.2.8, 2.4.2.9 in chapter 2 and matrices $\mathbf{K}$ and Σ are defined as

$$4.2.8 \qquad \Sigma = \mathbf{D + ZAZ'}$$

$$4.2.9 \qquad \mathbf{K = D^{-1} - D^{-1}X(X'D^{-1}X)^{-}X'D^{-1}}.$$

where $\mathbf{K = K'}$, and $\mathbf{X'KX} = 0$ implies $\mathbf{KX}=0$.

If the variance components σ_j^2, σ^2 and ρ are unknown, the method needs to estimate variance components and then iterate between two steps of estimation, viz. prediction of β, $\mathbf{u}$ and estimation of variance components until the whole process converges. The derivatives of $l = l_1 + l_2$ with respect to variance components σ_j^2, σ^2 and ρ are

4.2.10 $\partial l / \partial \sigma^2 = -(1/2)[n\sigma^{-2} - \sigma^{-4}(\mathbf{y} - \mathbf{X}\beta - \mathbf{Zu})'\mathbf{D}^{-1}(\mathbf{y} - \mathbf{X}\beta - \mathbf{Zu})]$,

4.2.11 $\partial l / \partial \sigma_j^2 = -(1/2)[v_j \sigma_j^{-2} - \sigma_j^{-4}\mathbf{u}_j' \mathbf{A}_j^{-1}\mathbf{u}_j]$ and

4.2.12 $\partial l / \partial \rho_s = -(1/2)\Sigma_{j=1}^{q}[\text{tr}\,\mathbf{A}_j^{-1}(\partial \mathbf{A}_j / \partial \rho_s) - \sigma_j^{-2}\tilde{\mathbf{u}}'\mathbf{A}_j^{-1}(\partial \mathbf{A}_j / \partial \rho_s)\mathbf{A}_j^{-1}\tilde{\mathbf{u}}]$ $s=1,2,...S$

Equating the above derivatives to zero and solving gives estimation equations for variance components σ_j^2, σ^2 and ρ as

4.2.13 $\tilde{\sigma}^2 = n^{-1}[(\mathbf{y} - \mathbf{X}\tilde{\beta} - \mathbf{Z}\tilde{\mathbf{u}})'\mathbf{D}^{-1}(\mathbf{y} - \mathbf{X}\tilde{\beta} - \mathbf{Z}\tilde{\mathbf{u}})]$,

4.2.14 $\tilde{\sigma}_j^2 = v_j^{-1}\tilde{\mathbf{u}}_j' \mathbf{A}_j^{-1}\tilde{\mathbf{u}}_j$ and

4.2.15 $\Sigma_{j=1}^{q}[\text{tr}\,\mathbf{A}_j^{-1}(\partial \mathbf{A}_j / \partial \rho_s) - \sigma_j^{-2}\tilde{\mathbf{u}}'\mathbf{A}_j^{-1}(\partial \mathbf{A}_j / \partial \rho_s)\mathbf{A}_j^{-1}\tilde{\mathbf{u}}] = 0$.

The estimation equation 4.2.15 clearly has no analytic solution and has to be solved numerically.

4.2.1: SOME ALGEBRA

1 $\Sigma^{-1} = \mathbf{D}^{-1} - \mathbf{D}^{-1}\mathbf{Z}\mathbf{T}^*\mathbf{Z}'\mathbf{D}^{-1}$, where $\mathbf{T}^* = (\mathbf{A}^{-1} + \mathbf{Z}'\mathbf{D}^{-1}\mathbf{Z})^{-1}$

2 $\mathbf{B}_{22} = (\mathbf{Z}'\mathbf{KZ} + \mathbf{A}^{-1})^{-} = \mathbf{T}$

3 $\mathbf{T}^*\mathbf{Z}'\mathbf{D}^{-1}\Sigma\mathbf{D}^{-1}\mathbf{Z}\mathbf{T}^* = \mathbf{A} - \mathbf{T}^*$

4 $\mathbf{Z}'\Sigma^{-1} = \mathbf{A}^{-1}\mathbf{T}^*\mathbf{Z}'\mathbf{D}^{-1}$

5 $\mathbf{Z}'\Sigma\mathbf{Z} = \mathbf{A}^{-1} - \mathbf{A}^{-1}\mathbf{T}^*\mathbf{A}^{-1}$

6 $\mathbf{T}^*\mathbf{Z}'\mathbf{D}^{-1} = \mathbf{A}\mathbf{Z}'\Sigma^{-1}$

7 $\mathbf{T}^*$ exists, ie, $|\mathbf{A}^{-1} + \mathbf{Z}'\mathbf{D}^{-1}\mathbf{Z}| \neq 0$

Proof:

1 $\quad \Sigma(\mathbf{D}^{-1} - \mathbf{D}^{-1}\mathbf{Z}\mathbf{T}^{*}\mathbf{Z}'\mathbf{D}^{-1}) = (\mathbf{D} + \mathbf{Z}\mathbf{A}\mathbf{Z}')(\mathbf{D}^{-1} - \mathbf{D}^{-1}\mathbf{Z}\mathbf{T}^{*}\mathbf{Z}'\mathbf{D}^{-1})$

$$= \mathbf{I} + \mathbf{Z}\mathbf{A}\mathbf{Z}'\mathbf{D}^{-1} - \mathbf{Z}\mathbf{T}^{*}\mathbf{Z}'\mathbf{D}^{-1} - \mathbf{Z}\mathbf{A}\mathbf{Z}'\mathbf{D}^{-1}\mathbf{Z}\mathbf{T}^{*}\mathbf{Z}'\mathbf{D}^{-1}$$

by substituting $\mathbf{T}^{*-1} - \mathbf{A}^{-1} = \mathbf{Z}'\mathbf{D}^{-1}\mathbf{Z}$ in the above expression, we have

$$= \mathbf{I} + \mathbf{Z}\mathbf{A}\mathbf{Z}'\mathbf{D}^{-1} - \mathbf{Z}\mathbf{T}^{*}\mathbf{Z}'\mathbf{D}^{-1} - \mathbf{Z}\mathbf{A}(\mathbf{T}^{*-1} - \mathbf{A}^{-1})\mathbf{T}^{*}\mathbf{Z}'\mathbf{D}^{-1}$$

$$= \mathbf{I} + \mathbf{Z}\mathbf{A}\mathbf{Z}'\mathbf{D}^{-1} - \mathbf{Z}\mathbf{T}^{*}\mathbf{Z}'\mathbf{D}^{-1} - \mathbf{Z}\mathbf{A}\mathbf{Z}'\mathbf{D}^{-1} + \mathbf{Z}\mathbf{T}^{*-1}\mathbf{Z}'\mathbf{D}^{-1} = \mathbf{I}.$$

2 From 2.4.2.8 and 2.4.2.9 in chapter 2 we have

$\mathbf{B}_{22} = \mathbf{T}^{*} + \mathbf{T}^{*}\mathbf{Z}'\mathbf{D}^{-1}\mathbf{X}\mathbf{B}_{11}\mathbf{X}'\mathbf{D}^{-1}\mathbf{Z}\mathbf{T}^{*}$, and $\mathbf{B}_{11} = [\mathbf{X}'\mathbf{D}^{-1}\mathbf{X} - \mathbf{X}'\mathbf{D}^{-1}\mathbf{Z}\mathbf{T}^{*}\mathbf{Z}'\mathbf{D}^{-1}\mathbf{X}]^{-1}$.

Replacing $\mathbf{B}_{11}$ in the right handside $\mathbf{B}_{22}$, gives

$$\mathbf{B}_{22} = \mathbf{T}^{*} + \mathbf{T}^{*}\mathbf{Z}'\mathbf{D}^{-1}\mathbf{X}[\mathbf{X}'\mathbf{D}^{-1}\mathbf{X} - \mathbf{X}'\mathbf{D}^{-1}\mathbf{Z}\mathbf{T}^{*}\mathbf{Z}'\mathbf{D}^{-1}\mathbf{X}]^{-1}\mathbf{X}'\mathbf{D}^{-1}\mathbf{Z}\mathbf{T}^{*},$$

$$= [\mathbf{T}^{*-1} - \mathbf{Z}'\mathbf{D}^{-1}\mathbf{X}(\mathbf{X}'\mathbf{D}^{-1}\mathbf{X})^{-}\mathbf{X}'\mathbf{D}^{-1}\mathbf{Z}]^{-1},$$

$= [\mathbf{Z}'\mathbf{D}^{-1}\mathbf{Z} + \mathbf{A}^{-1} - \mathbf{Z}'\mathbf{D}^{-1}\mathbf{X}(\mathbf{X}'\mathbf{D}^{-1}\mathbf{X})^{-}\mathbf{X}'\mathbf{D}^{-1}\mathbf{Z}]^{-1}$, using $\mathbf{T}^{*-1} = \mathbf{Z}'\mathbf{D}^{-1}\mathbf{Z} + \mathbf{A}^{-1}$

$$= [\mathbf{Z}'(\mathbf{D}^{-1} - \mathbf{D}^{-1}\mathbf{X}(\mathbf{X}'\mathbf{D}^{-1}\mathbf{X})^{-}\mathbf{X}'\mathbf{D}^{-1})\mathbf{Z} + \mathbf{A}^{-1}]^{-1} = [\mathbf{Z}'\mathbf{K}\mathbf{Z} + \mathbf{A}^{-1}]^{-1} = \mathbf{T}.$$

3 $\quad \mathbf{T}^{*}\mathbf{Z}'\mathbf{D}^{-1}\Sigma\mathbf{D}^{-1}\mathbf{Z}\mathbf{T}^{*} = \mathbf{T}^{*}\mathbf{Z}'\mathbf{D}^{-1}\mathbf{Z}\mathbf{T}^{*} + \mathbf{T}^{*}\mathbf{Z}'\mathbf{D}^{-1}\mathbf{Z}\mathbf{A}\mathbf{Z}'\mathbf{D}^{-1}\mathbf{Z}\mathbf{T}^{*}$

$$= \mathbf{T}^{*}(\mathbf{T}^{*-1} - \mathbf{A}^{-1})\mathbf{T}^{*} + \mathbf{T}^{*}(\mathbf{T}^{*-1} - \mathbf{A}^{-1})\mathbf{A}\mathbf{T}^{*}(\mathbf{T}^{*-1} - \mathbf{A}^{-1})\mathbf{T}^{*}$$

$$= (\mathbf{A} - \mathbf{T}^{*})(\mathbf{I} - \mathbf{A}^{-1}\mathbf{T}^{*}) = \mathbf{A} - \mathbf{T}^{*}.$$

4 From 1 we have,

$$\mathbf{Z}'\Sigma^{-1} = \mathbf{Z}'\mathbf{D}^{-1} - \mathbf{Z}'\mathbf{D}^{-1}\mathbf{Z}\mathbf{T}^{*}\mathbf{Z}'\mathbf{D}^{-1}$$

$= \mathbf{Z}'\mathbf{D}^{-1} - (\mathbf{T}^{*-1} - \mathbf{A}^{-1})\mathbf{T}^{*}\mathbf{Z}'\mathbf{D}^{-1} = \mathbf{A}^{-1}\mathbf{T}^{*}\mathbf{Z}'\mathbf{D}^{-1}$, using $\mathbf{T}^{*-1} - \mathbf{A}^{-1} = \mathbf{Z}'\mathbf{D}^{-1}\mathbf{Z}$.

5 Using 4 and $\mathbf{T}^{-1} - \mathbf{A}^{-1} = \mathbf{Z}'\mathbf{D}^{-1}\mathbf{Z}$, we have

$$\mathbf{Z}'\Sigma^{-1}\mathbf{Z} = \mathbf{A}^{-1}\mathbf{T}^{*}\mathbf{Z}'\mathbf{D}^{-1}\mathbf{Z} = \mathbf{A}^{-1}\mathbf{T}^{*}(\mathbf{T}^{*-1} - \mathbf{A}^{-1}) = \mathbf{A}^{-1} - \mathbf{A}^{-1}\mathbf{T}^{*}\mathbf{A}^{-1}.$$

The expression 6 follows from 2, and the proof of 7 is given in theorem 1 of appendix A.

4.3 MAXIMUM LIKELIHOOD (ML)

The log-likelihood function for a normally distributed observation vector $\mathbf{y}$ with $\mathbf{X}\beta$ mean and variance-covariance matrix $\sigma^2\Sigma$ is given by

4.3.1 $\quad l = -(1/2)[n\ln 2\pi\sigma^2 + \ln|\Sigma| + \sigma^{-2}(\mathbf{y}-\mathbf{X}\beta)'\Sigma^{-1}(\mathbf{y}-\mathbf{X}\beta)].$

From now on, the variance of random components $\mathbf{u}_j$ is taken as $\sigma^2\varphi_j\mathbf{A}_j$ where $\sigma_j^2 = \sigma^2\varphi_j$. Therefore, matrix $\mathbf{A}$ is a block diagonal matrix with blocks $\varphi_j\mathbf{A}_j$. Differentiation of 4.3.1 with respect to the parameters β, σ^2, φ_j and ρ_s gives

4.3.2 $\quad \partial l / \partial\beta = \sigma^{-2}\mathbf{X}'\Sigma^{-1}(\mathbf{y}-\mathbf{X}\beta),$

4.3.3 $\quad \partial l / \partial\sigma^2 = -(1/2)[n\sigma^{-2} - \sigma^{-4}(\mathbf{y}-\mathbf{X}\beta)'\Sigma^{-1}(\mathbf{y}-\mathbf{X}\beta)],$

4.3.4 $\quad \partial l / \partial\varphi_j = -(1/2)[\mathrm{tr}(\Sigma^{-1}\mathbf{Z}_j\mathbf{A}_j\mathbf{Z}_j') - \sigma^{-2}(\mathbf{y}-\mathbf{X}\beta)'\Sigma^{-1}\mathbf{Z}_j\mathbf{A}_j\mathbf{Z}_j'\Sigma^{-1}(\mathbf{y}-\mathbf{X}\beta)],$

4.3.5 $\quad \partial l / \partial\rho_s =$

$$= -(1/2)[\mathrm{tr}(\Sigma^{-1}\mathbf{Z}(\partial\mathbf{A}/\partial\rho_s)\mathbf{Z}') - \sigma^{-2}(\mathbf{y}-\mathbf{X}\beta)'\Sigma^{-1}\mathbf{Z}(\partial\mathbf{A}/\partial\rho_s)\mathbf{Z}'\Sigma^{-1}(\mathbf{y}-\mathbf{X}\beta)].$$

Equating the above derivatives to zero yields ML estimation equations for corresponding parameters. For given variance components, the ML estimator of parameter β coincides with the best linear unbiased estimator $\tilde{\beta}$,

4.3.6 $\quad \tilde{\beta} = \hat{\beta}_{ML} = (\mathbf{X}'\Sigma^{-1}\mathbf{X})^{-}\mathbf{X}'\Sigma^{-1}\mathbf{y}.$

However, the estimation equations for the variance components clearly have no analytic solution and have to be solved numerically. The asymptotic variance-covariance matrix for the ML estimators of the parameters

β, σ^2, φ and ρ is the inverse of the information matrix $\mathbf{I}_{ML}$ which is given by

4.3.7 $$\mathbf{I}_{ML} = 0.5 \times \begin{bmatrix} 2\sigma^{-2}(\mathbf{X}'\Sigma^{-1}\mathbf{X}) & 0 & 0 & 0 \\ . & n\sigma^{-4} & \sigma^{-2}[\mathrm{tr}\Sigma_{\varphi_j}] & \sigma^{-2}[\mathrm{tr}\Sigma_{\rho_t}] \\ . & . & [\mathrm{tr}\Sigma_{\varphi_i}\Sigma_{\varphi_j}] & [\mathrm{tr}\Sigma_{\varphi_i}\Sigma_{\rho_t}] \\ . & . & . & [\mathrm{tr}\Sigma_{\rho_s}\Sigma_{\rho_t}] \end{bmatrix}$$

where $\Sigma_{\varphi_j} = \Sigma^{-1}\partial\Sigma / \partial\varphi_j$ and $\Sigma_{\rho_s} = \Sigma^{-1}\partial\Sigma / \partial\rho_s$. The variance-covariance matrix for ML estimators of the variance components $(\sigma_1^2, \sigma_2^2, \ldots, \sigma_q^2)'$ is given by

4.3.9 $$\mathrm{var}(\hat{\sigma}_1^2, \hat{\sigma}_2^2, \ldots, \hat{\sigma}_q^2)') = \mathbf{B}\mathrm{var}(\hat{\varphi}_{ML})\mathbf{B}'$$

where $\mathrm{var}(\hat{\varphi}_{ML})$ is calculated from information matrix $\mathbf{I}_{ML}$ and $\mathbf{B} = [\partial\sigma_i^2 / \varphi_j]$ is the jacobian matrix.

Using 4.3.6 and algebra in 4.2.1, it can be easily proved that

4.3.10 $\Sigma^{-1}(\mathbf{y} - \mathbf{X}\hat{\beta}) = \mathbf{D}^{-1}(\mathbf{y} - \mathbf{X}\tilde{\beta} - \mathbf{Z}\tilde{\mathbf{u}})$,

4.3.11 $\mathbf{Z}'\Sigma^{-1}(\mathbf{y} - \mathbf{X}\hat{\beta}) = \mathbf{A}^{-1}\tilde{\mathbf{u}}$

4.3.12 $(\mathbf{y} - \mathbf{X}\hat{\beta})'\partial\Sigma^{-1} / \partial\rho_s(\mathbf{y} - \mathbf{X}\hat{\beta}) = -\tilde{\mathbf{u}}'\mathbf{A}^{-1}\partial\mathbf{A} / \partial\rho_s\mathbf{A}^{-1}\tilde{\mathbf{u}} = \sum_{j=1}^{q}\varphi_j^{-1}\tilde{\mathbf{u}}_j'\partial\mathbf{A}_j^{-1} / \partial\rho_s\tilde{\mathbf{u}}_j$

4.3.13 $(\mathbf{y} - \mathbf{X}\hat{\beta})'\partial\Sigma^{-1} / \partial\varphi_j(\mathbf{y} - \mathbf{X}\hat{\beta}) = -\varphi_j^{-2}\tilde{\mathbf{u}}_j'\mathbf{A}_j^{-1}\tilde{\mathbf{u}}_j$.

Note that in the above expressions, we have used the following relations.

4.3.14 $\Sigma = \mathbf{D} + \mathbf{Z}\mathbf{A}\mathbf{Z}' = \mathbf{D} + \sum_{j=1}^{q}\varphi_j\mathbf{Z}_j\mathbf{A}_j\mathbf{Z}_j'$, $\partial\mathbf{A}_j / \partial\varphi_j = -\mathbf{A}_j(\partial\mathbf{A}_j^{-1} / \partial\varphi_j)\mathbf{A}_j$,

4.3.15 $\partial\Sigma / \partial\varphi_j = \mathbf{Z}_j\mathbf{A}_j\mathbf{Z}_j'$, and $\partial\Sigma / \partial\rho_s = \sum_{j=1}^{q}\varphi_j\mathbf{Z}_j(\partial\mathbf{A}_j / \partial\rho_s)\mathbf{Z}_j'$.

Now using the above expressions, an iterative method to obtain ML estimators is as follows.

(1) Assign initial values to variance components.

(2) Solve 4.2.5.

(3) Use $\tilde{\beta}$ and $\tilde{u}$ to obtain a new value for variance component σ^2 for given φ_j and ρ_s by

4.3.16 $\hat{\sigma}^2_{(ML)} = n^{-1}\mathbf{y}'\Sigma^{-1}(\mathbf{y} - \mathbf{X}\hat{\beta}) = n^{-1}\mathbf{y}'\mathbf{D}^{-1}(\mathbf{y} - \mathbf{X}\tilde{\beta} - \mathbf{Z}\tilde{\mathbf{u}})$.

(4) Use $\tilde{\beta}$, $\tilde{\mathbf{u}}$, $\hat{\sigma}^2_{(ML)}$ and given values of ρ_s and φ_j to set up ML estimation equation for φ_j as

4.3.17 $\hat{\varphi}_{j(ML)} = (v_j - \mathrm{tr}\,\varphi_{j0}^{-1}\mathbf{A}_j^{-1}\mathbf{T}^*_{jj0})^{-1}\hat{\sigma}^{-2}_{(ML)}\tilde{\mathbf{u}}_j'\mathbf{A}_j^{-1}\tilde{\mathbf{u}}_j'$

where $\mathbf{T}^*_{jj0}$ is value of $\mathbf{T}^*_{jj}$ corresponding to the initial value of φ_{j0}.

(5) Use $\tilde{\beta}$, $\tilde{\mathbf{u}}$, $\hat{\sigma}^2_{(ML)}$, $\hat{\varphi}_{j(ML)}$ and given values of ρ_s to calculate new ρ_s values

that make 4.3.5 closer to zero,

4.3.18 $f(\rho_s) = \Sigma_{j=1}^{q}[-v_j^{*(s)} + r_j^{*(s)} + \hat{\varphi}^{-1}_{j(ML)}\hat{\sigma}^{-2}_{(ML)}\tilde{\mathbf{u}}_j'(\partial\mathbf{A}_j^{-1}/\partial\rho_s)\tilde{\mathbf{u}}_j]=0.$

where $v_j^{*(s)}$ and $r_j^{*(s)}$ are given in the below by 6 in 4.3.1. The equation 4.3.18 is a nonlinear function of ρ_s and the equation for $\hat{\rho}_{s(ML)}$ can be solved by appropriate convergence methods such as Newton-Raphson. For new values of $\hat{\rho}_{s(ML)}$, whole processes among (2)-(5) continues until the processes converge.

4.3.1 SIMPLIFICATIONS AND NOTIONS

1 $\mathrm{tr}\Sigma_{\varphi_j} = \mathrm{tr}\Sigma^{-1}\partial\Sigma/\partial\varphi_j = \mathrm{tr}\mathbf{Z}_j'\Sigma^{-1}\mathbf{Z}_j\mathbf{A}_j = \varphi_j^{-1}[v_j - \varphi_j^{-1}\mathrm{tr}\,\mathbf{A}_j^{-1}\mathbf{T}^*_{jj}] = \varphi_j^{-1}[v_j - r_j^*]$

2 $\mathrm{tr}\,\Sigma_{\rho_s} = \mathrm{tr}\Sigma^{-1}\partial\Sigma/\partial\rho_s = \Sigma_{j=1}^{q}[\mathrm{tr}\,\varphi_j^{-1}(\partial\mathbf{A}_j^{-1}/\partial\rho_s)\mathbf{T}^*_{jj} - \mathrm{tr}(\partial\mathbf{A}_j^{-1}/\partial\rho_s)\mathbf{A}_j]$

3

$\mathrm{tr}\Sigma_{\varphi_i}\Sigma_{\varphi_j} = \mathrm{tr}\Sigma^{-1}\partial\Sigma/\partial\varphi_i\Sigma^{-1}\partial\Sigma/\partial\varphi_j = [\varphi_i^{-2}(v_j - \varphi_j^{-1}\mathrm{tr}\,\mathbf{A}_j^{-1}\mathbf{T}^*_{jj})\delta_{ij} + \varphi_i^{-1}\varphi_j^{-1}\mathrm{tr}\,\mathbf{A}_j^{-1}\mathbf{T}^*_{ij}\mathbf{A}_i^{-1}\mathbf{T}^*_{ji}]$
$= [\varphi_i^{-2}\{(v_i - 2r_i^*)\delta_{ij} + \varphi_i^{-2}\varphi_j^{-2}r_{ij}^*\}]$

4 $\quad \mathrm{tr}\,\Sigma_{\rho_t}\Sigma_{\rho_s} = \mathrm{tr}\Sigma^{-1}(\sum_{j=1}^{q}\varphi_j \mathbf{Z}_j(\partial \mathbf{A}_j^{-1}/\partial\rho_t)\mathbf{Z}_j')\Sigma^{-1}(\sum_{j=1}^{q}\varphi_j \mathbf{Z}_j(\partial \mathbf{A}_j^{-1}/\partial\rho_s)\mathbf{Z}_j')$

$= \sum_{j=1}^{q}[\{\sum_{k=1}^{q}\varphi_j^{-1}\varphi_k^{-1} r_{jk}^{*(st)}\} + v_j^{*(st)} - 2r_j^{*(st)}]$

5 $\quad \mathrm{tr}\,\Sigma_{\rho_t}\Sigma_{\varphi_i} = \mathrm{tr}\Sigma^{-1}(\sum_{j=1}^{q}\varphi_j \mathbf{Z}_j(\mathbf{A}_j/\partial\rho_t)\mathbf{Z}_j')\Sigma^{-1}\mathbf{Z}_i\mathbf{Z}_i' = \varphi_i^{-1}[2\,r_i^{*(t)} - v_i^{(t)} - \sum_{j=1}^{q}\varphi_i^{-1}\varphi_j^{-1} r_{ij}^{*(t)}]$

where δ_{ij} = Kronecker delta,

6 $\quad r_j^{*} = \varphi_j^{-1}\,\mathrm{tr}\,\mathbf{A}_j^{-1}\mathbf{T}_{jj}^{*}$, $\quad r_{ij}^{*} = \mathrm{tr}\,\mathbf{T}_{ij}^{*}\mathbf{A}_j^{-1}\mathbf{T}_{ji}^{*}\mathbf{A}_i^{-1}$, $\quad r_j^{*(s)} = \varphi_j^{-1}\,\mathrm{tr}\partial\mathbf{A}_j^{-1}/\partial\rho_s\,\mathbf{T}_{jj}^{*}$

$r_{ij}^{*(st)} = \mathrm{tr}\,\mathbf{T}_{ij}^{*}\partial\mathbf{A}_j^{-1}/\partial\rho_s\,\mathbf{T}_{ji}^{*}\partial\mathbf{A}_i^{-1}/\partial\rho_t$, $\quad v_j^{*(st)} = \mathrm{tr}(\partial\mathbf{A}_j^{-1}/\partial\rho_s)\mathbf{A}_j\partial\mathbf{A}_i^{-1}/\partial\rho_t\,\mathbf{A}_j$,

$r_j^{*(st)} = \varphi_j^{-1}[(\mathrm{tr}\,\partial\mathbf{A}_j^{-1}/\partial\rho_s\,\mathbf{T}_{jj}^{*}\partial\mathbf{A}_i^{-1}/\partial\rho_t\,\mathbf{A}_j)]$

$v_j^{(s)} = \mathrm{tr}\partial\mathbf{A}_j^{-1}/\partial\rho_s\,\mathbf{A}_j$ and $\quad r_{ij}^{*(s)} = \mathrm{tr}\,\mathbf{T}_{ij}^{*}\partial\mathbf{A}_j^{-1}/\partial\rho_s\,\mathbf{T}_{ji}^{*}\mathbf{A}_j^{-1}$.

Using the above simplifications, the $\mathbf{I}_{(ML)}$ (information) multiply by 2, is

$$\begin{bmatrix} 2\sigma^{-2}\mathbf{H} & 0 & 0 & 0 \\ . & n\sigma^{-4} & \sigma^{-2}[\varphi_j^{-1}(v_j - r_j^{*})] & \sigma^{-2}[\sum_{j=1}^{q}(-v_j^{(t)} + r_j^{*(t)})] \\ . & . & [\varphi_i^{-2}\{(v_i - 2r_i^{*})\delta_{ij} + \varphi_i^{-2}\varphi_j^{-2}r_{ij}^{*}\}] & \varphi_i^{-1}[2r_i^{*(t)} - v_i^{(t)} - \sum_{j=1}^{q}\varphi_i^{-1}\varphi_j^{-1}r_{ij}^{*(t)}] \\ . & . & . & \sum_{j=1}^{q}[\{\sum_{k=1}^{q}\varphi_j^{-1}\varphi_k^{-1}r_{jk}^{*(ts)}\} + v_j^{*(ts)} - 2r_j^{*(ts)}] \end{bmatrix}$$

where $\mathbf{H} = \mathbf{X}'\Sigma\mathbf{X}$.

4.4 RESIDUAL MAXIMUM LIKELIHOOD (REML)

The log-likelihood function of the $\mathbf{Ky}$ is given by

$$l_{REML} = -(1/2)[(n-p)\ln 2\pi\sigma^2 + |\mathbf{K\Sigma K}| + \sigma^{-2}\mathbf{y}'\mathbf{K}(\mathbf{K\Sigma K})^{-}\mathbf{Ky}].$$

where $|\mathbf{K\Sigma K}|$ must be interpreted as the determinant of linearly independent rows and columns. Following Patterson and Thompson (1971), the residual maximum likelihood estimates of variance components σ^2, φ and ρ are, those values of the variance components σ^2, φ and ρ that maximise l_{REML}. Differentiation of l_{REML} with respect variance components σ^2, φ and ρ, yields REML estimation equations as

4.4.1 $\partial l_{REML} / \partial\sigma^2 = -(1/2)[(n-p)\sigma^{-2} - \sigma^{-4}\mathbf{y}'\mathbf{K}(\mathbf{K\Sigma K})^{-}\mathbf{K}\mathbf{y}]$

4.4.2

$$\partial l_{REML} / \partial\varphi_j = -(1/2)[\{tr(\mathbf{K\Sigma K})^{-}\mathbf{K}\partial\Sigma/\partial\varphi_j\mathbf{K}\} - \sigma^{-2}\mathbf{y}'\mathbf{K}(\mathbf{K\Sigma K})^{-}\mathbf{K}\partial\Sigma/\partial\varphi_j\mathbf{K}(\mathbf{K\Sigma K})^{-}\mathbf{K}\mathbf{y}]$$
$$= -(1/2)[tr\mathbf{K}_{\varphi_j} - \sigma^{-2}\mathbf{y}'\mathbf{K}_{\varphi_j}\mathbf{K}(\mathbf{K\Sigma K})^{-}\mathbf{y}]$$

4.4.3

$$\partial l_{REML} / \partial\rho_s = -(1/2)[\{tr(\mathbf{K\Sigma K})^{-}\mathbf{K}\partial\Sigma/\partial\rho_s\mathbf{K}\} - \sigma^{-2}\mathbf{y}'\mathbf{K}(\mathbf{K\Sigma K})^{-}\mathbf{K}\partial\Sigma/\partial\rho_s\mathbf{K}(\mathbf{K\Sigma K})^{-}\mathbf{K}\mathbf{y}]$$
$$= -(1/2)[tr\mathbf{K}_{\rho_s} - \sigma^{-2}\mathbf{y}'\mathbf{K}_{\rho_s}\mathbf{K}(\mathbf{K\Sigma K})^{-}\mathbf{K}\mathbf{y}]$$

where $\mathbf{K}_{\varphi_j} = \mathbf{K}(\mathbf{K\Sigma K})^{-}\mathbf{K}\partial\Sigma/\partial\varphi_j$ and $\mathbf{K}_{\rho_s} = \mathbf{K}(\mathbf{K\Sigma K})^{-}\mathbf{K}\partial\Sigma/\partial\rho_s$. The REML information matrix is given by

4.4.4 $$\mathbf{I}_{REML} = 0.5 \times \begin{bmatrix} (n-p)\sigma^{-4} & \sigma^{-2}tr\mathbf{K}_{\varphi_j} & \sigma^{-2}tr\mathbf{K}_{\rho_t} \\ . & tr\mathbf{K}_{\varphi_i}\mathbf{K}_{\varphi_j} & tr\mathbf{K}_{\varphi_i}\mathbf{K}_{\rho_t} \\ . & . & tr\mathbf{K}_{\rho_s}\mathbf{K}_{\rho_t} \end{bmatrix}.$$

The approximate variance-covariance matrix for the REML estimators of the variance components $(\sigma_1^2, \sigma_2^2, \ldots, \sigma_q^2)'$ can be obtained from 4.3.9 by replacing the ML estimators $\hat{\varphi}_{ML}$ by REML estimators $\hat{\varphi}_{REML}$.

4.4.1 ALGEBRA

1 $\mathbf{KDK} = \mathbf{K}$,

2 $(\mathbf{K\Sigma K})^{-} = \mathbf{K}^{-} - \mathbf{K}^{-}\mathbf{KZTZ'KK}^{-}$,

3 $\mathbf{K}(\mathbf{K\Sigma K})^{-}\mathbf{K} = \mathbf{K} - \mathbf{KZ}(\mathbf{A}^{-1} + \mathbf{Z'KZ})^{-1}\mathbf{Z'K} = \mathbf{K} - \mathbf{KZTZ'K}$,

4 $\mathbf{Z'K(K\Sigma K)^{-}K = A^{-1}(A^{-1} + Z'KZ)^{-1}Z'K = A^{-1}TZ'K}$

5 $\mathbf{Z'K(K\Sigma K)^{-}KZ = A^{-1} - A^{-1}(A^{-1} + Z'KZ)^{-1}A^{-1} = A^{-1} - A^{-1}TA^{-1}}$.

Proof

1 From 4.2.7, $\mathbf{K = D^{-1} - D^{-1}X(X'D^{-1}X)^{-}X'D^{-1}}$

$$\mathbf{DK = DD^{-1} - DD^{-1}X(X'D^{-1}X)^{-}X'D^{-1}}$$

$$\mathbf{DK = I - X(X'D^{-1}X)^{-}X'D^{-1}}, \text{ so}$$

$$\mathbf{KDK = K - KX(X'D^{-1}X)^{-}X'D^{-1}}, \text{ and } \mathbf{KX=0}$$

$$\mathbf{KDK = K - 0(X'D^{-1}X)^{-}X'D^{-1} = K}, \text{ which is 1.}$$

2 We have to show that

$$\mathbf{(K\Sigma K)(K^{-} - K^{-}KZTZ'KK^{-})K\Sigma K = K\Sigma K}$$

$$\mathbf{(K\Sigma K)(K^{-} - K^{-}KZTZ'KK^{-})K\Sigma K =}$$

$$\mathbf{= K\Sigma KK^{-}K\Sigma K - K\Sigma KK^{-}KZTZ'KK^{-}K\Sigma K}, \text{ using } \mathbf{KK^{-}K = K}$$

$$\mathbf{= K\Sigma K\Sigma K - K\Sigma KZTZ'K\Sigma K}, \text{ using 1 and } \mathbf{\Sigma = D + ZAZ'}$$

$$\mathbf{= K\Sigma K + K\Sigma KZAZ'K - K\Sigma KZTZ'K - K\Sigma KZTZ'KZAZ'K}$$

replacing $\mathbf{Z'KZ = T^{-1} - A^{-1}}$ gives

$$\mathbf{= K\Sigma K + K\Sigma KZAZ'K - K\Sigma KZTZ'K - K\Sigma KZAZ'K + K\Sigma KZTZ'K}$$

$$\mathbf{= K\Sigma K}, \text{ which is 2.}$$

The expression 3 follows from 2 and using $\mathbf{KK^{-}K = K}$.

4 From 3 we have

$$\mathbf{Z'K(K\Sigma K)^{-}K = Z'K - Z'KZTZ'K}, \text{ and using } \mathbf{Z'KZ = T^{-1} - A^{-1}} \text{ results}$$

$$\mathbf{Z'K(K\Sigma K)^{-}K = Z'K - (T^{-1} - A^{-1})TZ'K}$$

$$\mathbf{Z'K(K\Sigma K)^{-}K = Z'K - Z'K + A^{-1}TZ'K}$$

$$\mathbf{Z'K(K\Sigma K)^{-}K = A^{-1}TZ'K}, \text{ which is 4.}$$

5 From 4 we have

$\mathbf{Z'K(K\Sigma K)^{-}KZ = A^{-1}TZ'KZ}$, and using $\mathbf{Z'KZ = T^{-1} - A^{-1}}$ yields

$\mathbf{Z'K(K\Sigma K)^{-}KZ = A^{-1}T(T^{-1} - A^{-1})}$

$\mathbf{Z'K(K\Sigma K)^{-}KZ = A^{-1} - A^{-1}TA^{-1}}$, which is 5.

Theorem 4.4.1: The $\mathbf{K^{-} - K^{-}KZTZ'KK^{-}}$ is the Moore-Penrose inverse of the $\mathbf{K\Sigma K}$ if $\mathbf{K^{-}}$ is Moore-Penrose inverse $\mathbf{K}$.

Proof:

Following the definition of the Moore-Pensrose inverse of a matrix which is given in appendix A, we have to show

1 $\mathbf{(K\Sigma K)(K^{-} - K^{-}KZTZ'KK^{-})K\Sigma K = K\Sigma K}$

2 $\mathbf{(K^{-} - K^{-}KZTZ'KK^{-})K\Sigma K(K^{-} - K^{-}KZTZ'KK^{-}) = K^{-} - K^{-}KZTZ'KK^{-}}$

3 $\mathbf{[(K\Sigma K)(K^{-} - K^{-}KZTZ'KK^{-})]' = K\Sigma K(K^{-} - K^{-}KZTZ'KK^{-})}$

4 $\mathbf{[(K^{-} - K^{-}KZTZ'KK^{-})K\Sigma K]' = (K^{-} - K^{-}KZTZ'KK^{-})K\Sigma K}$.

Proof:

The proof of 1 is given by 2 of algebra 4.4.1.

2 $\mathbf{(K^{-} - K^{-}KZTZ'KK^{-})K\Sigma K(K^{-} - K^{-}KZTZ'KK^{-}) =}$

$\mathbf{K^{-}K\Sigma KK^{-} - K^{-}KZTZ'K\Sigma KK^{-} - K^{-}K\Sigma KZTZ'KK^{-} +}$

$\mathbf{K^{-}KZTZ'K\Sigma KZTZ'KK^{-}}$

using $\mathbf{K\Sigma K = K + KZAZ'K}$, the expression 2 becomes

$\mathbf{= K^{-} - K^{-}KZAZ'KK^{-} - K^{-}KZTZ'KK^{-} -}$

$\mathbf{K^{-}KZTZ'KZAZ'KK^{-} - K^{-}KZTZ'KK^{-} -}$

$\mathbf{K^{-}KZAZ'KZTZ'KK^{-} + K^{-}KZTZ'KZTZ'KK^{-} +}$

$\mathbf{K^{-}KZTZ'KZAZ'KZTZ'KK^{-}}$

replacing $\mathbf{Z'KZ = T^{-1} - A^{-1}}$ in the above equation gives

$$\mathbf{= K^- + K^-KZAZ'KK^- - K^-KZTZ'KK^- -}$$

$$\mathbf{K^-KZAZ'K + K^-KZTZ'KK^- - K^-KZTZ'KK^- -}$$

$$\mathbf{K^-KZTZ'KK^- - K^-KZAZ'KK^- +}$$

$$\mathbf{K^-KZTZ'K + K^-KZTZ'KZTZ'KK^- -}$$

$$\mathbf{K^-KZTZ'KZTZ'KK^- + K^-KZAZ'KK^- - K^-KZTZ'KK^-}$$

$\mathbf{= K^- - K^-KZTZ'KK^-}$ which is right handside of 2. Thus

$$\mathbf{(K^- - K^-KZTZ'KK^-)K\Sigma K(K^- - K^-KZTZ'KK^-) = K^- - K^-KZTZ'KK^-}.$$

Similarly it can be proved that

3 $\mathbf{[(K\Sigma K)(K^- - K^-KZTZ'KK^-)]' = [KK^-]'}$ and

4 $\mathbf{[(K^- - K^-KZTZ'KK^-)K\Sigma K]' = [K^-K]'}$.

Since $\mathbf{K^-}$ is taken to be Moore-Penrose inverse of the matrix $\mathbf{K}$ then $\mathbf{K^- - K^-KZTZ'KK^-}$ satisfies the four Penrose conditions.

Theorem 4.4.2: $\mathbf{Q = \Sigma^{-1} - \Sigma^{-1}X(X'\Sigma^{-1}X)^-X'\Sigma^{-1} = K(K\Sigma K)^-K}$

Proof: For symmetric idempotent matrix $\mathbf{X(X'X)X'}$, the matrix $\mathbf{W=I-X(X'X)X'}$ is also a symmetric idempotent. The symmetric idempotent matrix $\mathbf{W}$ has n-p (=rank of the matrix **W**) non-zero characteristic roots and they are each equal to +1. Thus, we have

$\mathbf{W = PP'}$ such that $\mathbf{P'P = I,\ WP = P,\ P'W = P'}$

and $\mathbf{P(P'\Sigma P)^-P'}$ is the Moore - Penrose inverse of $\mathbf{W\Sigma W}$. The matrix $\mathbf{Q}$ is also the Moore-Penrose inverse of $\mathbf{W\Sigma W}$. Since the Moore-Penrose inverse is unique then $\mathbf{Q = P(P'\Sigma P)^-P'}$. Since **KX=0** it follows that $\mathbf{Q = K(K\Sigma K)'K}$.

The following expressions are results of using the above theory, as well as the algebra and BLUP estimation equations from the previous section.

4.4.5 $\mathbf{K}(\mathbf{K\Sigma K})^{-}\mathbf{Ky} = \mathbf{K}(\mathbf{y}-\mathbf{Z}\tilde{\mathbf{u}}) =$

$$\mathbf{D}^{-1}(\mathbf{I}-\mathbf{X}(\mathbf{X}'\mathbf{D}^{-1}\mathbf{X})^{-}\mathbf{X}'\mathbf{D}^{-1})(\mathbf{y}-\mathbf{Z}\tilde{\mathbf{u}}) = \mathbf{D}^{-1}(\mathbf{y}-\mathbf{X}\tilde{\beta}-\mathbf{Z}\tilde{\mathbf{u}})$$

4.4.6 $\mathbf{Z}'\mathbf{K}(\mathbf{K\Sigma K})^{-}\mathbf{Ky} = \mathbf{Z}'\mathbf{K}(\mathbf{y}-\mathbf{Z}\tilde{\mathbf{u}}) = \mathbf{Z}'\mathbf{D}^{-1}(\mathbf{y}-\mathbf{X}\tilde{\beta}-\mathbf{Z}\tilde{\mathbf{u}}) = \mathbf{A}^{-1}\tilde{\mathbf{u}}$, so

4.4.7 $\mathbf{Z}_j'\mathbf{K}(\mathbf{K\Sigma K})^{-}\mathbf{Ky} = \mathbf{Z}_j'\mathbf{K}(\mathbf{y}-\mathbf{Z}\tilde{\mathbf{u}}) = \mathbf{Z}_j'\mathbf{D}^{-1}(\mathbf{y}-\mathbf{X}\tilde{\beta}-\mathbf{Z}\tilde{\mathbf{u}}) = \varphi_j^{-1}\mathbf{A}_j^{-1}\tilde{\mathbf{u}}_j$,

4.4.8 $\mathbf{y}'\mathbf{K}(\mathbf{K\Sigma K})^{-}\mathbf{K}(\partial\Sigma/\partial\varphi_j)\mathbf{K}(\mathbf{K\Sigma K})^{-}\mathbf{Ky} = \varphi_j^{-2}\tilde{\mathbf{u}}_j'\mathbf{A}_j^{-1}\tilde{\mathbf{u}}_j$, and

4.4.9 $\mathbf{y}'\mathbf{K}(\mathbf{K\Sigma K})^{-}\mathbf{K}(\partial\Sigma/\partial\rho_s)\mathbf{K}(\mathbf{K\Sigma K})^{-}\mathbf{Ky} = -\sum_{j=1}^{q}\varphi_j^{-1}\tilde{\mathbf{u}}_j'(\partial\mathbf{A}_j^{-1}/\partial\rho_s)\tilde{\mathbf{u}}_j$.

Using these expressions, the REML estimation equations for the variance components are given by

4.4.10 $\hat{\sigma}^2_{\text{REML}} = (n-p)^{-1}\mathbf{y}'\mathbf{D}^{-1}(\mathbf{y}-\mathbf{X}\tilde{\beta}-\mathbf{Z}\tilde{\mathbf{u}})$

4.4.11 $\hat{\varphi}_{j(\text{REML})} = (v_j - r_j)^{-1}\hat{\sigma}^{-2}_{(\text{REML})}\tilde{\mathbf{u}}_j'\mathbf{A}_j^{-1}\tilde{\mathbf{u}}_j'$

where $\mathbf{T}_{jj0}$ is value of $\mathbf{T}_{jj}$ corresponding to the initial value of φ_{j0} and ρ_0,

4.4.12 $f(\rho_s) = \sum_{j=1}^{q}[-v_j^{(s)} + r_j^{(s)} + \hat{\varphi}^{-1}_{j(\text{REML})}\hat{\sigma}^{-2}_{(\text{REML})}\tilde{\mathbf{u}}_j'(\partial\mathbf{A}_j^{-1}/\partial\rho_s)\tilde{\mathbf{u}}_j] = 0$.

The information matrix $\mathbf{I}_{(\text{REML})}$ for REML estimators of the variance components is

$$0.5\times\begin{bmatrix}(n-p)\sigma^{-4} & \sigma^{-2}[\varphi_j^{-1}(v_j - r_j)] & \sigma^{-2}[\sum_{j=1}^{q}(-v_j^{(t)}+r_j^{(t)})] \\ . & [\varphi_i^{-2}\{(v_i-2r_i)\delta_{ij}+\varphi_i^{-2}\varphi_j^{-2}r_{ij}\}] & \varphi_i^{-1}[2r_i^{(t)} - v_i^{(t)} - \sum_{j=1}^{q}\varphi_i^{-1}\varphi_j^{-1}r_{ij}^{(t)}] \\ . & . & \sum_{j=1}^{q}[\{\sum_{k=1}^{q}\varphi_j^{-1}\varphi_k^{-1}r_{jk}^{(st)}\}+v_j^{(st)}-2r_j^{(st)}]\end{bmatrix}$$

where r_j, $r_j^{(t)}$, $r_j^{(st)}$, $r_{ij}^{(t)}$ and $r_{ij}^{(st)}$ are obtained by 6 of 4.3.1 simply by deleting * in the corresponding terms.

4.5 GENERALIZED LINEAR MIXED MODELS (GLMMs)

In the generalized linear mixed model (GLMM), the distribution of the response vector $\mathbf{y}$ depends on a vector quantity η which is related to vector regression variables and random components through the equation

4.5.1 $\eta = \mathbf{X}\beta + \mathbf{Zu}$.

Let $f(\mathbf{y};\beta|\mathbf{u})$ to be the probability density function of $\mathbf{y}$ conditional on fixed $\mathbf{u}$. The log-likelihood of the observation vector $\mathbf{y}$ conditional on fixed $\mathbf{u}$ is

4.5.2 $l_1 = \ln f(\mathbf{y};\beta|\mathbf{u})$.

As in the previous section, for a normal random component $\mathbf{u}$ with zero mean and matrix $\sigma^2\mathbf{A}$ as variance-covariance, the log of the probability density function of $\mathbf{u}$ is denoted by l_2 and it is

4.5.3 $l_2 = -(1/2)[v\ln 2\pi\sigma^2 + \ln|\mathbf{A}| + \sigma^{-2}\mathbf{u}'\mathbf{A}^{-1}\mathbf{u}]$

where $v = \sum_{j=1}^{q} v_j$. The function l_2 may be considered to be a penalty function so that the parameters that maximise $l = l_1 + l_2$ are also called penalised likelihood (PL) estimators (BLUP estimators in the previous sections). Differentiating l with respect to β and $\mathbf{u}$ gives

4.5.4 $\partial l / \partial\beta = \mathbf{X}' dl_1 / d\eta$,

4.5.5 $\partial l / \partial\mathbf{u} = \mathbf{Z}' dl_1 / d\eta - \sigma^{-2}\mathbf{A}^{-1}\mathbf{u}$.

Apart from the second derivative of l with respect to random component $\mathbf{u}$ the second derivatives of l are the same as the second derivatives of l_1. The second order derivative of l with respect to the random component $\mathbf{u}$ is

4.4.6 $$\partial l^2 / \partial \mathbf{u} \partial \mathbf{u}' = -\mathbf{Z}'\mathbf{B}\mathbf{Z} - \sigma^{-2}\mathbf{A}^{-1}$$

where $\mathbf{B} = -d^2 l_1 / d\eta d\eta'$.

For given values of variance components ρ_s and φ_j, the Newton-Raphson iterative procedure for estimating $\boldsymbol{\beta}$, $\mathbf{u}$ is

4.5.7 $$\begin{bmatrix} \tilde{\boldsymbol{\beta}} \\ \tilde{\mathbf{u}} \end{bmatrix} = \begin{bmatrix} \boldsymbol{\beta}_0 \\ \mathbf{u}_0 \end{bmatrix} - \mathbf{V}^{-1} \begin{bmatrix} 0 \\ \sigma_0^{-2} \mathbf{A}_0^{-1} \mathbf{u}_0 \end{bmatrix} + \mathbf{V}^{-1} \begin{bmatrix} \mathbf{X}' \\ \mathbf{Z}' \end{bmatrix} dl_1 / \partial \eta$$

where $\boldsymbol{\beta}_0$, $\mathbf{u}_0$ are initial values for $\boldsymbol{\beta}$, $\mathbf{u}$ and $\mathbf{A}_0$ is the value of matrix $\mathbf{A}$ corresponding to the initial values φ_0 and ρ_0. The matrix $\mathbf{V}$ is

4.5.8 $$\mathbf{V} = \begin{bmatrix} \mathbf{X}' \\ \mathbf{Z}' \end{bmatrix} \mathbf{B} [\mathbf{X} \quad \mathbf{Z}] + \begin{bmatrix} 0 & 0 \\ 0 & \sigma^{-2}\mathbf{A}^{-1} \end{bmatrix}.$$

If second derivative matrix $\mathbf{V}$ replaced by E($\mathbf{V}$) then the iterative procedure becomes the method of scoring.

The general estimating approach in McGilchrist (1994) approximates the log-likelihood (l) by a quadratic approximation in the region of its maximum $(\tilde{\boldsymbol{\beta}}', \tilde{\mathbf{u}}')'$, i.e,

4.5.9 $$l = \text{constant} + (1/2) \begin{bmatrix} \boldsymbol{\beta} - \tilde{\boldsymbol{\beta}} \\ \mathbf{u} - \tilde{\mathbf{u}} \end{bmatrix}' \mathbf{V} \begin{bmatrix} \boldsymbol{\beta} - \tilde{\boldsymbol{\beta}} \\ \mathbf{u} - \tilde{\mathbf{u}} \end{bmatrix}.$$

In that case $\tilde{\beta}$, $\tilde{\mathbf{u}}$ have approximately a joint normal distribution with means β, $\mathbf{u}$ and variance-covariance matrix $\mathbf{V}^{-}$.

An alternative formulation of the problem is given in McGilchrist and Aisbett (1991) in which the component l_1 of the PL procedure is replaced by the log-likelihood of $\hat{\beta}$, $\hat{\mathbf{u}}$ as given by its approximate asymptotic distribution, viz. normal with means β, $\mathbf{u}$ and variance-covariance matrix inverse given by the information matrix for $\hat{\beta}$, $\hat{\mathbf{u}}$. The resulting PL log-likelihood obtained using the approximation is identical to the quadratic expression given above. The estimating equations for β, $\mathbf{u}$ are exactly those given by the method of scoring. Therefore, we may consider the PL (or BLUP) estimation as having been derived from the very approximate asymptotic distribution of $\hat{\beta}$, $\hat{\mathbf{u}}$.

If $\mathbf{I}(\beta,\mathbf{u})$ is the information matrix for β, $\mathbf{u}$ derived from l_1 then

4.5.10 $$\mathbf{I}(\beta,\mathbf{u}) = \begin{bmatrix}\mathbf{X}'\\ \mathbf{Z}'\end{bmatrix}\mathbf{B}[\mathbf{X} \quad \mathbf{Z}].$$

Replacing l_1 by l_1^*, the log-likelihood based on the asymptotic distribution of $\hat{\beta}$, $\hat{\mathbf{u}}$ gives

4.5.11 $$l_1^* = \text{constant} - (1/2)\begin{bmatrix}\hat{\beta}-\beta\\ \hat{\mathbf{u}}-\mathbf{u}\end{bmatrix}'\begin{bmatrix}\mathbf{X}'\\ \mathbf{Z}'\end{bmatrix}\mathbf{B}[\mathbf{X} \quad \mathbf{Z}]\begin{bmatrix}\hat{\beta}-\beta\\ \hat{\mathbf{u}}-\mathbf{u}\end{bmatrix}$$

$$= \text{constant} - (1/2)(\mathbf{y}^* - \mathbf{X}\beta - \mathbf{Z}\mathbf{u})'\mathbf{B}(\mathbf{y}^* - \mathbf{X}\beta - \mathbf{Z}\mathbf{u})$$

where $\mathbf{y}^* = \mathbf{X}\hat{\beta} + \mathbf{Z}\hat{\mathbf{u}}$.

The formulation of the problem is now exactly as described for normal theory models with $\mathbf{y}^*$ replacing $\mathbf{y}$, $\mathbf{B}$ in place of $\mathbf{D}^{-1}$ and $\sigma^2 = 1$

implying $\varphi_j = \sigma_j^2$. It follows that PL (or BLUP) estimators $\tilde{\beta}$, $\tilde{\mathbf{u}}$ may be used to find ML and REML estimates for the parameter β and variance components φ, ρ.

Thus, following the general estimation approach for normal theory, the steps of obtaining the approximate maximum likelihood (ML) and residual maximum likelihood (REML) estimates of parameters and variance components φ and ρ are as follows.

(1) Set up the log-likelihood l_1 conditional on the fixed random component $\mathbf{u}$ as a function of $\eta = \mathbf{X}\beta + \mathbf{Z}\mathbf{u}$.

(2) Given initial values β_0, $\mathbf{u}_0$, φ_0 and ρ_0 for β, $\mathbf{u}$, φ and ρ, solve 4.5.7.

(3) Use values of $\tilde{\beta}$ and $\tilde{\mathbf{u}}$ at convergence to obtain new values for variance components φ_j for given φ_j and ρ by

4.5.12 $\hat{\varphi}_{j(ML)} = \hat{\sigma}^2_{j(ML)} = (v_j - r_j^*)^{-1} \tilde{\mathbf{u}}_j' \mathbf{A}_j^{-1} \tilde{\mathbf{u}}_j'$ or

4.5.13 $\hat{\varphi}_{j(REML)} = \hat{\sigma}^2_{j(REML)} = (v_j - r_j)^{-1} \tilde{\mathbf{u}}_j' \mathbf{A}_j^{-1} \tilde{\mathbf{u}}_j'$.

(4) After convergence of the first two steps, the new estimation equations for the approximate ML and REML estimators of ρ are

4.5.14 $\sum_{j=1}^{q} [-v_j^{*(s)} + r_j^{*(s)} + \varphi_j^{-1} \tilde{\mathbf{u}}_j' (\partial \mathbf{A}_j^{-1} / \partial \rho_s) \tilde{\mathbf{u}}_j]_{\varphi_j = \hat{\varphi}_{j(ML)}} = 0$, for s=1,2,...,S,

and

4.5.15 $\sum_{j=1}^{q} [-v_j^{(s)} + r_j^{(s)} + \varphi_j^{-1} \tilde{\mathbf{u}}_j' (\partial \mathbf{A}_j^{-1} / \partial \rho_s) \tilde{\mathbf{u}}_j]_{\varphi_j = \hat{\varphi}_{j(REML)}} = 0$ for s=1,2,...,S.

Once convergences are obtained in the all three steps, approximate variance-covariance matrices of the ML and REML estimators can be obtained from previous sections.

4.6 APPLICATION TO ORDINAL AND DISCRETE RESPONSE DATA

A particular polytomous data that occur more frequently in applications are ordinal responses variables. The most widely used model in analysing ordinal responses data is the threshold model (ordinal regression model, McCullagh 1980). Chapter 1 has described two possible types of data for ordinal responses variables. That chapter has also mentioned some of the reasons to extend McCullagh (1980) by introducing terms corresponding to the random components into the linear predictor. A flexible estimation approach to derive approximate maximum likelihood (ML) and residual maximum likelihood (REML) estimates of parameters and variance components is the GLMM of McGilchrist (1994).

4.6.1 ORDINAL RESPONSE DATA

Let Y_{it} be observation for subject i at time t taking on possible values 0,1,2,...,M. It is assumed that the observable variable Y_{it} is a categorised value of an unobservable continuous variable U_{it} with G(.) as cumulative distribution function, viz.

4.6.1.1 $\quad Y_{it} = y_{it} \quad \Leftrightarrow \; \theta_{y_{it}-1} < U_{it} \le \theta_{y_{it}} \qquad$ or

4.6.1.2 $\quad Y_{it} = y_{it} \quad \Leftrightarrow \; \theta_{y_{it}-1} - \eta_{it} < U_{it} - \eta_{it} \le \theta_{y_{it}} - \eta_{it}$

where $y_{it} = 0,\ 1,\dots,M$ and $\theta_{-1} = -\infty < \theta_0 < \theta_1,\dots < \theta_{M-1} < \infty$. The η_{it} is

4.6.1.3 $\quad \eta_{it} = \mathbf{x}_{it}'\beta + \mathbf{z}_{it}'\mathbf{u}$

where $\mathbf{x}_{it}$ is a vector of p known regression variables with fixed regression coefficient β and $\mathbf{z}_{it}$ is an incidence vector for the normal random component $\mathbf{u}$ with zero mean and $\mathbf{A}$ as variance-covariance matrix. An extension of McCullagh (1980) is given by

4.6.1.4 $P(Y_{it} \leq y_{it}) = G(\theta_{y_{it}} - \eta_{it})$.

The probability of the observation from subject i at time t being y_{it} is

4.6.1.5 $P(Y_{it} = y_{it}) = G(\theta_{y_{it}} - \eta_{it}) - G(\theta_{y_{it}-1} - \eta_{it})$.

Therefore, the log-likelihood function of the observation vector $\mathbf{Y}$ conditional on fixed $\mathbf{u}$ is

4.6.1.6 $l_1 = \sum_{i=1}^{N} \sum_{t=1}^{n_i} \ln[G(\theta_{y_{it}} - \eta_{it}) - G(\theta_{y_{it}-1} - \eta_{it})]$.

Here threshold parameters $\theta_{y_{it}}$ are fixed and are very similar in nature to the β.

Given first and second order derivatives of l_1 with respect to the parameters, the approximate ML and REML estimators are obtained from 4.5.7, 4.5.12-4.5.15. Their asymptotic variance-covariance can be obtained from corresponding ML and REML expressions in normal theory development as given in section 4.3 and 4.4 of this chapter.

4.6.2 FREQUENCY OR DISCRETE DATA

In some problems there are categories of data for each subject (i) and within each category $\mathbf{x}_i$ and $\mathbf{z}_i$ are fixed and the total number of observations in the category are known. In that case the frequency of $y=k$ is denoted by f_{ik} and the distribution of f_{ik} for given $f_{i.}$ (sum of f_{ik} over k) is multinomial with probabilities dependent on fixed unknown parameters and random components corresponding to $\mathbf{x}_i$ and $\mathbf{z}_i$.

Although frequency data is a special case of ordinal data, there are some differences in terms of model fitting and inferences. Because the probability distribution is multinomial, we introduce another form for log-likelihood function l_i conditional on the fixed random component $\mathbf{u}$. For the observed frequencies vector $\mathbf{f} = [f_1', f_2', \ldots, f_N']'$, it is

4.6.2.1 $$l_i = \sum_{i=1}^{N} \sum_{j=0}^{M} f_{ik} \ln P_{ik}$$

where $\mathbf{f}_i = [f_{i0}, f_{i1}, \ldots, f_{iM}]'$. The probabilities P_{ik} are given by

4.6.2.2 $$P_{ik} = \begin{cases} G(\tau_{i0}) & \text{for } k=0 \\ G(\tau_{ik}) - G(\tau_{i(k-1)}) & \text{for } 0<k\le M-1 \\ 1-G(\tau_{iM}) & \text{for } k=M \end{cases}$$

where

4.6.2.3 $$\tau_{ik} = \begin{cases} \theta_k - \eta_i & \text{for } 0\le k\le M-1 \\ \theta_{k-1} - \eta_i & \text{for } k=M \end{cases}, \quad \eta_i = \mathbf{x}_i'\beta + \mathbf{z}_i'\mathbf{u}.$$

The $\mathbf{x}_i$ and $\mathbf{z}_i$ are risk variables and incidence vector for the random component $\mathbf{u}$ respectively. In matrix notation, we have

4.6.2.4 $$\mu_i = E(\mathbf{Y}_i|\mathbf{u}) = f_{i.}\mathbf{P}_i = \mathbf{C}_i G(\tau_i)$$

4.6.2.5 $$\tau_i = \mathbf{S}_i \alpha$$

4.6.2.6 $$\alpha = [\theta', \beta', \mathbf{u}']'$$

where threshold parameters are collected in θ. Let $\mathbf{J}_M = [0_{M-1}', 1]'$ and $\mathbf{U} = [\mathbf{I}_M, \mathbf{J}_M]'$ then $\mathbf{S}_i = [\mathbf{U}, -1_{M+1} \otimes (\mathbf{x}_i', \mathbf{z}_i')]$. The $\mathbf{C}_i$ is a (M+1)×(M+1) matrix with principal diagonal elements equal to 1, diagonal below the principal of the elements (-1, -1, ...,-1, 0) and all other elements zero.

From the above expressions it follows that the conditional log-likelihood l_i is a function of τ_{ik} . As in ordinal data, for given first and second order derivatives, the approximate ML and REML estimators can be obtained from 4.5.7, 4.5.12-4.5.15. The approximated variance-covariance of ML and REML estimators are obtained from sections 4.3 and 4.4.

In both ordinal and frequency data different choices of the distribution function G(.) result in different threshold models. In the following chapters, we will use four threshold models. These are models corresponding to the four common distributions; standard normal, logistic, extreme minimal and extreme maximal value for G.

CHAPTER FIVE

RANDOM COMPONENT THRESHOLD MODELS

5.1 INTRODUCTION

The preceding chapter has described the general structure of GLMM approaches for ordinal response variables. This and the following chapters are going to exhibit GLMM approaches to ordinal response variables in specific problems. This usually involves representing various forms of the matrix **A** (variance-covariance matrix of random components) in chapter 4.

This chapter extends the ordinal regression models of McCullagh (1980). Four threshold models, in which the response variable is related to regression variables with fixed coefficients as well as random components, are fitted to ordinal response variables.

Ordinal or ordered categorical data often occur as response variables in statistical applications, although some arise from grouping an underlying continuous random variable. McCullagh and Nelder (1989) have summarised different situations which result in such polytomous data and a sequence of models for ordinal data have been described in McCullagh (1980). The essence of such modelling is conveyed by introducing a continuous variable U and if U lies in the interval $(\theta_{y-1}, \theta_y]$ then response variable Y=y is recorded. The underlying variable U is not observed. Regression is introduced into the model by replacing θ_y with $\theta_y - \eta$, where η is the appropriate combination of regression variables involving unknown regression parameters and random components. Equivalently the underlying response variable U could be considered as being replaced by U-η. The resulting cumulative distribution function for Y is G(y-η) where G(.) is the cumulative distribution function for U.

When η contains not only fixed effects but also random components then a mixed threshold model results. Section 5.2 provides more detail on the data being considered, models for that data, with estimation techniques provided in section 5.3.

Sections 5.4 and 5.5 provide applications to dairy produce testing and an arthritis clinical trial. The dairy produce testing data were analysed in Zhaorong et al (1992) by using best linear unbiased prediction or penalised likelihood method that has negatively biased estimates of variance components. The arthritis clinical data have been analysed in Fitzmaurice (1995) by the GEE approach. Besides the ML and REML estimates, we also reproduce penalised likelihood (PL) estimates.

5.2 THRESHOLD MODELS

Since the discrete values of Y are usually denoted by 0, 1, ..., M, and U has a distribution over $(-\infty, \infty)$ for most models, we take $\theta_{-1} = -\infty$, $\theta_M = \infty$. The threshold model for Y is

5.2.1 $$P(Y \le y) = G(\theta_y - \eta)$$

It is clear that, if η contains a constant term, there is a lack of identifiability which may be overcome by setting $\theta_0 = 0$ leaving θ_1, θ_2, ..., θ_{M-1} and the parameters in η to be estimated. The observations Y_i, i= 1, 2, ..., N have associated vectors of regression variables $\mathbf{x}_i$ with fixed regression coefficient β, together with incidence vectors $\mathbf{z}_{ij}$ for vectors of random components $\mathbf{u}_j$, j=1, 2, ..., q. The vector $\mathbf{u}_j$ has v_j components. Thus

5.2.2 $$\eta_i = \mathbf{x}_i'\beta + \sum_j \mathbf{z}_{ij}'\mathbf{u}_j$$

gives the structure of the regression relationship. Expressed in matrix format, let η be the vector of η_i and $\mathbf{X}$ and $\mathbf{Z}_j$ be the matrices constructed from rows given by $\mathbf{x}_i'$, $\mathbf{z}_{ij}'$ respectively, and

5.2.3 $$\mathbf{Z} = [\mathbf{Z}_1, \mathbf{Z}_2, \ldots, \mathbf{Z}_q], \ \mathbf{u}' = [\mathbf{u}_1', \mathbf{u}_2', \ldots, \mathbf{u}_q']$$

so that

5.2.4 $$\eta = \mathbf{X}\beta + \mathbf{Z}\mathbf{u}.$$

In what follows we take the $\mathbf{u}_j$ to be independent $N(0, \varphi_j\mathbf{A}_j)$ and the variance matrix of $\mathbf{u}$ is denoted by $\mathbf{A}$. Thus $\mathbf{A}$ has block diagonal form with $\varphi_j\mathbf{A}_j$ forming the blocks on the diagonal.

Four threshold models result from giving four different structures to the G function. They are set out below.

Model 1: If $G(.) = \Phi(.)$, where Φ denotes the cumulative distribution function for a standard normal distribution, the standard *threshold model* is obtained.

Model 2: if $G(.) = e^{(.)} / [1+e^{(.)}]$ (logistic), the *proportional odds model* is obtained.

Model 3: if $G(.) = 1 - \exp[-e^{(.)}]$ (extreme minimal value) , the *proportional hazards model* is obtained.

Model 4: $G(.) = \exp[-e^{-(.)}]$ (extreme maximal value) , gives another model.

In the application to dairy produce data and arthritis clinical trial considered in sections 5.4 and 5.5, these are the four threshold models fitted.

5.3 METHOD OF ESTIMATION

Estimation in random component threshold models is described in general in chapter 4. The method requires a definition two components of the best linear unbiased prediction or penalised likelihood (PL) function. The

5.3.1 l_1 = log-likelihood of observation vector **y** conditional on fixed u

and

5.3.2 l_2 = logarithm of the probability density function of u

$$= -(1/2)\Sigma_{j=1}^{q}[v_j \ln 2\pi\varphi_j + \ln|\mathbf{A}_j| + \varphi_j^{-1}\mathbf{u}_j'\mathbf{A}_j^{-1}\mathbf{u}_j].$$

The function l_2 may be considered to be a penalty function so that the method of maximising the sum of l_1+l_2, is called a PL method. It has obvious links to shrinkage estimation and ridge regression. To allow for possible missing observations, we define $d_i = 1$ if observation for i present and $d_i = 0$ if missing. For the current problem, the log of conditional likelihood of the observations given the random components is

5.3.3 $\quad l_1 = \sum_{i=1}^{N} d_i \ln[G(\theta_{y_i} - \eta_i) - G(\theta_{y_i - 1} - \eta_i)]$

where the model for Y given in section 5.2 has been applied.

The steps of computing approximate maximum likelihood (ML) and residual maximum likelihood (REML) estimators are as follows. Letting θ be the vector of $[\theta_1, \theta_2, ..., \theta_{M-1}]$, the penalised likelihood estimators of $\theta, \beta, \mathbf{u}$ are found using a Newton-Raphson iterative scheme beginning with initial values $\theta_0, \beta_0, u_0, \eta_0 = \mathbf{X}\beta_0 + \mathbf{Z}u_0$ and solving the following equations for changes $\Delta\theta, \Delta\beta, \Delta u$ to be made to the initial values for the next iteration.

5.3.5
$$\mathbf{V}\begin{bmatrix}\Delta\theta \\ \Delta\beta \\ \Delta\mathbf{u}\end{bmatrix} = \begin{bmatrix}\mathbf{I} & 0 \\ 0 & \mathbf{X}' \\ 0 & \mathbf{Z}'\end{bmatrix}\begin{bmatrix}\partial l_1/\partial\theta_0 \\ \partial l_1/\partial\eta_0\end{bmatrix} - \begin{bmatrix}0 \\ 0 \\ \mathbf{A}_0^{-1}\mathbf{u}_0\end{bmatrix}$$

where

5.3.6
$$\mathbf{V} = \begin{bmatrix}\mathbf{V}_{11} & \mathbf{V}_{12} & \mathbf{V}_{13} \\ \mathbf{V}_{21} & \mathbf{V}_{22} & \mathbf{V}_{23} \\ \mathbf{V}_{31} & \mathbf{V}_{32} & \mathbf{V}_{33}\end{bmatrix} = \begin{bmatrix}\mathbf{I} & 0 \\ 0 & \mathbf{X}' \\ 0 & \mathbf{Z}'\end{bmatrix}\begin{bmatrix}-\partial^2 l_1/\partial\theta_0\partial\theta_0' & -\partial^2 l_1/\partial\theta_0\partial\eta_0' \\ -\partial^2 l_1/\partial\eta_0\partial\theta_0' & -\partial^2 l_1/\partial\eta_0\partial\eta_0'\end{bmatrix}\begin{bmatrix}\mathbf{I} & 0 & 0 \\ 0 & \mathbf{X} & \mathbf{Z}\end{bmatrix} + \begin{bmatrix}0 & 0 & 0 \\ 0 & 0 & 0 \\ 0 & 0 & \mathbf{A}_0^{-1}\end{bmatrix}$$

and

$\mathbf{A}_0$, $\partial l_1/\partial\theta_0$, $\partial l_1/\partial\eta_0$, $\partial^2 l_1/\partial\theta_0\partial\theta_0'$, $\partial^2 l_1/\partial\theta_0\partial\eta_0'$ and $\partial^2 l_1/\partial\eta_0\partial\eta_0'$ are the values of $\mathbf{A}$, $\partial l_1/\partial\theta$, $\partial l_1/\partial\eta$, $\partial^2 l_1/\partial\theta\partial\theta'$, $\partial^2 l_1/\partial\theta\partial\eta'$ and $\partial^2 l_1/\partial\eta\partial\eta'$ corresponding to initial estimates of their components. At convergence, the values $\tilde{\theta}, \tilde{\beta}, \tilde{u}$ obtained are the penalised likelihood (PL) estimates of θ, β and $\mathbf{u}$ corresponding to the initial estimates of φ_j used in $\mathbf{A}_0$. At the end of each converged sequence of iterations, new estimates of φ_j are obtained but the method of obtaining new estimates of φ_j depends on which of PL, ML or REML is being used. Recalling expressions from section 4, the three methods are

5.3.6 $\tilde{\varphi}_{j(PL)} = \tilde{\mathbf{u}}_j' \mathbf{A}_j^{-1} \tilde{\mathbf{u}}_j / v_j$ or $\hat{\varphi}_{j(ML)} = [\tilde{\mathbf{u}}_j' \mathbf{A}_j^{-1} \tilde{\mathbf{u}}_j + \mathrm{tr}\, \mathbf{A}_j^{-1} \mathbf{T}_{jj}^*] / v_j$ or

$$\tilde{\varphi}_{j(REML)} = [\tilde{\mathbf{u}}_j' \mathbf{A}_j^{-1} \tilde{\mathbf{u}}_j + \mathrm{tr}\, \mathbf{A}_j^{-1} \mathbf{T}_{jj}] / v_j$$

If $\qquad \mathbf{V}^{-1} = \begin{bmatrix} . & . & . \\ . & . & . \\ . & . & \mathbf{T} \end{bmatrix}, \qquad \mathbf{T}^* = \mathbf{V}_{33}^{-1}$

and $\mathbf{T} = [\mathbf{T}_{ij}]$, $\mathbf{T}^* = [\mathbf{T}_{ij}^*]$ are partitions of $\mathbf{T}$, $\mathbf{T}^*$ conformably to the partition of u into $\mathbf{u}_1$, $\mathbf{u}_2$, ..., $\mathbf{u}_q$, then the asymptotic variance matrix for the maximum likelihood estimators of the φ parameters is

5.3.7 $\qquad 2[\varphi_i^{-2}(v_i - 2\varphi_i^{-1} \mathrm{tr}\, \mathbf{A}_i^{-1} \mathbf{T}_{ii}^*) \delta_{ij} + \varphi_i^{-2} \varphi_j^{-2} \mathrm{tr}\, \mathbf{A}_i^{-1} \mathbf{T}_{ij}^* \mathbf{A}_j^{-1} \mathbf{T}_{ji}^*]^{-1}_{\varphi_i = \varphi_{i(ML)},\, \varphi_j = \varphi_{j(ML)}}$.

The asymptotic variance matrix for the maximum likelihood estimators of the θ and β is given by the corresponding row and column of the matrix $\mathbf{V}^{-1}$. If all asterisks are deleted, the REML results are obtained.

Finally ML (REML) estimates of β, θ are equal to the converged $\tilde{\beta}$, $\tilde{\theta}$ when corresponding ML (REML) estimates of φ_j are used. Thus the only changes to the penalised likelihood approach made in obtaining ML and REML estimators, is the way in which $\tilde{\mathbf{u}}$ is used to compute new estimates of the φ_j parameters. The above process is iterated until the estimates of the φ_j parameters converge. The three methods give different converged values of the φ_j and hence the corresponding estimates of β, θ will also be different for the three methods.

The estimation equations for β, θ, $\mathbf{u}$ and calculation of asymptotic variance-covariance matrices requires the evaluation of first and second derivatives of l_i. Letting

5.3.8 $\quad P_i = G(\theta_{y_i} - \eta_i) - G(\theta_{y_i-1} - \eta_i)$, $p_i = g(\theta_{y_i} - \eta_i) - g(\theta_{y_i-1} - \eta_i)$

where $g(.) = G'(.)$ and δ be the usual Kronecker delta, the first derivatives are

5.3.9 $\quad \partial l_i / \partial \eta_i = -d_i p_i / P_i$ and

5.3.10 $\quad \partial l_i / \partial \theta_k = \sum_{i=1}^{N} d_i P_i^{-1} [\delta_{y_i,k} g(\theta_{y_i} - \eta_i) - \delta_{y_i-1,k} g(\theta_{y_i-1} - \eta_i)]$.

The second order derivatives are given by

5.3.11

$$\partial^2 l_i / \partial\theta_k \partial\theta_h = \begin{cases} \sum_{i=1}^{N} d_i P_i^{-1} \{\delta_{y_i,k}[g'(\theta_{y_i} - \eta_i) - P_i^{-1} g^2(\theta_{y_i} - \eta_i)] - \\ \quad \delta_{(y_i-1)k}[g'(\theta_{y_i-1} - \eta_i) - P_i^{-1} g^2(\theta_{y_i-1} - \eta_i)]\}, & k = h \\ \sum_{i=1}^{N} d_i P_i^{-2} \delta_{y_i-1,k} [g(\theta_{y_i} - \eta_i) g(\theta_{y_i-1} - \eta_i)], & k = h-1 \\ \sum_{i=1}^{N} d_i P_i^{-2} \delta_{y_i,k} [g(\theta_{y_i} - \eta_i) g(\theta_{y_i-1} - \eta_i)], & k = h+1 \\ 0 \text{ , otherwise} \end{cases}$$

5.3.12

$$\partial^2 l_i / \partial\theta_k \partial\eta_i = \{d_i P_i^{-1} \delta_{y_i,k}[-g'(\theta_{y_i} - \eta_i) + p_i P_i^{-1} g(\theta_{y_i} - \eta_i)] + \delta_{y_i,k}[g'(\theta_{y_i} - \eta_i) - p_i P_i^{-1} g(\theta_{y_i} - \eta_i)]\}$$

and

5.3.13

$$\partial^2 l_i / \partial\eta_i \partial\eta_j = \begin{cases} d_i P_i^{-1}[g'(\theta_{y_i} - \eta_i) - g'(\theta_{y_i-1} - \eta_i) - p_i^2 P_i^{-1}], & j = i \\ 0 \text{ , otherwise} \end{cases}.$$

Armed with these derivatives the method may be applied to find PL , ML and REML estimates. Replacing second order derivatives in 5.3.6 yields information matrix **V** and this matrix is potentially large. However, some of the components of the partitioned matrix **V** are structured and easy to invert so that repeated use of the result formula of the lemma 1 in appendix A for inversion of partitioned matrices, often simplifies the problem. The formula for inversion of partitioned matrices is given in Searle (1982, p260, equation 14).

5.4 APPLICATION TO DAIRY PRODUCE DATA

The methods are applied to data arising in the investigation of twenty different techniques of using a presumptive coliform test for evaluation of dairy product. In New Zealand, the dairy industry used the presumptive coliform test as an important manufacturing hygiene indicator. It is required, in detection techniques, to be practical and very efficient. In this regard, some discussion queried the influence of media-type on coliform recovery. In devising an experiment to investigate this effect, it was decided to also look at the effect of innoculum size. Four medium types such as lactose broth and five product sizes, 0.01 g, 0.1 g, 1 g, 2.5 g, 5 g, were used, in a 4×5 factorial design, for testing each sample.

From dairy food plants throughout New Zealand, 1192 milk product samples were obtained. The response variable is the coded time it takes until gas production occurs in the sample added to one of four media, with Y = 0,1,2 indicating that gas production occurs >48hr, >24hr and ≤48hr, ≤24hr respectively. The samples that responded uniformly to the 4×5 factorial treatment design, by showing the same extent of gas production of all combinations of design levels, were discounted because of their lack of information in distinguishing between levels. A total of 125 samples remained for the statistical analysis. Details of the experiments are available in Cooke, et al (1985), and results for 125 samples are given in Table 1 in appendix B.

The aim of the study is to see if product size and medium type has any influence on the presumptive coliform test and if there is any interaction between these factors. A standardised presumptive coliform test may standardise for any factors influencing the result. Accordingly a selection of models with different dependencies on the factors of interest, are fitted to the data. Detail of these models follows.

Let Y_{rst} be the response variable for sample r added to medium-type s and having product size t (r = 1, 2,..., 125; s = 1, 2, 3, 4; t = 1, 2, ..., 4). Possible models for the distribution of Y are given in section 5.2 , with the corresponding linear predictor η_{rst} given by

5.4.1 $\eta_{rst} = \tau_{st} + u_r$, all twenty methods different,

5.4.2 $\eta_{rst} = \alpha_s + \beta_t + u_r$, additive medium and size effects,

5.4.3 $\eta_{rst} = \beta_t + u_r$, size effects only where u_r is the sample effect taken to be random and distributed as independent $N(0,\varphi)$. The above models each have implied **X** matrices for the fixed effects, while the **Z** matrix is the same for the three models. Zhaorong, McGilchrist and Jorgensen (1992) fitted these three models (5.4.1, 5.4.2, 5.4.3) with the first three of the models in section 5.2 , using the penalised likelihood estimation procedure only. They concluded that the model 5.4.3 seemed adequate to describe the data.

To support this conclusion the ML and REML estimates and standard errors of the parameters of the three η structures (5.4.1, 5.4.2 and 5.4.3) are given in Tables 5.4a and 5.4b , and 5.4c and 5.4d . The Tables 5.4a and 5.4b refer to the most general η structure by applying standard normal, logistic, extreme minimal and maximal distributions for the G function. It is clear that the pattern of $\hat{\tau}_{st}$, t=1,2,3,4,5 is the same for all s by using any of four distributions for the G. Hence it is to be expected that, in fitting additive medium and size effects model 5.4.2, the results are shown in Table 5.4c, the estimate of the medium effects α_s are all close to zero, i.e corresponding z-values are smaller than the 1.96 critical value. However, the z-value for the $\hat{\alpha}_1$ is bigger than 1.96 corresponding to the threshold model 4 of section 5.2. Nevertheless, since z-value for $\hat{\alpha}_1$ is about 2, close to 1.96, and on the other hand, z-values for $\hat{\alpha}_2$ and $\hat{\alpha}_3$ are smaller than 1.96, the preferred model is therefore 5.4.3 . Note that estimates of threshold parameter θ and φ are consistent for all models 5.4.1 , 5.4.2 and 5.4.3.

Thus the general conclusion is that size of sample is an important effect but medium type is not and there is no significant interaction. The estimates of β indicate that increasing the sample size substantially decreases the time to gas production.

The estimates and standard errors of the parameters are provided in tables 5.4d by using three methods PL, ML and REML. It can be seen that the estimates of regression parameters are obtained by PL, ML and REML methods being in close agreement with standard errors of the PL, although estimates somewhat smaller than those of ML and REML.

The estimated values of the conditional loglikelihood (l_1) for the models 5.4.1, 5.4.2 and 5.4.3 for all four threshold models of section 5.2 by PL, ML and REML methods is given in Table 5.4e.

Table 5.4a PL, ML and REML estimates of parameters in the threshold models for the model 5.4.1 . Est =Estimate, SE=Standard Error, Z-v = Est/SE .

		PL			ML			REML		
		Est	SE	Z-v	Est	SE	Z-v	Est	SE	Z-v
Standard Normal	φ	1.41			1.54	0.07	23.1	1.56	0.05	34.2
	θ_1	0.87	0.04	22.5	0.87	0.04	22.5	0.87	0.04	22.5
	τ_{11}	-1.56	0.19	-8.08	-1.57	0.20	-8.00	-1.57	0.20	-8.00
	τ_{12}	-0.38	0.17	-2.30	-0.38	0.17	-2.27	-0.39	0.17	-2.27
	τ_{13}	0.39	0.16	2.39	0.39	0.17	2.35	0.39	0.17	2.34
	τ_{14}	1.06	0.17	6.45	1.07	0.17	6.35	1.07	0.17	6.34
	τ_{15}	1.64	0.17	9.62	1.64	0.17	9.49	1.65	0.17	9.47
	τ_{21}	-1.51	0.19	-7.91	-1.52	0.19	-7.83	-1.52	0.20	-7.83
	τ_{22}	-0.37	0.17	-2.23	-0.38	0.17	-2.20	-0.38	0.17	-2.20
	τ_{23}	0.53	0.16	3.29	0.53	0.17	3.24	0.53	0.17	3.23
	τ_{24}	1.11	0.17	6.70	1.11	0.17	6.60	1.11	0.17	6.58
	τ_{25}	1.34	0.17	8.00	1.34	0.17	7.89	1.35	0.17	7.87
	τ_{31}	-2.00	0.22	-9.13	-2.01	0.22	-9.07	-2.01	0.22	-9.06
	τ_{32}	-0.73	0.17	-4.29	-0.74	0.17	-4.23	-0.74	0.18	-4.23
	τ_{33}	0.32	0.16	2.00	0.32	0.16	1.97	0.32	0.16	1.97
	τ_{34}	1.00	0.16	6.16	1.00	0.17	6.06	1.01	0.17	6.05
	τ_{35}	1.35	0.17	8.13	1.36	0.17	8.01	1.36	0.17	8.00
	τ_{41}	-1.71	0.20	-8.63	-1.72	0.20	-8.55	-1.72	0.20	-8.54
	τ_{42}	-0.55	0.17	-3.27	-0.56	0.17	-3.23	-0.56	0.17	-3.22
	τ_{43}	0.30	0.16	1.84	0.30	0.16	1.81	0.30	0.17	1.81
	τ_{44}	1.01	0.16	6.22	1.02	0.17	6.12	1.02	0.17	6.11
	τ_{45}	1.34	0.17	8.01	1.35	0.17	7.89	1.35	0.17	7.88
Logistic	φ	4.26			4.69	0.07	70.36	4.74	0.42	11.24
	θ_1	1.50	0.07	21.97	1.51	0.07	21.96	1.51	0.07	21.96
	τ_{11}	-2.68	0.34	-7.93	-2.71	0.34	-7.85	-2.71	0.35	-7.85
	τ_{12}	-0.65	0.29	-2.27	-0.66	0.29	-2.25	-0.66	0.29	-2.24
	τ_{13}	0.71	0.28	2.57	0.72	0.28	2.53	0.72	0.28	2.53
	τ_{14}	1.85	0.28	6.53	1.86	0.29	6.43	1.86	0.29	6.42
	τ_{15}	2.82	0.29	9.64	2.85	0.30	9.50	2.85	0.30	9.49
	τ_{21}	-2.56	0.33	-7.69	-2.59	0.34	-7.61	-2.59	0.34	-7.61
	τ_{22}	-0.64	0.29	-2.21	-0.65	0.30	-2.19	-0.65	0.30	-2.19
	τ_{23}	0.96	0.28	3.48	0.97	0.28	3.42	0.97	0.28	3.42
	τ_{24}	1.94	0.29	6.81	1.96	0.29	6.71	1.96	0.29	6.70
	τ_{25}	2.34	0.29	8.19	2.36	0.29	8.07	2.36	0.29	8.05
	τ_{31}	-3.48	0.40	-8.75	-3.51	0.40	-8.70	-3.51	0.40	-8.69
	τ_{32}	-1.36	0.31	-4.44	-1.38	0.31	-4.39	-1.38	0.31	-4.38
	τ_{33}	0.59	0.28	2.14	0.60	0.28	2.10	0.60	0.28	2.10
	τ_{34}	1.82	0.28	6.50	1.83	0.29	6.40	1.83	0.29	6.39
	τ_{35}	2.33	0.29	8.20	2.35	0.29	8.07	2.35	0.29	8.06
	τ_{41}	-2.99	0.36	-8.32	-3.01	0.37	-8.26	-3.02	0.37	-8.25
	τ_{42}	-0.92	0.29	-3.14	-0.93	0.30	-3.10	-0.93	0.30	-3.09
	τ_{43}	0.52	0.28	1.89	0.52	0.28	1.86	0.52	0.28	1.86
	τ_{44}	1.79	0.28	6.41	1.80	0.29	6.31	1.80	0.29	6.29
	τ_{45}	2.34	0.29	8.10	2.36	0.30	7.98	2.36	0.30	7.97

Table 5.4b PL, ML and REML estimates of parameters in the threshold models for the model 5.4.1 . Est =Estimate, SE=Standard Error, Z-v = Est/SE .

		PL			ML			REML		
		Est	SE	Z-v	Est	SE	Z-v	Est	SE	Z-v
	φ	1.87			2.03	0.07	30.89	2.06	0.08	26.25
	θ_1	0.99	0.04	22.16	0.99	0.05	22.15	0.99	0.05	22.15
	τ_{11}	-1.23	0.20	-6.18	-1.24	0.20	-6.11	-1.24	0.20	-6.10
	τ_{12}	0.04	0.18	0.20	0.04	0.19	0.20	0.04	0.19	0.20
	τ_{13}	0.85	0.18	4.66	0.86	0.19	4.60	0.86	0.19	4.59
	τ_{14}	1.63	0.19	8.49	1.64	0.20	8.38	1.64	0.20	8.37
	τ_{15}	2.28	0.21	11.13	2.29	0.21	11.01	2.30	0.21	11.00
	τ_{21}	-1.25	0.20	-6.25	-1.26	0.20	-6.18	-1.26	0.20	-6.17
	τ_{22}	0.08	0.18	0.43	0.08	0.19	0.42	0.08	0.19	0.42
	τ_{23}	1.03	0.18	5.66	1.04	0.19	5.58	1.04	0.19	5.57
Extreme	τ_{24}	1.74	0.19	8.94	1.75	0.20	8.84	1.75	0.20	8.82
Minimal	τ_{25}	1.95	0.20	9.89	1.97	0.20	9.78	1.97	0.20	9.76
	τ_{31}	-1.70	0.22	-7.85	-1.72	0.22	-7.78	-1.72	0.22	-7.77
	τ_{32}	-0.14	0.19	-0.76	-0.14	0.19	-0.74	-0.14	0.19	-0.74
	τ_{33}	0.82	0.18	4.58	0.83	0.18	4.52	0.83	0.19	4.51
	τ_{34}	1.60	0.19	8.48	1.61	0.19	8.38	1.61	0.19	8.36
	τ_{35}	1.97	0.20	10.00	1.98	0.20	9.89	1.98	0.20	9.88
	τ_{41}	-1.39	0.20	-6.82	-1.40	0.21	-6.75	-1.40	0.21	-6.74
	τ_{42}	-0.13	0.19	-0.70	-0.13	0.19	-0.69	-0.13	0.19	-0.69
	τ_{43}	0.78	0.18	4.32	0.78	0.18	4.26	0.79	0.19	4.25
	τ_{44}	1.57	0.19	8.35	1.58	0.19	8.24	1.58	0.19	8.23
	τ_{45}	2.00	0.20	10.02	2.02	0.20	9.92	2.02	0.20	9.90
	φ	1.69			1.88	0.07	27.76	1.90	0.07	27.58
	θ_1	1.01	0.05	21.98	1.02	0.05	21.97	1.02	0.05	21.97
	τ_{11}	-2.32	0.26	-9.00	-2.33	0.26	-8.95	-2.34	0.26	-8.94
	τ_{12}	-0.85	0.19	-4.49	-0.86	0.20	-4.43	-0.86	0.20	-4.43
	τ_{13}	0.04	0.18	0.23	0.04	0.18	0.21	0.04	0.18	0.21
	τ_{14}	0.79	0.18	4.48	0.79	0.18	4.39	0.79	0.18	4.38
	τ_{15}	1.37	0.18	7.74	1.38	0.18	7.59	1.38	0.18	7.57
	τ_{21}	-2.21	0.25	-8.88	-2.23	0.25	-8.83	-2.23	0.25	-8.83
	τ_{22}	-0.87	0.19	-4.48	-0.88	0.20	-4.43	-0.88	0.20	-4.43
	τ_{23}	0.19	0.18	1.06	0.18	0.18	1.03	0.18	0.18	1.02
Extreme	τ_{24}	0.80	0.18	4.52	0.80	0.18	4.43	0.80	0.18	4.42
Maximal	τ_{25}	1.10	0.18	6.21	1.10	0.18	6.09	1.10	0.18	6.08
	τ_{31}	-2.99	0.33	-9.13	-3.01	0.33	-9.11	-3.01	0.33	-9.11
	τ_{32}	-1.49	0.21	-7.06	-1.50	0.22	-7.00	-1.50	0.22	-6.99
	τ_{33}	-0.06	0.18	-0.32	-0.06	0.18	-0.33	-0.06	0.18	-0.33
	τ_{34}	0.68	0.17	3.88	0.68	0.18	3.78	0.68	0.18	3.77
	τ_{35}	1.10	0.18	6.29	1.11	0.18	6.16	1.11	0.18	6.15
	τ_{41}	-2.58	0.27	-9.40	-2.60	0.28	-9.37	-2.60	0.28	-9.36
	τ_{42}	-1.14	0.20	-5.69	-1.15	0.20	-5.63	-1.15	0.20	-5.63
	τ_{43}	-0.04	0.18	-0.22	-0.04	0.18	-0.23	-0.04	0.18	-0.23
	τ_{44}	0.73	0.17	4.22	0.74	0.18	4.13	0.74	0.18	4.12
	τ_{45}	1.05	0.18	5.94	1.05	0.18	5.82	1.05	0.18	5.80

Table 5.4c PL, ML and REML estimates of parameters in the threshold models for model 5.4.2 . Est =Estimate, SE=Standard Error, Z-v = Est/SE .

		PL			ML			REML		
		Est	SE	Z-v	Est	SE	Z-v	Est	SE	Z-v
	φ	1.40			1.54	0.07	23.19	1.55	0.05	34.28
	θ_1	0.86	0.04	22.49	0.87	0.04	22.49	0.87	0.04	22.49
Standard	α_1	0.15	0.08	1.84	0.15	0.08	1.85	0.15	0.08	1.85
Normal	α_2	0.14	0.08	1.68	0.14	0.08	1.69	0.14	0.08	1.69
	α_3	-0.06	0.08	-0.72	-0.06	0.08	-0.72	-0.06	0.08	-0.72
	β_1	-1.74	0.15	-11.8	-1.75	0.15	-11.6	-1.75	0.15	-11.6
	β_2	-0.57	0.14	-4.19	-0.57	0.14	-4.09	-0.57	0.14	-4.08
	β_3	0.33	0.13	2.45	0.33	0.14	2.38	0.33	0.14	2.38
	β_4	0.99	0.14	7.33	0.99	0.14	7.15	0.99	0.14	7.13
	β_5	1.35	0.14	9.91	1.36	0.14	9.68	1.36	0.14	9.65
	φ	4.22			4.65	0.07	70.29	4.70	0.42	11.33
	θ_1	1.49	0.07	21.98	1.50	0.07	21.96	1.50	0.07	21.96
	α_1	0.26	0.14	1.83	0.26	0.14	1.84	0.26	0.14	1.84
	α_2	0.25	0.14	1.78	0.25	0.14	1.79	0.25	0.14	1.79
Logistic	α_3	-0.10	0.14	-0.72	-0.10	0.14	-0.73	-0.10	0.14	-0.73
	β_1	-3.00	0.26	-11.6	-3.02	0.27	-11.3	-3.02	0.27	-11.3
	β_2	-0.99	0.24	-4.19	-0.99	0.24	-4.10	-1.00	0.24	-4.09
	β_3	0.59	0.23	2.57	0.59	0.24	2.51	0.60	0.24	2.50
	β_4	1.74	0.23	7.48	1.76	0.24	7.30	1.76	0.24	7.28
	β_5	2.35	0.24	9.89	2.37	0.25	9.66	2.37	0.25	9.64
	φ	1.85			2.02	0.07	30.84	2.04	0.08	26.48
	θ_1	0.98	0.04	22.16	0.99	0.05	22.15	0.99	0.05	22.15
	α_1	0.14	0.09	1.60	0.15	0.09	1.60	0.15	0.09	1.60
	α_2	0.15	0.09	1.70	0.16	0.09	1.70	0.16	0.09	1.70
Extreme	α_3	-0.03	0.09	-0.38	-0.03	0.09	-0.38	-0.03	0.09	-0.38
Minimal	β_1	-1.44	0.16	-9.02	-1.45	0.16	-8.85	-1.45	0.17	-8.83
	β_2	-0.11	0.15	-0.71	-0.11	0.16	-0.69	-0.11	0.16	-0.68
	β_3	0.80	0.15	5.29	0.81	0.16	5.18	0.81	0.16	5.17
	β_4	1.57	0.16	10.00	1.58	0.16	9.80	1.58	0.16	9.77
	β_5	1.98	0.16	12.30	1.99	0.17	12.06	1.99	0.17	12.03
	φ	1.69			1.87	0.07	27.87	1.89	0.07	27.70
	θ_1	1.00	0.05	22.00	1.01	0.05	21.99	1.01	0.05	21.99
	α_1	0.18	0.09	2.00	0.19	0.09	2.02	0.19	0.09	2.02
Extreme	α_2	0.16	0.09	1.70	0.16	0.09	1.71	0.16	0.09	1.71
Maximal	α_3	-0.08	0.09	-0.91	-0.09	0.09	-0.92	-0.09	0.09	-0.92
	β_1	-2.55	0.18	-14.0	-2.57	0.19	-13.8	-2.57	0.19	-13.7
	β_2	-1.15	0.15	-7.43	-1.16	0.16	-7.27	-1.16	0.16	-7.25
	β_3	-0.04	0.15	-0.24	-0.04	0.15	-0.25	-0.04	0.15	-0.26
	β_4	0.68	0.15	4.64	0.68	0.15	4.49	0.68	0.15	4.48
	β_5	1.08	0.15	7.33	1.09	0.15	7.11	1.09	0.15	7.09

* α_4 is fixed at zero to achieve identifiability.

Table 5.4d PL, ML and REML estimates of parameters in the threshold models for the model 5.4.3 . Est =Estimate, SE=Standard Error, Z-v = Est/SE .

		PL			ML			REML		
		Est	SE	Z-v	Est	SE	Z-v	Est	SE	Z-v
Standard Normal	φ	1.39			1.52	0.04	35.50	1.54	0.05	34.56
	θ_1	0.86	0.04	22.49	0.86	0.04	22.49	0.86	0.04	22.49
	β_1	-1.67	0.14	-12.2	-1.68	0.14	-11.9	-1.68	0.14	-11.9
	β_2	-0.51	0.13	-4.06	-0.51	0.13	-3.95	-0.51	0.13	-3.94
	β_3	0.38	0.12	3.09	0.38	0.13	3.00	0.38	0.13	2.99
	β_4	1.04	0.13	8.32	1.04	0.13	8.08	1.04	0.13	8.05
	β_5	1.41	0.13	11.09	1.41	0.13	10.78	1.42	0.13	10.75
Logistic	φ	4.18			4.60	0.39	11.75	4.65	0.41	11.42
	θ_1	1.49	0.07	21.97	1.50	0.07	21.96	1.50	0.07	21.96
	β_1	-2.88	0.24	-11.9	-2.91	0.25	-11.6	-2.91	0.25	-11.6
	β_2	-0.88	0.22	-4.02	-0.88	0.23	-3.91	-0.88	0.23	-3.90
	β_3	0.69	0.21	3.24	0.69	0.22	3.14	0.69	0.22	3.13
	β_4	1.83	0.22	8.45	1.85	0.23	8.21	1.85	0.23	8.18
	β_5	2.44	0.22	11.04	2.46	0.23	10.74	2.46	0.23	10.70
Extreme Minimal	φ	1.85			2.01	0.07	27.30	2.03	0.08	26.55
	θ_1	0.98	0.04	22.16	0.98	0.04	22.14	0.98	0.04	22.14
	β_1	-1.37	0.15	-9.15	-1.38	0.15	-8.94	-1.38	0.16	-8.92
	β_2	-0.04	0.14	-0.28	-0.04	0.15	-0.27	-0.04	0.15	-0.27
	β_3	0.87	0.14	6.13	0.87	0.15	5.98	0.88	0.15	5.96
	β_4	1.63	0.15	11.07	1.64	0.15	10.81	1.64	0.15	10.77
	β_5	2.04	0.15	13.51	2.06	0.16	13.20	2.06	0.16	13.17
Extreme Maximal	φ	1.65			1.84	0.06	28.96	1.86	0.07	28.17
	θ_1	1.00	0.05	22.00	1.00	0.05	21.99	1.00	0.05	21.99
	β_1	-2.48	0.17	-14.4	-2.49	0.18	-14.1	-2.50	0.18	-14.1
	β_2	-1.08	0.14	-7.64	-1.09	0.15	-7.43	-1.09	0.15	-7.41
	β_3	0.03	0.13	0.20	0.02	0.14	0.18	0.02	0.14	0.17
	β_4	0.74	0.13	5.49	0.74	0.14	5.29	0.74	0.14	5.27
	β_5	1.14	0.14	8.39	1.14	0.14	8.10	1.14	0.14	8.07

Table 5.4e: Estimated value of conditional log-likelihood (l_1) for the threshold models.

Model	Method	Standard normal	Logistic	Extreme minimal	Extreme maximal
5.4.1	REML	-1414.94	-1409.84	-1414.15	-1437.96
	ML	-1415.08	-1410.01	-1414.32	-1438.12
	PL	-1416.44	-1411.63	-1415.66	-1439.88
5.4.2	REML	-1418.77	-1414.74	-1417.91	-1443.5
	ML	-1418.91	-1414.91	-1418.07	-1443.66
	PL	-1420.27	-1416.54	-1419.42	-1445.41
5.4.3	REML	-1424.1	-1420.29	-1421.53	-1450.51
	ML	-1424.24	-1420.46	-1421.68	-1450.67
	PL	-1425.61	-1422.09	-1423.03	-1452.45

5.5 APPLICATION TO ARTHRITIS CLINICAL TRIAL DATA

A second application of the models in section 5.2 is to binary response variables. We introduce models in section 5.2 for binary data by assuming that there is only one cut-point (threshold parameter, θ_0). It is, without loss of generality, taken that $\theta_0 = 0$.

The motivating example is reported in Fitzmaurice and Lipsitz (1995) and represented in table 2 of appendix B. It is a subset of data on 51 subjects from an arthritis clinical trial (Bombardier et al , 1986). In this study, patients have at most five unequally spaced binary self-assessment measurements of arthritis, where self-assessment equals 0 if 'poor' and 1 if 'good'. Patients had a base-line self-assessment measurement (week 0) and follow-up self-assessment measurements at weeks 1, 5, 9 and 13. Randomization to one of the two treatments, placebo or auranofin, occurred following the second self-assessment. After randomization, patients remained on the assigned treatment for the entire study period. In addition to treatments and time, age and gender of patients were recorded. Note that the treatment remains the same at all times for patients randomized to have the placebo but changes for the patients randomized to have auronofin after the second self-assessment measurement.

The main interest of the study is to investigate the difference in response to two treatment groups and whether age and gender of patients have any influence on the responses.

Fitzmaurice and Lipsitz (1995) have fitted two different models; the marginal and conditional, by using GEEs methods. They have concluded that the patients on auranofin are more likely to give positive self-assessment and that there are not statistically significant influences due to age, time or gender.

We develop the following model with all four threshold models in section 5.2 viz PL, ML and REML methods.

5.5.1 $\eta_{it} = \beta_0 + \alpha(\text{gender}_i) + \gamma(\text{age}_i) + \beta_t(\text{treat}_{it}) + u_i$,

where risk variables are age in years at the base-line, gender (gender_i, 1=male, 0=female), treatment (treat_{it}, $1 = \text{auranofin}$, $0 = \text{placebo}$). The significant changes in β_t (t=1, 2, 3, 4) indicates influences of time on the treatment auranofin. The u_i is the patient effect taken to be random and distributed as independent $N(0,\varphi)$. The relationship between Y_{it} response (1, 0) for patient i at time t is equation 5.2.1 altered by inserting suffix i,t in y , Y and η.

Table 5.5a provides estimates and standard errors of the parameters for the model 5.5.1 for three methods (PL, ML and REML). The PL, ML and REML estimates are obtained for all four threshold models of section 5.2.

The PL method shows that the variability between patients is always close to zero. However, both ML and REML methods give a significant variance of patients random effects for each of four threshold models. The factors of age and gender do not have a statistically significant influence on self-assessment.

The test of overall treatment effect is obtained by using the asymptotic joint distribution of the $\hat{\beta}_t$ (t=1,2,3,4). Table 5.5b gives estimate and standard errors of the treatment effects and corresponding asymptotic z-values which are shown with the z-v column. In this table, the z-value is greater than the 1.96 critical value by each method (PL, ML and REML) for all four threshold models. Note, the estimated treatment effect is positive. It indicates that the η increases and θ-η decreases, so that observations of the patients on the treatment auranofin are more likely in the highest category (1) viz. good.

Thus fitting model 5.5.1 by ML or REML methods provides conclusions that are the same as those in the Fitzmaurice et al (1995) i.e, significant treatment auranofin effect, with age and gender not significant risk variables. Nevertheless ML and REML methods give prediction of random components and estimate of variance of random component which the GEEs methods do not. Additionally model 5.5.1 provides estimates of the treatment effect at each time. Looking through z-v column in the Table 5.2a, we see that the PL method provides significant treatment effect at times 2, 3 and 4 by giving z-values greater than the 1.96 critical value for all four threshold models. However the ML and REML methods show a significant treatment effect at times 2, 4 for threshold models 1 and 4 of section 5.2 and the significance has disappeared at time 4 for threshold models 2 and 3 from section 5.2.

Given that the treatment effect has influence through time, we use asymptotic joint distribution of $\hat{\beta}_t$ for further investigating changes in the treatment effects over time.

For the threshold model 1 of section 5.2, the asymptotic variance covariance matrix is

5.5.2
$$\begin{bmatrix} 0.146 & 0.066 & 0.066 & 0.066 \\ 0.066 & 0.328 & 0.063 & 0.065 \\ 0.066 & 0.063 & 0.189 & 0.069 \\ 0.066 & 0.065 & 0.069 & 0.225 \end{bmatrix}.$$

The pairwise contrast between β_t, their standard errors and the ratio of estimate to the standard errors (z-v) are given in Table 5.5c. The results show a significant increase in the treatment effect from time 1 to 2.
This conclusion is consistent with the results obtained using the other three threshold models (2, 3, 4) of section 5.2.

In short, the treatment auranofin has a statistically significant effect. Since the estimated value is positive, it decreases the $\theta - \eta$ and causes the highest response (1) for the patients on the treatment auranofin. On the treatment auranofin, the possibility of giving a 1 result increases as the patients move from time 1 to 2. This possibility becomes constant from time 2 up to 4. There are no statistically significant age and gender effects.

The estimates and standard errors of the parameters are provided in tables 5.5a and 5.5b by using three methods PL, ML and REML. In the previous section, the general conclusion was the same for any of three methods (PL, ML, REML) applied to dairy produce data. For the arthritis data, the results in the Table 5.5a and 5.5b indicate a clear variation among those three methods. In the table 5.5a, the PL estimates of φ is always zero for all four threshold mixed models of section 5.2. This is in agreement with general simulation results, these being that the PL estimates of standard errors often under-report the true standard errors while those of REML, in particular, are usually quite close to those obtained through simulation (McGilchrist 1993, 1994) and (Saei and McGilchrist 1996).

Table 5.5d gives estimates of conditional loglikelihood (l_1) for the models 5.5.1 for all four threshold mixed models by using PL, ML and REML methods.

Table 5.5a Estimates of parameters, standard errors and z-values for the model 5.5.1. Est =Estimate, SE=Standard Error, Z-v = Est/SE .

		PL			ML			REML		
		Est	SE	z-v	Est	SE	z-v	Est	SE	z-v
Standard Normal	φ	0.00			0.43	0.21	2.04	0.55	0.25	2.20
	β_0	0.05	0.56	0.09	0.10	0.79	0.13	0.11	0.84	0.13
	α	0.36	0.23	1.52	0.38	0.33	1.14	0.38	0.36	1.08
	γ	0.00	0.01	-0.20	0.00	0.01	-0.19	0.00	0.02	-0.19
	β_1	0.44	0.29	1.49	0.48	0.37	1.32	0.49	0.38	1.29
	β_2	1.53	0.47	3.25	1.64	0.55	2.97	1.68	0.57	2.93
	β_3	0.69	0.34	2.04	0.72	0.42	1.71	0.72	0.44	1.66
	β_4	0.87	0.38	2.31	0.92	0.46	2.01	0.93	0.47	1.96
Logistic	φ	0.00			1.05	0.54	1.94	1.36	0.65	2.10
	β_0	0.12	0.96	0.13	0.23	1.29	0.18	0.26	1.37	0.19
	α	0.60	0.39	1.54	0.62	0.53	1.16	0.63	0.57	1.10
	γ	0.00	0.02	-0.26	-0.01	0.02	-0.27	-0.01	0.02	-0.26
	β_1	0.73	0.49	1.47	0.75	0.59	1.28	0.77	0.62	1.25
	β_2	2.86	1.05	2.73	2.95	1.10	2.68	3.00	1.12	2.68
	β_3	1.17	0.60	1.96	1.14	0.69	1.66	1.15	0.72	1.61
	β_4	1.45	0.67	2.17	1.46	0.76	1.93	1.48	0.79	1.89
Extreme Minimal	φ	0.00			0.76	0.36	2.08	0.96	0.44	2.20
	β_0	0.43	0.82	0.53	0.53	1.06	0.50	0.57	1.13	0.50
	α	0.48	0.31	1.57	0.50	0.43	1.15	0.51	0.46	1.09
	γ	0.00	0.01	-0.22	-0.01	0.02	-0.30	-0.01	0.02	-0.30
	β_1	0.60	0.41	1.44	0.59	0.49	1.21	0.60	0.51	1.17
	β_2	2.59	1.01	2.55	2.71	1.05	2.58	2.75	1.06	2.59
	β_3	0.99	0.53	1.87	0.95	0.60	1.60	0.95	0.62	1.54
	β_4	1.22	0.60	2.03	1.21	0.66	1.83	1.22	0.68	1.79
Extreme Maximal	φ	0.00			0.37	0.19	1.99	0.49	0.23	2.16
	β_0	-0.32	0.52	-0.62	-0.23	0.74	-0.31	-0.23	0.79	-0.29
	α	0.33	0.23	1.43	0.36	0.32	1.13	0.37	0.34	1.07
	γ	0.00	0.01	-0.12	0.00	0.01	-0.13	0.00	0.01	-0.13
	β_1	0.43	0.28	1.52	0.47	0.35	1.36	0.49	0.36	1.33
	β_2	1.27	0.34	3.79	1.39	0.46	3.06	1.44	0.49	2.96
	β_3	0.65	0.30	2.15	0.69	0.38	1.81	0.69	0.40	1.75
	β_4	0.82	0.32	2.55	0.87	0.41	2.14	0.89	0.43	2.08

Table 5.5b: Estimate of the treatment effect, standard errors and z-value for model 5.5.1. $\hat{\beta}$ = average of $\hat{\beta}_t$ (t=1,2,3,4), SE=Standard Error, Z-v = Est/SE .

	PL			ML			REML		
	$\hat{\beta}$	SE	z-v	$\hat{\beta}$	SE	z-v	$\hat{\beta}$	SE	z-v
ST Normal	0.881	0.22	4.004	0.939	0.304	3.086	0.956	0.324	2.952
Logistic	1.549	0.411	3.774	1.576	0.52	3.045	1.599	0.55	2.926
Ex Minimal	1.347	0.37	3.661	1.368	0.452	3.032	1.376	0.473	2.913
Ex maximal	0.792	0.197	4.022	0.855	0.28	3.06	0.877	0.3	2.925

* ST = Standard and Ex = Extreme.

Table 5.5c: Estimate of the contrast between treatment effect, standard errors (SE) and the ratio of estimate to their standard errors (z-v) for model 5.5.1.

		REML		
Distribution	Contrast	Est	SE	z-v
Standard Normal	$\beta_1 - \beta_2$	-1.188	0.556	-2.135
	$\beta_1 - \beta_3$	-0.229	0.447	-0.513
	$\beta_1 - \beta_4$	-0.437	0.407	-1.073
	$\beta_2 - \beta_3$	0.959	0.593	1.617
	$\beta_2 - \beta_4$	0.751	0.614	1.224
	$\beta_3 - \beta_4$	-0.208	0.505	-0.412

Table 5.5d: Estimated value of conditional log-likelihood (l_1) for the threshold models.

Model	Method	Standard normal	Logistic	Extreme minimal	Extreme maximal
5.5.1	REML	-60.73	-62.49	-66.08	-68.75
	ML	-62.67	-64.42	-69.09	-70.21
	PL	-74.09	-73.43	-76.81	-114.96

CHAPTER SIX

THRESHOLD MODELS IN A METHADONE PROGRAM EVALUATION

6.1 INTRODUCTION

In chapter 5, the ordinal regression models of McCullagh (1980) are extended to ordinal mixed models by introducing random components into the linear predictor. Estimation equations of variance components are given for four threshold models using both ML and REML methods. The developed approach is applied to two real data sets.

Basically the theory underlying this chapter is the same as that of chapter 5, indeed it is an application of the theory developed in that chapter. The application is of sufficient interest to justify a separate chapter.

The response variable in evaluating a methadone program usually measures the extent of noncompliance with the aims of the program and, for those who are successful in these aims, the response is zero. It is not unusual, therefore, to attempt to model response data with a large zero frequency and with remaining values either distributed continuously over the positive range or perhaps grouped into intervals. The aim is to relate the response variable to the treatment variable acting in the presence of the other covariables.

One approach to this problem has been to model the zero occurrences separately from the positive occurrences and to attempt a marrying of the two separate inferences at a later stage. Another approach has been to use zero-inflated or zero added distributions. For each of these approaches, the eventual inference procedures are not simple, particularly when the regression model includes both fixed and random components.

We advance here a very versatile approach to these problems by using threshold models (models developed in chapter 5) in which there is considered to be an underlying unobservable variable U such that if U lies in the interval from $\theta_{y-1} - \eta$ to $\theta_y - \eta$ then response Y=y is observed, where θ_k , k = -1, 0, ,1, ...,M are threshold parameters ($\theta_{-1} = -\infty$, $\theta_M = \infty$) and η is linear combination of fixed regression and random components describing the characteristics of the subject being observed. The combination of risk variable values η , moves all thresholds $\theta - \eta$ up or down by the same amount. When the positive response is continuous, responses are grouped into intervals. Green (1984) showed that, even with very coarse grouping, the parameter estimates and their standard errors are close to those for ungrouped data. Note that if η includes a constant term, there is lack of identifiability of the θ parameters which may be solved by setting $\theta_0 = 0$.

If G(.) is the cumulative distribution function for the underlying unobservable variable U , then $P(Y \le y|\eta) = G(\theta_y - \eta)$ and examples of G(.) are given in chapter 5. Here, we use all four models of chapter 5 in which G(.) is taken to be standard normal, logistic, extreme minimal and extreme maximal distributions respectively. The estimation and inference by ML and REML methods are consistent within each of the four threshold models when applied to the study data.

For the methadone program, the regression variables consist of subject characteristics and the treatment program. However, in some cases subjects cohabit so that a further factor is a household effect which is included in the model as a random effect. Details of the program are given in section 6.2, while later sections are concerned with the method of analysis.

6.2 METHADONE PROGRAM

The Kirketon Road Centre (KRC) is a primary health care in Sydney, Australia. It was set up to service sex workers, drug users and at risk youth as part of a nationwide strategy to prevent the spread of human immunodeficiency virus (HIV). This methadone program is the first in Australia to be set up within a primary health program rather than as a separate clinic. A randomised control trial was carried out to evaluate the methadone maintainance program of the centre. In the trial 70 subjects were assigned randomly to one of two treatments, methadone and control. Subjects are interviewed at baseline and at three months, with a urine sample for drug toxicology collected at the same times. The interview collected information on demographic data, drug use, previous treatment experiences, use of KRC services and a number of structured questionnaires including the Opiate Treatment Index (Dark et al, 1992). Opiate Treatment Index (OTI) is a multi-dimensional instrument designed to assess outcome from treatments for opioid dependence. It measures drug use, HIV risk-taking behaviour, crime, drug related health problems, psychological functioning for the month prior to interview, and social functioning for the previous six months.

Included in the OTI is the 28 item version of the general health questionaire (GHQ). Life events were measured by the Life Experiences Survey (Goldberg et al, 1979).

Patients were questioned about their use of heroin, opioids other than heroin, alcohol, cocaine and benzodiazepines. Sixteen patients did not complete the study for various reasons and the data for the remainder are shown in Table 3 of appendix B. Of the sixteen drop-outs, four were from the methadone treatment group: one did not return for treatment after the initial interview, one was in prison and the fate of two remained unknown. Of twelve drop-outs from the control group, one died, three were in prison and the fate of eight remained unknown. Every attempt was made to locate each of the drop-outs. Since the response data were obtained at the follow-up interview, the drop-outs could not be included in the analysis. Originally 72 subjects were randomised with 89% of the treatment group and 66% of the control group completing valid follow-up interviews. However, two members of the study control group were excluded because they had been in prison for the whole of the follow-up period. The analysis is based on the original randomisation, the intention to treat, although 76% of the control group attended other methadone clinics during the study period. Covariables 2,3,4 in the list given below record methadone use from any clinic and hence the leakage of control to treatment is partially recorded in the covariables.

From the collected data, four response variables have been selected for separate analysis. Three of the variables are the average number of drug usages per day (injection or pill) for the three drugs heroin (H), cocaine (Co) and benzodiazepine (B) with the average taken over the month prior to interview. The average is denoted by S. For these three variables, the response is categorised with

6.2.1
$$Y = \begin{cases} 0 & \text{if} \quad S = 0 \\ 1 & \text{if} \quad 0 \le S < 1/7 \\ 2 & \text{if} \quad 1/7 \le S < 1 \\ 3 & \text{if} \quad S \ge 1 \end{cases} .$$

The fourth response variable is the number of crimes committed during the previous three months (Cr). This is a discrete response variable and is modelled directly, but with all values ≥ 5 grouped together in one category at $Y = 5$.

The treatment and covariables fitted in the model are described in semitabular form below.

Covariable	Description
1	Treatment group , 1 =treatment, 0=control
2	Number of weeks received methadone in follow-up period
3	Receiving methadone at time of follow-up interview, 0=no, 1=yes
4	Methadone dose at time of follow-up interview
5	Number of negative life events reported at follow-up interview
6	Number of positive life events reported at follow-up interview
7	GHQ total score at follow-up interview
8	OTI social score at follow-up interview
9	Age in years

10 Gender, 0=male, 1=female

11 Years of education

12 Number of years since first addicted to heroin

13 Age when first charged

14 Total months in prison before enrolled for study

The last two covariables (13 and 14) are used only when the response variable is the number of crimes committed (Cr). In this case, the three first response variables, self reported use of heroin (H), cocaine (Co), benzodiazepine (B) at the follow-up interview are also used as covariables. Note, the three covariables H, Co and B are used as they are observed not in the categorised form. They are coded in the Table 3 of appendix B as the first three variables. For all models there is a random household effect which is distributed independently for different households as $N(0,\varphi)$.

6.3 MODELS AND ESTIMATION

The response variable Y is now considered to be a discrete random variable, perhaps as a result of values being grouped into intervals as described in section 6.2, and is distributed according to the threshold mixed model

6.3.1 $$P(Y \le y) = G(\theta_y - \eta) \quad , \quad y = 0,1,\ldots,M$$

where η is a linear combination of risk variables and the random household component. Letting $\mathbf{X}$ be the matrix of risk variables and $\mathbf{u}$ the vector of household variables, then

6.3.2 $\eta = \mathbf{X}\beta + \mathbf{Z}\mathbf{u}$,

where β and $\mathbf{Z}$ are vector of regression coefficients and incidence matrix for vector of household variables respectively. Let θ be the vector of threshold parameters. The best linear unbiased predictor (BLUP) or penalised likelihood (PL) estimators of θ, β and $\mathbf{u}$ are obtained by maximising the sum of the log-likelihood of $\mathbf{y}$ conditional on given $\mathbf{u}$, denoted by l_1 , and the logarithm of the probability density function of $\mathbf{u}$, denoted by l_2 , where

6.3.3 $l_1 = \sum_{i=1}^{52} \ln[G(\theta_{y_i} - \eta_i) - G(\theta_{y_i - 1} - \eta_i)]$, and

6.3.4 $l_2 = -(1/2)[q\ln 2\pi\varphi + \varphi^{-1}\mathbf{u}'\mathbf{u}]$.

where 52 is the number of patients and q is the number of households (the dimension of random component vector $\mathbf{u}$). The resulting equations are iterative beginning with initial estimates θ_0, β_0 and $\mathbf{u}_0$ as well as φ_0 . Changes in estimates from one iteration to the next are $\Delta\theta$, $\Delta\beta$ and $\Delta\mathbf{u}$ are given by

6.3.5
$$\mathbf{V}\begin{bmatrix}\Delta\theta \\ \Delta\beta \\ \Delta\mathbf{u}\end{bmatrix} = \begin{bmatrix}\mathbf{I} & 0 \\ 0 & \mathbf{X}' \\ 0 & \mathbf{Z}'\end{bmatrix}\begin{bmatrix}\partial l_1/\partial\theta_0 \\ \partial l_1/\partial\eta_0\end{bmatrix} - \begin{bmatrix}0 \\ 0 \\ \varphi_0^{-1}\mathbf{u}_0\end{bmatrix},$$

where

6.3.6
$$\mathbf{V} = \begin{bmatrix}\mathbf{V}_{11} & \mathbf{V}_{12} & \mathbf{V}_{13} \\ \mathbf{V}_{21} & \mathbf{V}_{22} & \mathbf{V}_{23} \\ \mathbf{V}_{31} & \mathbf{V}_{32} & \mathbf{V}_{33}\end{bmatrix}$$

$$
= \begin{bmatrix} \mathbf{I} & 0 \\ 0 & \mathbf{X}' \\ 0 & \mathbf{Z}' \end{bmatrix} \begin{bmatrix} -\partial^2 l_1 / \partial\theta_0 \partial\theta' & -\partial^2 l_1 / \partial\theta_0 \partial\eta_0' \\ -\partial^2 l_1 / \partial\eta_0 \partial\theta_0' & -\partial^2 l_1 / \partial\eta_0 \partial\eta' \end{bmatrix} \begin{bmatrix} \mathbf{I} & 0 & 0 \\ 0 & \mathbf{X} & \mathbf{Z} \end{bmatrix} + \begin{bmatrix} 0 & 0 & 0 \\ 0 & 0 & 0 \\ 0 & 0 & \varphi_0^{-1}\mathbf{I} \end{bmatrix}
$$

and φ_0, $\partial l_1 / \partial\theta_0$, $\partial l_1 / \partial\eta_0$, $\partial^2 l_1 / \partial\theta_0 \partial\theta_0'$, $\partial^2 l_1 / \partial\theta_0 \partial\eta_0'$ and $\partial^2 l_1 / \partial\eta_0 \partial\eta_0'$ are the values of φ, $\partial l_1 / \partial\theta$, $\partial l_1 / \partial\eta$, $\partial^2 l_1 / \partial\theta \partial\theta'$, $\partial^2 l_1 / \partial\theta \partial\eta'$ and $\partial^2 l_1 / \partial\eta \partial\eta'$ corresponding to initial estimates of their components. Upon convergence, an approximation to the maximum likelihood (ML) estimate of φ is given by

6.3.7 $$\tilde{\varphi}_{(ML)} = [\tilde{\mathbf{u}}'\tilde{\mathbf{u}} + \mathrm{tr}\,\mathbf{V}_{33}^{-1}] / q \ .$$

A second tier of iterations on φ take the ML estimate as the new initial value for φ. At the converged value of φ say $\hat{\varphi}$, the asymptotic variance of the $\hat{\varphi}$ is

6.3.8 $$2\varphi^2[(q - 2\varphi^{-1}\mathrm{tr}\mathbf{V}_{33}^{-1}) + \varphi^{-2}\mathrm{tr}\mathbf{V}_{33}^{-1}\mathbf{V}_{33}^{-1}]^{-1}{}_{\varphi = \varphi(ML)} \ .$$

If

6.3.9 $$\mathbf{V}^{-1} = \begin{bmatrix} \mathbf{T}_{11} & \mathbf{T}_{12} & \mathbf{T}_{31} \\ \mathbf{T}_{21} & \mathbf{T}_{22} & \mathbf{T}_{23} \\ \mathbf{T}_{31} & \mathbf{T}_{32} & \mathbf{T}_{33} \end{bmatrix},$$

then replacement of $\mathbf{V}_{33}^{-1}$ by $\mathbf{T}_{33}$ in the equation 6.3.7 yields the REML estimate of the variance component in each iteration and using this value in the equation 6.3.5 yields REML estimates for threshold and fixed parameters (θ and β). The asymptotic variance of the REML estimate of the variance component φ is given by replacing $\mathbf{V}_{33}^{-1}$ by $\mathbf{T}_{33}$ in the equation 6.3.8 .

The necessary derivatives calculations for the estimation equations 6.3.5 are obtained by slightly modifications to the derivatives given in section 5.3 of chapter 5.

6.4 RESULTS

The results of fitting all regression variables to heroin, cocaine and benzodiazepine, are given in Tables 6.4a and 6.4b which give REML estimates of all parameters. Tables 6.4c and 6.4d provide corresponding ML estimates of parameters. The ML and REML estimates of the parameters are given in Tables 6.4e and 6.4f for number of crimes committed. Significance of the regression coefficients can be judged by using the asymptotic distribution of the estimators of regression coefficients. In each table, we provide z-value (ratio of estimate to its standard error) shown by z-v column. A z-v greater than 1.96 in absolute value, indicates that the corresponding regression coefficient contributes a significant variation to the data. It is important to realise that a positive coefficient for a regression variable in $\eta = \mathbf{X}\beta + \mathbf{u}$ means that η is increased for an increase in $\mathbf{X}$ component values, so that θ-η values are decreased and higher $\mathbf{Y}$ observations are likely. The results of the separate analyses of the four response variables (H, Co, B and Cr) can be summarised in the following discussion, where a significant result is declared if a two-tailed test would reject a null hypothesis of no effect at the 5% significance level. Roughly speaking, in terms of looking for significant regression coefficients, the same conclusion is obtained using any of four distributions (standard normal, logistic, extreme minimal and maximal) for G(.) function. To save repetition, we continue our discussion by using the REML result only applied to the standard normal distribution for the G(.) function (threshold model 1 of chapter 5).

Heroin (H) Use:

The treatment (methadone) is not a significant factor after allowing for all covariables. Significant covariables are gender (estimate=1.4, 95%CI 0.09,2.71) and years of education (estimate=0.53, 95%CI 0.20,0.86) with being female and longer education providing greater risk of noncompliance. More positive life events (estimate=-0.30, 95%CI -0.46,-0.14) also significantly support compliance with the program. Although the traditional relationships between heroin use and time spent on methadone treatment and on methadone dose are not statistically significant here, they are in the expected direction. Additionally there is a significant variance of the random household effect (estimate=2.12, 95%CI 0.20,4.40) indicating that the type of household is an important factor in compliance with the program. There is a possibility in future studies that these random household effects, which can be estimated, may be matched to household descriptors in an effort to delineate what is important in households occupied by cohabiting drug users.

Cocaine Use:

The treatment is again not a significant effect after allowing for covariables. The only significant covariable is OTI social score (estimate=0.09, 95%CI 0.01,0.17) at the follow-up interview. The positive coefficient indicates higher levels of social dysfunction associated with cocaine use. Again, as with heroin (H), the random household effect is a significant factor with variance estimated at 1.83 (95%CI 0.52,3.14).

Benzodiazepine Use:

In this case the only reported significant variable is the number of weeks receiving methadone in the follow-up period (estimate=-0.05, 95%CI -.09,-0.01). The coefficient is negative indicating less risk of benzodiazepine use for the more frequent methadone program participants.

The results also show that the difference between threshold parameters θ_1 and $\theta_0 = 0$ is not significant. Thus it might be an idea to combine categories 1 and 2 for this data.

Crime:

Again the treatment effect is not significant and the only significant covariable is the age at first charge (estimate=-0.06, 95%CI -0.10,-0.02). The older the person when first charged, the fewer the crimes likely to have been committed in the study period. Note that number of crimes does not have a significant relationship to drug use in this analysis. The variance of the random household effect (estimate=8.00, 95%CI 1.82,12.18) is quite significant indicating that the household formed by people (drug users) cohabiting is an important factor in committing crime.

An examination of the threshold parameters indicates that categories 2 and 3 can be combined to reduce number of category from 6 to 5.

Some other effects come close to 5% significance level but have not been commented on specially. In Tables 6.4a, 6.4b, 6.4c, 6.4d, 6.4e and 6.4f, estimates and standard errors with their ratio (z-v), give an effective idea of these factors.

In terms of comparing the performance of the four threshold models given in section 5.2 of chapter 5, we have obtained the value for the log conditional likelihood (l_1) at REML estimate points. These values are; -18.9, -19.7, -19.3, -20.1 for the H, -29.4, -30.9, -31.3, -27.7 for the Co, -23.7, -24.5, -26.1, -21.3 for the B, and -14.1, -14.9, -16.7, -13.6 for the Cr data with threshold models 1, 2, 3 and 4 in section 5.2 of chapter 5 respectively. The general indication is that the threshold model 4 in section 5.2 of chapter 5 (extreme maximal value distribution for the G(.)) may be the best of the four models apart possibly for heroin (h) use.

In conclusion a characteristic of the response variables for this study is the high proportion of zero responses. When the response is non-zero, observations of heroin (H), cocaine (Co) and benzodiazepine (B) use are distributed over a positive continuum of values while crime (Cr) takes only positive integer values. The high frequency of zeros makes standard modelling procedures difficult and often the model is separated into two parts - first a zero-nonzero record for which a logit model is often used and secondly a model for the remaining variation conditional on it being nonzero Manning et al (1987). The regression on underlying risk or explanatory variables is fitted separately in these two models and, if appropriate, significance levels combined subsequently.

The approach advocated in this chapter fits a unified regression model which has the additional feature that it can handle mixed models for clustered data in which these is dependence among observations within each cluster. Threshold models are surprisingly versatile in handling quite difficult data distributions. There is no inherent difficulty in handling missing data but observations in which the response variable is missing, as is the case here, can't contribute to the analysis.

Finally we have provided estimates of parameters, prediction of random components and their corresponding asymptotic variances by both ML and REML methods. Our conclusions are based on the results of the REML method that provides smaller bias than the ML method for estimating the parameters and variance components.

Table 6.4a: REML estimates of parameters in the threshold models fitted to heroin, cocaine and benzodiazepine use.
Est = Estimate, SE =Standard error and z-v = Est/SE.

Dis	Response Variable		HEROIN			COCAINE			BENZODIAZEPINE		
	Parameter		**Est**	SE	**z-v**	**Est**	SE	**z-v**	**Est**	SE	**z-v**
	Variance Component		2.12	0.99	2.14	1.82	0.82	2.24	1.77	0.99	1.78
ST	Threshold	θ_1	2.34	0.56	4.2	1.46	0.34	4.33	0.37	0.2	1.82
		θ_2	4.15	0.71	5.84	2.67	0.46	5.84	1.03	0.32	3.21
	Treatment group		0.41	0.74	0.55	1.18	0.68	1.74	-0.55	0.79	-0.7
	No. of weeks received methadone		-0.15	0.11	-1.33	0.04	0.1	0.41	-0.33	0.14	-2.48
	Recieving methadone at 3 months		0.15	1.39	0.1	-1.24	1.13	-1.09	0.93	1.41	0.66
	Methadone dose at 3 months		-0.02	0.01	-1.64	0.02	0.01	1.78	0.02	0.01	1.1
	Negative life events		0.15	0.08	1.92	-0.15	0.07	-1.94	0.12	0.08	1.48
	Positive life events		-0.3	0.08	-3.65	-0.1	0.07	-1.39	0.01	0.08	0.18
	GHQ total		-0.06	0.05	-1.17	0.07	0.05	1.35	0.01	0.05	0.13
	OTI social		0.03	0.05	0.64	0.09	0.04	2.02	-0.06	0.06	-0.98
	Age		-0.04	0.06	-0.66	0.02	0.06	0.32	-0.03	0.09	-0.32
	Gender		1.4	0.67	2.09	-0.04	0.58	-0.06	0.34	0.65	0.52
	Years of Education		0.53	0.17	3.19	-0.17	0.14	-1.17	0.12	0.2	0.57
	Years of addiction		0.09	0.09	1.02	-0.06	0.09	-0.73	0.08	0.11	0.7
Lo	Variance Component		5.39	2.53	2.14	4.37	1.98	2.21	4.41	2.48	1.78
	Threshold	θ_1	3.78	0.92	4.11	2.26	0.53	4.29	0.59	0.32	1.82
		θ_2	6.66	1.18	5.65	4.18	0.73	5.72	1.63	0.51	3.2
	Treatment group		0.65	1.18	0.56	1.84	1.08	1.71	-0.88	1.26	-0.7
	No. of weeks received methadone		-0.23	0.18	-1.33	0.06	0.16	0.4	-0.54	0.22	-2.46
	Recieving methadone at 3 months		0.22	2.21	0.1	-1.91	1.76	-1.08	1.52	2.26	0.68
	Methadone dose at 3 months		-0.03	0.02	-1.62	0.03	0.02	1.75	0.02	0.02	1.1
	Negative life events		0.25	0.13	1.92	-0.23	0.12	-1.95	0.19	0.13	1.46
	Positive life events		-0.47	0.13	-3.56	-0.16	0.12	-1.38	0.02	0.12	0.14
	GHQ total		-0.09	0.08	-1.16	0.11	0.08	1.33	0.01	0.09	0.14
	OTI social		0.05	0.07	0.64	0.14	0.07	1.98	-0.09	0.09	-0.98
	Age		-0.07	0.1	-0.66	0.03	0.1	0.36	-0.05	0.14	-0.34
	Gender		2.23	1.07	2.07	0.03	0.91	0.03	0.56	1.03	0.54
	Years of Education		0.85	0.27	3.14	-0.26	0.22	-1.18	0.19	0.32	0.59
	Years of addiction		0.15	0.14	1.03	-0.1	0.13	-0.75	0.13	0.18	0.74

* Dis=Distribution, ST= Standard Normal, Lo=Logistic, E= Extreme,

Mi= Minimal and Ma=Maximal.

Table 6.4b: REML estimates of parameters in the threshold models fitted to heroin, cocaine and benzodiazepine use .
Est = Estimate, SE =Standard error and z-v = Est/SE.

Dis	Response Variable		HEROIN			COCAINE			BENZODIAZEPINE		
	Parameter		Est	SE	z-v	Est	SE	z-v	Est	SE	z-v
	Variance Component		2.75	1.28	2.15	1.69	0.79	2.15	1.4	0.84	1.66
	Threshold	θ_1	2.77	0.7	3.98	1.47	0.34	4.35	0.34	0.19	1.82
		θ_2	4.74	0.86	5.54	2.65	0.45	5.84	0.94	0.29	3.22
	Treatment group		0.43	0.83	0.51	1.19	0.68	1.76	-0.41	0.72	-0.57
	No. of weeks received methadone		-0.17	0.13	-1.36	0.05	0.1	0.53	-0.29	0.13	-2.3
E	Recieving methadone at 3 months		0.19	1.56	0.12	-1.27	1.11	-1.15	0.71	1.31	0.54
Mi	Methadone dose at 3 months		-0.02	0.01	-1.66	0.02	0.01	1.67	0.01	0.01	1.1
	Negative life events		0.18	0.09	1.96	-0.15	0.08	-1.93	0.1	0.08	1.33
	Positive life events		-0.33	0.09	-3.46	-0.1	0.07	-1.4	0.01	0.07	0.21
	GHQ total		-0.06	0.06	-1.11	0.07	0.05	1.29	0.01	0.05	0.26
	OTI social		0.04	0.05	0.77	0.1	0.04	2.16	-0.05	0.05	-0.94
	Age		-0.04	0.08	-0.59	0.02	0.06	0.29	-0.02	0.08	-0.21
	Gender		1.55	0.77	2.01	0.08	0.6	0.13	0.3	0.61	0.49
	Years of Education		0.61	0.2	3.09	-0.15	0.14	-1.09	0.1	0.19	0.55
	Years of addiction		0.1	0.1	1	-0.06	0.08	-0.69	0.06	0.1	0.57
	Variance Component		2.32	1.09	2.12	3	1.27	2.37	3.53	1.81	1.95
	Threshold	θ_1	2.34	0.57	4.14	1.74	0.41	4.26	0.49	0.27	1.82
		θ_2	4.27	0.74	5.75	3.29	0.59	5.61	1.39	0.43	3.19
	Treatment group		0.43	0.78	0.55	1.4	0.86	1.64	-0.88	1.09	-0.81
	No. of weeks received methadone		-0.15	0.12	-1.27	0.04	0.12	0.33	-0.46	0.19	-2.44
	Recieving methadone at 3 months		0.13	1.48	0.09	-1.45	1.41	-1.02	1.37	1.95	0.7
	Methadone dose at 3 months		-0.02	0.01	-1.59	0.03	0.01	1.79	0.02	0.02	1.08
E	Negative life events		0.16	0.09	1.79	-0.18	0.09	-1.94	0.17	0.11	1.53
Ma	Positive life events		-0.31	0.09	-3.49	-0.13	0.09	-1.36	0.01	0.11	0.11
	GHQ total		-0.06	0.05	-1.18	0.09	0.07	1.32	0	0.08	0
	OTI social		0.02	0.05	0.51	0.1	0.05	1.8	-0.07	0.08	-0.94
	Age		-0.05	0.07	-0.71	0.03	0.08	0.43	-0.05	0.12	-0.4
	Gender		1.46	0.73	2.01	0.01	0.72	0.02	0.44	0.87	0.5
	Years of Education		0.54	0.18	3.07	-0.22	0.18	-1.25	0.16	0.28	0.58
	Years of addiction		0.1	0.09	1.03	-0.09	0.11	-0.83	0.12	0.15	0.81

* Dis=Distribution, ST= Standard Normal, Lo=Logistic, E= Extreme,

Mi= Minimal and Ma=Maximal.

Table 6.4c: ML estimates of parameters in the threshold models fitted to heroin, cocaine, benzodiazepine use and number of crimes commited.
Est = Estimate, SE =Standard Error and z-v = Est/SE.

Dis	Response Variable		HEROIN			COCAINE			BENZODIAZEPINE		
	Parameter		Est	SE	z-v	Est	SE	z-v	Est	SE	z-v
	Variance Component		0.24	0.31	0.76	0	0	1.57	0.05	0.14	0.34
ST	Threshold	θ_1	1.65	0.39	4.25	0.91	0.22	4.24	0.21	0.12	1.8
		θ_2	2.87	0.49	5.89	1.7	0.3	5.72	0.6	0.19	3.11
	Treatment group		0.41	0.46	0.87	0.87	0.41	2.14	-0.35	0.49	-0.7
	No. of weeks received methadone		-0.1	0.07	-1.39	0.05	0.06	0.76	-0.25	0.09	-2.89
	Recieving methadone at 3 months		-0.08	0.89	-0.09	-0.99	0.7	-1.4	0.7	0.9	0.78
	Methadone dose at 3 months		-0.01	0.01	-1.62	0.01	0.01	1.94	0.01	0.01	1.36
	Negative life events		0.08	0.05	1.52	-0.12	0.05	-2.56	0.06	0.05	1.12
	Positive life events		-0.23	0.05	-4.31	-0.09	0.05	-2.02	0	0.05	-0.03
	GHQ total		-0.03	0.04	-0.85	0.04	0.03	1.25	0.01	0.04	0.32
	OTI social		0.03	0.03	1.05	0.07	0.03	2.57	-0.04	0.04	-1.06
	Age		-0.05	0.04	-1.06	0.01	0.04	0.21	-0.03	0.06	-0.54
	Gender		1	0.47	2.15	0.16	0.37	0.44	0.44	0.43	1.02
	Years of Education		0.41	0.11	3.63	-0.11	0.09	-1.26	0.1	0.13	0.77
	Years of addiction		0.07	0.06	1.13	-0.04	0.05	-0.78	0.06	0.07	0.76
Lo	Variance Component		0.94	0.95	0.99	0	0	1.31	0.02	0.04	0.47
	Threshold	θ_1	2.85	0.69	4.11	1.54	0.38	4.08	0.35	0.2	1.78
		θ_2	4.91	0.88	5.57	2.88	0.54	5.37	1.01	0.33	3.02
	Treatment group		0.6	0.8	0.75	1.5	0.74	2.02	-0.59	0.84	-0.7
	No. of weeks received methadone		-0.17	0.12	-1.42	0.08	0.11	0.74	-0.4	0.14	-2.83
	Recieving methadone at 3 months		-0.11	1.5	-0.07	-1.69	1.18	-1.42	1.18	1.46	0.81
	Methadone dose at 3 months		-0.02	0.01	-1.65	0.02	0.01	1.85	0.02	0.01	1.33
	Negative life events		0.15	0.09	1.59	-0.2	0.08	-2.45	0.1	0.09	1.05
	Positive life events		-0.38	0.1	-3.9	-0.15	0.08	-1.96	-0.02	0.08	-0.28
	GHQ total		-0.06	0.06	-0.91	0.07	0.06	1.28	0.02	0.06	0.24
	OTI social		0.05	0.05	1.02	0.11	0.05	2.31	-0.06	0.06	-0.92
	Age		-0.08	0.08	-1	0.03	0.06	0.48	-0.06	0.1	-0.6
	Gender		1.66	0.81	2.05	0.34	0.62	0.55	0.81	0.72	1.13
	Years of Education		0.7	0.2	3.41	-0.21	0.15	-1.45	0.17	0.22	0.79
	Years of addiction		0.12	0.1	1.15	-0.1	0.09	-1.06	0.1	0.13	0.75

* Dis=Distribution, ST= Standard Normal, Lo=Logistic, E= Extreme,

Mi= Minimal and Ma=Maximal.

Table 6.4d: ML estimates of parameters in the threshold models fitted to heroin, cocaine, benzodiazepine use and number of crimes commited. Est = Estimate, SE =Standard Error and z-v = Est/SE.

Dis	Response Variable		HEROIN			COCAINE			BENZODIAZEPINE		
	Parameter		Est	SE	z-v	Est	SE	z-v	Est	SE	z-v
	Variance Component		0	0	1.05	0	0	0.98	0.01	0.01	0.71
E Mi	Threshold	θ_1	1.97	0.5	3.97	0.95	0.23	4.22	0.2	0.11	1.8
		θ_2	3.25	0.61	5.36	1.71	0.3	5.6	0.55	0.18	3.11
	Treatment group		0.31	0.53	0.6	0.81	0.41	1.97	-0.24	0.48	-0.51
	No. of weeks received methadone		-0.12	0.08	-1.62	0.07	0.06	1.08	-0.23	0.09	-2.6
	Recieving methadone at 3 months		-0.08	0.99	-0.08	-0.98	0.7	-1.4	0.5	0.91	0.55
	Methadone dose at 3 months		-0.01	0.01	-1.45	0.01	0.01	1.68	0.01	0.01	1.36
	Negative life events		0.09	0.06	1.44	-0.13	0.05	-2.54	0.05	0.05	0.93
	Positive life events		-0.24	0.06	-4.04	-0.11	0.05	-2.09	0.01	0.04	0.28
	GHQ total		-0.02	0.04	-0.6	0.05	0.03	1.47	0.02	0.04	0.55
	OTI social		0.06	0.04	1.6	0.08	0.03	2.83	-0.03	0.03	-0.98
	Age		-0.05	0.06	-0.94	0	0.04	-0.06	-0.02	0.05	-0.3
	Gender		0.85	0.51	1.67	0.24	0.41	0.59	0.35	0.43	0.8
	Years of Education		0.48	0.14	3.34	-0.08	0.09	-0.89	0.09	0.13	0.71
	Years of addiction		0.08	0.07	1.13	-0.01	0.05	-0.28	0.05	0.07	0.68
E Ma	Variance Component		0.31	0.34	0.9	0	0	1.62	0	0	2.7
	Threshold	θ_1	1.72	0.42	4.13	1.11	0.27	4.1	0.29	0.16	1.78
		θ_2	3.09	0.55	5.62	2.22	0.43	5.16	0.86	0.29	2.97
	Treatment group		0.57	0.52	1.09	1.08	0.5	2.15	-0.67	0.72	-0.94
	No. of weeks received methadone		-0.09	0.08	-1.13	0.02	0.08	0.27	-0.35	0.11	-3.18
	Recieving methadone at 3 months		-0.13	1.02	-0.12	-1.18	0.92	-1.28	1.14	1.16	0.98
	Methadone dose at 3 months		-0.02	0.01	-1.7	0.02	0.01	2.28	0.02	0.01	1.44
	Negative life events		0.08	0.06	1.33	-0.14	0.06	-2.18	0.1	0.08	1.29
	Positive life events		-0.27	0.07	-4.13	-0.11	0.06	-1.92	-0.02	0.07	-0.37
	GHQ total		-0.04	0.04	-0.94	0.04	0.05	0.92	0	0.05	0.01
	OTI social		0.02	0.03	0.75	0.07	0.03	2.18	-0.05	0.05	-1.05
	Age		-0.06	0.05	-1.23	0.03	0.05	0.49	-0.06	0.08	-0.76
	Gender		1.26	0.52	2.4	0.02	0.45	0.05	0.77	0.57	1.36
	Years of Education		0.44	0.12	3.57	-0.16	0.12	-1.37	0.14	0.17	0.8
	Years of addiction		0.07	0.06	1.14	-0.08	0.07	-1.11	0.09	0.11	0.83

* Dis=Distribution, ST= Standard Normal, Lo=Logistic, E= Extreme,

Mi= Minimal and Ma=Maximal.

Table 6.4e: ML and REML estimates of parameters in the threshold models fitted to number of crimes commited. Est = Estimate, SE =Standard error and z-v= Est/SE, Dist =distribution.

Dist	Response Variable		ML			REML		
	Parameter		Est	SE	z-v	Est	SE	z-v
Standard Normal	Variance Component		0	0	1.28	3.15	2.54	2.54
	Threshold	θ_1	1.19	0.29	4.08	2.58	0.63	4.11
		θ_2	1.36	0.3	4.47	3.13	0.7	4.47
		θ_3	1.78	0.34	5.21	4.36	0.84	5.11
		θ_4	2.71	0.48	5.59	6.56	1.15	5.7
	Treatment group		-0.87	0.47	-1.83	-1.03	1.29	-0.8
	No. of weeks received methadone		-0.2	0.09	-2.32	-0.42	0.25	-1.68
	Recieving methadone at 3 months		-1	0.89	-1.13	-1.52	2.46	-0.62
	Methadone dose at 3 months		0.03	0.01	2.23	0.04	0.03	1.48
	Negative life events		0.15	0.05	2.76	0.18	0.13	1.37
	Positive life events		-0.05	0.05	-0.87	-0.13	0.15	-0.92
	GHQ total		0.01	0.04	0.3	0.14	0.1	1.33
	OTI social		-0.07	0.04	-1.69	-0.09	0.11	-0.83
	Age		-0.02	0.06	-0.36	0.03	0.16	0.21
	Gender		0.55	0.48	1.16	1.93	1.11	1.74
	Years of Education		0.28	0.14	1.98	0.39	0.36	1.1
	Years of addiction		0	0.01	-0.29	-0.11	0.23	-0.5
	Age at the first charge		-0.03	0.01	-2.94	-0.06	0.02	-2.7
	Total months in prison		0.01	0.08	0.12	0	0.02	0.17
	Heroin at 3 months		0.34	0.17	2.08	0.57	0.47	1.21
	Cocaine at 3 months		0.49	0.24	2.04	1.12	0.66	1.68
	Bezodiazepine at 3 months		-0.16	0.09	-1.82	-0.38	0.26	-1.47
Logistic	Variance Component		0.67	0.91	0.74	20.9	8.36	2.5
	Threshold	θ_1	2.14	0.54	3.96	4.13	1.05	3.92
		θ_2	2.46	0.57	4.32	5	1.16	4.31
		θ_3	3.23	0.65	4.96	6.98	1.39	5.04
		θ_4	4.96	0.95	5.22	10.5	1.91	5.49
	Treatment group		-1.35	0.93	-1.46	-1.68	2.12	-0.79
	No. of weeks received methadone		-0.36	0.17	-2.15	-0.68	0.4	-1.68
	Recieving methadone at 3 months		-1.55	1.66	-0.94	-2.53	4.02	-0.63
	Methadone dose at 3 months		0.04	0.02	2.04	0.07	0.05	1.5
	Negative life events		0.26	0.1	2.51	0.28	0.21	1.35
	Positive life events		-0.1	0.11	-0.91	-0.22	0.24	-0.94
	GHQ total		0.02	0.08	0.31	0.22	0.17	1.31
	OTI social		-0.11	0.07	-1.46	-0.15	0.18	-0.83
	Age		-0.04	0.12	-0.32	0.05	0.26	0.18
	Gender		0.97	0.89	1.08	3.12	1.8	1.74
	Years of Education		0.47	0.27	1.71	0.66	0.59	1.12
	Years of addiction		0	0.02	-0.27	0.01	0.04	0.14
	Age at the first charge		-0.05	0.02	-2.8	-0.1	0.04	-2.68
	Total months in prison		0.02	0.18	0.14	-0.18	0.37	-0.49
	Heroin at 3 months		0.62	0.3	2.05	0.93	0.77	1.21
	Cocaine at 3 months		0.87	0.45	1.92	1.78	1.08	1.65
	Bezodiazepine at 3 months		-0.28	0.16	-1.72	-0.61	0.42	-1.46

Table 6.4f: ML and REML estimates of parameters in the threshold models fitted to number of crimes commited. Est = Estimate, SE =Standard error and z-v = Est/SE, Dist =distribution.

Dist	Response Variable		ML			REML		
	Parameter		Est	SE	z-v	Est	SE	z-v
Extreme Minimal	Variance Component		0	0	4.23	6.92	.65	2.54
		θ_1	1.31	0.33	3.97	2.64	0.65	4.08
	Threshold	θ_2	1.5	0.34	4.34	3.16	0.71	4.46
		θ_3	1.97	0.4	4.96	4.29	0.82	5.21
		θ_4	2.96	0.56	5.31	6.26	1.06	5.89
	Treatment group		-1.27	0.55	-2.32	-0.93	1.19	-0.79
	No. of weeks received methadone		-0.21	0.09	-2.22	-0.4	0.23	-1.71
	Recieving methadone at 3 months		-1.29	0.83	-1.55	-1.46	2.3	-0.63
	Methadone dose at 3 months		0.03	0.01	2.4	0.04	0.03	1.5
	Negative life events		0.18	0.07	2.59	0.17	0.12	1.38
	Positive life events		-0.03	0.06	-0.51	-0.12	0.14	-0.88
	GHQ total		-0.01	0.05	-0.13	0.13	0.1	1.37
	OTI social		-0.08	0.05	-1.46	-0.09	0.1	-0.83
	Age		0	0.06	0.03	0.05	0.15	0.32
	Gender		0.65	0.54	1.22	1.78	1.06	1.68
	Years of Education		0.36	0.16	2.25	0.36	0.33	1.09
	Years of addiction		-0.01	0.01	-0.67	-0.12	0.21	-0.56
	Age at the first charge		-0.04	0.01	-3.12	-0.06	0.02	-2.69
	Total months in prison		-0.02	0.08	-0.23	0	0.02	0.17
	Heroin at 3 months		0.35	0.18	1.95	0.56	0.45	1.24
	Cocaine at 3 months		0.49	0.24	2.01	1.06	0.64	1.68
	Bezodiazepine at 3 months		-0.15	0.09	-1.64	-0.36	0.24	-1.48
Extreme Maximal	Variance Component		0	0	4.11	11.7	4.72	2.53
		θ_1	1.57	0.41	3.85	2.82	0.71	3.95
	Threshold	θ_2	1.82	0.44	4.16	3.47	0.8	4.32
		θ_3	2.42	0.52	4.7	4.98	1	5
		θ_4	3.83	0.79	4.85	7.75	1.46	5.32
	Treatment group		-0.83	0.63	-1.32	-1.3	1.6	-0.81
	No. of weeks received methadone		-0.31	0.13	-2.39	-0.5	0.3	-1.67
	Recieving methadone at 3 months		-0.59	1.27	-0.46	-1.9	3.01	-0.63
	Methadone dose at 3 months		0.03	0.01	2.06	0.05	0.04	1.51
	Negative life events		0.2	0.07	2.89	0.22	0.16	1.38
	Positive life events		-0.08	0.08	-1.02	-0.17	0.18	-0.94
	GHQ total		0.02	0.05	0.39	0.15	0.13	1.2
	OTI social		-0.09	0.04	-2.07	-0.12	0.14	-0.86
	Age		-0.08	0.09	-0.94	0.02	0.2	0.09
	Gender		0.48	0.58	0.83	2.32	1.33	1.74
	Years of Education		0.36	0.2	1.78	0.5	0.45	1.12
	Years of addiction		0	0.01	-0.16	-0.12	0.28	-0.43
	Age at the first charge		-0.03	0.01	-2.54	-0.08	0.03	-2.76
	Total months in prison		0.08	0.14	0.61	0	0.03	0.13
	Heroin at 3 months		0.61	0.22	2.81	0.68	0.57	1.2
	Cocaine at 3 months		0.77	0.36	2.12	1.31	0.79	1.66
	Bezodiazepine at 3 months		-0.24	0.12	-2.02	-0.45	0.31	-1.45

CHAPTER SEVEN

LONGITUDINAL THRESHOLD MODELS WITH RANDOM COMPONENTS

7.1 INTRODUCTION

Chapter 5 has introduced four threshold mixed models. It also provided estimation equations for the parameters, standard errors and an estimate of the variance component. Chapter 6 has demonstrated the capacity of threshold mixed models to deal with very interesting data types, including data for which the frequency of a zero response is large and also data for which the distribution of the discrete response is not well known. In this chapter we develop threshold mixed models for longitudinal ordinal data.

In longitudinal studies the same variables are observed at several time points for each subject of the study. The object of such studies is to relate a response variable to a vector of regression or explanatory variables and observe how that relationship changes over time. When the response variables are Gaussian, there are existing methods of analysis which may be applied, but fewer methods have been developed for categorical or ordinal discrete responses. The purpose of this chapter is to propose a general method of analysis for longitudinal ordered response variables with correlations between observations on the same subject. The next two sections outline the models considered and the estimation procedure. In the following section, we introduce different structures for the linear predictor η. In a later section after, a goodness of fit for the threshold model is given by using discriminant analysis. The last sections apply the method to a skin treatment study of Standish, Gillings and Koch (1978), to data reported in Koch et al (1990 and 1992).

7.2 MODELS AND NOTATION

Typically in a longitudinal study, the data set consists of an outcome variable measured at different time points for each individual. This chapter is concerned specially with ordinal outcomes in which the observation Y_{it} for subject i at time t is an ordinal variable and can take on values denoted by $0, 1, ...,M$. The distribution of Y_{it} depends on linear predictor

7.2.1 $$\eta_{it} = \mathbf{x}'_{it}\beta + \mathbf{z}'_{it}\mathbf{u}_i$$

where $\mathbf{x}_{it}$ is a vector of p known regression variables with fixed regression coefficient β and $\mathbf{z}_{it}$ is an incidence vector for the random component vector $\mathbf{u}_i$. The cumulative distribution function for Y_{it} conditional on $\mathbf{u}_i$, for a *time independent longitudinal threshold model*, may be modelled by

7.2.2 $$P(Y_{it} \le y_{it}) = G(\theta_{y_{it}} - \eta_{it})$$

where $G(.)$ is a cumulative distribution function, y_{it} is the observed value for Y_{it} and $\theta_{y_{it}}$ are break point parameters which are increased or decreased by η_{it} depending on the values of regression variables and the random components. Four different cumulative distributions for the $G(.)$

are given in section 5.2 of chapter 5 . We use all four distributions for G(.) in this chapter again.

A *time independent longitudinal threshold model* is defined above in which the break points $\theta_{y_{it}}$ remain constant over time. This model contrasts with a *time dependent longitudinal threshold model*,

$$P(Y_{it} \le y_{it}) = G(\theta_{y_{it}}(t) - \eta_{it}) \tag{7.2.3}$$

where the break points $\theta(t)_{y_{it}}$ depend on the time at which the response is observed. The parameter θ_{-1} is always taken as $-\infty$ so that $G(\theta_{-1} - \eta_{it})$ is always zero while θ_M is taken to be $+\infty$ indicating that $G(\theta_M - \eta_{it})$ is always 1. Additionally η usually contains a constant term so that there is a lack of identifiability arising from the notion that any quantity added to all θ values can be subtracted by similarly adding it to the constant term of the η values. This lack of identifiability is removed by setting θ_0=0. Thus for the time independent model there are M-2 unknown θ parameters, while for the time dependent model with n times, there are n(M-2) different θ parameters. These parameters are collected into a vector $\boldsymbol{\theta}$.

When the observations Y_{it} are collected into a vector $\mathbf{y}$ and the η_{it} into a vector η where $\mathbf{y} = [Y_{it}, i = 1, 2, ..., N, t = 1, 2, ..., n_i]'$, $\eta = [\eta_{it}, i = 1, 2, ..., N, t = 1, 2, ..., n_i]'$ then $\eta = \mathbf{X}\beta + \mathbf{Zu}$ where matrices $\mathbf{X}$, $\mathbf{Z}$ have rows made up of $\mathbf{x}'_{it}$, $\mathbf{z}'_{it}$ respectively. The vector $\mathbf{u}$ may be partitioned into $\mathbf{u}' = [\mathbf{u}'_1, \mathbf{u}'_2, ..., \mathbf{u}'_q]$ such that the $\mathbf{u}_j$ are mutually independent. Let $\mathbf{Z} = [\mathbf{Z}_1, \mathbf{Z}_2, ..., \mathbf{Z}_q]$ be a conformal partition of the $\mathbf{Z}$

matrix. The random components vectors $\mathbf{u}_j$ are taken to be distributed as $N(0, \varphi_j \mathbf{I})$. By letting $\mathbf{A}(\varphi) = \text{diag}[\varphi_1 \mathbf{I}, \varphi_1 \mathbf{I}, \ldots, \varphi_q \mathbf{I}]$ we have $\mathbf{u}$ distributed as $N[0, \mathbf{A}(\varphi)]$.

7.3 ESTIMATION

The maximum likelihood (ML) and residual maximum likelihood (REML) estimation equations for the parameters in threshold mixed models are given in previous sections. The method essentially uses BLUP (or PL) estimators of the fixed parameters $\boldsymbol{\theta}$, $\boldsymbol{\beta}$ and the realisations of the random components $\mathbf{u}$ as an initial step in the computation of approximate ML and REML estimators. Specially, if l_1 is the log-likelihood of $\mathbf{y}$ conditional on fixed $\mathbf{u}$ and l_2 is the logarithm of the probability density function of $\mathbf{u}$, then BLUP (or PL) estimators $\tilde{\boldsymbol{\theta}}$, $\tilde{\boldsymbol{\beta}}$, $\tilde{\mathbf{u}}$ maximise $l_1 + l_2$. This is achieved using a Newton-Raphson iterative technique starting with the initial values $\boldsymbol{\theta}_0$, $\boldsymbol{\beta}_0$, $\mathbf{u}_0$ and $\mathbf{A}_0 = \mathbf{A}(\varphi_0)$ with φ_0 being initial value of the vector parameter φ. Successive iterations are obtained by finding changes $\Delta\tilde{\boldsymbol{\theta}}$, $\Delta\tilde{\boldsymbol{\beta}}$, $\Delta\tilde{\mathbf{u}}$ to the current estimates from the equations,

7.3.1
$$\mathbf{V}\begin{bmatrix} \Delta\tilde{\boldsymbol{\theta}} \\ \Delta\tilde{\boldsymbol{\beta}} \\ \Delta\tilde{\mathbf{u}} \end{bmatrix} = \begin{bmatrix} \mathbf{I} & 0 \\ 0 & \mathbf{X}' \\ 0 & \mathbf{Z}' \end{bmatrix} \begin{bmatrix} \partial l_1 / \partial \boldsymbol{\theta}_0 \\ \partial l_1 / \partial \boldsymbol{\eta}_0 \end{bmatrix} - \begin{bmatrix} 0 \\ 0 \\ \mathbf{A}_0^{-1}\mathbf{u}_0 \end{bmatrix}$$

where

7.3.2
$$\mathbf{V} = \begin{bmatrix} \mathbf{V}_{11} & \mathbf{V}_{12} & \mathbf{V}_{13} \\ \mathbf{V}_{21} & \mathbf{V}_{22} & \mathbf{V}_{23} \\ \mathbf{V}_{31} & \mathbf{V}_{32} & \mathbf{V}_{33} \end{bmatrix}$$
$$= \begin{bmatrix} \mathbf{I} & 0 \\ 0 & \mathbf{X}' \\ 0 & \mathbf{Z}' \end{bmatrix} \begin{bmatrix} -\partial^2 l_1 / \partial \boldsymbol{\theta}_0 \partial \boldsymbol{\theta}' & -\partial^2 l_1 / \partial \boldsymbol{\theta}_0 \partial \boldsymbol{\eta}_0' \\ -\partial^2 l_1 / \partial \boldsymbol{\eta}_0 \partial \boldsymbol{\theta}_0' & -\partial^2 l_1 / \partial \boldsymbol{\eta}_0 \partial \boldsymbol{\eta}' \end{bmatrix} \begin{bmatrix} \mathbf{I} & 0 & 0 \\ 0 & \mathbf{X} & \mathbf{Z} \end{bmatrix} + \begin{bmatrix} 0 & 0 & 0 \\ 0 & 0 & 0 \\ 0 & 0 & \mathbf{A}_0^{-1} \end{bmatrix}$$

and $\mathbf{A}_0$, $\partial l_1/\partial\theta_0$, $\partial l_1/\partial\eta_0$, $\partial^2 l_1/\partial\theta_0\partial\theta_0'$, $\partial^2 l_1/\partial\theta_0\partial\eta_0$ and $\partial^2 l_1/\partial\eta_0\partial\eta_0'$ are values of the $\mathbf{A}$, $\partial l_1/\partial\theta$, $\partial l_1/\partial\eta$, $\partial^2 l_1/\partial\theta\partial\theta'$, $\partial^2 l_1/\partial\theta\partial\eta$ and $\partial^2 l_1/\partial\eta\partial\eta'$ corresponding to initial estimates of their components.

After convergence

7.3.3 $$\hat{\varphi}_{j(ML)} = [\tilde{\mathbf{u}}_j'\tilde{\mathbf{u}}_j + \operatorname{tr}\mathbf{T}_{jj}^*]/v_j$$

where $\mathbf{T}^* = [\mathbf{T}_{ij}^*] = \mathbf{V}_{33}^{-1}$ and $\mathbf{T}_{ij}^*$ is the i,j block in the partition of the $\mathbf{T}^*$ conformally to the partition of u into $\mathbf{u}_1$, $\mathbf{u}_2,\ldots,\mathbf{u}_q$. After replacing φ_0 with $\hat{\varphi}_{(ML)}$ as the new initial value for φ, the whole process is iterated again from this new initial value. Eventually convergence is obtained for $\hat{\varphi}_{(ML)}$ and the BLUP (or PL) estimates of θ, β are then the ML estimates $\hat{\theta}_{(ML)}$, $\hat{\beta}_{(ML)}$ which have an approximate variance matrix given by

7.3.4 $$\operatorname{Var}\begin{bmatrix}\hat{\theta}\\ \hat{\beta}\end{bmatrix} \cong \Omega \quad \text{where}$$

7.3.5 $$\mathbf{V}^{-1} = \begin{bmatrix}\mathbf{V}_{12} & \mathbf{V}_{11} & \mathbf{V}_{13}\\ \mathbf{V}_{21} & \mathbf{V}_{22} & \mathbf{V}_{23}\\ \mathbf{V}_{31} & \mathbf{V}_{32} & \mathbf{V}_{33}\end{bmatrix}^{-1} = \left[\begin{array}{cc|c} . & . & .\\ . & . & .\\ \hline . & . & .\end{array}\right] = \begin{bmatrix}\Omega & .\\ . & \mathbf{T}\end{bmatrix}.$$

The approximate variance matrix for $\hat{\varphi}_{(ML)}$ is

7.3.5 $$2[\varphi_i^{-2}(v_i - 2\varphi_i^{-1}\operatorname{tr}\mathbf{T}_{ii}^*)\delta_{ij} + \varphi_i^{-2}\varphi_j^{-2}\operatorname{tr}\mathbf{T}_{ij}^*\mathbf{T}_{ji}^*]^{-1}_{\varphi_i=\varphi_{i(ML)},\,\varphi_j=\varphi_{j(ML)}}$$

where the term in square brackets is the i,j term corresponding to $\hat{\varphi}_i$, $\hat{\varphi}_j$. The REML estimators of φ are obtained by replacing all $\mathbf{T}^*$ terms with $\mathbf{T}$ terms. Corresponding estimators of θ, β which are obtained are then REML estimators and all approximate variance matrices are similarly obtained by replacing $\mathbf{T}^*$ terms with $\mathbf{T}$ terms.

Implementation of the above procedure depends on an expression for l_1 in terms of η and its first and second derivatives with respect to η and θ. Let $g(.) = G'(.)$. For the time independent longitudinal model, we define

7.3.6 $\quad \Delta_{it} = G(\theta_{y_{it}} - \eta_{it}) - G(\theta_{y_{it}-1} - \eta_{it})$,

7.3.7 $\quad \nabla_{it} = g(\theta_{y_{it}} - \eta_{it}) - g(\theta_{y_{it}-1} - \eta_{it})$

and for the time dependent model, $\theta_{y_{it}}$, $\theta_{y_{it}-1}$ are replaced by $\theta_{y_{it}}(t)$, $\theta_{y_{it}-1}(t)$ in the expressions 7.3.6 and 7.3.7 . To allow for possible missing observations, we define $d_{it} = 1$ if observation at t for subject i is present and $d_{it} = 0$ if missing. With this notation, the conditional log-likelihood of the observations given the random components $\mathbf{u}$ is

7.3.8 $\quad l_1 = \sum_{i=1}^{N} \sum_{t=1}^{n_i} d_{it} \ln \Delta_{it}$.

First and second order derivatives of l_1 with respect to the parameters may be written using the notation

7.3.9 $\quad w_{kit} = \delta_{k,y_{it}} g(\theta_{y_{it}} - \eta_{it}) - \delta_{k,y_{it}-1} g(\theta_{y_{it}-1} - \eta_{it})$,

7.310 $\quad w^*_{kit} = \delta_{k,y_{it}} g'(\theta_{y_{it}} - \eta_{it}) - \delta_{k,y_{it}-1} g'(\theta_{y_{it}-1} - \eta_{it})$

where g' denotes differentiation with respect to the argument and δ_{ij} is the usual Kronecker delta. For the time dependent longitudinal model, θ terms are replaced by $\theta(t)$ terms as indicated above. Thus

7.3.11 $\quad \partial l_1 / \partial \eta_{it} = -d_{it} \Delta_{it}^{-1} \nabla_{it}$

7.312 $\quad \partial l_1 / \partial \theta_k = \sum_{i=1}^{N} \sum_{t=1}^{n_i} d_{it} \Delta_{it}^{-1} w_{kit}$

7.3.13 $\quad \partial l_1 / \partial \theta_k(t) = \sum_{i=1}^{N} d_{it} \Delta_{it}^{-1} w_{kit}$

7.3.14

$$\partial^2 l_1 / \partial \eta_{it} \partial \eta_{i't'} = \begin{cases} -d_{it} \{\Delta_{it}^{-2} \nabla_{it}^2 - \Delta_{it}^{-1}[g'(\theta_{y_{it}} - \eta_{it}) - g'(\theta_{y_{it}-1} - \eta_{it})]\} & i = i',\ t = t' \\ 0 & i \neq i',\ t \neq t' \end{cases}$$

7.3.15 $\quad \partial^2 l_1 / \partial \eta_{it} \partial \theta_k = d_{it} [-\Delta_{it}^{-1} w_{kit}^{*} + \nabla_{it} \Delta_{it}^{-2} w_{kit}] = \partial^2 l_1 / \partial \eta_{it} \partial \theta_k(t)$

7.3.16 $\quad \partial^2 l_1 / \partial \theta_k \partial \theta_{k'} =$

$$\begin{cases} \sum_{i=1}^{N} \sum_{t=1}^{n_i} d_{it} [\Delta_{it}^{-1} w_{kk}^{*} - \Delta_{it}^{-2} (\delta_{k,y_{it}} g^2(\theta_{y_{it}} - \eta_{it}) - \delta_{k,y_{it}-1} g^2(\theta_{y_{it}-1} - \eta_{it}))] & \text{for } k = k' \\ \sum_{i=1}^{N} \sum_{t=1}^{n_i} d_{it} \delta_{k,y_{it}} \Delta_{it}^{-2} g(\theta_{y_{it}} - \eta_{it}) g(\theta_{y_{it}-1} - \eta_{it})] & \text{for } k = k'+1 \\ \sum_{i=1}^{N} \sum_{t=1}^{n_i} d_{it} \delta_{k,y_{it}-1} \Delta_{it}^{-2} g(\theta_{y_{it}} - \eta_{it}) g(\theta_{y_{it}-1} - \eta_{it})] & \text{for } k = k'-1 \\ 0 & \text{else} \end{cases}$$

7.3.17 $\quad \partial^2 l_1 / \partial \theta_k(t) \partial \theta_{k'}(t) =$

$$\begin{cases} \sum_{i=1}^{N} d_{it} [\Delta_{it}^{-1} w_{kk}^{*} - \Delta_{it}^{-2} (\delta_{y_{it}} g^2(\theta_{k,y_{it}} - \eta_{it}) - \delta_{k,y_{it}-1} g^2(\theta_{y_{it}-1} - \eta_{it}))] & \text{for } k = k' \\ \sum_{i=1}^{N} d_{it} \delta_{k,y_{it}} \Delta_{it}^{-2} g(\theta_{y_{it}} - \eta_{it}) g(\theta_{y_{it}-1} - \eta_{it})] & \text{for } k = k'+1 \\ \sum_{i=1}^{N} d_{it} \delta_{k,y_{it}-1} \Delta_{it}^{-2} g(\theta_{y_{it}} - \eta_{it}) g(\theta_{y_{it}-1} - \eta_{it})] & \text{for } k = k'-1 \\ 0 & \text{else} \end{cases}$$

7.4 DIFFERENT MODELS FOR η

The longitudinal response models for Y_{it} are given in section 7.2 with expressions 7.2.2 and 7.2.3 for the time independent and time dependent longitudinal models respectively. The term η_{it} depends on the risk variables and on random components which describe the dependence of observations on the same patient. In the applications which follow the main focus is on treatment as the risk variable and develop 6 different models for η.

Model 1: $\quad \eta_{it} = \beta_0 + \beta_t(\text{treat}_i) + u_i$, t=1,2,...,n where risk variable is treatment (treat_i, $1 = \text{active}$, $0 = \text{placebo}$). The u_i are independent subject effects distributed as $N(0, \varphi_1)$.

Model 2: $\eta_{it} = \beta_0 + \beta_t(\text{treat}_i) + u_{1i} + z_t u_{2i}$

where u_{1i}, u_{2i} are independent normal variables with zero mean and variances φ_1, φ_2 respectively and z_t =0, t=1 ; z_t=1, t=2,3,...n. The term u_{2i} allows a possible increase in variance and pattern of association in the second and following times periods consistent with the idea that any individual departures from the model in the first time period are likely to be carried over into subsequent time periods and be augmented by further errors.

These first two models do not contain any risk variables except the treatment effect. The next model does include further individual characteristic (risk variables) into model 2 as fixed effects. This involves modelling random variables u_{1i} and u_{2i} in terms of individual characteristics, eg, age, gender. Let $\mathbf{x}_{2i}$ be a vector of risk variables for individual characteristics and vectors α_1 and α_2 consist of the parameters corresponding to $\mathbf{x}_{2i}$ at baseline and follow-up time. Then the regression models for the two component u_{1i} and u_{2i} are given by

7.4.1 $u_{1i} = \mathbf{x}'_{2i}\alpha_1 + b_{1i}$

7.4.2 $u_{2i} = \mathbf{x}'_{2i}\alpha_2 + b_{2i}$

where b_{1i}, b_{2i} are independent normal variables with mean zero and variances φ_1, φ_2 respectively. Replacing expressions 7.4.1 and 7.4.2 in the model 2 induces model 3 as

Model 3: $\eta_{it} = \beta_0 + \beta_t(\text{treat}_i) + \mathbf{x}'_{2i}\alpha_1 + z_t\mathbf{x}'_{2i}\alpha_2 + b_{1i} + z_t b_{2i}$.

Models 4, 5 and **6** are the corresponding models to 1, 2, and 3 but replace the fixed break point by time varying break point (threshold parameter).

7.5 GOODNESS OF FITS

The models may also be used to predict ordinal response observations by using estimates of the parameters and random components, thereby extending the work of Anderson and Philips (1981) and Albert and Anderson (1981) to include random effects in the linear predictor η. The estimators of fixed parameters and the predictors of the random components in each model, allow a predicted value for the linear predictor η_{it} say $\hat{\eta}_{it}$ for subject i at time t and a predicted profile over time, denoted by Y_{it} . For time independent and dependent longitudinal threshold models, we have

7.5.1 $\hat{\theta}_{y_{it}-1} < \hat{\eta}_{it} \le \hat{\theta}_{y_{it}} \Leftrightarrow \hat{Y}_{it} = y_{it}$

7.5.2 $\hat{\theta}_{y_{it}-1}(t) < \hat{\eta}_{it} \le \hat{\theta}_{y_{it}}(t) \Leftrightarrow \hat{Y}_{it} = y_{it}$

respectively. Such predicted values may be compared to the actual observed values and give some idea of the performance of different threshold models of section 5.2 in chapter 5 for the different structures of the linear predictor η. A comparison of the frequency distributions of observed and predicted values in active treatment and placebo groups at each of the follow-up observation times is also provided. In this and following chapters, we use this technique to give some idea of the application of different threshold models for different structures of the η. Note that the results are only given for the final (preferred) models.

7.6 APPLICATION TO STUDY OF SKIN CONDITION DATA

The preceding theory and models are applied to the results of a multicentre clinical trial which test the efficacy and safety of a new treatment of a skin condition. Details of the trial are given in Standish et al (1978). In all 172 subjects were randomly allocated to either a treatment or a placebo. Initially each patient was examined to determine severity of skin condition and then, at each of three follow-up visits, patients were evaluated as

1 = rapidly improving; 2 = slowly improving; 3 = stable

4 = slowly worsening; 5 = rapidly worsening.

These are ordinal responses and Y_{it} is the response for patient i at time t. The results are reprinted in Table 4 in appendix B.

Patient and treatment effects are used in model 1. A second component is added to account for changes of patient effect over time in the model 2. Model 3 is created by including initial stages of disease and clinic effect. Thus all 6 models of section 7.4 are applicable for this data.

Tables 7.6.i and 7.6.ij provide ML and REML estimates of the parameters, standard errors and the ratio of estimates to their standard errors (z-value) for the models 1, 2, 3, 4, 5 and 6. In tabling, the i represents model and the j shows further results for the model i. For example, Table 7.6.1 provides results for the model 1, Table 7.6.6j (j=a, b, c, d) give results for the model 6. The estimate of treatment effect is obtained by using the asymptotic distribution of $\hat{\beta}_t$ (t=1,2,3). Table 7.6 gives the results for all 6 models.

Model 1:

From Table 7.6a, the estimate of treatment effect is negative and highly significant. It is indicating that the treatment improves the skin condition. In addition, this improvement appears more clearly across time. We also use the asymptotic distribution of $\hat{\beta}_t$ (t=1,2,3) to build pairwise contrasts. The results show that there are significant differences between treatment at time 1-2 and 1-3. The difference between treatment at times 2 and 3 appears significant for threshold models 2 and 4 of chapter 5, whereas it does not significant for the threshold models 1 and 3 of chapter 5.

Model 2:

Firstly we note that the estimate of φ_2 is always close to zero, whereas the estimate of φ_1 is large compared to its standard error. Thus there is a substantial patient effect but there is no evidence that this patient effect changes over time. The results for the treatment effect are the same as in the model 1.

Model 3:

The initial skin condition (γ) has not a statistically significant effects. The clinic effects α_1 also are not statistically significant. The clinic effects α_2 are found to be barely ever significant indicating that there is initially only limited variation among clinics.

Models 4:

Although the break points (threshold parameters) are lower for the third time period, an examination of the estimates of the breakpoints $\theta_y(t)$ indicates that the break points (threshold parameters) do not seem to vary over time. The results support the conclusion in the previous models for the treatment effect. Moreover, the pairwise contrasts show that there are significant changes between treatment effect at times 1-2, 1-3 and 2-3 for all four threshold models of chapter 5.

Models 5 and **6:**

In terms of treatment effect and threshold parameters, the results support the conclusions in the model 4 for both models 5 and 6. As in model 2, the results of model 5 indicate a significant variation among patients with no significant changes of patient effect over time.

The results of the model 6 do not indicate significant changes from the model 3 for the clinic effect (α) and initial skin condition (γ).

From the above results, model 1, which includes patients random effect in addition to the fixed treatment effect, is an appropriate model for summarising the results of the experiment. Using the developed technique in section 7.5, application of this model 1 provides a predicted value the same as observed in 84%, 84.65%, 83.73%, 83.73% by ML and 84.16%, 84.65%, 83.73%, 83.73% by REML methods for the threshold models of chapter 5 (using standard normal, logistic, extreme minimal and maximal value distributions for the G function) respectively.

Table 7.6b provides frequency distributions of observed and predicted values in active treatment and placebo groups at each observations times for the threshold models listed in chapter 5.

Table 7.6.1: **ML** and **REML** estimates of parameters, standard errors and their ratio for the model 1.

		ML			REML		
		Est	SE	Z-v	Est	SE	Z-v
Standard Normal	φ	3.358	0.434	7.742	3.473	0.45	7.714
	θ_1	1.95	0.157	12.424	1.965	0.158	12.415
	θ_2	3.889	0.217	17.912	3.921	0.219	17.879
	θ_3	6.38	0.308	20.738	6.427	0.31	20.701
	β_0	3.573	0.277	12.878	3.602	0.281	12.815
	β_1	-2.308	0.336	-6.872	-2.326	0.34	-6.835
	β_2	-3.172	0.355	-8.946	-3.196	0.359	-8.899
	β_3	-3.616	0.364	-9.94	-3.644	0.368	-9.891
Logistic	φ	9.065	1.173	7.73	9.407	1.221	7.703
	θ_1	3.181	0.264	12.061	3.21	0.266	12.045
	θ_2	6.37	0.368	17.331	6.432	0.372	17.289
	θ_3	10.554	0.537	19.639	10.645	0.543	19.599
	β_0	5.864	0.463	12.656	5.92	0.47	12.592
	β_1	-3.787	0.555	-6.829	-3.822	0.563	-6.791
	β_2	-5.173	0.586	-8.826	-5.221	0.595	-8.781
	β_3	-5.948	0.607	-9.799	-6.004	0.616	-9.753
Extreme Minimal	φ	3.899	0.498	7.821	4.055	0.521	7.79
	θ_1	2.075	0.171	12.151	2.094	0.173	12.131
	θ_2	4.202	0.243	17.258	4.246	0.247	17.207
	θ_3	6.759	0.339	19.922	6.827	0.344	19.858
	β_0	4.156	0.312	13.32	4.199	0.317	13.251
	β_1	-2.501	0.365	-6.847	-2.527	0.371	-6.809
	β_2	-3.405	0.383	-8.882	-3.439	0.389	-8.829
	β_3	-3.822	0.396	-9.657	-3.862	0.402	-9.604
Extreme Maximal	φ	4.192	0.549	7.639	4.353	0.572	7.615
	θ_1	2.216	0.185	11.986	2.237	0.187	11.967
	θ_2	4.342	0.249	17.43	4.384	0.252	17.385
	θ_3	7.521	0.398	18.906	7.577	0.401	18.893
	β_0	3.673	0.307	11.975	3.709	0.311	11.909
	β_1	-2.56	0.379	-6.761	-2.583	0.384	-6.722
	β_2	-3.48	0.4	-8.699	-3.511	0.406	-8.651
	β_3	-4.106	0.418	-9.814	-4.141	0.424	-9.765

Table 7.6.2: **ML** and **REML** estimates of parameters, standard errors and their ratio for the model 2.

		ML			REML		
		Est	SE	Z-v	Est	SE	Z-v
Standard Normal	φ_1	3.345	0.439	7.626	3.457	0.457	7.558
	φ_2	0.08	0.142	0.563	0.108	0.183	1
	θ_1	1.96	0.158	12.428	1.979	0.159	12.421
	θ_2	3.907	0.218	17.946	3.946	0.22	17.924
	θ_3	6.415	0.309	20.749	6.474	0.313	20.715
	β_0	3.596	0.278	12.922	3.633	0.282	12.873
	β_1	-2.323	0.336	-6.91	-2.347	0.341	-6.885
	β_2	-3.193	0.357	-8.956	-3.224	0.362	-8.912
	β_3	-3.642	0.366	-9.953	-3.678	0.371	-9.907
Logistic	φ_1	9.034	1.172	7.705	9.341	1.226	7.617
	φ_2	0.06	0.111	0.539	0.132	0.366	1
	θ_1	3.183	0.264	12.064	3.215	0.267	12.052
	θ_2	6.372	0.367	17.343	6.437	0.372	17.316
	θ_3	10.558	0.537	19.651	10.656	0.543	19.623
	β_0	5.868	0.463	12.67	5.931	0.47	12.623
	β_1	-3.791	0.554	-6.84	-3.83	0.562	-6.816
	β_2	-5.178	0.586	-8.831	-5.233	0.595	-8.789
	β_3	-5.955	0.607	-9.805	-6.018	0.616	-9.764
Extreme Minimal	φ_1	3.892	0.498	7.812	4.039	0.52	7.768
	φ_2	0.01	0.008	1.309	0.024	0.028	1
	θ_1	2.075	0.171	12.153	2.095	0.173	12.136
	θ_2	4.202	0.243	17.264	4.247	0.247	17.222
	θ_3	6.76	0.339	19.928	6.828	0.344	19.871
	β_0	4.157	0.312	13.325	4.199	0.317	13.263
	β_1	-2.502	0.365	-6.853	-2.529	0.371	-6.823
	β_2	-3.406	0.383	-8.884	-3.44	0.389	-8.833
	β_3	-3.823	0.396	-9.66	-3.865	0.402	-9.61
Extreme Maximal	φ_1	4.192	0.549	7.638	4.352	0.572	7.613
	φ_2	0.002	0.001	2.914	0.003	0.001	1
	θ_1	2.216	0.185	11.986	2.237	0.187	11.967
	θ_2	4.343	0.249	17.431	4.384	0.252	17.386
	θ_3	7.521	0.398	18.907	7.578	0.401	18.894
	β_0	3.673	0.307	11.976	3.71	0.311	11.911
	β_1	-2.56	0.379	-6.762	-2.584	0.384	-6.723
	β_2	-3.48	0.4	-8.699	-3.511	0.406	-8.652
	β_3	-4.107	0.418	-9.815	-4.142	0.424	-9.766

Table 7.6.3a: ML and REML estimates of parameters, standard errors and their ratio for the model 3.

		ML			REML		
		Est	SE	Z-v	Est	SE	Z-v
Standard Normal	φ_1	3.258	0.432	7.549	3.73	0.508	7.34
	φ_2	0.089	0.158	0.563	0.184	0.285	0.645
	θ_1	2.001	0.161	12.432	2.078	0.168	12.4
	θ_2	4.021	0.225	17.894	4.18	0.235	17.786
	θ_3	6.648	0.326	20.407	6.888	0.34	20.246
	β_0	4.111	0.633	6.498	4.298	0.672	6.393
	β_1	-2.356	0.34	-6.935	-2.448	0.359	-6.824
	β_2	-3.243	0.361	-8.99	-3.369	0.382	-8.819
	β_3	-3.933	0.399	-9.865	-4.094	0.421	-9.725
	γ_{11}	-0.576	0.61	-0.944	-0.614	0.647	-0.948
	γ_{12}	-0.331	0.572	-0.579	-0.357	0.607	-0.588
	γ_{21}	-0.324	0.377	-0.858	-0.332	0.385	-0.861
	γ_{22}	-0.454	0.316	-1.435	-0.461	0.322	-1.43
	α_{11}	0.659	0.497	1.325	0.673	0.528	1.276
	α_{12}	0.307	0.503	0.611	0.304	0.533	0.57
	α_{13}	-0.589	0.516	-1.143	-0.622	0.547	-1.137
	α_{14}	-0.469	1.08	-0.434	-0.501	1.147	-0.437
	α_{15}	-0.552	0.555	-0.995	-0.581	0.589	-0.986
	α_{21}	0.987	0.448	2.205	1.022	0.458	2.233
	α_{22}	0.558	0.413	1.351	0.59	0.422	1.4
	α_{23}	1.07	0.406	2.636	1.104	0.414	2.665
	α_{24}	-0.321	0.772	-0.415	-0.325	0.785	-0.414
	α_{25}	0.399	0.472	0.846	0.413	0.481	0.859

* γ_{13}, γ_{23}, α_{16} and α_{26} are fixed to achieve identifiability.

Table 7.6.3b: ML and REML estimates of parameters, standard errors and their ratio for the model 3.

Logistic	φ_1	8.751	1.153	7.591	10.034	1.365	7.349
	φ_2	0.133	0.325	0.411	0.415	0.736	0.564
	θ_1	3.245	0.269	12.077	3.377	0.281	12.027
	θ_2	6.555	0.379	17.304	6.829	0.398	17.177
	θ_3	10.909	0.56	19.467	11.318	0.586	19.328
	β_0	6.686	1.038	6.44	7.012	1.104	6.349
	β_1	-3.846	0.559	-6.874	-4.006	0.591	-6.773
	β_2	-5.26	0.593	-8.871	-5.483	0.629	-8.712
	β_3	-6.385	0.658	-9.709	-6.671	0.696	-9.587
	γ_{11}	-0.909	1	-0.909	-0.979	1.061	-0.923
	γ_{12}	-0.544	0.936	-0.581	-0.591	0.995	-0.595
	γ_{21}	-0.563	0.621	-0.907	-0.569	0.635	-0.896
	γ_{22}	-0.742	0.516	-1.437	-0.755	0.528	-1.431
	α_{11}	1.078	0.814	1.324	1.105	0.865	1.278
	α_{12}	0.541	0.822	0.658	0.534	0.874	0.612
	α_{13}	-0.937	0.844	-1.11	-0.993	0.897	-1.107
	α_{14}	-0.76	1.762	-0.431	-0.814	1.876	-0.434
	α_{15}	-0.92	0.907	-1.014	-0.967	0.964	-1.003
	α_{21}	1.591	0.742	2.146	1.64	0.76	2.157
	α_{22}	0.872	0.675	1.292	0.929	0.69	1.345
	α_{23}	1.7	0.673	2.524	1.764	0.687	2.567
	α_{24}	-0.506	1.23	-0.411	-0.518	1.257	-0.413
	α_{25}	0.696	0.772	0.902	0.712	0.789	0.903

*** γ_{13}, γ_{23}, α_{16} and α_{26} are fixed to achieve identifiability.**

Table 7.6.3c: ML and REML estimates of parameters, standard errors and their ratio for the model 3.

		ML			REML		
		Est	SE	Z-v	Est	SE	Z-v
Extreme Minimal	φ_1	3.791	0.489	7.753	4.387	0.579	7.578
	φ_2	0.007	0.004	1.601	0.072	0.135	0.537
	θ_1	2.119	0.175	12.104	2.2	0.183	12.033
	θ_2	4.321	0.251	17.182	4.506	0.265	17.007
	θ_3	6.997	0.357	19.622	7.279	0.375	19.403
	β_0	4.66	0.683	6.825	4.869	0.729	6.682
	β_1	-2.537	0.37	-6.863	-2.647	0.392	-6.753
	β_2	-3.461	0.389	-8.894	-3.603	0.414	-8.705
	β_3	-4.106	0.431	-9.525	-4.288	0.457	-9.389
	γ_{11}	-0.567	0.653	-0.868	-0.6	0.696	-0.862
	γ_{12}	-0.37	0.611	-0.605	-0.392	0.652	-0.601
	γ_{21}	-0.462	0.412	-1.122	-0.48	0.422	-1.137
	γ_{22}	-0.449	0.346	-1.296	-0.463	0.354	-1.31
	α_{11}	0.736	0.534	1.379	0.756	0.569	1.33
	α_{12}	0.412	0.54	0.763	0.411	0.576	0.714
	α_{13}	-0.554	0.553	-1.002	-0.589	0.589	-0.999
	α_{14}	-0.522	1.156	-0.452	-0.554	1.233	-0.449
	α_{15}	-0.603	0.594	-1.014	-0.636	0.633	-1.004
	α_{21}	1.05	0.479	2.193	1.09	0.492	2.214
	α_{22}	0.502	0.45	1.115	0.533	0.461	1.157
	α_{23}	1.181	0.447	2.642	1.228	0.458	2.684
	α_{24}	-0.384	0.811	-0.473	-0.392	0.827	-0.474
	α_{25}	0.541	0.507	1.067	0.561	0.519	1.081

* γ_{13}, γ_{23}, α_{16} and α_{26} are fixed to achieve identifiability.

Table 7.6.3d: ML and REML estimates of parameters, standard errors and their ratio for the model 3.

Extreme Maximal	φ_1	4.098	0.54	7.588	4.767	0.637	7.482
	φ_2	0.002	0.001	2.685	0.033	0.045	0.724
	θ_1	2.257	0.188	12.012	2.348	0.197	11.935
	θ_2	4.472	0.258	17.337	4.652	0.271	17.153
	θ_3	7.755	0.414	18.748	8.004	0.429	18.669
	β_0	4.253	0.714	5.953	4.453	0.761	5.848
	β_1	-2.609	0.383	-6.805	-2.708	0.407	-6.66
	β_2	-3.544	0.405	-8.742	-3.68	0.43	-8.562
	β_3	-4.388	0.455	-9.646	-4.559	0.48	-9.507
	γ_{11}	-0.62	0.697	-0.889	-0.678	0.741	-0.914
	γ_{12}	-0.313	0.654	-0.479	-0.353	0.695	-0.507
	γ_{21}	-0.382	0.437	-0.874	-0.384	0.445	-0.863
	γ_{22}	-0.567	0.348	-1.629	-0.582	0.354	-1.644
	α_{11}	0.713	0.56	1.273	0.744	0.597	1.248
	α_{12}	0.275	0.564	0.487	0.289	0.602	0.48
	α_{13}	-0.721	0.579	-1.244	-0.745	0.618	-1.206
	α_{14}	-0.522	1.202	-0.434	-0.559	1.286	-0.435
	α_{15}	-0.631	0.624	-1.01	-0.647	0.666	-0.972
	α_{21}	1.108	0.53	2.091	1.137	0.54	2.104
	α_{22}	0.657	0.469	1.401	0.7	0.477	1.467
	α_{23}	1.119	0.471	2.377	1.162	0.478	2.432
	α_{24}	-0.227	0.842	-0.27	-0.23	0.856	-0.269
	α_{25}	0.446	0.548	0.814	0.455	0.557	0.816

* γ_{13}, γ_{23}, α_{16} and α_{26} are fixed to achieve identifiability.

Table 7.6.4a: ML and REML estimates of parameters, standard errors and their ratio for the model 4.

		ML			REML		
		Est	SE	Z-v	Est	SE	Z-v
Standard Normal	φ_1	3.544	0.456	7.776	3.676	0.475	7.745
	θ_{11}	2.019	0.209	9.671	2.036	0.211	9.671
	θ_{12}	2.168	0.226	9.59	2.187	0.228	9.59
	θ_{13}	1.655	0.233	7.096	1.668	0.235	7.096
	θ_{21}	3.79	0.25	15.132	3.825	0.253	15.124
	θ_{22}	4.214	0.272	15.47	4.252	0.275	15.465
	θ_{23}	3.884	0.276	14.094	3.918	0.278	14.099
	θ_{31}	6.832	0.446	15.312	6.895	0.452	15.269
	θ_{32}	6.499	0.401	16.216	6.549	0.404	16.231
	θ_{33}	6.06	0.408	14.854	6.106	0.411	14.872
	β_0	3.643	0.284	12.815	3.675	0.288	12.746
	β_1	-2.357	0.35	-6.729	-2.377	0.355	-6.691
	β_2	-3.15	0.364	-8.648	-3.177	0.369	-8.599
	β_3	-3.775	0.378	-9.995	-3.808	0.383	-9.943
Logistic	φ_1	9.582	1.233	7.768	9.977	1.289	7.737
	θ_{11}	3.294	0.346	9.518	3.327	0.35	9.514
	θ_{12}	3.532	0.378	9.349	3.567	0.382	9.341
	θ_{13}	2.7	0.39	6.93	2.726	0.393	6.928
	θ_{21}	6.185	0.419	14.764	6.252	0.424	14.749
	θ_{22}	6.908	0.456	15.155	6.982	0.461	15.141
	θ_{23}	6.406	0.463	13.825	6.473	0.468	13.824
	θ_{31}	11.297	0.77	14.675	11.418	0.78	14.644
	θ_{32}	10.722	0.708	15.141	10.821	0.714	15.163
	θ_{33}	10.061	0.719	13.995	10.152	0.724	14.019
	β_0	5.986	0.475	12.605	6.05	0.483	12.537
	β_1	-3.876	0.579	-6.695	-3.915	0.588	-6.656
	β_2	-5.154	0.603	-8.543	-5.207	0.613	-8.496
	β_3	-6.207	0.629	-9.873	-6.272	0.638	-9.824

Table 7.6.4b: ML and REML estimates of parameters, standard errors and their ratio for the model 4.

		ML			REML		
		Est	SE	Z-v	Est	SE	Z-v
Extreme Minimal	φ_1	4.191	0.533	7.859	4.375	0.559	7.822
	θ_{11}	2.157	0.229	9.438	2.179	0.231	9.435
	θ_{12}	2.326	0.25	9.297	2.35	0.253	9.287
	θ_{13}	1.76	0.254	6.926	1.776	0.257	6.921
	θ_{21}	4.043	0.279	14.505	4.089	0.282	14.486
	θ_{22}	4.659	0.305	15.265	4.713	0.309	15.239
	θ_{23}	4.258	0.31	13.746	4.307	0.314	13.737
	θ_{31}	7.221	0.461	15.672	7.308	0.468	15.602
	θ_{32}	6.941	0.408	16.997	7.016	0.413	16.98
	θ_{33}	6.584	0.442	14.902	6.656	0.447	14.891
	β_0	4.257	0.321	13.243	4.305	0.327	13.169
	β_1	-2.574	0.384	-6.709	-2.603	0.39	-6.671
	β_2	-3.379	0.398	-8.483	-3.416	0.405	-8.43
	β_3	-4.05	0.419	-9.671	-4.098	0.426	-9.62
Extreme Maximal	φ_1	4.379	0.572	7.661	4.565	0.598	7.635
	θ_{11}	2.284	0.239	9.56	2.308	0.242	9.551
	θ_{12}	2.429	0.254	9.559	2.456	0.257	9.553
	θ_{13}	1.912	0.271	7.055	1.932	0.274	7.046
	θ_{21}	4.231	0.288	14.676	4.278	0.292	14.656
	θ_{22}	4.645	0.312	14.863	4.693	0.316	14.852
	θ_{23}	4.369	0.323	13.532	4.413	0.326	13.533
	θ_{31}	8.007	0.595	13.449	8.084	0.6	13.467
	θ_{32}	7.59	0.577	13.148	7.652	0.58	13.193
	θ_{33}	7.104	0.577	12.316	7.159	0.579	12.358
	β_0	3.742	0.315	11.896	3.784	0.32	11.825
	β_1	-2.618	0.393	-6.655	-2.645	0.4	-6.614
	β_2	-3.482	0.41	-8.502	-3.517	0.416	-8.452
	β_3	-4.242	0.43	-9.86	-4.285	0.437	-9.807

Table 7.6.5a: ML and REML estimates of parameters, standard errors and their ratio for the model 5.

		ML			REML		
		Est	SE	Z-v	Est	SE	Z-v
Standard Normal	φ_1	3.525	0.458	7.692	3.644	0.481	7.58
	φ_2	0.063	0.11	0.573	0.113	0.191	0.59
	θ_{11}	2.028	0.21	9.676	2.051	0.212	9.679
	θ_{12}	2.175	0.227	9.583	2.2	0.23	9.577
	θ_{13}	1.662	0.234	7.098	1.681	0.237	7.1
	θ_{21}	3.799	0.251	15.13	3.841	0.254	15.121
	θ_{22}	4.231	0.274	15.47	4.282	0.277	15.465
	θ_{23}	3.899	0.277	14.093	3.944	0.28	14.097
	θ_{31}	6.832	0.445	15.344	6.895	0.45	15.325
	θ_{32}	6.532	0.403	16.197	6.608	0.408	16.197
	θ_{33}	6.095	0.411	14.828	6.167	0.416	14.828
	β_0	3.657	0.285	12.85	3.701	0.289	12.806
	β_1	-2.367	0.35	-6.764	-2.395	0.355	-6.751
	β_2	-3.163	0.366	-8.651	-3.199	0.372	-8.605
	β_3	-3.792	0.379	-10	-3.837	0.386	-9.951
Logistic	φ_1	9.574	1.233	7.764	9.908	1.289	7.686
	φ_2	0.011	0.009	1.223	0.102	0.236	0.433
	θ_{11}	3.294	0.346	9.519	3.33	0.35	9.518
	θ_{12}	3.532	0.378	9.349	3.57	0.382	9.338
	θ_{13}	2.7	0.39	6.93	2.729	0.394	6.928
	θ_{21}	6.185	0.419	14.765	6.253	0.424	14.756
	θ_{22}	6.908	0.456	15.155	6.985	0.461	15.143
	θ_{23}	6.406	0.463	13.825	6.474	0.468	13.826
	θ_{31}	11.294	0.77	14.676	11.399	0.778	14.654
	θ_{32}	10.723	0.708	15.14	10.834	0.715	15.158
	θ_{33}	10.062	0.719	13.995	10.164	0.725	14.018
	β_0	5.986	0.475	12.608	6.053	0.482	12.56
	β_1	-3.876	0.579	-6.698	-3.918	0.587	-6.677
	β_2	-5.154	0.603	-8.544	-5.21	0.613	-8.499
	β_3	-6.208	0.629	-9.874	-6.278	0.639	-9.829

Table 7.6.5b: ML and REML estimates of parameters, standard errors and their ratio for the model 5.

		ML			REML		
		Est	SE	Z-v	Est	SE	Z-v
Extreme Minimal	φ_1	4.19	0.533	7.857	4.372	0.559	7.819
	φ_2	0.002	0.001	2.98	0.003	0.001	2.296
	θ_{11}	2.157	0.229	9.438	2.179	0.231	9.436
	θ_{12}	2.326	0.25	9.296	2.35	0.253	9.287
	θ_{13}	1.76	0.254	6.927	1.776	0.257	6.921
	θ_{21}	4.043	0.279	14.506	4.089	0.282	14.487
	θ_{22}	4.659	0.305	15.265	4.713	0.309	15.24
	θ_{23}	4.258	0.31	13.747	4.307	0.314	13.737
	θ_{31}	7.22	0.461	15.674	7.307	0.468	15.605
	θ_{32}	6.941	0.408	16.996	7.016	0.413	16.979
	θ_{33}	6.584	0.442	14.902	6.656	0.447	14.89
	β_0	4.257	0.321	13.244	4.305	0.327	13.17
	β_1	-2.574	0.384	-6.711	-2.603	0.39	-6.673
	β_2	-3.379	0.398	-8.484	-3.416	0.405	-8.431
	β_3	-4.05	0.419	-9.672	-4.098	0.426	-9.621
Extreme Maximal	φ_1	4.378	0.572	7.659	4.562	0.598	7.631
	φ_2	0.003	0.001	2.511	0.006	0.004	1.681
	θ_{11}	2.284	0.239	9.56	2.308	0.242	9.551
	θ_{12}	2.429	0.254	9.559	2.456	0.257	9.553
	θ_{13}	1.913	0.271	7.055	1.932	0.274	7.047
	θ_{21}	4.231	0.288	14.677	4.278	0.292	14.657
	θ_{22}	4.645	0.313	14.863	4.694	0.316	14.853
	θ_{23}	4.369	0.323	13.532	4.414	0.326	13.533
	θ_{31}	8.007	0.595	13.449	8.083	0.6	13.467
	θ_{32}	7.591	0.577	13.149	7.653	0.58	13.194
	θ_{33}	7.105	0.577	12.317	7.16	0.579	12.359
	β_0	3.742	0.315	11.897	3.784	0.32	11.828
	β_1	-2.618	0.393	-6.656	-2.646	0.4	-6.616
	β_2	-3.482	0.41	-8.502	-3.517	0.416	-8.453
	β_3	-4.243	0.43	-9.861	-4.285	0.437	-9.807

Table 7.6.6a: ML and REML estimates of parameters, standard errors and their ratio for the model 6.

		ML			REML		
		Est	SE	Z-v	Est	SE	Z-v
Standard Normal	φ_1	3.426	0.445	7.703	3.895	0.531	7.339
	φ_2	0.014	0.013	1.09	0.204	0.295	0.69
	θ_{11}	2.078	0.234	8.88	2.152	0.243	8.867
	θ_{12}	2.178	0.238	9.17	2.286	0.25	9.156
	θ_{13}	1.66	0.241	6.897	1.743	0.252	6.913
	θ_{21}	3.916	0.289	13.561	4.061	0.301	13.501
	θ_{22}	4.281	0.293	14.599	4.495	0.309	14.569
	θ_{23}	3.936	0.294	13.389	4.128	0.308	13.399
	θ_{31}	7.067	0.486	14.541	7.293	0.506	14.427
	θ_{32}	6.671	0.434	15.388	6.984	0.454	15.377
	θ_{33}	6.198	0.434	14.278	6.497	0.456	14.256
	β_0	4.19	0.646	6.483	4.412	0.688	6.41
	β_1	-2.446	0.365	-6.697	-2.537	0.384	-6.61
	β_2	-3.222	0.374	-8.615	-3.377	0.4	-8.446
	β_3	-3.857	0.388	-9.946	-4.049	0.415	-9.764
	γ_{11}	-0.422	0.649	-0.649	-0.487	0.685	-0.711
	γ_{12}	-0.076	0.608	-0.125	-0.133	0.642	-0.208
	γ_{21}	-0.514	0.391	-1.315	-0.503	0.412	-1.221
	γ_{22}	-0.725	0.351	-2.065	-0.716	0.37	-1.932
	α_{11}	0.543	0.555	0.979	0.539	0.583	0.924
	α_{12}	0.08	0.553	0.145	0.063	0.582	0.108
	α_{13}	-0.815	0.565	-1.443	-0.866	0.594	-1.457
	α_{14}	-0.543	1.182	-0.459	-0.602	1.244	-0.484
	α_{15}	-0.729	0.612	-1.19	-0.769	0.643	-1.196
	α_{21}	0.61	0.421	1.45	0.667	0.444	1.502
	α_{22}	0.65	0.395	1.647	0.7	0.417	1.68
	α_{23}	0.859	0.395	2.177	0.911	0.417	2.184
	α_{24}	-0.116	0.768	-0.151	-0.096	0.811	-0.118
	α_{25}	0.494	0.441	1.121	0.523	0.466	1.124

* γ_{13}, γ_{23}, α_{16} and α_{26} are fixed to achieve identifiability.

Table 7.6.6b: ML and REML estimates of parameters, standard errors and their ratio for the model 6.

		ML			REML		
		Est	SE	Z-v	Est	SE	Z-v
Logistic	φ_1	9.286	1.205	7.707	10.576	1.438	7.356
	φ_2	0.004	0.002	2.17	0.424	0.773	0.549
	θ_{11}	3.391	0.387	8.763	3.51	0.402	8.735
	θ_{12}	3.546	0.396	8.95	3.715	0.417	8.919
	θ_{13}	2.712	0.402	6.749	2.841	0.421	6.746
	θ_{21}	6.402	0.481	13.317	6.643	0.501	13.264
	θ_{22}	7.019	0.492	14.264	7.351	0.517	14.221
	θ_{23}	6.491	0.496	13.087	6.784	0.518	13.089
	θ_{31}	11.663	0.828	14.09	12.045	0.862	13.967
	θ_{32}	10.992	0.76	14.468	11.465	0.79	14.511
	θ_{33}	10.248	0.755	13.58	10.687	0.783	13.64
	β_0	6.872	1.066	6.447	7.218	1.134	6.365
	β_1	-4.014	0.604	-6.65	-4.158	0.634	-6.555
	β_2	-5.263	0.619	-8.501	-5.509	0.66	-8.342
	β_3	-6.333	0.645	-9.816	-6.637	0.688	-9.652
	γ_{11}	-0.669	1.071	-0.624	-0.781	1.129	-0.692
	γ_{12}	-0.141	1.003	-0.141	-0.226	1.057	-0.214
	γ_{21}	-0.843	0.642	-1.312	-0.816	0.673	-1.212
	γ_{22}	-1.166	0.575	-2.027	-1.161	0.602	-1.927
	α_{11}	0.882	0.914	0.965	0.895	0.96	0.932
	α_{12}	0.135	0.91	0.148	0.115	0.957	0.12
	α_{13}	-1.286	0.932	-1.38	-1.364	0.98	-1.392
	α_{14}	-0.919	1.934	-0.475	-0.998	2.036	-0.49
	α_{15}	-1.237	1.007	-1.228	-1.279	1.058	-1.208
	α_{21}	0.991	0.694	1.427	1.056	0.729	1.449
	α_{22}	1.098	0.646	1.7	1.176	0.678	1.735
	α_{23}	1.311	0.655	2.003	1.399	0.685	2.043
	α_{24}	-0.161	1.232	-0.131	-0.143	1.295	-0.11
	α_{25}	0.847	0.721	1.175	0.867	0.757	1.145

* γ_{13}, γ_{23}, α_{16} and α_{26} are fixed to achieve identifiability.

Table 7.6.6c: ML and REML estimates of parameters, standard errors and their ratio for the model 6.

		ML			REML		
		Est	SE	Z-v	Est	SE	Z-v
Extreme Minimal	φ_1	3.994	0.513	7.784	4.66	0.611	7.625
	φ_2	0.001	0	3.279	0.051	0.087	0.592
	θ_{11}	2.202	0.253	8.703	2.287	0.263	8.699
	θ_{12}	2.317	0.261	8.895	2.411	0.272	8.854
	θ_{13}	1.769	0.262	6.755	1.836	0.272	6.74
	θ_{21}	4.148	0.319	12.99	4.327	0.334	12.972
	θ_{22}	4.693	0.329	14.247	4.906	0.346	14.187
	θ_{23}	4.282	0.33	12.992	4.475	0.345	12.971
	θ_{31}	7.403	0.503	14.707	7.716	0.529	14.578
	θ_{32}	7.089	0.449	15.774	7.386	0.469	15.735
	θ_{33}	6.681	0.466	14.33	6.966	0.487	14.296
	β_0	4.76	0.701	6.792	4.977	0.751	6.631
	β_1	-2.629	0.399	-6.583	-2.741	0.423	-6.479
	β_2	-3.451	0.408	-8.467	-3.6	0.434	-8.293
	β_3	-4.124	0.428	-9.642	-4.314	0.455	-9.472
	γ_{11}	-0.414	0.699	-0.593	-0.445	0.744	-0.597
	γ_{12}	-0.109	0.654	-0.167	-0.129	0.697	-0.186
	γ_{21}	-0.56	0.433	-1.295	-0.582	0.444	-1.309
	γ_{22}	-0.701	0.391	-1.794	-0.723	0.401	-1.804
	α_{11}	0.585	0.6	0.975	0.601	0.636	0.945
	α_{12}	0.132	0.599	0.22	0.126	0.636	0.198
	α_{13}	-0.725	0.61	-1.189	-0.767	0.648	-1.184
	α_{14}	-0.646	1.274	-0.507	-0.689	1.352	-0.51
	α_{15}	-0.808	0.659	-1.226	-0.85	0.699	-1.216
	α_{21}	0.702	0.457	1.537	0.735	0.471	1.562
	α_{22}	0.687	0.435	1.58	0.728	0.446	1.631
	α_{23}	0.829	0.433	1.917	0.869	0.444	1.958
	α_{24}	-0.056	0.829	-0.068	-0.049	0.847	-0.057
	α_{25}	0.599	0.477	1.256	0.632	0.491	1.286

* γ_{13}, γ_{23}, α_{16} and α_{26} are fixed to achieve identifiability.

Table 7.6.6d: ML and REML estimates of parameters, standard errors and their ratio for the model 6.

		ML			REML		
		Est	SE	Z-v	Est	SE	Z-v
Extreme Maximal	φ_1	4.312	0.566	7.616	5.048	0.676	7.474
	φ_2	0.001	0	3.656	0.062	0.114	0.545
	θ_{11}	2.37	0.272	8.729	2.467	0.284	8.694
	θ_{12}	2.454	0.27	9.099	2.568	0.283	9.081
	θ_{13}	1.913	0.28	6.829	1.997	0.293	6.814
	θ_{21}	4.417	0.334	13.212	4.604	0.35	13.165
	θ_{22}	4.742	0.338	14.043	4.95	0.354	13.998
	θ_{23}	4.437	0.345	12.862	4.625	0.36	12.857
	θ_{31}	8.311	0.631	13.167	8.616	0.652	13.217
	θ_{32}	7.783	0.605	12.869	8.056	0.62	12.993
	θ_{33}	7.243	0.599	12.096	7.484	0.612	12.234
	β_0	4.398	0.734	5.99	4.63	0.786	5.892
	β_1	-2.741	0.412	-6.646	-2.853	0.438	-6.521
	β_2	-3.561	0.423	-8.422	-3.713	0.45	-8.245
	β_3	-4.334	0.444	-9.766	-4.519	0.472	-9.574
	γ_{11}	-0.376	0.753	-0.5	-0.447	0.799	-0.559
	γ_{12}	-0.013	0.705	-0.019	-0.058	0.748	-0.078
	γ_{21}	-0.693	0.453	-1.532	-0.707	0.466	-1.517
	γ_{22}	-0.856	0.396	-2.159	-0.884	0.409	-2.161
	α_{11}	0.521	0.629	0.829	0.553	0.668	0.829
	α_{12}	-0.014	0.626	-0.023	-0.011	0.664	-0.017
	α_{13}	-1.035	0.646	-1.601	-1.071	0.686	-1.562
	α_{14}	-0.661	1.323	-0.5	-0.709	1.41	-0.503
	α_{15}	-0.951	0.696	-1.368	-0.972	0.738	-1.316
	α_{21}	0.737	0.482	1.531	0.76	0.498	1.527
	α_{22}	0.778	0.449	1.733	0.827	0.462	1.79
	α_{23}	0.955	0.474	2.015	0.998	0.488	2.047
	α_{24}	-0.029	0.851	-0.034	-0.03	0.876	-0.034
	α_{25}	0.701	0.506	1.386	0.718	0.52	1.379

* γ_{13}, γ_{23}, α_{16} and α_{26} are fixed to achieve identifiability.

Table 7.6a: ML and REML estimates of treatment effect, standard errors and their z-v for the model 1, 2, 3, 4, 5, 6 by using four threshold models.

Model		ML			REML		
		Est	SE	z-v	Est	SE	z-v
1	Standard Nor	-3.03	0.328	-9.23	-3.06	0.334	-9.17
	Logistic	-4.97	0.546	-9.1	-5.02	0.555	-9.05
	Extreme Min	-3.243	0.358	-9.07	-3.28	0.365	-9
	Extreme Max	-3.38	0.371	-9.12	-3.42	0.378	-9.06
2	Standard Nor	-3.053	0.3	-9.262	-3.083	0.34	-9.211
	Logistic	-4.975	0.546	-9.121	-5.027	0.554	-9.075
	Extreme Min	-3.243	0.358	-9.073	-3.278	0.364	-9.016
	Extreme Max	-3.382	0.371	-9.123	-3.412	0.38	-9.059
3	Standard Nor	-3.117	0.329	-9.483	-3.251	0.351	-9.272
	Logistic	-5.091	0.545	-9.337	-5.313	0.581	-9.144
	Extreme Min	-3.321	0.357	-9.295	-3.463	0.381	-9.078
	Extreme Max	-3.472	0.372	-9.329	-3.604	0.397	-9.074
4	Standard Nor	-3.094	0.337	-9.183	-3.121	0.342	-9.118
	Logistic	-5.079	0.56	-9.074	-5.131	0.569	-9.011
	Extreme Min	-3.334	0.37	-9.016	-3.372	0.377	-8.949
	Extreme Max	-3.448	0.38	-9.083	-3.482	0.386	-9.014
5	Standard Nor	-3.107	0.337	-9.21	-3.144	0.343	-9.164
	Logistic	-5.079	0.56	-9.076	-5.135	0.569	-9.028
	Extreme Min	-3.334	0.37	-9.017	-3.372	0.377	-8.951
	Extreme Max	-3.448	0.38	-9.084	-3.483	0.386	-9.016
6	Standard Nor	-3.175	0.338	-9.401	-3.321	0.361	-9.211
	Logistic	-5.203	0.561	-9.275	-5.435	0.598	-9.088
	Extreme Min	-3.401	0.368	-9.23	-3.552	0.395	-8.995
	Extreme Max	-3.545	0.383	-9.251	-3.695	0.411	-8.997

* Nor = Normal, Min =Minimal, Max =Maximal.

Table 7.6b: Observed and predicted frequencies for subjects undergoing active treatment or placebo using model 1 for skin condition data of section 7.4.

Time		1									2								
			ML				REML					ML				REML			
	Y	O	1	2	3	4	1	2	3	4	O	1	2	3	4	1	2	3	4
T	1	22	23	23	23	23	22	22	22	22	37	35	35	35	38	33	33	33	36
	2	34	41	41	37	41	40	40	36	40	30	40	39	38	37	36	35	34	33
	3	24	16	16	19	20	15	16	19	20	8	9	10	9	10	8	9	8	8
	4	4	8	8	9	4	8	7	8	3	5	4	4	6	3	3	3	5	3
	5	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
P	1	5	3	3	3	5	3	3	3	5	4	3	3	3	5	2	2	2	4
	2	14	14	14	12	12	14	14	12	12	13	18	18	15	16	14	14	12	12
	3	16	29	29	30	35	29	29	30	35	30	32	32	34	37	29	29	30	34
	4	46	38	38	35	32	38	38	35	32	25	31	31	31	26	31	31	31	26
	5	3	0	0	4	0	0	0	4	0	4	0	0	1	0	0	0	1	0

Time		3								
			ML				REML			
	Y	O	1	2	3	4	1	2	3	4
T	1	48	49	49	35	53	45	45	31	49
	2	18	26	26	39	27	23	23	36	23
	3	7	9	9	10	8	8	8	9	7
	4	6	4	4	4	0	3	3	3	0
	5	0	0	0	0	0	0	0	0	0
P	1	5	6	6	6	8	2	2	2	4
	2	7	24	24	22	22	12	12	10	10
	3	20	33	33	34	39	28	28	29	34
	4	19	21	21	21	15	21	21	21	15
	5	4	0	0	1	0	0	0	1	0

* T = Treatment, P= Placebo, O = Observed, 1 = Standard Normal,

2 = Logistic, 3 = Extreme Minimal value and 4 = Extreme Maximal value.

7.7 APPLICATION TO SKIN DISORDER DATA

A second longitudinal study of skin disorder was reported in Koch et al (1992) with data for 36 subjects receiving active treatment and 36 receiving a placebo. Subjects were observed 3, 7, 10 and 14 days after entry to the study. Data are reprinted in Table 5 in appendix B. The response variable Y_{it} for subject i at time t (i=1,2,...,72; t=1,2,3,4) is coded as 0 = excellent, 1=good, 2=fair, 3 =poor.

Note that there are only two observations for category 4 (poor) in the placebo group. Because of the small number of observation in category 4, categories 4 (poor) and 3 (fair) are combined, reducing the number of categories under consideration to 3. Thus the observation for subject i at time t (i=1,2,...,72; t=1,2,3,4) is coded as 0 = excellent, 1=good, 2=fair. We use models 1, 2, 4 and 5 of section 7.4 since the only risk variable for this data is the treatment variable.

The results of fitting models are given in Tables 7.7.1, 7.7.2, 7.7.4 and 7.7.5 for the models 1, 2, 4 and 5 respectively. Table 7.7a provides ML and REML estimates of treatment effect for the models 1, 2, 4, and 5.

Model 1:

Estimates of average treatment effect for the model 1, 2, 4, 5 are obtained by using the asymptotic distribution of $\hat{\beta}_t$ (t=1,2,3,4). If $\beta = 4^{-1}\sum_{j=1}^{4}\beta_j$ then estimate of β are given in Table 7.7a, we see that the z-values are greater than the 1.96 critical value for all four threshold models of chapter 5. Since the estimate of treatment effect is negative, patients on active treatment are more likely to give responses in the lowest category (excellent). Moreover, from Table 7.7.1, it can be seen that the z-value is negatively increasing as patients move from day 3 to day 14. Thus patients on active treatment improve more the longer they stay. However, the pairwise comparisons show that except for the threshold model 2 of chapter 5, there is not significant changes for the treatment effect from day 7 and after.

Model 2:

In spite of increase in the estimates of the second variance component (φ_2) for the threshold model 3 of chapter 5, it does not seem that statistically significant patient effects change over time. The highest z-value (ratio estimate to standard error) is 1.347, it belongs to model 4 of section 5.2 in chapter 5 (G(.) = extreme maximal). The z-value for the ML and REML estimates of φ_1 is greater than 1.96 critical value. Thus there is a substantial patient effect.

Models 4 and 5:

The results in the Table 7.7.4 indicate that the estimate of the threshold parameter increases over time. However, the difference between the threshold parameters at day 7 and day 10 is not significant. In terms of the treatment effect, as in the models 1 and 2, the results show that the treatment has a highly significant effect. Nevertheless, the results of pairwise comparisons show that except between β_1 and β_4, there are not significant changes for the treatment effect over time. The results of model 5 (Table 7.7.5) indicate that the φ_2 is always close to zero and the conclusion about the treatment effect and threshold parameter follows from model 4.

Therefore, model 4 is a suitable model for this data. For this model, the predicted values are the same as observed in 72.92% , 73.61%, 73.61%, 70.83% by ML and 72.92% , 73.96%, 73.61%, 70.83% REML methods for threshold models of section 5.2 respectively.

A comparison of the frequency distributions of observed and predicted values in active treatment and placebo groups at each observations times are given in Table 7.7b.

In conclusion, for this data, it is not necessary to include a second variance component in the model. The treatment has a statistically significant effect. While the estimate of treatment effect is negative, thereby increasing the probability of observing the lowest (excellent) category of result for patients in the active treatment group. The treatment shows more improvement as patients move from day 3 to day 14. Furthermore, the threshold parameter is also affected by time.

Table 7.7.1: ML and REML estimates of parameters, standard errors and ratio for the model 1.

		ML			REML		
		Est	SE	Z-v	Est	SE	Z-v
Standard Normal	φ	0.46	0.135	3.399	0.494	0.143	3.443
	θ_1	1.823	0.125	14.552	1.835	0.126	14.533
	β_0	1.212	0.167	7.253	1.22	0.17	7.165
	β_1	-0.023	0.271	-0.086	-0.023	0.275	-0.084
	β_2	-0.812	0.275	-2.95	-0.817	0.279	-2.929
	β_3	-0.81	0.275	-2.944	-0.816	0.279	-2.923
	β_4	-1.356	0.286	-4.741	-1.366	0.29	-4.71
Logistic	φ	1.246	0.37	3.366	1.341	0.393	3.412
	θ_1	3.001	0.217	13.82	3.024	0.219	13.797
	β_0	2.024	0.285	7.092	2.039	0.291	7.015
	β_1	-0.064	0.447	-0.144	-0.065	0.454	-0.142
	β_2	-1.367	0.457	-2.988	-1.377	0.464	-2.967
	β_3	-1.361	0.457	-2.978	-1.371	0.464	-2.957
	β_4	-2.268	0.477	-4.75	-2.288	0.484	-4.722
Extreme Minimal	φ	0.592	0.168	3.523	0.641	0.18	3.565
	θ_1	2.08	0.151	13.788	2.097	0.152	13.764
	β_0	1.802	0.209	8.639	1.815	0.213	8.542
	β_1	-0.094	0.304	-0.308	-0.094	0.31	-0.304
	β_2	-0.97	0.302	-3.213	-0.98	0.307	-3.193
	β_3	-0.947	0.303	-3.121	-0.957	0.309	-3.1
	β_4	-1.562	0.315	-4.96	-1.576	0.32	-4.921
Extreme Maximal	φ	0.531	0.158	3.355	0.576	0.169	3.407
	θ_1	2.034	0.146	13.93	2.05	0.147	13.905
	β_0	0.887	0.169	5.266	0.897	0.173	5.194
	β_1	0.081	0.292	0.277	0.083	0.297	0.278
	β_2	-0.769	0.303	-2.535	-0.776	0.308	-2.519
	β_3	-0.749	0.303	-2.477	-0.756	0.307	-2.458
	β_4	-1.38	0.326	-4.232	-1.394	0.331	-4.217

Table 7.7.2: ML and REML estimates of parameters, standard errors and their ratio for the model 2.

		ML			REML		
		Est	SE	Z-v	Est	SE	Z-v
Standard Normal	φ_1	0.44	0.146	3.011	0.465	0.162	2.874
	φ_2	0.045	0.098	0.461	0.067	0.139	0.48
	θ_1	1.83	0.126	14.56	1.845	0.127	14.544
	β_0	1.238	0.168	7.372	1.258	0.172	7.334
	β_1	-0.046	0.27	-0.172	-0.057	0.274	-0.207
	β_2	-0.838	0.277	-3.022	-0.855	0.282	-3.032
	β_3	-0.836	0.277	-3.016	-0.853	0.282	-3.026
	β_4	-1.386	0.288	-4.807	-1.408	0.293	-4.804
Logistic	φ_1	1.21	0.393	3.082	1.281	0.446	2.874
	φ_2	0.079	0.233	0.337	0.136	0.386	0.353
	θ_1	3.005	0.217	13.831	3.032	0.219	13.816
	β_0	2.049	0.286	7.168	2.083	0.292	7.143
	β_1	-0.088	0.447	-0.197	-0.105	0.452	-0.233
	β_2	-1.391	0.459	-3.031	-1.419	0.467	-3.039
	β_3	-1.386	0.459	-3.02	-1.414	0.467	-3.029
	β_4	-2.297	0.479	-4.79	-2.337	0.488	-4.79
extreme Minimal	φ_1	0.492	0.192	2.566	0.529	0.203	2.605
	φ_2	0.218	0.223	0.979	0.245	0.235	1.044
	θ_1	2.11	0.153	13.777	2.13	0.155	13.755
	β_0	1.897	0.209	9.059	1.921	0.213	9
	β_1	-0.175	0.298	-0.589	-0.187	0.302	-0.617
	β_2	-1.078	0.308	-3.495	-1.099	0.314	-3.497
	β_3	-1.042	0.31	-3.362	-1.062	0.316	-3.361
	β_4	-1.677	0.322	-5.206	-1.703	0.328	-5.186
Extreme Maximal	φ_1	0.526	0.159	3.309	0.562	0.174	3.227
	φ_2	0.011	0.013	0.814	0.029	0.059	0.497
	θ_1	2.035	0.146	13.933	2.052	0.148	13.91
	β_0	0.893	0.169	5.293	0.913	0.174	5.263
	β_1	0.075	0.292	0.257	0.066	0.296	0.224
	β_2	-0.774	0.304	-2.547	-0.79	0.309	-2.552
	β_3	-0.755	0.303	-2.492	-0.772	0.309	-2.5
	β_4	-1.386	0.326	-4.245	-1.411	0.332	-4.252

Table 7.7.4: **ML** and **REML** estimates of parameters, standard errors and their ratio for the model.

		ML			REML		
		Est	SE	Z-v	Est	SE	Z-v
Standard	φ_1	0.562	0.156	3.597	0.603	0.166	3.631
	θ_{11}	1.362	0.176	7.723	1.371	0.177	7.726
	θ_{12}	2.069	0.223	9.264	2.085	0.225	9.268
	θ_{13}	1.77	0.211	8.381	1.784	0.213	8.394
	θ_{14}	2.988	0.358	8.336	3.01	0.36	8.361
	β_0	1.269	0.179	7.089	1.279	0.183	7.002
	β_1	-0.347	0.292	-1.189	-0.35	0.296	-1.184
	β_2	-0.788	0.296	-2.666	-0.794	0.3	-2.647
	β_3	-0.891	0.293	-3.04	-0.897	0.297	-3.017
	β_4	-1.257	0.309	-4.061	-1.266	0.314	-4.033
Logistic	φ_1	1.563	0.435	3.595	1.681	0.463	3.63
	θ_{11}	2.255	0.294	7.678	2.272	0.296	7.677
	θ_{12}	3.431	0.38	9.034	3.462	0.383	9.042
	θ_{13}	2.958	0.356	8.307	2.987	0.359	8.32
	θ_{14}	5.428	0.776	6.998	5.473	0.778	7.03
	β_0	2.163	0.308	7.018	2.183	0.315	6.941
	β_1	-0.647	0.478	-1.353	-0.654	0.486	-1.346
	β_2	-1.385	0.495	-2.8	-1.396	0.502	-2.78
	β_3	-1.517	0.486	-3.124	-1.529	0.493	-3.1
	β_4	-2.249	0.523	-4.298	-2.269	0.531	-4.27
Extreme Minimal	φ_1	0.758	0.202	3.751	0.822	0.218	3.776
	θ_{11}	1.619	0.205	7.878	1.631	0.207	7.879
	θ_{12}	2.334	0.24	9.736	2.357	0.242	9.719
	θ_{13}	2.045	0.235	8.714	2.068	0.237	8.722
	θ_{14}	3.099	0.334	9.274	3.136	0.339	9.254
	β_0	1.838	0.223	8.251	1.854	0.228	8.15
	β_1	-0.459	0.336	-1.365	-0.462	0.342	-1.351
	β_2	-0.891	0.338	-2.632	-0.902	0.345	-2.617
	β_3	-1.013	0.334	-3.028	-1.021	0.34	-3
	β_4	-1.374	0.36	-3.822	-1.388	0.366	-3.796
Extreme Maximal	φ_1	0.687	0.188	3.646	0.746	0.202	3.687
	θ_{11}	1.451	0.199	7.279	1.465	0.201	7.287
	θ_{12}	2.365	0.295	8.025	2.385	0.296	8.053
	θ_{13}	1.971	0.262	7.515	1.991	0.264	7.541
	θ_{14}	4.215	0.719	5.859	4.248	0.721	5.896

Table 7.7.4: (continued).

Extreme Maximal	β_0	1.003	0.187	5.369	1.017	0.192	5.301
	β_1	-0.265	0.31	-0.856	-0.273	0.316	-0.862
	β_2	-0.829	0.326	-2.546	-0.84	0.332	-2.533
	β_3	-0.874	0.322	-2.717	-0.885	0.328	-2.701
	β_4	-1.41	0.349	-4.04	-1.428	0.355	-4.023

Table 7.7.5: ML and **REML** estimates of parameters, standard errors and their ratio for the model 5.

		ML			REML		
		Est	SE	Z-v	Est	SE	Z-v
Standard Normal	φ_1	0.488	0.178	2.751	0.516	0.188	2.754
	φ_2	0.125	0.184	0.679	0.149	0.197	0.756
	θ_{11}	1.372	0.178	7.723	1.383	0.179	7.726
	θ_{12}	2.088	0.226	9.241	2.107	0.228	9.24
	θ_{13}	1.779	0.213	8.36	1.795	0.215	8.369
	θ_{14}	3.014	0.361	8.342	3.04	0.363	8.367
	β_0	1.309	0.179	7.309	1.326	0.183	7.256
	β_1	-0.384	0.286	-1.344	-0.394	0.289	-1.362
	β_2	-0.826	0.299	-2.759	-0.839	0.305	-2.755
	β_3	-0.931	0.296	-3.142	-0.946	0.302	-3.136
	β_4	-1.299	0.313	-4.146	-1.316	0.318	-4.132
Logistic	φ_1	1.295	0.478	2.708	1.376	0.504	2.729
	φ_2	0.441	0.536	0.822	0.505	0.565	0.894
	θ_{11}	2.261	0.294	7.698	2.281	0.296	7.702
	θ_{12}	3.458	0.384	9.008	3.493	0.388	9.011
	θ_{13}	2.973	0.359	8.27	3.004	0.363	8.276
	θ_{14}	5.472	0.78	7.016	5.523	0.783	7.049
	β_0	2.228	0.306	7.292	2.257	0.312	7.245
	β_1	-0.718	0.463	-1.552	-0.734	0.469	-1.566
	β_2	-1.439	0.499	-2.881	-1.458	0.508	-2.871
	β_3	-1.58	0.491	-3.215	-1.602	0.5	-3.203
	β_4	-2.315	0.529	-4.373	-2.345	0.539	-4.354
Extreme Minimal	φ_1	0.628	0.228	2.757	0.668	0.242	2.763
	φ_2	0.223	0.25	0.893	0.264	0.267	0.989
	θ_{11}	1.643	0.209	7.848	1.661	0.212	7.847
	θ_{12}	2.358	0.244	9.676	2.385	0.247	9.646
	θ_{13}	2.062	0.238	8.674	2.088	0.241	8.673
	θ_{14}	3.149	0.344	9.164	3.193	0.35	9.128
	β_0	1.888	0.222	8.491	1.913	0.227	8.425

Table 7.7.5: (continued).

Extreme Minimal	β_1	-0.523	0.328	-1.598	-0.537	0.332	-1.618
	β_2	-0.957	0.344	-2.781	-0.977	0.351	-2.784
	β_3	-1.065	0.34	-3.136	-1.082	0.346	-3.122
	β_4	-1.441	0.365	-3.95	-1.465	0.372	-3.939
Extreme Maximal	φ_1	0.51	0.212	2.406	0.548	0.225	2.442
	φ_2	0.322	0.254	1.27	0.363	0.27	1.347
	θ_{11}	1.453	0.198	7.328	1.468	0.2	7.344
	θ_{12}	2.411	0.299	8.064	2.437	0.301	8.092
	θ_{13}	2.008	0.267	7.525	2.033	0.269	7.549
	θ_{14}	4.294	0.723	5.939	4.337	0.725	5.985
	β_0	1.118	0.189	5.921	1.146	0.194	5.902
	β_1	-0.376	0.297	-1.266	-0.393	0.302	-1.299
	β_2	-0.913	0.335	-2.724	-0.934	0.342	-2.729
	β_3	-0.992	0.332	-2.993	-1.017	0.339	-3.003
	β_4	-1.526	0.359	-4.252	-1.558	0.366	-4.256

Table 7.7a: ML and REML estimates of treatment effect, standard errors and their ratio for the model 1, 2, 4, 5 by using four threshold models.

		ML			REML		
Model		Est	SE	z-v	Est	SE	z-v
1	Standard Nor	-0.75	0.215	-3.497	-0.756	0.219	-3.447
	Logistic	-1.265	0.358	-3.532	-1.275	0.366	-3.484
	Extreme Min	-0.893	0.241	-3.705	-0.902	0.247	-3.651
	Extreme Max	-0.704	0.232	-3.035	-0.711	0.238	-2.991
2	Standard Nor	-0.821	0.231	-3.547	-0.827	0.237	-3.497
	Logistic	-1.449	0.39	-3.712	-1.462	0.399	-3.661
	Extreme Min	-0.934	0.265	-3.529	-0.944	0.272	-3.472
	Extreme Max	-0.845	0.254	-3.319	-0.856	0.261	-3.276
4	Standard Nor	-0.776	0.216	-3.602	-0.793	0.221	-3.595
	Logistic	-1.291	0.359	-3.595	-1.319	0.367	-3.59
	Extreme Min	-0.993	0.242	-4.099	-1.013	0.249	-4.074
	Extreme Max	-0.71	0.232	-3.057	-0.726	0.238	-3.047
5	Standard Nor	-0.86	0.231	-3.724	-0.874	0.236	-3.699
	Logistic	-1.513	0.387	-3.909	-1.535	0.396	-3.878
	Extreme Min	-0.997	0.264	-3.774	-1.015	0.271	-3.746
	Extreme Max	-0.952	0.256	-3.722	-0.975	0.263	-3.711

* Nor = Normal, Min =Minimal, Max =Maximal.

Table 7.7b: Observed and predicted frequencies for subjects undergoing active treatment or placebo using model 4 for skin disorder data of section 7.4.

Time		1									2								
			ML				REML					ML				REML			
	Y	O	1	2	3	4	1	2	3	4	O	1	2	3	4	1	2	3	4
	0	5	3	3	0	3	3	3	0	3	13	8	8	3	13	8	8	3	13
T	1	21	23	24	22	27	23	24	22	27	19	28	28	32	23	28	28	32	23
	2	10	10	9	14	6	10	9	14	6	4	0	0	1	0	0	0	1	0
	0	1	0	0	0	1	0	0	0	1	4	0	0	0	1	0	0	0	1
P	1	12	16	15	14	24	16	15	14	24	23	30	30	26	35	30	30	26	35
	2	23	20	21	22	11	20	21	22	11	9	6	6	10	0	6	6	10	0
Time		3									4								
			ML				REML					ML				REML			
	Y	O	1	2	3	4	1	2	3	4	O	1	2	3	4	1	2	3	4
	0	13	8	8	8	14	11	8	8	14	19	20	20	11	27	20	20	11	27
T	1	19	28	28	26	22	25	28	26	22	16	16	16	25	9	16	16	25	9
	2	4	0	0	2	0	0	0	2	0	1	0	0	0	0	0	0	0	0
	0	8	0	0	0	1	0	0	0	1	11	0	0	0	1	0	0	0	1
P	1	15	30	30	36	35	30	29	22	29	24	36	36	36	35	36	36	36	35
	2	13	6	6	0	0	6	7	14	6	1	0	0	0	0	0	0	0	0

* T = Treatment, P= Placebo, O = Observed, 1 = Standard Normal,

2= Logistic, 3 = Extreme Minimal value and 4 = Extreme Maximal value.

7.8 APPLICATION TO RESPIRATORY DISORDER DATA

The third application is to respiratory disorder data reported by Koch et al (1990). A total of 111 patients within two centres were randomly assigned to two treatments (active , placebo). At the baseline, status of each patient was recorded according to a five ordinal response scale (0 = terrible, 1 = poor, 2= fair, 3 = good, 4 = excellent), and also at each of four visits (visit 1, visit 2, visit 3, visit 4) during the time period over which the treatments were administered. Individual characteristics like age and gender of patients were also recorded at the time of entry to the study. The data are shown in Table 6 in appendix B.

We developed all 6 models of section 7.4 for the threshold models given in section 5.2. The treatment and patient effects are included in the model 1. The model 2 includes a second component of variance to take account of possible increase in the variance. The center, age and gender risk variables (individual characteristics) are included in the model 3.

The results of fitting models are tabled by 7.8.i and 7.8.ij. The i refers to the model and j indicates more results about model i. For example Table 7.8.1 gives results for the model 1, tables 7.8.5j (j =a, b, c, d) provide results for the model 5. The estimate of overall treatment effect is obtained by assuming treatment effect is constant over time and by using asymptotic distribution of $\hat{\beta}_t$ (t=1,2,3,4). The results are shown in the Table 7.8a.

Model 1:

The results indicate that treatment has a statistical significance effect. Moreover the estimate is positive, in that it increases η , so that observations are more expected in the highest category (excellent) from patients in the active treatment group.

From the tables 7.8.1 , we can see that the treatment effects β_t (t=1,2,3,4) are significant by comparing their corresponding z-values to the 1.96 critical value. Nevertheless, in spite of the treatment effect decreasing in magnitude for visits 2-4, the results of pair comparison between β_t (t=1,2,3,4), show that the treatment effect stays steady over time.

Model 2:

The results show that both variance components φ_1 and φ_2 are highly significant. Thus, there is significant variation between patients, and the patient effect does significantly change over time. The predicted values of the second random component may be used to show the direction of patient effect change (increase or decrease over time) and identify patients who show the greatest changes over time.

Model 3:

The center α_i and gender λ_i effects (i=1,2) do not appear significant. The risk variable age γ_1 does not contribute a significant variation on the first random component, however, the age effect γ_2 involves a significant reduction for the second random component. Also the results address the initial status of the disease effects ω_{ij} (i=1,2; j=1,2,3,4), another important significant risk variable.

Models 4, 5 and **6:**

In these models, the equality of break points $\theta_y(t)$ are tested across visits. The results support the null hypothesis, ie, the threshold parameters have no significant changes over time. The results for the models 4, 5 and 6 are the same as models 1, 2 and 3 respectively.

Consequently, model 3 of section 7.4 that includes second variance components along with risk variable corresponding to initial status of disease, adequately summarises this data. In this model, the observed and predicted Y values agree in 67.12%, 68.0%, 67.8%, 66%, by ML and 67.57%, 70.1%, 69.82%, 67.57% by REML methods for the model 3 by using the threshold models of section 5.2 respectively.

A comparison of the frequency distributions of observed and predicted values in active treatment and placebo groups at each observations times are given in Table 7.8b.

The data also have been analysed by Miller , Davis and Landis (1993) using GEEs and WLS methods. Our results are consistent with their results. Nevertheless they concluded that the treatment effect does not appear significant at first visit, whereas application of models in section 7.2 give a highly significant effect at every visit including the first visit.

Table 7.8.1: ML and REML estimates of parameters, standard errors and z-v of estimates to their standard errors for the model 1.

		ML			REML		
		Est	SE	Z-v	Est	SE	Z-v
Standard Normal	φ	1.859	0.299	6.218	1.923	0.311	6.183
	θ_1	0.828	0.121	6.829	0.832	0.122	6.829
	θ_2	2.18	0.152	14.306	2.19	0.153	14.304
	θ_3	3.2	0.169	18.89	3.214	0.17	18.883
	β_0	1.934	0.227	8.527	1.943	0.23	8.463
	β_1	0.822	0.315	2.61	0.825	0.319	2.59
	β_2	1.217	0.323	3.772	1.222	0.326	3.745
	β_3	1.063	0.319	3.328	1.067	0.323	3.304
	β_4	0.784	0.316	2.482	0.787	0.32	2.462
Logistic	φ	5.278	0.846	6.24	5.476	0.883	6.203
	θ_1	1.452	0.218	6.664	1.462	0.22	6.661
	θ_2	3.728	0.278	13.429	3.751	0.28	13.414
	θ_3	5.449	0.31	17.561	5.482	0.313	17.535
	β_0	3.266	0.391	8.359	3.286	0.396	8.296
	β_1	1.419	0.529	2.682	1.428	0.536	2.663
	β_2	2.053	0.54	3.804	2.065	0.547	3.777
	β_3	1.81	0.537	3.368	1.821	0.545	3.344
	β_4	1.338	0.533	2.512	1.346	0.54	2.493
Extreme Minimal	φ	2.562	0.411	6.231	2.655	0.429	6.191
	θ_1	1.076	0.163	6.586	1.082	0.164	6.585
	θ_2	2.716	0.207	13.144	2.729	0.208	13.133
	θ_3	3.885	0.227	17.136	3.905	0.228	17.119
	β_0	2.793	0.289	9.66	2.808	0.293	9.597
	β_1	0.904	0.369	2.45	0.909	0.374	2.433
	β_2	1.313	0.382	3.435	1.319	0.387	3.409
	β_3	1.193	0.379	3.151	1.199	0.383	3.127
	β_4	0.913	0.375	2.432	0.917	0.38	2.411
Extreme Maximal	φ	2.189	0.344	6.368	2.275	0.36	6.326
	θ_1	0.872	0.128	6.818	0.879	0.129	6.814
	θ_2	2.317	0.166	13.958	2.334	0.167	13.936
	θ_3	3.461	0.189	18.283	3.485	0.191	18.248
	β_0	1.719	0.238	7.211	1.73	0.242	7.148
	β_1	0.862	0.337	2.554	0.867	0.342	2.532
	β_2	1.367	0.343	3.99	1.376	0.348	3.961
	β_3	1.103	0.34	3.245	1.11	0.345	3.22
	β_4	0.789	0.337	2.342	0.795	0.342	2.324

Table 7.8.2: ML and REML estimates of parameters, standard errors and z-v of estimates to their standard errors for the model 2.

		ML			REML		
		Est	SE	Z-v	Est	SE	Z-v
Standard Normal	φ_1	1.588	0.312	5.087	1.65	0.325	5.078
	φ_2	0.857	0.287	2.988	0.892	0.296	3.015
	θ_1	0.931	0.136	6.858	0.939	0.137	6.859
	θ_2	2.382	0.168	14.217	2.399	0.169	14.21
	θ_3	3.481	0.186	18.744	3.505	0.187	18.731
	β_0	2.209	0.237	9.318	2.227	0.24	9.267
	β_1	0.749	0.308	2.434	0.751	0.312	2.409
	β_2	1.224	0.343	3.566	1.23	0.348	3.533
	β_3	1.061	0.34	3.122	1.066	0.345	3.093
	β_4	0.753	0.336	2.243	0.755	0.341	2.218
Logistic	φ_1	4.26	0.824	5.168	4.43	0.86	5.154
	φ_2	2.047	0.729	2.81	2.147	0.753	2.85
	θ_1	1.56	0.232	6.709	1.574	0.235	6.707
	θ_2	3.917	0.29	13.501	3.949	0.293	13.486
	θ_3	5.711	0.323	17.698	5.758	0.326	17.675
	β_0	3.59	0.393	9.132	3.625	0.399	9.087
	β_1	1.246	0.5	2.492	1.25	0.507	2.466
	β_2	2.012	0.557	3.61	2.023	0.566	3.576
	β_3	1.751	0.554	3.159	1.76	0.563	3.129
	β_4	1.25	0.548	2.28	1.254	0.556	2.254
Extreme Minimal	φ_1	2.258	0.437	5.166	2.356	0.457	5.157
	φ_2	1.397	0.417	3.346	1.451	0.431	3.366
	θ_1	1.22	0.183	6.656	1.231	0.185	6.655
	θ_2	2.982	0.225	13.266	3.005	0.227	13.252
	θ_3	4.253	0.245	17.333	4.287	0.248	17.312
	β_0	3.066	0.303	10.116	3.091	0.307	10.055
	β_1	0.779	0.362	2.15	0.782	0.368	2.126
	β_2	1.454	0.417	3.486	1.466	0.423	3.462
	β_3	1.304	0.413	3.154	1.314	0.42	3.132
	β_4	0.971	0.409	2.37	0.978	0.416	2.352
Extreme Maximal	φ_1	1.774	0.343	5.164	1.844	0.359	5.143
	φ_2	0.75	0.289	2.592	0.792	0.3	2.64
	θ_1	0.924	0.134	6.882	0.933	0.136	6.881
	θ_2	2.419	0.172	14.03	2.442	0.174	14.01

Table 7.8.2: (continued).

Extreme Maximal	θ_3	3.613	0.196	18.427	3.645	0.198	18.396
	β_0	1.924	0.24	8.026	1.946	0.244	7.989
	β_1	0.855	0.323	2.647	0.861	0.328	2.627
	β_2	1.313	0.352	3.728	1.319	0.358	3.686
	β_3	1.066	0.349	3.054	1.07	0.355	3.018
	β_4	0.745	0.346	2.156	0.747	0.351	2.127

Table 7.8.3a: ML and **REML** estimates of parameters, standard errors and z-v of estimates to their standard errors for the model 3.

		ML			REML		
		Est	SE	Z-v	Est	SE	Z-v
Standard Normal	φ_1	0.85	0.22	3.862	1.022	0.261	3.921
	φ_2	0.974	0.283	3.44	1.177	0.334	3.527
	θ_1	0.953	0.138	6.888	0.991	0.144	6.89
	θ_2	2.476	0.173	14.285	2.557	0.18	14.239
	θ_3	3.622	0.193	18.757	3.739	0.2	18.673
	β_0	4.325	0.603	7.175	4.475	0.644	6.953
	β_1	0.697	0.298	2.34	0.716	0.311	2.303
	β_2	1.576	0.344	4.584	1.624	0.367	4.428
	β_3	1.411	0.34	4.15	1.455	0.363	4.008
	β_4	1.083	0.335	3.236	1.116	0.358	3.119
	α_1	-0.463	0.307	-1.505	-0.478	0.321	-1.488
	α_2	0.113	0.348	0.324	0.112	0.363	0.309
	γ_1	-0.001	0.011	-0.092	-0.001	0.011	-0.107
	γ_2	-0.022	0.01	-2.316	-0.023	0.01	-2.296
	λ_1	-0.188	0.371	-0.506	-0.198	0.39	-0.509
	λ_2	-0.256	0.373	-0.686	-0.264	0.389	-0.678
	ω_{11}	-3.526	0.975	-3.615	-3.631	1.018	-3.567
	ω_{12}	-2.575	0.527	-4.884	-2.655	0.552	-4.808
	ω_{13}	-1.935	0.468	-4.133	-1.995	0.49	-4.07
	ω_{14}	-0.777	0.47	-1.653	-0.804	0.492	-1.634
	ω_{21}	1.099	1.059	1.037	1.133	1.103	1.027
	ω_{22}	0.375	0.542	0.692	0.388	0.565	0.686
	ω_{23}	0.614	0.484	1.27	0.634	0.504	1.258
	ω_{24}	0.529	0.48	1.102	0.547	0.5	1.095

* ω_{15} and ω_{25} are fixed at zero to achieve identifiability.

Table 7.8.3b: ML and REML estimates of parameters, standard errors and z-v of estimates to their standard errors for the model 3.

		ML			REML		
		Est	SE	Z-v	Est	SE	Z-v
Logistic	φ_1	2.291	0.585	3.913	2.786	0.7	3.979
	φ_2	2.59	0.757	3.423	3.193	0.904	3.532
	θ_1	1.591	0.235	6.76	1.668	0.247	6.749
	θ_2	4.085	0.3	13.614	4.244	0.314	13.522
	θ_3	5.968	0.336	17.77	6.195	0.351	17.638
	β_0	7.084	0.994	7.129	7.364	1.066	6.907
	β_1	1.141	0.484	2.359	1.177	0.506	2.326
	β_2	2.562	0.565	4.539	2.658	0.607	4.381
	β_3	2.289	0.561	4.081	2.375	0.603	3.939
	β_4	1.778	0.554	3.208	1.84	0.596	3.088
	α_1	-0.748	0.499	-1.498	-0.776	0.522	-1.488
	α_2	0.178	0.566	0.315	0.178	0.592	0.3
	γ_1	-0.003	0.017	-0.174	-0.003	0.018	-0.173
	γ_2	-0.035	0.016	-2.205	-0.037	0.017	-2.196
	λ_1	-0.298	0.602	-0.495	-0.318	0.634	-0.501
	λ_2	-0.426	0.611	-0.696	-0.434	0.639	-0.678
	ω_{11}	-5.69	1.574	-3.615	-5.893	1.649	-3.574
	ω_{12}	-4.201	0.866	-4.852	-4.348	0.909	-4.782
	ω_{13}	-3.118	0.773	-4.032	-3.23	0.811	-3.982
	ω_{14}	-1.249	0.771	-1.62	-1.301	0.81	-1.606
	ω_{21}	1.736	1.703	1.019	1.796	1.783	1.008
	ω_{22}	0.599	0.884	0.678	0.613	0.926	0.662
	ω_{23}	0.989	0.796	1.242	1.022	0.832	1.228
	ω_{24}	0.847	0.787	1.076	0.876	0.823	1.064

* ω_{15} and ω_{25} are fixed at zero to achieve identifiability.

Table 7.8.3c: **ML** and **REML** estimates of parameters, standard errors and z-v of estimates to their standard errors for the model 3.

		ML			REML		
		Est	SE	Z-v	Est	SE	Z-v
Extreme Minimal	φ_1	1.342	0.322	4.168	1.619	0.387	4.184
	φ_2	1.316	0.389	3.383	1.633	0.467	3.5
	θ_1	1.244	0.186	6.68	1.301	0.195	6.673
	θ_2	3.075	0.231	13.331	3.189	0.241	13.239
	θ_3	4.414	0.255	17.344	4.578	0.266	17.211
	β_0	5.745	0.763	7.53	5.962	0.819	7.282
	β_1	0.769	0.36	2.136	0.803	0.377	2.128
	β_2	1.866	0.418	4.465	1.934	0.448	4.313
	β_3	1.707	0.411	4.149	1.77	0.442	4.001
	β_4	1.391	0.408	3.405	1.437	0.439	3.272
	α_1	-0.621	0.374	-1.662	-0.636	0.391	-1.626
	α_2	0.267	0.411	0.651	0.265	0.431	0.615
	γ_1	-0.004	0.013	-0.306	-0.004	0.014	-0.311
	γ_2	-0.025	0.012	-2.15	-0.026	0.012	-2.13
	λ_1	-0.197	0.455	-0.434	-0.222	0.478	-0.465
	λ_2	-0.444	0.447	-0.993	-0.448	0.468	-0.958
	ω_{11}	-4.233	1.158	-3.656	-4.396	1.218	-3.609
	ω_{12}	-3.165	0.647	-4.891	-3.292	0.682	-4.824
	ω_{13}	-2.375	0.59	-4.028	-2.474	0.62	-3.989
	ω_{14}	-1.045	0.595	-1.755	-1.098	0.626	-1.755
	ω_{21}	1.153	1.208	0.955	1.216	1.269	0.958
	ω_{22}	0.46	0.64	0.719	0.504	0.672	0.75
	ω_{23}	0.741	0.591	1.253	0.789	0.618	1.277
	ω_{24}	0.713	0.591	1.205	0.758	0.617	1.228

* ω_{15} and ω_{25} are fixed at zero to achieve identifiability.

Table 7.8.3d: ML and REML estimates of parameters, standard errors and z-v of estimates to their standard errors for the model 3.

		ML			REML		
		Est	SE	Z-v	Est	SE	Z-v
Extreme Maximal	φ_1	0.8	0.223	3.587	1.006	0.271	3.709
	φ_2	1.199	0.318	3.774	1.438	0.379	3.795
	θ_1	0.956	0.138	6.929	1.003	0.145	6.92
	θ_2	2.548	0.181	14.042	2.656	0.191	13.933
	θ_3	3.797	0.207	18.343	3.95	0.217	18.188
	β_0	4.084	0.597	6.843	4.269	0.644	6.633
	β_1	0.789	0.301	2.62	0.807	0.317	2.545
	β_2	1.639	0.356	4.598	1.699	0.383	4.431
	β_3	1.403	0.354	3.966	1.453	0.38	3.821
	β_4	1.026	0.349	2.942	1.067	0.375	2.845
	α_1	-0.408	0.313	-1.302	-0.433	0.329	-1.314
	α_2	0.002	0.371	0.005	0.003	0.387	0.009
	γ_1	0.001	0.011	0.083	0	0.011	0.038
	γ_2	-0.025	0.01	-2.457	-0.026	0.011	-2.429
	λ_1	-0.259	0.37	-0.7	-0.259	0.392	-0.662
	λ_2	-0.121	0.39	-0.311	-0.141	0.408	-0.346
	ω_{11}	-3.617	1.016	-3.561	-3.733	1.063	-3.511
	ω_{12}	-2.651	0.537	-4.937	-2.734	0.566	-4.831
	ω_{13}	-2.018	0.465	-4.336	-2.074	0.493	-4.212
	ω_{14}	-0.733	0.46	-1.593	-0.751	0.488	-1.539
	ω_{21}	1.3	1.146	1.134	1.324	1.193	1.11
	ω_{22}	0.455	0.576	0.789	0.447	0.602	0.742
	ω_{23}	0.693	0.501	1.385	0.698	0.525	1.331
	ω_{24}	0.499	0.492	1.015	0.504	0.515	0.977

* ω_{15} and ω_{25} are fixed at zero to achieve identifiability.

Table 7.8.4a: ML and REML estimates of parameters, standard errors and z-v of estimates to their standard errors for the model 4.

		ML			REML		
		Est	SE	Z-v	Est	SE	Z-v
Standard Normal	φ_1	1.901	0.305	6.233	1.967	0.317	6.196
	θ_{11}	0.635	0.17	3.735	0.638	0.171	3.737
	θ_{12}	1.043	0.215	4.842	1.048	0.216	4.849
	θ_{13}	0.841	0.205	4.105	0.846	0.206	4.11
	θ_{14}	0.886	0.199	4.447	0.891	0.2	4.451
	θ_{21}	2.019	0.207	9.736	2.027	0.208	9.744
	θ_{22}	2.501	0.23	10.89	2.513	0.23	10.903
	θ_{23}	2.086	0.226	9.241	2.096	0.227	9.252
	θ_{24}	2.239	0.221	10.131	2.25	0.222	10.141
	θ_{31}	3.204	0.232	13.798	3.218	0.233	13.806
	θ_{32}	3.528	0.259	13.639	3.545	0.26	13.649
	θ_{33}	3.197	0.246	12.982	3.212	0.247	12.994
	θ_{34}	3.028	0.236	12.836	3.043	0.237	12.848
	β_0	1.959	0.229	8.542	1.969	0.232	8.476
	β_1	0.714	0.338	2.11	0.716	0.342	2.094
	β_2	1.489	0.353	4.221	1.496	0.356	4.196
	β_3	1.012	0.347	2.914	1.017	0.351	2.898
	β_4	0.714	0.342	2.089	0.717	0.346	2.076
Logistic	φ_1	5.408	0.864	6.257	5.613	0.903	6.217
	θ_{11}	1.142	0.303	3.769	1.149	0.305	3.771
	θ_{12}	1.804	0.368	4.897	1.816	0.37	4.905
	θ_{13}	1.485	0.355	4.183	1.496	0.357	4.189
	θ_{14}	1.533	0.34	4.508	1.543	0.342	4.513
	θ_{21}	3.542	0.372	9.533	3.563	0.374	9.535
	θ_{22}	4.273	0.403	10.598	4.3	0.406	10.603
	θ_{23}	3.554	0.387	9.174	3.576	0.39	9.181
	θ_{24}	3.782	0.378	9.992	3.805	0.381	9.997
	θ_{31}	5.602	0.421	13.299	5.636	0.424	13.3
	θ_{32}	5.981	0.452	13.231	6.019	0.455	13.233
	θ_{33}	5.415	0.427	12.685	5.449	0.429	12.69
	θ_{34}	5.101	0.406	12.549	5.132	0.409	12.553
	β_0	3.315	0.396	8.377	3.336	0.401	8.313
	β_1	1.332	0.574	2.321	1.34	0.581	2.306
	β_2	2.507	0.594	4.221	2.523	0.601	4.197
	β_3	1.699	0.584	2.907	1.709	0.591	2.89
	β_4	1.167	0.574	2.031	1.173	0.581	2.018

Table 7.8.4b: **ML** and **REML** estimates of parameters, standard errors and z-v of estimates to their standard errors for the model 4.

		ML			REML		
		Est	SE	Z-v	Est	SE	Z-v
Extreme Minimal	φ_1	2.652	0.424	6.256	2.752	0.443	6.21
	θ_{11}	0.806	0.219	3.687	0.809	0.219	3.688
	θ_{12}	1.34	0.277	4.835	1.348	0.278	4.842
	θ_{13}	1.137	0.274	4.153	1.144	0.275	4.159
	θ_{14}	1.185	0.261	4.532	1.192	0.263	4.537
	θ_{21}	2.503	0.263	9.509	2.515	0.265	9.507
	θ_{22}	3.111	0.283	10.991	3.127	0.284	10.993
	θ_{23}	2.667	0.283	9.433	2.682	0.284	9.439
	θ_{24}	2.806	0.275	10.221	2.821	0.276	10.224
	θ_{31}	3.863	0.289	13.348	3.883	0.291	13.34
	θ_{32}	4.28	0.314	13.65	4.304	0.315	13.643
	θ_{33}	3.964	0.305	12.976	3.986	0.307	12.976
	θ_{34}	3.712	0.291	12.744	3.732	0.293	12.745
	β_0	2.836	0.294	9.655	2.852	0.297	9.589
	β_1	0.748	0.399	1.876	0.752	0.404	1.861
	β_2	1.65	0.418	3.952	1.659	0.422	3.928
	β_3	1.192	0.416	2.866	1.199	0.421	2.849
	β_4	0.82	0.409	2.005	0.824	0.414	1.99
Extreme Maximal	φ_1	2.231	0.35	6.374	2.323	0.367	6.328
	θ_{11}	0.725	0.189	3.841	0.731	0.19	3.845
	θ_{12}	1.102	0.227	4.855	1.111	0.228	4.864
	θ_{13}	0.856	0.206	4.148	0.864	0.208	4.155
	θ_{14}	0.884	0.201	4.399	0.891	0.202	4.404
	θ_{21}	2.258	0.238	9.474	2.275	0.24	9.483
	θ_{22}	2.642	0.258	10.243	2.661	0.259	10.258
	θ_{23}	2.157	0.24	8.971	2.173	0.242	8.983
	θ_{24}	2.326	0.239	9.75	2.344	0.24	9.758
	θ_{31}	3.635	0.278	13.062	3.66	0.28	13.075
	θ_{32}	3.772	0.294	12.828	3.798	0.296	12.844
	θ_{33}	3.374	0.271	12.445	3.398	0.273	12.459
	θ_{34}	3.21	0.261	12.305	3.232	0.262	12.316
	β_0	1.743	0.241	7.238	1.755	0.245	7.173
	β_1	0.852	0.366	2.329	0.857	0.371	2.311
	β_2	1.627	0.378	4.31	1.639	0.382	4.286
	β_3	0.992	0.366	2.71	0.998	0.371	2.692
	β_4	0.69	0.362	1.907	0.694	0.367	1.892

Table 7.8.5a: ML and REML estimates of parameters, standard errors and z-v of estimates to their standard errors for the model 5.

		ML			REML		
		Est	SE	Z-v	Est	SE	Z-v
Standard Normal	φ_1	1.63	0.317	5.136	1.692	0.331	5.111
	φ_2	0.827	0.284	2.909	0.881	0.297	2.965
	θ_{11}	0.753	0.198	3.806	0.762	0.2	3.808
	θ_{12}	1.134	0.232	4.891	1.145	0.234	4.901
	θ_{13}	0.929	0.223	4.171	0.938	0.224	4.18
	θ_{14}	0.971	0.216	4.493	0.98	0.218	4.5
	θ_{21}	2.183	0.23	9.492	2.203	0.232	9.485
	θ_{22}	2.701	0.246	10.976	2.723	0.248	10.991
	θ_{23}	2.293	0.245	9.372	2.313	0.246	9.388
	θ_{24}	2.446	0.239	10.229	2.467	0.241	10.241
	θ_{31}	3.375	0.253	13.347	3.404	0.255	13.336
	θ_{32}	3.841	0.281	13.685	3.874	0.283	13.692
	θ_{33}	3.51	0.266	13.187	3.541	0.268	13.203
	θ_{34}	3.319	0.256	12.975	3.348	0.258	12.988
	β_0	2.171	0.241	9.024	2.192	0.244	8.968
	β_1	0.645	0.325	1.981	0.647	0.329	1.966
	β_2	1.566	0.382	4.096	1.576	0.388	4.063
	β_3	1.084	0.376	2.883	1.092	0.382	2.86
	β_4	0.747	0.37	2.02	0.751	0.376	1.999

Table 7.8.5b: ML and REML estimates of parameters, standard errors and z-v of estimates to their standard errors for the model 2.

		ML			REML		
		Est	SE	Z-v	Est	SE	Z-v
	φ_1	4.402	0.844	5.216	4.564	0.881	5.182
	φ_2	2.02	0.73	2.767	2.19	0.768	2.85
	θ_{11}	1.282	0.333	3.843	1.298	0.338	3.847
	θ_{12}	1.904	0.389	4.899	1.927	0.393	4.908
	θ_{13}	1.583	0.375	4.219	1.603	0.379	4.229
	θ_{14}	1.626	0.36	4.518	1.644	0.363	4.524
Logistic	θ_{21}	3.624	0.385	9.41	3.658	0.389	9.401
	θ_{22}	4.51	0.425	10.6	4.557	0.43	10.603
	θ_{23}	3.79	0.41	9.251	3.831	0.414	9.26
	θ_{24}	4.016	0.4	10.035	4.058	0.404	10.039
	θ_{31}	5.582	0.429	13.026	5.63	0.433	13.013
	θ_{32}	6.358	0.479	13.277	6.426	0.484	13.276
	θ_{33}	5.786	0.45	12.847	5.848	0.455	12.855
	θ_{34}	5.438	0.43	12.644	5.496	0.435	12.648
	β_0	3.553	0.4	8.873	3.592	0.407	8.823
	β_1	1.083	0.532	2.035	1.082	0.538	2.012
	β_2	2.616	0.629	4.16	2.641	0.639	4.131
	β_3	1.79	0.616	2.905	1.808	0.627	2.885
	β_4	1.21	0.605	2.001	1.221	0.615	1.983

Table 7.8.5c: ML and REML estimates of parameters, standard errors and z-v of estimates to their standard errors for the model 5.

		ML			REML		
		Est	SE	Z-v	Est	SE	Z-v
	φ_1	2.324	0.448	5.186	2.426	0.47	5.162
	φ_2	1.333	0.413	3.223	1.423	0.435	3.271
	θ_{11}	1.016	0.264	3.845	1.031	0.268	3.851
	θ_{12}	1.411	0.294	4.792	1.425	0.297	4.798
	θ_{13}	1.245	0.295	4.22	1.259	0.298	4.23
	θ_{14}	1.279	0.281	4.554	1.292	0.283	4.561
Extreme	θ_{21}	2.781	0.289	9.613	2.812	0.293	9.607
Minimal	θ_{22}	3.327	0.307	10.838	3.357	0.31	10.83
	θ_{23}	2.904	0.305	9.514	2.932	0.308	9.52
	θ_{24}	3.039	0.297	10.226	3.067	0.3	10.225
	θ_{31}	4.122	0.309	13.33	4.167	0.313	13.315
	θ_{32}	4.654	0.345	13.481	4.7	0.349	13.461
	θ_{33}	4.333	0.331	13.092	4.376	0.334	13.087
	θ_{34}	4.057	0.317	12.797	4.096	0.32	12.792
	β_0	3.015	0.309	9.755	3.045	0.314	9.686
	β_1	0.676	0.383	1.764	0.68	0.388	1.752
	β_2	1.849	0.466	3.971	1.867	0.474	3.941
	β_3	1.372	0.461	2.975	1.386	0.469	2.954
	β_4	0.948	0.454	2.089	0.957	0.462	2.072

Table 7.8.5d: ML and **REML** estimates of parameters, standard errors and z-v of estimates to their standard errors for the model 5.

		ML			REML		
		Est	SE	Z-v	Est	SE	Z-v
Extreme Maximal	φ_1	1.815	0.348	5.214	1.879	0.364	5.167
	φ_2	0.772	0.292	2.645	0.849	0.309	2.748
	θ_{11}	0.765	0.199	3.856	0.775	0.201	3.858
	θ_{12}	1.179	0.241	4.895	1.195	0.244	4.906
	θ_{13}	0.913	0.219	4.177	0.926	0.221	4.187
	θ_{14}	0.949	0.214	4.433	0.961	0.217	4.439
	θ_{21}	2.236	0.243	9.216	2.255	0.245	9.204
	θ_{22}	2.817	0.272	10.348	2.853	0.275	10.368
	θ_{23}	2.311	0.255	9.076	2.341	0.257	9.092
	θ_{24}	2.485	0.253	9.83	2.516	0.256	9.842
	θ_{31}	3.566	0.281	12.691	3.593	0.283	12.682
	θ_{32}	4.027	0.31	13.01	4.077	0.313	13.032
	θ_{33}	3.622	0.286	12.666	3.667	0.289	12.689
	θ_{34}	3.433	0.275	12.472	3.475	0.278	12.488
	β_0	1.92	0.243	7.889	1.947	0.248	7.856
	β_1	0.744	0.344	2.162	0.744	0.348	2.14
	β_2	1.671	0.396	4.217	1.687	0.403	4.183
	β_3	1.04	0.383	2.713	1.05	0.39	2.691
	β_4	0.712	0.379	1.88	0.717	0.386	1.86

Table 7.8.6a: **ML** and **REML** estimates of parameters, standard errors and z-v of estimates to their standard errors for the model 6.

		ML			REML		
		Est	SE	Z-v	Est	SE	Z-v
Standard Normal	φ_1	0.99	0.237	4.184	1.191	0.284	4.197
	φ_2	0.831	0.271	3.067	1.05	0.325	3.23
	θ_{11}	1.013	0.291	3.479	1.058	0.303	3.488
	θ_{12}	1.063	0.228	4.654	1.109	0.236	4.697
	θ_{13}	0.861	0.216	3.978	0.902	0.224	4.019
	θ_{14}	0.908	0.211	4.305	0.946	0.218	4.334
	θ_{21}	2.711	0.343	7.901	2.808	0.356	7.882
	θ_{22}	2.641	0.252	10.502	2.73	0.259	10.556
	θ_{23}	2.228	0.249	8.961	2.311	0.256	9.019
	θ_{24}	2.393	0.244	9.816	2.478	0.251	9.86
	θ_{31}	4.047	0.368	10.989	4.19	0.382	10.955
	θ_{32}	3.8	0.288	13.175	3.932	0.298	13.189
	θ_{33}	3.467	0.272	12.726	3.591	0.281	12.775
	θ_{34}	3.276	0.261	12.55	3.391	0.269	12.588
	β_0	4.464	0.63	7.085	4.65	0.678	6.859
	β_1	0.774	0.313	2.473	0.795	0.327	2.43
	β_2	1.754	0.369	4.756	1.809	0.393	4.597
	β_3	1.273	0.362	3.515	1.318	0.387	3.404
	β_4	0.931	0.356	2.615	0.961	0.381	2.52
	α_1	-0.495	0.319	-1.551	-0.513	0.334	-1.536
	α_2	0.148	0.341	0.433	0.148	0.358	0.412
	γ_1	0.002	0.011	0.157	0.001	0.012	0.118
	γ_2	-0.028	0.01	-2.676	-0.028	0.011	-2.648
	λ_1	-0.123	0.388	-0.316	-0.138	0.408	-0.338
	λ_2	-0.39	0.378	-1.03	-0.402	0.396	-1.015
	ω_{11}	-3.759	1.021	-3.684	-3.886	1.069	-3.636
	ω_{12}	-2.71	0.549	-4.935	-2.806	0.577	-4.863
	ω_{13}	-2.015	0.486	-4.149	-2.086	0.51	-4.09
	ω_{14}	-0.732	0.488	-1.501	-0.766	0.512	-1.495
	ω_{21}	1.313	1.048	1.253	1.357	1.096	1.237
	ω_{22}	0.481	0.542	0.887	0.497	0.568	0.876
	ω_{23}	0.648	0.483	1.341	0.67	0.506	1.323
	ω_{24}	0.423	0.489	0.867	0.44	0.511	0.861

* ω_{15} and ω_{25} are fixed at zero to achieve identifiability.

Table 7.8.6b: **ML** and **REML** estimates of parameters, standard errors and z-v of estimates to their standard errors for the model 6.

		ML			REML		
		Est	SE	Z-v	Est	SE	Z-v
Logistic	φ_1	2.665	0.635	4.194	3.226	0.766	4.21
	φ_2	2.248	0.731	3.075	2.914	0.891	3.269
	θ_{11}	1.654	0.478	3.462	1.737	0.5	3.473
	θ_{12}	1.788	0.384	4.656	1.883	0.401	4.696
	θ_{13}	1.472	0.366	4.018	1.556	0.383	4.059
	θ_{14}	1.522	0.352	4.321	1.599	0.368	4.346
	θ_{21}	4.402	0.568	7.748	4.572	0.592	7.728
	θ_{22}	4.434	0.438	10.126	4.624	0.456	10.13
	θ_{23}	3.711	0.421	8.823	3.877	0.438	8.853
	θ_{24}	3.958	0.412	9.607	4.127	0.429	9.617
	θ_{31}	6.593	0.616	10.697	6.838	0.641	10.665
	θ_{32}	6.332	0.497	12.735	6.603	0.519	12.716
	θ_{33}	5.76	0.465	12.376	6.006	0.485	12.382
	θ_{34}	5.411	0.443	12.204	5.638	0.462	12.2
	β_0	7.306	1.04	7.023	7.637	1.124	6.795
	β_1	1.266	0.513	2.467	1.301	0.537	2.424
	β_2	2.904	0.613	4.74	3.024	0.658	4.595
	β_3	2.076	0.599	3.465	2.165	0.644	3.359
	β_4	1.506	0.589	2.557	1.563	0.634	2.463
	α_1	-0.8	0.521	-1.536	-0.833	0.545	-1.526
	α_2	0.234	0.559	0.419	0.232	0.588	0.395
	γ_1	0	0.019	0.023	0	0.02	-0.002
	γ_2	-0.042	0.017	-2.473	-0.044	0.018	-2.447
	λ_1	-0.205	0.632	-0.325	-0.236	0.666	-0.354
	λ_2	-0.614	0.624	-0.985	-0.622	0.656	-0.948
	ω_{11}	-6.071	1.655	-3.667	-6.297	1.737	-3.624
	ω_{12}	-4.428	0.909	-4.873	-4.595	0.956	-4.808
	ω_{13}	-3.251	0.807	-4.031	-3.381	0.847	-3.99
	ω_{14}	-1.183	0.804	-1.472	-1.251	0.845	-1.48
	ω_{21}	2.09	1.694	1.234	2.157	1.784	1.209
	ω_{22}	0.787	0.895	0.879	0.803	0.942	0.853
	ω_{23}	1.054	0.805	1.31	1.09	0.845	1.291
	ω_{24}	0.69	0.809	0.852	0.727	0.85	0.856

* ω_{15} and ω_{25} are fixed at zero to achieve identifiability.

Table 7.8.6c: ML and REML estimates of parameters, standard errors and z-v of estimates to their standard errors for the model 6.

		ML			REML		
		Est	SE	Z-v	Est	SE	Z-v
Extreme Minimal	φ_1	1.522	0.345	4.405	1.842	0.42	4.386
	φ_2	1.16	0.377	3.075	1.505	0.462	3.261
	θ_{11}	1.271	0.374	3.402	1.334	0.39	3.42
	θ_{12}	1.351	0.293	4.616	1.415	0.305	4.642
	θ_{13}	1.169	0.289	4.041	1.236	0.303	4.085
	θ_{14}	1.214	0.277	4.384	1.275	0.289	4.412
	θ_{21}	3.294	0.434	7.596	3.423	0.45	7.603
	θ_{22}	3.276	0.319	10.275	3.403	0.332	10.24
	θ_{23}	2.823	0.312	9.039	2.944	0.325	9.057
	θ_{24}	2.989	0.306	9.755	3.108	0.319	9.743
	θ_{31}	4.828	0.458	10.532	5.019	0.477	10.523
	θ_{32}	4.625	0.359	12.893	4.811	0.376	12.804
	θ_{33}	4.287	0.342	12.543	4.463	0.357	12.512
	θ_{34}	4.025	0.327	12.308	4.184	0.341	12.273
	β_0	5.873	0.789	7.442	6.134	0.854	7.186
	β_1	0.843	0.376	2.243	0.881	0.395	2.231
	β_2	2.078	0.448	4.642	2.157	0.481	4.484
	β_3	1.573	0.44	3.578	1.638	0.473	3.465
	β_4	1.196	0.435	2.749	1.238	0.468	2.642
	α_1	-0.662	0.388	-1.709	-0.68	0.407	-1.671
	α_2	0.32	0.408	0.785	0.318	0.429	0.74
	γ_1	-0.001	0.014	-0.076	-0.002	0.015	-0.11
	γ_2	-0.03	0.012	-2.445	-0.031	0.013	-2.417
	λ_1	-0.122	0.473	-0.258	-0.155	0.499	-0.311
	λ_2	-0.588	0.455	-1.293	-0.596	0.478	-1.246
	ω_{11}	-4.456	1.214	-3.672	-4.644	1.281	-3.626
	ω_{12}	-3.282	0.666	-4.927	-3.429	0.705	-4.864
	ω_{13}	-2.432	0.605	-4.022	-2.545	0.638	-3.99
	ω_{14}	-0.982	0.613	-1.602	-1.044	0.646	-1.617
	ω_{21}	1.36	1.21	1.124	1.437	1.278	1.124
	ω_{22}	0.555	0.646	0.859	0.608	0.681	0.893
	ω_{23}	0.761	0.6	1.269	0.815	0.629	1.296
	ω_{24}	0.602	0.612	0.984	0.651	0.641	1.015

* ω_{15} and ω_{25} are fixed at zero to achieve identifiability.

Table 7.8.6d: ML and REML estimates of parameters, standard errors and z-v of estimates to their standard errors for the model 6.

		ML			REML		
		Est	SE	Z-v	Est	SE	Z-v
Extreme Maximal	φ_1	0.953	0.244	3.907	1.176	0.297	3.954
	φ_2	1.025	0.305	3.364	1.297	0.372	3.491
	θ_{11}	1.004	0.284	3.534	1.054	0.297	3.545
	θ_{12}	1.117	0.241	4.646	1.18	0.252	4.688
	θ_{13}	0.864	0.217	3.99	0.915	0.227	4.03
	θ_{14}	0.9	0.212	4.238	0.947	0.222	4.264
	θ_{21}	2.762	0.351	7.866	2.867	0.365	7.846
	θ_{22}	2.788	0.28	9.954	2.922	0.292	10.004
	θ_{23}	2.287	0.263	8.707	2.401	0.274	8.757
	θ_{24}	2.464	0.261	9.435	2.583	0.273	9.465
	θ_{31}	4.23	0.395	10.708	4.379	0.409	10.707
	θ_{32}	4.029	0.32	12.584	4.213	0.334	12.63
	θ_{33}	3.638	0.297	12.233	3.806	0.31	12.277
	θ_{34}	3.428	0.284	12.054	3.585	0.297	12.082
	β_0	4.246	0.631	6.729	4.455	0.683	6.521
	β_1	0.87	0.323	2.692	0.885	0.339	2.612
	β_2	1.846	0.386	4.781	1.924	0.415	4.634
	β_3	1.243	0.375	3.316	1.294	0.404	3.204
	β_4	0.86	0.37	2.328	0.896	0.399	2.248
	α_1	-0.437	0.33	-1.324	-0.462	0.346	-1.333
	α_2	0.037	0.367	0.099	0.037	0.385	0.096
	γ_1	0.003	0.011	0.267	0.002	0.012	0.188
	γ_2	-0.029	0.011	-2.687	-0.03	0.011	-2.624
	λ_1	-0.215	0.39	-0.55	-0.223	0.413	-0.539
	λ_2	-0.232	0.397	-0.584	-0.247	0.418	-0.592
	ω_{11}	-3.864	1.069	-3.615	-3.986	1.118	-3.565
	ω_{12}	-2.828	0.578	-4.895	-2.918	0.607	-4.806
	ω_{13}	-2.145	0.498	-4.305	-2.206	0.525	-4.201
	ω_{14}	-0.712	0.488	-1.459	-0.736	0.515	-1.43
	ω_{21}	1.517	1.137	1.335	1.539	1.19	1.293
	ω_{22}	0.591	0.587	1.007	0.578	0.615	0.94
	ω_{23}	0.77	0.508	1.517	0.772	0.534	1.446
	ω_{24}	0.407	0.503	0.808	0.418	0.53	0.789

* ω_{15} and ω_{25} are fixed at zero to achieve identifiability.

Table 7.8a: ML and REML estimates of treatment effect, standard errors and their z-v for the model 1, 2, 3, 4, 5, 6 by using four threshold models.

		ML			REML		
Model		Est	SE	z-v	Est	SE	z-v
1	Standard Nor	0.971	0.285	3.403	0.975	0.29	3.369
	Logistic	1.655	0.481	3.438	1.665	0.489	3.404
	Extreme Min	1.081	0.335	3.226	1.086	0.34	3.192
	Extreme Max	1.03	0.306	3.363	1.037	0.311	3.329
2	Standard Nor	1.192	0.27	4.409	1.228	0.292	4.207
	Logistic	1.943	0.444	4.371	2.013	0.483	4.168
	Extreme Min	1.433	0.329	4.36	1.486	0.357	4.16
	Extreme Max	1.214	0.277	4.382	1.257	0.302	4.163
3	Standard Nor	1.192	0.27	4.409	1.228	0.292	4.207
	Logistic	1.943	0.444	4.371	2.013	0.483	4.168
	Extreme Min	1.433	0.329	4.36	1.486	0.357	4.16
	Extreme Max	1.214	0.277	4.382	1.257	0.302	4.163
4	Standard Nor	0.982	0.288	3.407	0.987	0.293	3.372
	Logistic	1.676	0.487	3.443	1.686	0.495	3.408
	Extreme Min	1.103	0.34	3.24	1.108	0.346	3.204
	Extreme Max	1.04	0.309	3.364	1.047	0.315	3.328
5	Standard Nor	1.01	0.3	3.366	1.017	0.306	3.325
	Logistic	1.675	0.491	3.414	1.688	0.5	3.374
	Extreme Min	1.211	0.363	3.335	1.223	0.371	3.297
	Extreme Max	1.042	0.31	3.357	1.05	0.317	3.316
6	Standard Nor	1.183	0.275	4.299	1.221	0.299	4.082
	Logistic	1.938	0.454	4.271	2.013	0.496	4.059
	Extreme Min	1.423	0.335	4.242	1.479	0.367	4.031
	Extreme Max	1.205	0.282	4.278	1.25	0.308	4.051

* Nor = Normal, Min =Minimal, Max =Maximal.

Table 7.8b: Observed and predicted frequencies for subjects undergoing active treatment or placebo using model 3 for skin treatment data of section 7.8.

Time		1									2								
			ML				REML					ML				REML			
	Y	O	1	2	3	4	1	2	3	4	O	1	2	3	4	1	2	3	4
T	1	1	0	0	0	1	1	1	0	1	0	0	0	0	0	0	0	0	0
	2	3	1	1	1	1	0	0	1	3	4	1	1	1	1	1	1	1	2
	3	13	17	16	13	19	16	16	13	17	12	14	14	10	17	14	14	10	17
	4	19	19	19	17	20	18	18	18	19	11	9	9	10	13	9	9	11	12
	5	18	17	18	23	13	19	19	22	14	27	30	30	33	23	30	30	32	23
P	1	4	3	3	0	4	3	3	0	4	9	9	8	7	9	9	9	8	10
	2	6	2	2	4	6	2	3	5	6	7	5	6	3	7	6	5	3	6
	3	19	21	22	19	22	21	20	17	22	19	18	17	20	21	16	17	19	21
	4	12	20	19	18	18	19	19	19	17	11	16	15	13	12	16	14	13	11
	5	16	11	11	16	7	12	12	16	8	11	9	11	14	8	10	12	14	9

Time		3									4								
			ML				REML					ML				REML			
	Y	O	1	2	3	4	1	2	3	4	O	1	2	3	4	1	2	3	4
T	1	2	0	0	0	1	0	0	0	1	1	1	1	0	1	1	1	0	1
	2	3	1	2	1	3	2	3	1	3	8	2	2	3	6	3	2	3	6
	3	10	14	13	11	15	13	12	11	15	12	15	15	12	15	15	15	12	15
	4	14	9	9	12	16	9	9	12	16	9	15	16	9	16	14	16	9	16
	5	25	30	30	30	19	30	30	30	19	24	21	20	30	16	21	20	30	16
P	1	11	9	8	7	9	9	9	8	10	12	9	8	7	9	9	9	8	10
	2	6	5	6	3	7	6	5	3	6	3	5	6	3	7	6	5	3	6
	3	14	18	17	20	21	16	17	19	21	17	18	17	20	21	16	17	19	21
	4	11	16	15	13	12	16	14	13	11	9	16	15	13	12	16	14	13	11
	5	15	9	11	14	8	10	12	14	9	16	9	11	14	8	10	12	14	9

* T = Treatment, P= Placebo, O = Observed, 1 = Standard Normal,

2= Logistic, 3 = Extreme Minimal value and 4 = Extreme Maximal value.

CHAPTER EIGHT

STATIONARY THRESHOLD MODELS

8.1 INTRODUCTION

Chapter 7 has described two types of longitudinal threshold models; time dependent and time independent threshold models, for ordinal response variables. Three different models of linear predictor η have been discussed for both longitudinal threshold models. In that chapter, model 2 for the linear predictor η involved a second random component that allowed possible increase in variance and pattern association in the second and following time periods. Although, an extension of the model 2 is possible by introducing a further n-1 random components, the assumptions of those models may not valid for some applications. In particular, random components may be correlated and if so the method needs to give estimation equations for hyperparameters describing covariances between those random components in addition to the variance parameters. In this chapter we develop models for the time series ordinal response variables.

Time series models need to account for the correlation between observations within each subject. A correlation parameter (ρ) is introduced into the variance-covariance matrix of the random components. Two threshold models are defined analogously to the two longitudinal threshold models in previous chapter. Two variance-covariance structures, viz. constant correlation (exchangeable) and AR(1) are taken for random components within a subject. The AR(1) assumes that two observations for one subject will be approximately independent if they are far removed from one another in time. The exchangeable correlation form assumes a constant correlation on every pair of observations for the same subject. Sections 8.2 and 8.3 give models and estimation procedures. In sections 8.4 and 8.5 estimation equations are simplified for two particular variance-covariance matrices. The last two sections give applications of the methods to the analysis of respiratory disorder data of Koch et al (1990) and to map data of Ten Have and Uttal (1994).

8.2 MODELS

Suppose that repeated observations are obtained (Y_{it}) at times $t=1,2,...,n_i$ from subject i, i=1, 2,...N. The observation Y_{it} is an ordinal variable, and can take on values denoted by 0, 1, ...,M. The distribution of Y_{it} depends on the linear predictor

8.2.1 $\eta_{it} = \mathbf{x}'_{it}\beta + u_{it}$

where $\mathbf{x}_{it}$ is a vector of p known regression variables with fixed regression coefficient β. The u_{it} is a random variable, and it accounts for variations in the η_{it} that are not explained by the known regression variables $\mathbf{x}_{it}$. The random variables u_{it} and u_{is}, for a subject are correlated; those from distinct subjects are independent. The variance-covariance matrix is characterised by two parameters φ and ρ for the random vector $\mathbf{u}_i = [u_{i1}, u_{i2}, \ldots u_{in_i}]'$.

The two possible cumulative distribution functions for Y_{it} conditional on u_{it}, are

8.2.2 $$P(Y_{it} \le k) = G(\theta_k - \eta_{it})$$ and

8.2.3 $$P(Y_{it} \le k) = G(\theta_k(t) - \eta_{it})$$

where k=1, 2,...M and G(.) is a cumulative distribution function for unobservable continuous random variable with conditional mean η_{it}. The θ_k are break point parameters and $\theta_k(t)$ are break points parameters at time t. Four different structures for the G(.) are given in section 5.2 of chapter 5. These are used for both models 8.2.2 and 8.2.3 in this chapter.

The parameter θ_{-1} is always taken as $-\infty$ so that $G(\theta_{-1} - \eta_{it})$ is always zero while θ_M is taken to be $+\infty$ indicating that $G(\theta_M - \eta_{it})$ is always 1. Additionally η usually contains a constant term so that there is a lack of identifiability arising from the notion that any quantity added to all θ values can be subtracted by similarly adding it to the constant term of the η values. This lack of identifiability is removed by setting θ_0=0. Thus for 8.2.2 there are M-2 unknown θ parameters, while for 8.2.3 there are n(M-2) different θ parameters where n is the maximum of the n_i. These parameters are collected into a vector θ.

The random component vector $\mathbf{u} = [\mathbf{u}_1', \mathbf{u}_2', ..., \mathbf{u}_N']'$, follows a normal distribution with a zero mean and $\varphi\mathbf{A} = \varphi \operatorname{diag}[\mathbf{A}_1, \mathbf{A}_2, ..., \mathbf{A}_N]$ as the variance-covariance matrix. The $\mathbf{A}_i$ are $n_i \times n_i$ matrices of the elements which are functions of the correlation parameter ρ.

8.3 ESTIMATION

What follows is an iterative method to obtain approximate ML estimators of the parameters and variance components that are obtained from the general estimation approach described in chapter 4. In the first step, penalised likelihood (PL) estimates $\tilde{\theta}$, $\tilde{\beta}$, $\tilde{\mathbf{u}}$ are obtained by maximising the $l_1 + l_2$ for the given initial values of the φ and ρ. The log of the conditional likelihood of the observations given random components (l_1), for the model 8.2.2, is

$$8.3.2 \qquad l_1 = \sum_{i=1}^{N} \sum_{t=1}^{n_i} \ln \Delta_{it}$$

where $\Delta_{it} = G(\theta_{y_{it}} - \eta_{it}) - G(\theta_{y_{it}-1} - \eta_{it})$ is identical to the expression 7.3.6 in chapter 7. For the model 8.2.3, $\theta_{y_{it}}$, $\theta_{y_{it}-1}$ is replaced by $\theta_{y_{it}}(t)$, $\theta_{y_{it}-1}(t)$ in the expressions 7.3.6 and 7.3.7 of chapter 7. The logarithm of the probability density function (l_2) for random components $\mathbf{u}$ is given by

$$8.3.3 \qquad l_2 = -(1/2)[\text{const.} + N_0 \ln\varphi + \ln|\mathbf{A}| + \varphi^{-1}\mathbf{u}'\mathbf{A}^{-1}\mathbf{u}]$$

where $N_0 = \sum_{i=1}^{N} n_i$.

For given initial values $\theta_0, \beta_0, \mathbf{u}_0, \varphi_0, \rho_0$, estimation equations are derived using the Newton-Raphson iterative method,

$$8.3.4 \qquad \begin{bmatrix} \tilde{\theta} \\ \tilde{\beta} \\ \tilde{\mathbf{u}} \end{bmatrix} = \begin{bmatrix} \theta_0 \\ \beta_0 \\ \mathbf{u}_0 \end{bmatrix} + \mathbf{V}^{-1} \begin{bmatrix} \mathbf{I} & 0 \\ 0 & \mathbf{X}' \\ 0 & \mathbf{Z}' \end{bmatrix} \begin{bmatrix} \partial l_1 / \partial \theta_0 \\ \partial l_1 / \partial \eta_0 \end{bmatrix} - \mathbf{V}^{-1} \begin{bmatrix} 0 \\ 0 \\ \varphi_0^{-1}\mathbf{A}_0^{-1}\mathbf{u}_0 \end{bmatrix}$$

$$8.3.5 \qquad \mathbf{V} = \begin{bmatrix} \mathbf{V}_{11} & \mathbf{V}_{12} & \mathbf{V}_{13} \\ \mathbf{V}_{21} & \mathbf{V}_{22} & \mathbf{V}_{23} \\ \mathbf{V}_{31} & \mathbf{V}_{32} & \mathbf{V}_{33} \end{bmatrix}$$

$$= \begin{bmatrix} \mathbf{I} & 0 \\ 0 & \mathbf{X}' \\ 0 & \mathbf{Z}' \end{bmatrix} \left(- \begin{bmatrix} \partial^2 l_1 / \partial\theta_0 \partial\theta_0' & \partial^2 l_1 / \partial\theta_0 \partial\eta_0' \\ \partial^2 l_1 / \partial\eta_0 \partial\theta_0' & \partial^2 l_1 / \partial\eta_0 \partial\eta_0' \end{bmatrix} \right) \begin{bmatrix} \mathbf{I} & 0 & 0 \\ 0 & \mathbf{X} & \mathbf{Z} \end{bmatrix} + \begin{bmatrix} 0 & 0 & 0 \\ 0 & 0 & 0 \\ 0 & 0 & \varphi_0^{-1}\mathbf{A}^{-1}(\rho_0) \end{bmatrix}$$

where

$\mathbf{A}(\rho_0)$, $\partial l_1 / \partial\theta_0$, $\partial l_1 / \partial\eta_0$, $\partial^2 l_1 / \partial\theta_0\partial\theta_0'$, $\partial^2 l_1 / \partial\theta_0\partial\eta_0'$ and $\partial^2 l_1 / \partial\eta_0\partial\eta_0'$ are values of the $\mathbf{A}(\rho)$, $\partial l_1 / \partial\theta$, $\partial l_1 / \partial\eta$, $\partial^2 l_1 / \partial\theta\partial\theta'$, $\partial^2 l_1 / \partial\theta\partial\eta'$ and $\partial^2 l_1 / \partial\eta\partial\eta'$ corresponding to initial estimates of their components. The necessary derivatives for the above equations are given by equations 7.3.11-7.3.17 in chapter 7.

Once the equation 8.3.4 has converged, the ML estimate of the variance component parameter φ is obtained from equation 8.3.5.

8.3.5 $$\hat{\varphi}_{(ML)} = (\textstyle\sum_{i=1}^{N} n_i)^{-1}[\mathrm{tr}\,\mathbf{A}^{-1}(\rho_0)\mathbf{T}^* + \tilde{\mathbf{u}}'\mathbf{A}^{-1}(\rho_0)\tilde{\mathbf{u}}]$$

where $\mathbf{T}^* = [\varphi_0^{-1}\mathbf{A}^{-1}(\rho_0) + \mathbf{Z}'\mathbf{B}\mathbf{Z}]^{-1}$, $\mathrm{B} = -\partial^2 l_1 / \partial\tilde{\eta}\partial\tilde{\eta}'$ and $\tilde{\eta} = \mathbf{X}\tilde{\beta} + \mathbf{Z}\tilde{\mathbf{u}}$. After replacing φ_0 with $\hat{\varphi}_{(ML)}$ as the new initial value for φ, the process between steps 1 and 2 is iterated from this initial value. The third step starts after the converging at steps 1 and 2. The estimation equation for the ML estimate of the variance component parameter ρ is given by

8.3.6 $$\mathrm{tr}(\partial\mathbf{A}^{-1}/\partial\rho)\mathbf{A}(\rho_0) = \hat{\varphi}_{(ML)}^{-1}[\mathrm{tr}(\partial\mathbf{A}^{-1}/\partial\rho)\mathbf{T}^* + \tilde{\mathbf{u}}'(\partial\mathbf{A}^{-1}/\partial\rho)\tilde{\mathbf{u}}].$$

The new values $\hat{\rho}_{(ML)}$, and $\hat{\varphi}_{(ML)}$ are substituted for the ρ and φ respectively in the step 1, and then the whole process is iterated again. The PL estimators of θ and β corresponding to the final values of the $\hat{\rho}_{(ML)}$, and $\hat{\varphi}_{(ML)}$, are the ML estimators $\hat{\theta}_{(ML)}$ and $\hat{\beta}_{(ML)}$. Their asymptotic variance-covariance then is given by

8.3.6 $$\mathrm{Var}\begin{bmatrix}\hat{\theta}\\ \hat{\beta}\end{bmatrix} \cong \Omega \quad \text{where}$$

8.3.7 $$\mathbf{V}^{-1} = \begin{bmatrix}\mathbf{V}_{11} & \mathbf{V}_{12} & \mathbf{V}_{13}\\ \mathbf{V}_{21} & \mathbf{V}_{22} & \mathbf{V}_{23}\\ \mathbf{V}_{31} & \mathbf{V}_{32} & \mathbf{V}_{33}\end{bmatrix}^{-1} = \begin{bmatrix} \cdot & \cdot & | & \cdot\\ \cdot & \cdot & | & \cdot\\ - & - & - & -\\ \cdot & \cdot & | & \cdot\end{bmatrix} = \begin{bmatrix}\Omega & \cdot\\ \cdot & \mathbf{T}\end{bmatrix}.$$

The asymptotic variance-covariance matrix for the maximum likelihood estimators $\hat{\varphi}_{(ML)}$ and $\hat{\rho}_{(ML)}$, is

8.3.8
$$\mathrm{Var}\begin{bmatrix}\hat{\varphi}_{(ML)}\\ \hat{\rho}_{(ML)}\end{bmatrix} \cong 2\begin{bmatrix}\mathrm{tr}\Sigma^{-1}(\partial\Sigma/\partial\varphi)\Sigma^{-1}\partial\Sigma/\partial\varphi & \mathrm{tr}\Sigma^{-1}(\partial\Sigma/\partial\varphi)\Sigma^{-1}\partial\Sigma/\partial\rho\\ \cdot & \mathrm{tr}\Sigma^{-1}(\partial\Sigma/\partial\rho)\Sigma^{-1}\partial\Sigma/\partial\rho\end{bmatrix}^{-1}_{\varphi=\hat{\varphi}_{(ML)},\,\rho=\hat{\rho}_{(ML)}}$$

where $\Sigma = \mathbf{B}^{-1} + \varphi\mathbf{ZAZ}'$. The REML estimators of the parameters are obtained by replacing $\mathbf{T}^{*}$ with $\mathbf{T}$ in all of the above three steps. The approximate variance-covariance matrix for the residual maximum likelihood estimators $\hat{\varphi}_{(REML)}$ and $\hat{\rho}_{(REML)}$ is given by

8.3.9
$$\mathrm{Var}\begin{bmatrix}\hat{\varphi}\\ \hat{\rho}\end{bmatrix}_{(REML)} \cong 2\begin{bmatrix}\mathrm{tr}\mathbf{Q}(\partial\Sigma/\partial\varphi)\mathbf{Q}\partial\Sigma/\partial\varphi & \mathrm{tr}\mathbf{Q}(\partial\Sigma/\partial\varphi)\mathbf{Q}\partial\Sigma/\partial\rho\\ \cdot & \mathrm{tr}\mathbf{Q}(\partial\Sigma/\partial\rho)\mathbf{Q}\partial\Sigma/\partial\rho\end{bmatrix}^{-1}_{\varphi=\hat{\varphi}_{(REML)},\,\rho=\hat{\rho}_{(REML)}}$$

where $\mathbf{Q} = \Sigma^{-1} - \Sigma^{-1}(\mathbf{X}'\Sigma^{-1}\mathbf{X})^{-}\mathbf{X}'\Sigma^{-1}$. The expressions 8.3.8 and 8.3.9 are analogous to the corresponding expressions for the normal response variables given in sections 4.3 and 4.4 of chapter 4.

The next section simplifies the above expressions for the two particular variance-covariance matrix structures. Structure 1 ignores distance and assumes a constant correlation between pairs of random components for the same subject. In the second structure, two random components for one subject are approximately independent if they are far from one another in time.

8.4 EXCHANGEABLE

Since observations are obtained for the same subject across time, the assumption of independence for the random components may not be valid for some applications. A very simple form of dependence is achieved by assuming that the random components for the subject are dependent with a constant correlation ρ. The variance-covariance matrix for the random components is a block diagonal matrix $\varphi\mathbf{A}$ with blocks $\varphi\mathbf{A}_i = \varphi[(1-\rho)\mathbf{I}_i + \rho\mathbf{J}_i]$. The inverse of the matrix $\mathbf{A}$ then is a block diagonal with blocks

8.4.1 $$\mathbf{A}_i^{-1} = (1-\rho)^{-1}[\mathbf{I}_i - \rho(1+(\mathbf{n}_i-1)\rho)\mathbf{J}_i]$$

where i=1,2,...N; $\mathbf{I}_i$ is an $n_i \times n_i$ identity matrix and $\mathbf{J}_i$ is a $n_i \times n_i$ matrix with all elements 1. The first order derivative of the matrix $\mathbf{A}^{-1}$ with respect to ρ, is a block diagonal matrix of the blocks given by

8.4.2 $$\partial\mathbf{A}^{-1}_i / \partial\rho = (1-\rho)^{-2}\mathbf{I}_i - (1+(n_i-1)\rho^2)[(1-\rho)(1+(n_i-1)\rho)]^{-2}\mathbf{J}_i.$$

The three components in 8.3.6, the ML estimation equation for the parameter ρ are simplified as follows:

8.4.3 $$\mathrm{tr}(\partial\mathbf{A}^{-1} / \partial\rho)\mathbf{A} = \sum_{i=1}^{N} n_i(n_i-1)\rho[(1-\rho)(1+(n_i-1)\rho)]^{-1},$$

8.4.4 $$\tilde{\mathbf{u}}'(\partial A/\partial\rho)\tilde{\mathbf{u}} =$$
$$= (1-\rho)^{-2}\tilde{\mathbf{u}}'\tilde{\mathbf{u}} - \sum_{i=1}^{N}(1+(n_i-1)\rho^2)[(1-\rho)(1+(n_i-1)\rho)]^{-2}\tilde{\mathbf{u}}_i'\mathbf{J}_i\tilde{\mathbf{u}}_i$$

8.4.5 $$\mathrm{tr}(\partial A^{-1}/\partial\rho)\mathbf{T}^* =$$
$$= (1-\rho)^{-2}\mathrm{tr}\mathbf{T}^* - \sum_{i=1}^{N}(1+(n_i-1)\rho^2)[(1-\rho)(1+(n_i-1)\rho)]^{-2}\mathrm{tr}\mathbf{J}_i\mathbf{T}_i^* .$$

Using equations 8.4.3, 8.4.4 and 8.4.5, the ML estimation equation for the parameter ρ is simplified to

8.4.6 $$f(\rho)=a\rho^3+b\rho^2+c\rho+d=0$$

where f is a function of the parameter ρ of degree 3 or more. The nonlinear equation 8.4.6 can be solved by

8.4.7 $$\hat{\rho}_{(ML)} = \rho_0 - f(\rho_0)f'^{-1}(\rho_0) .$$

Let $b_{1i} = \tilde{\mathbf{u}}_i'\tilde{\mathbf{u}}_i$, $b_{2i} = \mathrm{tr}\mathbf{T}_i^*$, $b_{3i} = \tilde{\mathbf{u}}_i'\mathbf{J}_i\tilde{\mathbf{u}}_i$, $b_{4i} = \mathrm{tr}\mathbf{J}_i\mathbf{T}_i^*$, then a, b, c in and d in 8.4.6 are given by

8.4.8 $$a=\sum_{i=1}^{N} n_i(n_i-1)^2,$$

8.4.9 $$b=\sum_{i=1}^{N}[\hat{\varphi}_{(ML)}^{-1}((n_i-1)^2(b_{1i}+b_{2i})-(n_i-1)(b_{3i}+b_{4i}))+n_i(n_i-1)(2-n_i)]$$

8.4.10 $$c=2\sum_{i=1}^{N}[\hat{\varphi}_{(ML)}^{-1}(b_{1i}+b_{2i})-n_i(n_i-1)],\ d=\sum_{i=1}^{N}\hat{\varphi}_{(ML)}^{-1}[b_{1i}+b_{2i})-(b_{3i}+b_{4i})].$$

Similarly, the ML estimation equation for the φ (8.3.5) and the approximate variance-covariance matrix for the ML estimators $\hat{\varphi}_{ML}$, and $\hat{\rho}_{ML}$ (8.3.8) , are simplified for the exchangeable correlation structure. The REML estimates and their approximate variances are obtained by replacing T with T^* in the above expressions.

8.5 AR(1)

In section 8.4, the random components are dependent with a constant correlation for the same subject. However, this ignores the influence of the distance between two observation. In this section, the random components are modelled as first order autoregressive, AR(1). The variance-covariance matrix $\varphi\mathbf{A}$, is a block diagonal matrix of the diagonal elements given by

8.5.1 $$\varphi\mathbf{A}_i = \varphi\begin{bmatrix} 1 & \rho & . & . & \rho^{n_i-1} \\ \rho & 1 & . & . & . \\ . & . & . & . & . \\ . & . & . & . & \rho \\ \rho^{n_i-1} & . & . & \rho & 1 \end{bmatrix}.$$

Matrix $\mathbf{A}_i$ has a closed form inverse like

8.5.2 $$\mathbf{A}_i^{-1} = (1-\rho^2)^{-1}[\mathbf{K}_i + (1+\rho^2)\Lambda_i + \rho\Gamma_i]$$

where $\mathbf{K}_i$ and Λ_i are $n_i \times n_i$ diagonal matrices with diagonal elements of $(1,0,0,0,...0,1)$ and $(0,1,1,1,...,1,0)$ and the matrix Γ_i has minus one above and one below principal diagonal, zero all other elements. Differentiating of $\mathbf{A}_i^{-1}$ with respect to ρ, yields equation 8.5.3,

8.5.3 $$\partial\mathbf{A}_i^{-1}/\partial\rho = (1-\rho^2)^{-2}[2\rho(\mathbf{K}_i + 2\Lambda_i) + (1+\rho^2)\Gamma_i].$$

The product of the matrix $\partial\mathbf{A}^{-1}/\partial\rho$ with the matrix $\mathbf{A}$ is a block diagonal matrix with the blocks of

8.5.4 $$(\partial\mathbf{A}_i^{-1}/\partial\rho)\mathbf{A}_i = [(1-\rho^2)^{-1}\rho(\mathbf{K}_i + 2\Lambda_i)] + (1-\rho^2)^{-2}\mathbf{H}_i$$

where matrix $\mathbf{H}_i$ has principal diagonal zero and all other elements are functions of the parameter ρ. From 8.5.3 and 8.5.4, the three components in 8.3.6, and the ML estimation equation for the parameter ρ, are simplified as follows.

8.5.5 $\quad tr(\partial \mathbf{A}^{-1}/\partial\rho)\mathbf{A} = \sum_{i=1}^{N} tr(\partial \mathbf{A}_i^{-1}/\partial\rho)\mathbf{A}_i = 2\rho(1-\rho^2)^{-1}\sum_{i=1}^{N}(n_i - 1),$

8.5.6 $\quad tr(\partial \mathbf{A}^{-1}/\partial\rho)\mathbf{T}^* = \sum_{i=1}^{N} tr(\partial \mathbf{A}_i^{-1}/\partial\rho)\mathbf{T}_i^* =$

$\quad = (1-\rho^2)^{-2}[2\rho\sum_{i=1}^{N}(K_i + 2\Lambda_i)\mathbf{T}_i^* + (1+\rho^2)\sum_{i=1}^{N}\Gamma_i\mathbf{T}_i^*],$

8.5.7 $\quad \tilde{\mathbf{u}}'(\partial \mathbf{A}^{-1}/\partial\rho)\tilde{\mathbf{u}} = \sum_{i=1}^{N}\tilde{\mathbf{u}}_i'(\partial \mathbf{A}_i^{-1}/\partial\rho)\tilde{\mathbf{u}}_i =$

$\quad = (1-\rho^2)^{-2}[2\rho\sum_{i=1}^{N}\tilde{\mathbf{u}}_i'(K_i + 2\Lambda_i)\tilde{\mathbf{u}}_i + (1+\rho^2)\sum_{i=1}^{N}\tilde{\mathbf{u}}_i'\Gamma_i\tilde{\mathbf{u}}_i],$

where $\mathbf{T}^* = [\varphi_{(ML)}^{-1}\mathbf{A}^{-1}(\rho_0) + \mathbf{Z}'\mathbf{B}\mathbf{Z}]^{-1}$ is a block diagonal matrix with diagonal elements of $\mathbf{T}_i^* = (\hat{\varphi}_{(ML)}^{-1}\mathbf{A}_i^{-1} + \mathbf{Z}_j'\mathbf{B}_i\mathbf{Z}_j)^{-1}$ that is corresponding to the vector $\mathbf{u}_i$ component of $\mathbf{u}$. From 8.3.6, 8.5.5, 8.5.6 and 8.5.7, the ML estimation equation for ρ is given by

8.5.8 $\quad f(\rho)=a\rho^3 + b\rho^2 + c\rho + d=0,$

where

$a = 2\sum_{i=1}^{N}(n_i - 1),\ \ b = \hat{\varphi}_{(ML)}^{-1}[\sum_{i=1}^{N}(tr\Gamma_i\mathbf{T}_i^* + \tilde{\mathbf{u}}_i'\Gamma_i\tilde{\mathbf{u}}_i)]$

$c = \sum_{i=1}^{N}\{\hat{\varphi}_{(ML)}^{-1}[tr(\mathbf{K}_i + 2\Lambda_i)\mathbf{T}_i^* + \tilde{\mathbf{u}}_i'(\mathbf{K}_i + 2\Lambda_i)\tilde{\mathbf{u}}_i] - (n_i - 1)\}$ and d=b.

The equation 8.5.8 is a nonlinear function of ρ of degree 3 or more and it can be solved by using 8.4.7. The ML estimation equation (8.3.5) and approximate variance-covariance matrix (8.3.8), are also simplified for the AR(1). The REML estimation equations are simply obtained from the ML equations replacing $\mathbf{T}^*$ with $\mathbf{T}$ and $\mathbf{T}_i^*$ with $\mathbf{T}_i$.

8.6 APPLICATION TO RESPIRATORY DISORDER DATA

The study has been explained and data analysed by fitting longitudinal threshold models in the previous chapter. The data is reanalysed by assuming that the patient random effect follows a normal distribution with zero mean and variance-covariance corresponding to the exchangeable and AR(1) structures. The model is

8.6.1 $\eta_{it} = \beta_0 + \alpha(c_i) + \gamma(age_i) + \lambda(gen_i) + \omega_j(stut_i) + \beta_t(treat_{it}) + u_{it}$

where risk variables are centre (c_i, $1 =$ centre 1, $0 =$ centre 2), age in years at base-line (age_i), gender ($gender_i$, $1 =$ male, $0 =$ female), status at base-line ($stut_i$, $j = 1, 2, 3, 4, 5$) treatment ($treat_{it}$, $1 =$ active, $0 =$ placebo) and u_{it} is i^{th} patient random effect. The results of fitting model 8.6.1 by ML and REML methods, are tabled as 8.6.1.2A.j , 8.6.1.2C.j for the model 8.2.2. Tables 8.6.1.3A.j, 8.6.1.3C.j give results for the model 8.2.3. The letters A, C refer to the AR(1), constant correlation respectively and j=a,b,c,d give more results for the same model.

Model 8.3.2:

The results show that the random components are highly correlated for a patient. The centre, gender effects α, λ and age regression coefficient γ are not significant. The initial status of patients has a statistically significant effect. It indicates that patient with status in lower category (terrible) at base-line pertains to give response in lower category in the end of study.

Although the treatment effects β_t increases from first visit to second visit and then decreases, the pair comparisons show that the changes are not statistically significant. Tables have not been reported in the thesis for these comparisons.

The results in the Table 8.6.1.4 are obtained by using the asymptotic distribution of the estimators $\hat{\beta}_t$ (t=1,2,3,4), and assuming that the β_t's are constant over time. It can be seen that the treatment is highly a statistically significant. The estimate of treatment effect β is positive; indicating that patients in the treatment active group are more likely to respond in the higher categories.

Model 8.3.3:

The results in Tables 8.6.1.3A.j and 8.6.1.3C.j (j=a,b, c, d) show that the changes of the threshold parameter θ over time are not statistically significant.

Thus, model 8.3.2 is a suitable model for this data. Using the discussion in section 7.5 of chapter 7, the predicted values are the same as observed in 71.4%, 72.3%, 73%, 73% for AR(1) and 67.8%, 68.92%, 69.14%, 67.6% for the constant correlation for the four threshold models described in section 5.2 of chapter 5.

Table 8.6.1.2A.a: **ML** and **REML** estimates of parameters (Est), standard errors (SE), the ratio of estimates to their standard errors (z-v) for the model 8.6.1.

		ML			REML		
		Est	SE	Z-v	Est	SE	Z-v
Standard Normal	φ	1.551	0.251	6.192	1.89	0.316	5.987
	ρ	0.901	0.046	19.556	0.9	0.042	21.462
	θ_1	0.902	0.131	6.886	0.946	0.137	6.896
	θ_2	2.397	0.166	14.414	2.494	0.173	14.38
	θ_3	3.537	0.186	19.03	3.68	0.194	18.969
	β_0	4.178	0.626	6.672	4.348	0.678	6.417
	α	-0.379	0.276	-1.376	-0.398	0.299	-1.332
	γ	-0.015	0.01	-1.545	-0.016	0.011	-1.474
	λ	-0.323	0.344	-0.939	-0.335	0.373	-0.898
	ω_1	-2.69	0.848	-3.172	-2.793	0.921	-3.033
	ω_2	-2.275	0.465	-4.888	-2.361	0.504	-4.682
	ω_3	-1.49	0.407	-3.663	-1.548	0.441	-3.514
	ω_4	-0.417	0.411	-1.014	-0.439	0.445	-0.986
	β_1	0.979	0.305	3.206	1.012	0.327	3.095
	β_2	1.401	0.315	4.449	1.445	0.336	4.297
	β_3	1.238	0.311	3.982	1.278	0.332	3.847
	β_4	0.93	0.306	3.033	0.959	0.328	2.923
Logistic	φ	3.998	0.651	6.141	4.869	0.819	5.945
	ρ	0.904	0.046	19.767	0.901	0.042	21.481
	θ_1	1.486	0.219	6.789	1.559	0.229	6.798
	θ_2	3.908	0.283	13.826	4.068	0.295	13.797
	θ_3	5.763	0.319	18.085	6	0.333	18.037
	β_0	6.755	1.017	6.642	7.029	1.098	6.402
	α	-0.598	0.444	-1.346	-0.627	0.481	-1.304
	γ	-0.026	0.016	-1.604	-0.027	0.018	-1.528
	λ	-0.535	0.555	-0.963	-0.554	0.601	-0.922
	ω_1	-4.314	1.364	-3.162	-4.486	1.479	-3.034
	ω_2	-3.655	0.757	-4.828	-3.793	0.818	-4.637
	ω_3	-2.335	0.663	-3.522	-2.428	0.716	-3.392
	ω_4	-0.635	0.67	-0.947	-0.671	0.724	-0.927
	β_1	1.589	0.492	3.23	1.646	0.526	3.127
	β_2	2.283	0.509	4.48	2.362	0.544	4.344
	β_3	2.012	0.506	3.978	2.083	0.54	3.858
	β_4	1.523	0.498	3.059	1.57	0.531	2.954

* ω_5 is fixed at zero to achieve identifialbility.

Table 8.6.1.2A.b: **ML** and **REML** estimates of parameters (Est), standard errors (SE), the ratio of estimates to their standard errors (z-v) for the model 8.6.1.

		ML			REML		
		Est	SE	Z-v	Est	SE	Z-v
Extreme Minimal	φ	2.103	0.338	6.219	2.607	0.434	6.003
	ρ	0.9	0.045	20.067	0.9	0.041	22.078
	θ_1	1.143	0.171	6.693	1.194	0.178	6.709
	θ_2	2.921	0.216	13.516	3.033	0.225	13.506
	θ_3	4.229	0.24	17.636	4.398	0.25	17.614
	β_0	5.466	0.752	7.266	5.671	0.818	6.936
	α	-0.478	0.323	-1.479	-0.497	0.353	-1.409
	γ	-0.017	0.012	-1.473	-0.018	0.013	-1.406
	λ	-0.382	0.402	-0.949	-0.399	0.44	-0.908
	ω_1	-3.387	0.991	-3.416	-3.523	1.085	-3.247
	ω_2	-2.859	0.556	-5.144	-2.962	0.605	-4.892
	ω_3	-1.928	0.491	-3.928	-2.001	0.534	-3.748
	ω_4	-0.665	0.497	-1.338	-0.694	0.54	-1.283
	β_1	1.06	0.355	2.985	1.107	0.383	2.891
	β_2	1.605	0.373	4.305	1.668	0.4	4.171
	β_3	1.467	0.368	3.983	1.524	0.396	3.853
	β_4	1.099	0.364	3.022	1.131	0.391	2.893
Extreme Maximal	φ	1.699	0.27	6.289	2.055	0.34	6.042
	ρ	0.909	0.044	20.585	0.907	0.041	22.276
	θ_1	0.912	0.132	6.922	0.961	0.139	6.929
	θ_2	2.464	0.174	14.186	2.573	0.182	14.122
	θ_3	3.7	0.199	18.61	3.856	0.208	18.515
	β_0	3.929	0.647	6.071	4.103	0.698	5.878
	α	-0.374	0.288	-1.3	-0.395	0.311	-1.272
	γ	-0.016	0.01	-1.576	-0.017	0.011	-1.517
	λ	-0.323	0.36	-0.897	-0.336	0.389	-0.864
	ω_1	-2.584	0.885	-2.92	-2.686	0.957	-2.806
	ω_2	-2.227	0.483	-4.609	-2.313	0.522	-4.434
	ω_3	-1.449	0.419	-3.456	-1.498	0.453	-3.307
	ω_4	-0.338	0.421	-0.801	-0.348	0.455	-0.765
	β_1	1.04	0.319	3.264	1.075	0.341	3.156
	β_2	1.486	0.326	4.56	1.536	0.348	4.414
	β_3	1.235	0.324	3.816	1.278	0.346	3.697
	β_4	0.926	0.32	2.897	0.968	0.342	2.836

* ω_5 is fixed at zero to achieve identifialbility.

Table 8.6.1.3A.a: **ML** and **REML** estimates of parameters (Est), standard errors (SE), the ratio of estimates to their standard errors (z-v) for the model 8.6.1.

		ML			REML		
		Est	SE	Z-v	Est	SE	Z-v
Standard Normal	φ	1.57	0.253	6.2	1.941	0.323	6.003
	ρ	0.901	0.046	19.625	0.9	0.042	21.44
	θ_{11}	0.704	0.188	3.743	0.74	0.197	3.763
	θ_{12}	1.137	0.233	4.886	1.198	0.242	4.947
	θ_{13}	0.904	0.22	4.108	0.956	0.23	4.158
	θ_{14}	0.951	0.216	4.399	1.002	0.226	4.43
	θ_{21}	2.249	0.231	9.754	2.345	0.24	9.777
	θ_{22}	2.73	0.249	10.978	2.846	0.258	11.051
	θ_{23}	2.28	0.245	9.298	2.386	0.255	9.372
	θ_{24}	2.444	0.244	10.006	2.556	0.255	10.039
	θ_{31}	3.58	0.258	13.879	3.73	0.268	13.897
	θ_{32}	3.859	0.28	13.758	4.024	0.291	13.813
	θ_{33}	3.513	0.267	13.148	3.669	0.277	13.224
	θ_{34}	3.34	0.261	12.781	3.495	0.273	12.82
	β_o	4.191	0.63	6.652	4.375	0.686	6.378
	α	-0.367	0.277	-1.325	-0.387	0.303	-1.279
	γ	-0.015	0.01	-1.535	-0.016	0.011	-1.46
	λ	-0.323	0.346	-0.933	-0.336	0.378	-0.888
	ω_1	-2.709	0.853	-3.177	-2.821	0.932	-3.028
	ω_2	-2.289	0.468	-4.889	-2.382	0.51	-4.668
	ω_3	-1.502	0.409	-3.671	-1.565	0.446	-3.51
	ω_4	-0.407	0.413	-0.984	-0.43	0.451	-0.955
	β_1	0.902	0.333	2.712	0.93	0.356	2.615
	β_2	1.688	0.351	4.814	1.747	0.374	4.675
	β_3	1.176	0.343	3.428	1.222	0.366	3.336
	β_4	0.852	0.337	2.532	0.887	0.36	2.463

* ω_5 is fixed at zero to achieve identifialbility.

Table 8.6.1.3A.b: ML and REML estimates of parameters (Est), standard errors (SE), the ratio of estimates to their standard errors (z-v) for the model 8.6.1.

		ML			REML		
		Est	SE	Z-v	Est	SE	Z-v
Logistic	φ	4.057	0.66	6.144	5.012	0.84	5.964
	ρ	0.907	0.045	20.06	0.901	0.042	21.482
	θ_{11}	1.175	0.312	3.765	1.236	0.327	3.783
	θ_{12}	1.849	0.378	4.887	1.949	0.395	4.94
	θ_{13}	1.498	0.362	4.141	1.586	0.379	4.189
	θ_{14}	1.563	0.352	4.436	1.648	0.369	4.461
	θ_{21}	3.7	0.386	9.595	3.859	0.402	9.608
	θ_{22}	4.457	0.416	10.718	4.655	0.432	10.77
	θ_{23}	3.713	0.403	9.208	3.89	0.42	9.267
	θ_{24}	3.963	0.4	9.92	4.149	0.418	9.935
	θ_{31}	5.896	0.439	13.417	6.148	0.458	13.431
	θ_{32}	6.286	0.47	13.375	6.566	0.489	13.42
	θ_{33}	5.717	0.444	12.881	5.981	0.462	12.944
	θ_{34}	5.407	0.429	12.598	5.663	0.449	12.621
	β_0	6.776	1.025	6.609	7.073	1.112	6.36
	α	-0.584	0.448	-1.305	-0.615	0.487	-1.263
	γ	-0.026	0.016	-1.59	-0.027	0.018	-1.51
	λ	-0.53	0.56	-0.947	-0.551	0.609	-0.904
	ω_1	-4.337	1.375	-3.155	-4.528	1.497	-3.024
	ω_2	-3.671	0.763	-4.813	-3.823	0.828	-4.616
	ω_3	-2.351	0.668	-3.52	-2.454	0.725	-3.387
	ω_4	-0.615	0.675	-0.911	-0.655	0.733	-0.893
	β_1	1.506	0.541	2.782	1.556	0.578	2.692
	β_2	2.758	0.572	4.821	2.866	0.609	4.705
	β_3	1.906	0.559	3.409	1.987	0.596	3.334
	β_4	1.367	0.545	2.51	1.422	0.581	2.446

* ω_5 is fixed at zero to achieve identifialbility.

Table 8.6.1.3A.c: ML and REML estimates of parameters (Est), standard errors (SE), the ratio of estimates to their standard errors (z-v) for the model 8.6.1.

		ML			REML		
		Est	SE	Z-v	Est	SE	Z-v
Extreme Minimal	φ	2.14	0.343	6.231	2.701	0.449	6.021
	ρ	0.901	0.045	20.108	0.9	0.041	21.986
	θ_{11}	0.888	0.238	3.738	0.928	0.247	3.754
	θ_{12}	1.4	0.289	4.849	1.467	0.3	4.892
	θ_{13}	1.167	0.282	4.133	1.23	0.294	4.177
	θ_{14}	1.237	0.276	4.481	1.3	0.289	4.506
	θ_{21}	2.74	0.283	9.678	2.851	0.294	9.684
	θ_{22}	3.303	0.301	10.986	3.438	0.312	11.003
	θ_{23}	2.805	0.297	9.435	2.929	0.309	9.477
	θ_{24}	3.005	0.296	10.134	3.137	0.309	10.14
	θ_{31}	4.255	0.31	13.719	4.439	0.324	13.69
	θ_{32}	4.583	0.335	13.69	4.779	0.35	13.661
	θ_{33}	4.235	0.324	13.084	4.423	0.338	13.102
	θ_{34}	4.042	0.317	12.756	4.227	0.331	12.757
	β_0	5.485	0.758	7.232	5.711	0.831	6.876
	α	-0.464	0.326	-1.424	-0.486	0.359	-1.353
	γ	-0.018	0.012	-1.483	-0.018	0.013	-1.41
	λ	-0.383	0.405	-0.946	-0.402	0.447	-0.9
	ω_1	-3.4	0.998	-3.408	-3.548	1.101	-3.224
	ω_2	-2.869	0.56	-5.124	-2.982	0.615	-4.851
	ω_3	-1.928	0.495	-3.898	-2.009	0.542	-3.705
	ω_4	-0.637	0.501	-1.273	-0.668	0.549	-1.218
	β_1	0.957	0.387	2.475	1.002	0.417	2.401
	β_2	1.937	0.414	4.678	2.016	0.444	4.542
	β_3	1.417	0.409	3.463	1.482	0.439	3.375
	β_4	1.02	0.402	2.539	1.061	0.431	2.459

* ω_5 is fixed at zero to achieve identifialbility.

Table 8.6.1.3A.d: ML and REML estimates of parameters (Est), standard errors (SE), the ratio of estimates to their standard errors (z-v) for the model 8.6.1.

		ML			REML		
		Est	SE	Z-v	Est	SE	Z-v
Extreme Maximal	φ	1.714	0.273	6.284	2.1	0.347	6.057
	ρ	0.911	0.044	20.821	0.904	0.041	22.068
	θ_{11}	0.747	0.197	3.8	0.789	0.206	3.823
	θ_{12}	1.161	0.238	4.878	1.23	0.249	4.94
	θ_{13}	0.902	0.218	4.138	0.958	0.229	4.188
	θ_{14}	0.922	0.212	4.35	0.975	0.222	4.385
	θ_{21}	2.378	0.251	9.462	2.486	0.262	9.484
	θ_{22}	2.815	0.271	10.39	2.952	0.282	10.475
	θ_{23}	2.312	0.255	9.05	2.433	0.267	9.129
	θ_{24}	2.457	0.254	9.663	2.579	0.266	9.699
	θ_{31}	3.859	0.295	13.095	4.025	0.306	13.152
	θ_{32}	4.031	0.309	13.032	4.222	0.321	13.142
	θ_{33}	3.628	0.287	12.644	3.805	0.298	12.754
	θ_{34}	3.414	0.277	12.341	3.584	0.289	12.412
	β_0	3.947	0.651	6.063	4.141	0.705	5.873
	α	-0.362	0.289	-1.252	-0.385	0.314	-1.226
	γ	-0.016	0.01	-1.549	-0.017	0.011	-1.49
	λ	-0.324	0.362	-0.894	-0.338	0.392	-0.862
	ω_1	-2.619	0.891	-2.941	-2.732	0.967	-2.827
	ω_2	-2.251	0.486	-4.63	-2.345	0.527	-4.454
	ω_3	-1.473	0.422	-3.492	-1.527	0.457	-3.339
	ω_4	-0.338	0.424	-0.798	-0.349	0.46	-0.76
	β_1	1.021	0.351	2.91	1.052	0.374	2.812
	β_2	1.776	0.366	4.85	1.848	0.39	4.739
	β_3	1.14	0.354	3.219	1.189	0.378	3.148
	β_4	0.809	0.347	2.33	0.852	0.371	2.298

*** ω_5 is fixed at zero to achieve identifialbility.**

Table 8.6.1.2C.a: **ML** and **REML** estimates of parameters (Est), standard errors (SE), the ratio of estimates to their standard errors (z-v) for the model 8.6.1.

		ML			REML		
		Est	SE	Z-v	Est	SE	Z-v
Standard Normal	φ	1.306	0.229	5.693	1.567	0.282	5.546
	ρ	0.908	0.082	11.014	0.902	0.072	12.5
	θ_1	0.837	0.122	6.861	0.868	0.126	6.868
	θ_2	2.257	0.156	14.444	2.329	0.161	14.424
	θ_3	3.336	0.175	19.077	3.443	0.181	19.037
	β_0	3.958	0.597	6.634	4.087	0.639	6.395
	α	-0.35	0.263	-1.333	-0.364	0.282	-1.288
	γ	-0.015	0.01	-1.604	-0.016	0.01	-1.545
	λ	-0.314	0.328	-0.956	-0.324	0.352	-0.919
	ω_1	-2.53	0.808	-3.131	-2.603	0.868	-2.997
	ω_2	-2.164	0.444	-4.874	-2.23	0.476	-4.683
	ω_3	-1.414	0.388	-3.644	-1.458	0.416	-3.504
	ω_4	-0.379	0.392	-0.967	-0.394	0.421	-0.936
	β_1	0.941	0.291	3.239	0.968	0.308	3.14
	β_2	1.353	0.3	4.503	1.39	0.318	4.371
	β_3	1.189	0.296	4.016	1.222	0.314	3.897
	β_4	0.896	0.292	3.073	0.92	0.309	2.975
Logistic	φ	3.517	0.619	5.678	4.237	0.768	5.517
	ρ	0.917	0.081	11.355	0.912	0.071	12.907
	θ_1	1.414	0.21	6.74	1.469	0.218	6.741
	θ_2	3.754	0.274	13.721	3.878	0.283	13.681
	θ_3	5.539	0.309	17.929	5.722	0.32	17.866
	β_0	6.515	0.99	6.582	6.728	1.062	6.332
	α	-0.56	0.432	-1.294	-0.579	0.466	-1.243
	γ	-0.027	0.016	-1.687	-0.028	0.017	-1.622
	λ	-0.536	0.541	-0.992	-0.556	0.582	-0.955
	ω_1	-4.095	1.327	-3.087	-4.217	1.43	-2.949
	ω_2	-3.521	0.737	-4.778	-3.627	0.792	-4.58
	ω_3	-2.225	0.645	-3.447	-2.291	0.693	-3.307
	ω_4	-0.563	0.653	-0.862	-0.581	0.701	-0.829
	β_1	1.566	0.478	3.279	1.619	0.508	3.187
	β_2	2.226	0.493	4.514	2.295	0.523	4.386
	β_3	1.962	0.489	4.009	2.024	0.519	3.898
	β_4	1.504	0.484	3.107	1.547	0.514	3.013

* ω_5 is fixed at zero to achieve identifialbility.

Table 8.6.1.2C.b: ML and REML estimates of parameters (Est), standard errors (SE), the ratio of estimates to their standard errors (z-v) for the model 8.6.1.

		ML			REML		
		Est	SE	Z-v	Est	SE	Z-v
Extreme Minimal	φ	1.732	0.302	5.74	2.096	0.378	5.546
	ρ	0.902	0.08	11.337	0.901	0.07	12.895
	θ_1	1.085	0.163	6.646	1.12	0.168	6.651
	θ_2	2.792	0.208	13.405	2.872	0.215	13.376
	θ_3	4.034	0.231	17.471	4.155	0.238	17.423
	β_0	5.306	0.714	7.431	5.467	0.767	7.127
	α	-0.456	0.305	-1.496	-0.47	0.329	-1.428
	γ	-0.017	0.011	-1.538	-0.018	0.012	-1.483
	λ	-0.373	0.379	-0.983	-0.388	0.41	-0.946
	ω_1	-3.209	0.932	-3.445	-3.304	1.008	-3.28
	ω_2	-2.768	0.527	-5.255	-2.851	0.567	-5.026
	ω_3	-1.866	0.466	-4.006	-1.925	0.501	-3.843
	ω_4	-0.644	0.471	-1.366	-0.668	0.507	-1.318
	β_1	1.021	0.336	3.041	1.059	0.358	2.961
	β_2	1.505	0.354	4.255	1.547	0.375	4.127
	β_3	1.371	0.348	3.937	1.407	0.37	3.807
	β_4	1.07	0.344	3.107	1.093	0.366	2.99
Extreme Maximal	φ	1.548	0.259	5.98	1.869	0.325	5.754
	ρ	0.915	0.073	12.55	0.91	0.065	14.071
	θ_1	0.872	0.127	6.882	0.913	0.133	6.883
	θ_2	2.377	0.168	14.144	2.471	0.176	14.07
	θ_3	3.569	0.193	18.531	3.704	0.201	18.421
	β_0	3.744	0.633	5.912	3.891	0.682	5.702
	α	-0.347	0.282	-1.229	-0.364	0.305	-1.194
	γ	-0.016	0.01	-1.572	-0.017	0.011	-1.517
	λ	-0.302	0.353	-0.855	-0.312	0.381	-0.82
	ω_1	-2.475	0.87	-2.844	-2.556	0.94	-2.718
	ω_2	-2.155	0.474	-4.551	-2.23	0.511	-4.367
	ω_3	-1.411	0.411	-3.434	-1.453	0.443	-3.278
	ω_4	-0.318	0.413	-0.771	-0.324	0.446	-0.728
	β_1	1.004	0.311	3.226	1.033	0.332	3.113
	β_2	1.477	0.318	4.643	1.527	0.339	4.505
	β_3	1.222	0.316	3.872	1.265	0.336	3.762
	β_4	0.878	0.312	2.818	0.915	0.332	2.753

* ω_5 is fixed at zero to achieve identifialbility.

Table 8.6.1.3C.a: **ML** and **REML** estimates of parameters (Est), standard errors (SE), the ratio of estimates to their standard errors (z-v) for the model 8.6.1.

		ML			REML		
		Est	SE	Z-v	Est	SE	Z-v
Standard Normal	φ	1.331	0.233	5.712	1.613	0.289	5.572
	ρ	0.909	0.082	11.154	0.901	0.072	12.575
	θ_{11}	0.649	0.174	3.721	0.674	0.18	3.737
	θ_{12}	1.055	0.22	4.787	1.099	0.228	4.825
	θ_{13}	0.838	0.208	4.038	0.875	0.215	4.071
	θ_{14}	0.89	0.203	4.393	0.927	0.21	4.421
	θ_{21}	2.108	0.216	9.77	2.176	0.222	9.799
	θ_{22}	2.583	0.238	10.846	2.672	0.245	10.895
	θ_{23}	2.142	0.234	9.172	2.221	0.241	9.224
	θ_{24}	2.308	0.229	10.069	2.391	0.236	10.111
	θ_{31}	3.365	0.242	13.9	3.474	0.249	13.927
	θ_{32}	3.663	0.269	13.63	3.793	0.277	13.671
	θ_{33}	3.316	0.255	12.989	3.436	0.263	13.044
	θ_{34}	3.146	0.245	12.848	3.26	0.253	12.898
	β_0	3.982	0.602	6.614	4.122	0.647	6.37
	α	-0.339	0.265	-1.28	-0.353	0.286	-1.236
	γ	-0.015	0.01	-1.594	-0.016	0.01	-1.534
	λ	-0.314	0.331	-0.95	-0.326	0.357	-0.913
	ω_1	-2.55	0.815	-3.13	-2.629	0.879	-2.991
	ω_2	-2.18	0.448	-4.869	-2.251	0.482	-4.671
	ω_3	-1.426	0.391	-3.645	-1.474	0.421	-3.499
	ω_4	-0.369	0.396	-0.934	-0.384	0.426	-0.901
	β_1	0.852	0.317	2.687	0.871	0.335	2.597
	β_2	1.629	0.335	4.866	1.679	0.353	4.755
	β_3	1.126	0.327	3.44	1.163	0.346	3.364
	β_4	0.819	0.321	2.552	0.844	0.339	2.487

* ω_5 is fixed at zero to achieve identifialbility.

Table 8.6.1.3C.b: ML and REML estimates of parameters (Est), standard errors (SE), the ratio of estimates to their standard errors (z-v) for the model 8.6.1.

		ML			REML		
		Est	SE	Z-v	Est	SE	Z-v
Logistic	φ	3.59	0.63	5.698	4.369	0.788	5.544
	ρ	0.919	0.08	11.535	0.91	0.07	12.962
	θ_{11}	1.118	0.298	3.751	1.162	0.309	3.765
	θ_{12}	1.762	0.366	4.821	1.836	0.378	4.855
	θ_{13}	1.422	0.348	4.088	1.487	0.361	4.12
	θ_{14}	1.491	0.336	4.441	1.554	0.348	4.467
	θ_{21}	3.565	0.372	9.573	3.684	0.384	9.584
	θ_{22}	4.29	0.404	10.609	4.442	0.418	10.64
	θ_{23}	3.555	0.39	9.106	3.688	0.403	9.144
	θ_{24}	3.811	0.383	9.963	3.949	0.395	9.99
	θ_{31}	5.691	0.425	13.387	5.882	0.439	13.396
	θ_{32}	6.059	0.457	13.257	6.28	0.473	13.285
	θ_{33}	5.485	0.431	12.73	5.687	0.445	12.769
	θ_{34}	5.187	0.411	12.623	5.377	0.425	12.656
	β_0	6.554	0.999	6.561	6.785	1.076	6.306
	α	-0.549	0.437	-1.257	-0.569	0.472	-1.205
	γ	-0.027	0.016	-1.671	-0.028	0.017	-1.605
	λ	-0.532	0.546	-0.975	-0.552	0.59	-0.936
	ω_1	-4.125	1.339	-3.081	-4.257	1.449	-2.939
	ω_2	-3.542	0.743	-4.766	-3.656	0.801	-4.562
	ω_3	-2.243	0.651	-3.446	-2.316	0.701	-3.302
	ω_4	-0.545	0.658	-0.829	-0.565	0.71	-0.796
	β_1	1.486	0.527	2.822	1.53	0.558	2.741
	β_2	2.677	0.553	4.841	2.768	0.584	4.737
	β_3	1.839	0.541	3.401	1.906	0.572	3.333
	β_4	1.338	0.529	2.53	1.382	0.56	2.467

* ω_5 is fixed at zero to achieve identifialbility.

Table 8.6.1.2C.c: **ML** and **REML** estimates of parameters (Est), standard errors (SE), the ratio of estimates to their standard errors (z-v) for the model 8.6.1.

		ML			REML		
		Est	SE	Z-v	Est	SE	Z-v
Extreme Minimal	φ	1.793	0.31	5.778	2.201	0.394	5.585
	ρ	0.904	0.078	11.633	0.901	0.069	13.095
	θ_{11}	0.833	0.224	3.712	0.857	0.23	3.719
	θ_{12}	1.354	0.281	4.817	1.404	0.29	4.848
	θ_{13}	1.117	0.273	4.093	1.162	0.282	4.121
	θ_{14}	1.175	0.262	4.485	1.219	0.271	4.507
	θ_{21}	2.605	0.27	9.638	2.68	0.278	9.63
	θ_{22}	3.194	0.292	10.952	3.298	0.301	10.957
	θ_{23}	2.696	0.288	9.361	2.788	0.297	9.383
	θ_{24}	2.869	0.282	10.175	2.962	0.291	10.185
	θ_{31}	4.045	0.296	13.648	4.172	0.307	13.596
	θ_{32}	4.42	0.323	13.673	4.574	0.335	13.64
	θ_{33}	4.062	0.313	12.988	4.204	0.324	12.988
	θ_{34}	3.849	0.301	12.789	3.978	0.311	12.792
	β_0	5.344	0.724	7.381	5.521	0.782	7.06
	α	-0.442	0.31	-1.428	-0.457	0.336	-1.359
	γ	-0.017	0.011	-1.547	-0.018	0.012	-1.489
	λ	-0.376	0.385	-0.976	-0.392	0.419	-0.936
	ω_1	-3.225	0.945	-3.415	-3.328	1.028	-3.239
	ω_2	-2.781	0.534	-5.208	-2.871	0.578	-4.965
	ω_3	-1.866	0.472	-3.952	-1.929	0.511	-3.778
	ω_4	-0.614	0.478	-1.284	-0.637	0.517	-1.233
	β_1	0.895	0.368	2.434	0.925	0.392	2.362
	β_2	1.847	0.394	4.683	1.909	0.418	4.571
	β_3	1.331	0.389	3.419	1.375	0.412	3.334
	β_4	0.975	0.382	2.551	1.001	0.405	2.469

* ω_5 is fixed at zero to achieve identifialbility.

Table 8.6.1.3C.d: **ML** and **REML** estimates of parameters (Est), standard errors (SE), the ratio of estimates to their standard errors (z-v) for the model 8.6.1.

		ML			REML		
		Est	SE	Z-v	Est	SE	Z-v
Extreme Maximal	φ	1.567	0.262	5.978	1.912	0.332	5.76
	ρ	0.916	0.073	12.615	0.909	0.065	13.993
	θ_{11}	0.72	0.19	3.798	0.756	0.198	3.822
	θ_{12}	1.102	0.23	4.796	1.157	0.239	4.841
	θ_{13}	0.852	0.209	4.076	0.897	0.218	4.113
	θ_{14}	0.887	0.204	4.345	0.931	0.213	4.379
	θ_{21}	2.314	0.243	9.505	2.409	0.252	9.541
	θ_{22}	2.703	0.263	10.262	2.816	0.273	10.328
	θ_{23}	2.208	0.247	8.925	2.307	0.257	8.983
	θ_{24}	2.381	0.245	9.717	2.485	0.254	9.769
	θ_{31}	3.747	0.286	13.107	3.888	0.295	13.177
	θ_{32}	3.882	0.302	12.873	4.043	0.312	12.963
	θ_{33}	3.482	0.279	12.463	3.628	0.289	12.545
	θ_{34}	3.297	0.267	12.345	3.437	0.277	12.422
	β_0	3.773	0.638	5.911	3.933	0.69	5.698
	α	-0.338	0.284	-1.189	-0.356	0.308	-1.154
	γ	-0.016	0.01	-1.548	-0.017	0.011	-1.494
	λ	-0.303	0.355	-0.854	-0.316	0.385	-0.82
	ω_1	-2.516	0.877	-2.87	-2.603	0.951	-2.738
	ω_2	-2.182	0.477	-4.574	-2.262	0.516	-4.383
	ω_3	-1.435	0.414	-3.469	-1.48	0.448	-3.304
	ω_4	-0.321	0.416	-0.772	-0.326	0.451	-0.724
	β_1	0.998	0.343	2.913	1.025	0.364	2.813
	β_2	1.741	0.357	4.883	1.807	0.378	4.775
	β_3	1.11	0.345	3.219	1.155	0.367	3.15
	β_4	0.772	0.339	2.279	0.807	0.361	2.239

* ω_5 is fixed at zero to achieve identifialbility.

Table 8.6.1.4: **ML** and **REML** estimates of treatment effect, standard errors and their z-v for the model 8.6.1 by AR(1) and constant correlation.

		ML			REML		
Model		Est	SE	z-v	Est	SE	z-v
AR(1) 8.3.2	Standard Nor	1.137	0.267	4.259	1.173	0.289	4.054
	Logistic	1.852	0.433	4.28	1.915	0.468	4.093
	Extreme Min	1.308	0.312	4.187	1.357	0.341	3.978
	Extreme Max	1.172	0.28	4.192	1.214	0.302	4.019
AR(1) 8.3.3	Standard Nor	1.155	0.269	4.297	1.196	0.293	4.08
	Logistic	1.884	0.436	4.317	1.958	0.475	4.126
	Extreme Min	1.333	0.315	4.226	1.39	0.347	4.003
	Extreme Max	1.187	0.281	4.22	1.235	0.305	4.05
Const. 8.3.2	Standard Nor	1.095	0.254	4.304	1.125	0.273	4.12
	Logistic	1.815	0.421	4.311	1.871	0.453	4.132
	Extreme Min	1.242	0.295	4.216	1.277	0.318	4.017
	Extreme Max	1.145	0.274	4.18	1.185	0.296	4.007
Const. 8.3.3	Standard Nor	1.106	0.257	4.311	1.139	0.276	4.121
	Logistic	1.835	0.425	4.317	1.897	0.459	4.133
	Extreme Min	1.262	0.299	4.218	1.303	0.325	4.011
	Extreme Max	1.155	0.276	4.189	1.199	0.299	4.011

* Nor = Normal, Min =Minimal, Max =Maximal, Const.= Constant correlation.

8.7 APPLICATION TO MAP DATA

A second application is to map rotation data given by Ten Have and Uttal (1994). In this study, there are 89 children, of ages 35-67 months, each of whom attempted to find a toy hidden under one of 20 buckets scattered throughout a room. The toy was hidden at 10 different locations, the order of which was the same for each child. For each of these 10 trials, each subject was allowed three attempts to find the toy after seeing a map indicating the location of the toy. Each subject was randomly assigned to one of two groups. In group 1 in the map was rotated when presented by an investigator while in group 2 the map was presented correctly.

The observation Y_{it} for the subject i at location t is an ordinal response coded by 1, 2, 3, 4. The results for the 89 children are given in Table 7 in appendix B. The main study interest was to investigate the ability of children in the two study groups; rotated and nonrotated. Here t=1,2,...,10 refers to the trial number and the model fitted has

8.7.1 $$\eta_{it} = \beta_0 + \beta_t(\text{treat}_i) + u_{it}$$

where risk variable is treatment (treat_i, $1 = \text{rotated}$, $0 = \text{nonrotated}$). The random components $\mathbf{u}_i = [u_{i1}, u_{i2}, \ldots, u_{i10}]'$ are distributed as a multivariate normal with zero mean and variance-covariance corresponding to an AR(1) process or to a constant correlation matrix. The ML and REML estimates of parameters, standard errors and the ratio of estimates to their standard errors (z-v) are given in tables 8.7.2.2C.j , 8.7.2.2A.j and 8.7.2.3C.j , 8.7.2.3A.j for the models 8.2.2. and 8.2.3 by applying four threshold models in section 5.2 of chapter 5. Tables with the letter C present results for constant correlation, those with the letter A show results for the AR(1) process.

Model 8.3.2:

The rotated effects β_t (t=1,2,...10) are shown to be significant by comparing their z-v to the 1.96 critical value. It is shown that β_t significantly varies over time. The estimates of β_t, $\hat{\beta}_t$ decrease for t=1 up to t=7 an then increase. This trend indicates that the chance of finding toys at first attempts increases across time (location) t=1,2,...7 for the children in the rotated group.

The average effect of rotation is obtained by assuming that the β_t are constant and using the asymptotic distribution of the $\hat{\beta}_t$. The results are shown in the Table 8.7.2.4. It shows that the rotation has a statistically highly significant effect. The results also show that random components for a child are highly correlated.

Model 8.3.3:

The results in Tables 8.7.2.3C.j , 8.7.2.3A.j indicate that the threshold parameters θ involve some changes over time. The changes of $\hat{\beta}$ are slightly different for the models 8.3.2 and 8.3.3. Figure 8.7.1 shows the changes of $\hat{\beta}$ and $\hat{\theta}$ over time for the models 8.3.2 and 8.3.3.

The results also show that the random component are highly correlated for a child.

Consequently, model 8.7.1 with 8.3.3 is a suitable model for this data. Figure 8.7.2 shows the predicted and observed frequencies at four attempts for both rotated and nonrotated groups for four threshold models, as described in section 5.2 of chapter 5.

Finally, estimates of the parameters, variance components and their standard errors are very close by ML and REML methods in both applications.

Table 8.7.2.2A.a: ML and REML estimates of parameters (Est), standard errors (SE), the ratio of estimates to their standard errors (z-v) for the model 8.7.1.

		ML			REML		
		Est	SE	Z-v	Est	SE	Z-v
Standard Normal	φ	0.55	0.101	5.426	0.578	0.107	5.422
	ρ	0.911	0.037	24.37	0.91	0.037	24.485
	θ_1	0.658	0.048	13.856	0.662	0.048	13.86
	θ_2	0.985	0.056	17.465	0.991	0.057	17.471
	β_0	-0.041	0.112	-0.362	-0.039	0.114	-0.346
	β_1	1.742	0.264	6.606	1.75	0.266	6.574
	β_2	1.732	0.271	6.388	1.74	0.274	6.358
	β_3	1.339	0.252	5.314	1.344	0.254	5.286
	β_4	1.2	0.244	4.915	1.204	0.246	4.886
	β_5	0.849	0.241	3.529	0.852	0.243	3.505
	β_6	1.04	0.247	4.205	1.044	0.25	4.18
	β_7	-0.305	0.254	-1.203	-0.308	0.256	-1.201
	β_8	0.308	0.238	1.295	0.309	0.241	1.285
	β_9	0.852	0.241	3.534	0.855	0.244	3.513
	β_{10}	1.017	0.246	4.134	1.022	0.248	4.112
Logistic	φ	1.297	0.249	5.201	1.362	0.262	5.199
	ρ	0.918	0.038	24.074	0.916	0.038	24.179
	θ_1	1.06	0.077	13.693	1.066	0.078	13.696
	θ_2	1.591	0.093	17.109	1.6	0.093	17.115
	β_0	-0.054	0.176	-0.308	-0.052	0.179	-0.291
	β_1	2.741	0.425	6.45	2.752	0.429	6.423
	β_2	2.742	0.44	6.237	2.752	0.443	6.211
	β_3	2.124	0.403	5.267	2.132	0.407	5.239
	β_4	1.897	0.389	4.88	1.904	0.392	4.852
	β_5	1.316	0.374	3.519	1.32	0.378	3.495
	β_6	1.657	0.398	4.166	1.663	0.401	4.143
	β_7	-0.463	0.407	-1.137	-0.466	0.41	-1.137
	β_8	0.511	0.382	1.337	0.512	0.386	1.327
	β_9	1.332	0.374	3.558	1.337	0.378	3.536
	β_{10}	1.622	0.387	4.185	1.628	0.391	4.163

Table 8.7.2.2A.b: ML and REML estimates of parameters (Est), standard errors (SE), the ratio of estimates to their standard errors (z-v) for the model 8.7.1.

AR(1)		ML			REML		
		Est	SE	Z-v	Est	SE	Z-v
Extreme Minimal	φ	0.709	0.123	5.762	0.746	0.13	5.749
	ρ	0.902	0.036	24.942	0.901	0.036	25.11
	θ_1	0.736	0.053	13.761	0.741	0.054	13.768
	θ_2	1.083	0.063	17.302	1.09	0.063	17.311
	β_0	0.315	0.124	2.529	0.315	0.127	2.491
	β_1	1.917	0.335	5.726	1.927	0.337	5.712
	β_2	1.954	0.354	5.522	1.962	0.356	5.509
	β_3	1.466	0.307	4.772	1.475	0.31	4.757
	β_4	1.292	0.291	4.444	1.3	0.294	4.429
	β_5	0.811	0.273	2.972	0.815	0.276	2.956
	β_6	1.188	0.296	4.013	1.194	0.299	3.998
	β_7	-0.335	0.265	-1.263	-0.339	0.269	-1.261
	β_8	0.364	0.261	1.394	0.367	0.264	1.39
	β_9	0.81	0.273	2.973	0.816	0.275	2.961
	β_{10}	1.057	0.287	3.685	1.062	0.29	3.667
Extreme Maximal	φ	0.706	0.127	5.541	0.747	0.135	5.532
	ρ	0.908	0.037	24.646	0.905	0.037	24.511
	θ_1	0.754	0.055	13.642	0.76	0.056	13.645
	θ_2	1.152	0.068	17.016	1.16	0.068	17.021
	β_0	-0.39	0.129	-3.028	-0.388	0.131	-2.957
	β_1	1.973	0.269	7.347	1.985	0.272	7.292
	β_2	1.933	0.273	7.076	1.944	0.277	7.023
	β_3	1.502	0.264	5.697	1.51	0.267	5.654
	β_4	1.331	0.259	5.142	1.337	0.262	5.095
	β_5	1.068	0.26	4.104	1.071	0.263	4.065
	β_6	1.121	0.267	4.2	1.126	0.27	4.167
	β_7	-0.381	0.319	-1.192	-0.383	0.322	-1.189
	β_8	0.305	0.276	1.104	0.304	0.279	1.09
	β_9	1.069	0.262	4.081	1.073	0.265	4.046
	β_{10}	1.193	0.266	4.476	1.201	0.27	4.453

Table 8.7.2.3A.a: **ML** and **REML** estimates of parameters (Est), standard errors (SE), the ratio of estimates to their standard errors (z-v) for the model 8.7.1.

		ML			REML		
		Est	SE	Z-v	Est	SE	Z-v
Standard Normal	φ	0.561	0.103	5.461	0.594	0.109	5.468
	ρ	0.91	0.037	24.399	0.908	0.037	24.35
	θ_{11}	0.85	0.158	5.373	0.857	0.159	5.378
	θ_{12}	0.622	0.148	4.197	0.628	0.149	4.201
	θ_{13}	0.439	0.119	3.705	0.443	0.119	3.707
	θ_{14}	0.817	0.143	5.729	0.822	0.143	5.732
	θ_{15}	0.835	0.182	4.588	0.842	0.183	4.591
	θ_{16}	0.421	0.11	3.846	0.424	0.11	3.847
	θ_{17}	0.711	0.163	4.361	0.716	0.164	4.363
	θ_{18}	0.789	0.15	5.24	0.792	0.151	5.24
	θ_{19}	0.787	0.161	4.878	0.793	0.162	4.881
	θ_{110}	0.469	0.117	4.013	0.473	0.118	4.014
	θ_{21}	1.386	0.193	7.191	1.398	0.194	7.198
	θ_{22}	0.819	0.164	4.981	0.827	0.166	4.987
	θ_{23}	0.755	0.145	5.192	0.761	0.146	5.197
	θ_{24}	1.192	0.165	7.237	1.2	0.166	7.242
	θ_{25}	1.158	0.203	5.714	1.167	0.204	5.719
	θ_{26}	0.633	0.129	4.918	0.637	0.129	4.919
	θ_{27}	0.907	0.184	4.926	0.913	0.185	4.929
	θ_{28}	1.243	0.19	6.556	1.249	0.191	6.555
	θ_{29}	1.177	0.188	6.263	1.186	0.189	6.268
	θ_{210}	0.777	0.144	5.397	0.783	0.145	5.4
	β_0	-0.04	0.113	-0.354	-0.038	0.115	-0.332
	β_1	2.034	0.295	6.902	2.047	0.298	6.876
	β_2	1.631	0.295	5.524	1.641	0.298	5.499
	β_3	1.173	0.27	4.345	1.18	0.273	4.321
	β_4	1.339	0.265	5.057	1.345	0.268	5.024
	β_5	0.966	0.27	3.575	0.97	0.273	3.552
	β_6	0.822	0.262	3.135	0.825	0.265	3.109
	β_7	-0.322	0.263	-1.223	-0.325	0.266	-1.223
	β_8	0.415	0.252	1.649	0.415	0.254	1.632
	β_9	0.963	0.263	3.657	0.968	0.266	3.635
	β_{10}	0.879	0.262	3.362	0.884	0.264	3.343

Table 8.7.2.3A.b: ML and REML estimates of parameters (Est), standard errors (SE), the ratio of estimates to their standard errors (z-v) for the model 8.7.1.

		ML			REML		
		Est	SE	Z-v	Est	SE	Z-v
Logistic	φ	1.326	0.253	5.233	1.401	0.268	5.234
	ρ	0.917	0.038	24.278	0.916	0.038	24.352
	θ_{11}	1.398	0.267	5.239	1.407	0.268	5.245
	θ_{12}	1	0.241	4.157	1.008	0.242	4.161
	θ_{13}	0.707	0.192	3.683	0.712	0.193	3.686
	θ_{14}	1.318	0.235	5.598	1.325	0.236	5.602
	θ_{15}	1.337	0.296	4.521	1.346	0.297	4.526
	θ_{16}	0.686	0.18	3.817	0.689	0.18	3.818
	θ_{17}	1.132	0.263	4.31	1.138	0.264	4.313
	θ_{18}	1.266	0.246	5.152	1.271	0.247	5.151
	θ_{19}	1.26	0.262	4.815	1.268	0.263	4.819
	θ_{110}	0.747	0.187	3.986	0.751	0.188	3.988
	θ_{21}	2.303	0.338	6.813	2.318	0.34	6.823
	θ_{22}	1.319	0.269	4.903	1.329	0.271	4.91
	θ_{23}	1.217	0.238	5.123	1.226	0.239	5.129
	θ_{24}	1.929	0.276	6.986	1.94	0.277	6.994
	θ_{25}	1.852	0.331	5.59	1.865	0.333	5.596
	θ_{26}	1.03	0.212	4.854	1.035	0.213	4.856
	θ_{27}	1.45	0.3	4.834	1.459	0.301	4.839
	θ_{28}	2.011	0.317	6.339	2.019	0.319	6.339
	θ_{29}	1.888	0.309	6.114	1.901	0.311	6.121
	θ_{210}	1.241	0.233	5.327	1.249	0.234	5.331
	β_0	-0.052	0.177	-0.294	-0.05	0.181	-0.274
	β_1	3.286	0.496	6.619	3.301	0.5	6.601
	β_2	2.563	0.481	5.334	2.576	0.484	5.316
	β_3	1.841	0.433	4.25	1.849	0.437	4.228
	β_4	2.135	0.431	4.956	2.143	0.435	4.929
	β_5	1.5	0.429	3.496	1.507	0.433	3.476
	β_6	1.291	0.42	3.074	1.294	0.424	3.052
	β_7	-0.49	0.418	-1.172	-0.495	0.422	-1.172
	β_8	0.674	0.408	1.651	0.675	0.412	1.636
	β_9	1.511	0.418	3.611	1.518	0.422	3.592
	β_{10}	1.376	0.413	3.333	1.382	0.417	3.316

Table 8.7.2.3A.c: ML and REML estimates of parameters (Est), standard errors (SE), the ratio of estimates to their standard errors (z-v) for the model 8.7.1.

		ML			REML		
		Est	SE	Z-v	Est	SE	Z-v
Extreme Minimal	φ	0.73	0.126	5.814	0.78	0.134	5.805
	ρ	0.902	0.036	25.317	0.901	0.035	25.463
	θ_{11}	0.919	0.162	5.667	0.929	0.164	5.669
	θ_{12}	0.711	0.163	4.365	0.717	0.164	4.366
	θ_{13}	0.502	0.132	3.809	0.506	0.133	3.812
	θ_{14}	0.908	0.149	6.088	0.915	0.15	6.088
	θ_{15}	0.932	0.197	4.725	0.94	0.199	4.728
	θ_{16}	0.463	0.118	3.928	0.466	0.119	3.928
	θ_{17}	0.785	0.172	4.562	0.792	0.174	4.563
	θ_{18}	0.884	0.162	5.458	0.888	0.163	5.454
	θ_{19}	0.893	0.176	5.073	0.901	0.178	5.075
	θ_{110}	0.539	0.131	4.128	0.544	0.132	4.128
	θ_{21}	1.47	0.192	7.643	1.486	0.195	7.641
	θ_{22}	0.927	0.178	5.203	0.936	0.18	5.205
	θ_{23}	0.846	0.157	5.404	0.854	0.158	5.409
	θ_{24}	1.309	0.168	7.769	1.319	0.17	7.768
	θ_{25}	1.27	0.215	5.91	1.281	0.217	5.914
	θ_{26}	0.691	0.136	5.062	0.695	0.137	5.062
	θ_{27}	0.994	0.191	5.194	1.004	0.193	5.195
	θ_{28}	1.36	0.197	6.895	1.369	0.199	6.887
	θ_{29}	1.298	0.198	6.559	1.31	0.2	6.561
	θ_{210}	0.873	0.156	5.597	0.881	0.158	5.597
	β_0	0.315	0.126	2.501	0.317	0.129	2.455
	β_1	2.235	0.366	6.101	2.252	0.37	6.089
	β_2	1.839	0.38	4.837	1.85	0.383	4.825
	β_3	1.271	0.329	3.868	1.281	0.332	3.856
	β_4	1.467	0.315	4.654	1.477	0.319	4.632
	β_5	0.959	0.314	3.052	0.965	0.318	3.036
	β_6	0.891	0.314	2.842	0.896	0.317	2.824
	β_7	-0.36	0.281	-1.282	-0.365	0.285	-1.279
	β_8	0.524	0.288	1.822	0.527	0.292	1.806
	β_9	0.965	0.305	3.161	0.973	0.309	3.148
	β_{10}	0.891	0.307	2.904	0.897	0.31	2.889

Table 8.7.2.3A.d: **ML** and **REML** estimates of parameters (Est), standard errors (SE), the ratio of estimates to their standard errors (z-v) for the model 8.7.1.

		ML			REML		
		Est	SE	Z-v	Est	SE	Z-v
Extreme Maximal	φ	0.713	0.129	5.542	0.761	0.137	5.544
	ρ	0.909	0.037	24.875	0.905	0.037	24.584
	θ_{11}	1.01	0.199	5.07	1.02	0.201	5.077
	θ_{12}	0.702	0.172	4.072	0.711	0.174	4.078
	θ_{13}	0.494	0.137	3.622	0.499	0.138	3.625
	θ_{14}	0.934	0.173	5.391	0.941	0.174	5.396
	θ_{15}	0.942	0.21	4.484	0.95	0.212	4.489
	θ_{16}	0.491	0.13	3.773	0.495	0.131	3.774
	θ_{17}	0.856	0.209	4.101	0.86	0.21	4.105
	θ_{18}	0.928	0.187	4.959	0.932	0.188	4.961
	θ_{19}	0.869	0.185	4.693	0.876	0.187	4.697
	θ_{110}	0.521	0.134	3.902	0.526	0.135	3.904
	θ_{21}	1.678	0.249	6.749	1.695	0.251	6.758
	θ_{22}	0.935	0.194	4.817	0.946	0.196	4.827
	θ_{23}	0.863	0.172	5.006	0.872	0.174	5.014
	θ_{24}	1.381	0.206	6.709	1.391	0.207	6.717
	θ_{25}	1.332	0.241	5.517	1.343	0.243	5.525
	θ_{26}	0.746	0.157	4.766	0.752	0.158	4.769
	θ_{27}	1.108	0.244	4.549	1.114	0.245	4.556
	θ_{28}	1.521	0.255	5.975	1.528	0.255	5.983
	θ_{29}	1.343	0.226	5.932	1.354	0.228	5.94
	θ_{210}	0.884	0.171	5.172	0.892	0.172	5.177
	β_0	-0.389	0.13	-3.001	-0.386	0.132	-2.918
	β_1	2.328	0.315	7.397	2.348	0.319	7.358
	β_2	1.82	0.301	6.048	1.832	0.305	6.002
	β_3	1.319	0.282	4.684	1.326	0.286	4.643
	β_4	1.467	0.283	5.188	1.474	0.287	5.139
	β_5	1.168	0.286	4.083	1.173	0.29	4.043
	β_6	0.925	0.279	3.312	0.928	0.283	3.274
	β_7	-0.381	0.323	-1.181	-0.384	0.326	-1.18
	β_8	0.384	0.283	1.354	0.384	0.287	1.337
	β_9	1.149	0.281	4.092	1.155	0.285	4.057
	β_{10}	1.046	0.28	3.739	1.054	0.284	3.715

Table 8.7.2.2C.a: ML and REML estimates of parameters (Est), standard errors (SE), the ratio of estimates to their standard errors (z-v) for the model 8.7.1.

		ML			REML		
		Est	SE	Z-v	Est	SE	Z-v
Standard Normal	φ	0.522	0.117	4.459	0.547	0.122	4.472
	ρ	0.9	0.137	6.558	0.9	0.133	6.773
	θ_1	0.641	0.046	13.841	0.643	0.046	13.843
	θ_2	0.957	0.055	17.445	0.96	0.055	17.449
	β_0	-0.058	0.118	-0.486	-0.057	0.12	-0.475
	β_1	1.714	0.262	6.546	1.719	0.264	6.51
	β_2	1.733	0.272	6.38	1.739	0.274	6.347
	β_3	1.329	0.252	5.264	1.333	0.255	5.233
	β_4	1.196	0.245	4.881	1.2	0.247	4.85
	β_5	0.85	0.242	3.518	0.853	0.244	3.493
	β_6	1.034	0.248	4.165	1.037	0.251	4.138
	β_7	-0.293	0.255	-1.15	-0.294	0.257	-1.146
	β_8	0.303	0.239	1.269	0.303	0.241	1.258
	β_9	0.843	0.242	3.479	0.846	0.245	3.455
	β_{10}	1	0.247	4.054	1.003	0.249	4.028
Logistic	φ	1.255	0.287	4.377	1.318	0.301	4.384
	ρ	0.9	0.138	6.502	0.9	0.135	6.687
	θ_1	1.045	0.077	13.654	1.049	0.077	13.654
	θ_2	1.566	0.092	17.041	1.572	0.092	17.042
	β_0	-0.083	0.185	-0.449	-0.083	0.189	-0.438
	β_1	2.789	0.432	6.459	2.801	0.436	6.428
	β_2	2.799	0.446	6.282	2.81	0.449	6.255
	β_3	2.145	0.408	5.258	2.153	0.412	5.228
	β_4	1.925	0.392	4.908	1.933	0.396	4.879
	β_5	1.333	0.377	3.535	1.338	0.381	3.51
	β_6	1.66	0.401	4.144	1.665	0.404	4.117
	β_7	-0.441	0.41	-1.076	-0.443	0.413	-1.072
	β_8	0.5	0.386	1.296	0.501	0.39	1.285
	β_9	1.331	0.378	3.521	1.335	0.382	3.496
	β_{10}	1.625	0.393	4.13	1.63	0.397	4.103

Table 8.7.2.2C.b: **ML** and **REML** estimates of parameters (Est), standard errors (SE), the ratio of estimates to their standard errors (z-v) for the model 8.7.1.

		ML			REML		
		Est	SE	Z-v	Est	SE	Z-v
Extreme Minimal	φ	0.667	0.135	4.943	0.703	0.142	4.932
	ρ	0.9	0.107	8.423	0.9	0.103	8.728
	θ_1	0.711	0.052	13.736	0.714	0.052	13.738
	θ_2	1.042	0.06	17.281	1.047	0.061	17.285
	β_0	0.327	0.132	2.467	0.328	0.135	2.423
	β_1	1.948	0.336	5.797	1.958	0.339	5.781
	β_2	1.961	0.355	5.524	1.969	0.357	5.508
	β_3	1.457	0.308	4.731	1.464	0.311	4.711
	β_4	1.273	0.292	4.365	1.28	0.295	4.345
	β_5	0.79	0.274	2.88	0.793	0.277	2.86
	β_6	1.15	0.297	3.869	1.154	0.3	3.846
	β_7	-0.348	0.266	-1.309	-0.352	0.269	-1.307
	β_8	0.347	0.262	1.323	0.35	0.266	1.316
	β_9	0.766	0.274	2.791	0.769	0.277	2.772
	β_{10}	1.04	0.288	3.611	1.045	0.291	3.589
Extreme Maximal	φ	0.652	0.139	4.698	0.689	0.147	4.678
	ρ	0.9	0.12	7.524	0.9	0.117	7.684
	θ_1	0.731	0.054	13.613	0.734	0.054	13.614
	θ_2	1.114	0.066	16.968	1.119	0.066	16.97
	β_0	-0.436	0.135	-3.234	-0.437	0.138	-3.173
	β_1	1.884	0.266	7.091	1.891	0.269	7.025
	β_2	1.917	0.272	7.041	1.927	0.276	6.986
	β_3	1.482	0.263	5.634	1.488	0.266	5.586
	β_4	1.331	0.258	5.154	1.336	0.262	5.104
	β_5	1.09	0.26	4.194	1.094	0.263	4.157
	β_6	1.121	0.265	4.224	1.126	0.269	4.189
	β_7	-0.355	0.319	-1.112	-0.355	0.322	-1.102
	β_8	0.29	0.275	1.056	0.29	0.278	1.042
	β_9	1.062	0.261	4.065	1.067	0.265	4.031
	β_{10}	1.111	0.265	4.191	1.116	0.268	4.158

Table 8.7.2.3C.a: ML and REML estimates of parameters (Est), standard errors (SE), the ratio of estimates to their standard errors (z-v) for the model 8.7.1.

Exch		ML			REML		
		Est	SE	Z-v	Est	SE	Z-v
Standard Normal	φ	0.525	0.118	4.461	0.552	0.123	4.472
	ρ	0.9	0.137	6.561	0.9	0.133	6.77
	θ_{11}	0.797	0.149	5.338	0.8	0.15	5.34
	θ_{12}	0.591	0.141	4.181	0.593	0.142	4.183
	θ_{13}	0.417	0.113	3.688	0.419	0.114	3.689
	θ_{14}	0.793	0.139	5.714	0.796	0.139	5.716
	θ_{15}	0.811	0.177	4.574	0.815	0.178	4.577
	θ_{16}	0.417	0.108	3.853	0.418	0.109	3.854
	θ_{17}	0.699	0.16	4.362	0.702	0.161	4.364
	θ_{18}	0.788	0.149	5.282	0.79	0.15	5.284
	θ_{19}	0.777	0.159	4.896	0.78	0.159	4.899
	θ_{110}	0.457	0.114	4.021	0.459	0.114	4.022
	θ_{21}	1.299	0.182	7.145	1.304	0.182	7.148
	θ_{22}	0.778	0.157	4.954	0.781	0.158	4.957
	θ_{23}	0.718	0.139	5.157	0.721	0.14	5.16
	θ_{24}	1.158	0.16	7.216	1.162	0.161	7.22
	θ_{25}	1.126	0.198	5.699	1.132	0.198	5.703
	θ_{26}	0.624	0.127	4.926	0.626	0.127	4.927
	θ_{27}	0.889	0.18	4.926	0.893	0.181	4.929
	θ_{28}	1.223	0.185	6.608	1.227	0.186	6.61
	θ_{29}	1.155	0.184	6.28	1.16	0.185	6.285
	θ_{210}	0.757	0.14	5.415	0.76	0.14	5.418
	β_0	-0.061	0.119	-0.514	-0.061	0.121	-0.501
	β_1	1.965	0.29	6.77	1.971	0.293	6.735
	β_2	1.624	0.293	5.544	1.631	0.296	5.518
	β_3	1.159	0.268	4.321	1.164	0.271	4.295
	β_4	1.334	0.264	5.063	1.339	0.266	5.032
	β_5	0.967	0.269	3.6	0.97	0.271	3.579
	β_6	0.832	0.262	3.178	0.834	0.264	3.156
	β_7	-0.301	0.262	-1.148	-0.303	0.265	-1.142
	β_8	0.422	0.252	1.677	0.422	0.254	1.662
	β_9	0.963	0.264	3.652	0.966	0.266	3.63
	β_{10}	0.867	0.261	3.321	0.87	0.264	3.299

Table 8.7.2.3C.b: ML and REML estimates of parameters (Est), standard errors (SE), the ratio of estimates to their standard errors (z-v) for the model 8.7.1.

		ML			REML		
		Est	SE	Z-v	Est	SE	Z-v
Logistic	φ	1.273	0.29	4.391	1.342	0.305	4.397
	ρ	0.9	0.138	6.539	0.9	0.134	6.719
	θ_{11}	1.353	0.261	5.191	1.358	0.261	5.194
	θ_{12}	0.969	0.234	4.135	0.973	0.235	4.137
	θ_{13}	0.679	0.186	3.662	0.682	0.186	3.664
	θ_{14}	1.294	0.232	5.576	1.299	0.233	5.58
	θ_{15}	1.309	0.291	4.499	1.315	0.292	4.502
	θ_{16}	0.683	0.179	3.822	0.686	0.18	3.823
	θ_{17}	1.123	0.261	4.308	1.129	0.262	4.311
	θ_{18}	1.278	0.246	5.198	1.282	0.247	5.2
	θ_{19}	1.261	0.261	4.825	1.267	0.262	4.829
	θ_{110}	0.738	0.185	3.986	0.741	0.186	3.987
	θ_{21}	2.237	0.332	6.736	2.245	0.333	6.741
	θ_{22}	1.278	0.263	4.864	1.284	0.264	4.868
	θ_{23}	1.172	0.231	5.078	1.177	0.232	5.081
	θ_{24}	1.896	0.273	6.952	1.903	0.274	6.957
	θ_{25}	1.819	0.327	5.561	1.828	0.328	5.566
	θ_{26}	1.023	0.211	4.858	1.027	0.211	4.86
	θ_{27}	1.435	0.297	4.83	1.443	0.298	4.834
	θ_{28}	2.002	0.313	6.386	2.009	0.314	6.388
	θ_{29}	1.878	0.307	6.116	1.887	0.308	6.121
	θ_{210}	1.227	0.23	5.334	1.232	0.231	5.336
	β_0	-0.086	0.187	-0.46	-0.085	0.19	-0.449
	β_1	3.312	0.502	6.6	3.326	0.506	6.578
	β_2	2.609	0.484	5.389	2.621	0.488	5.371
	β_3	1.849	0.435	4.251	1.857	0.439	4.228
	β_4	2.163	0.432	5.003	2.171	0.436	4.977
	β_5	1.515	0.43	3.525	1.521	0.434	3.506
	β_6	1.309	0.421	3.107	1.313	0.425	3.086
	β_7	-0.46	0.42	-1.097	-0.463	0.424	-1.092
	β_8	0.678	0.412	1.647	0.679	0.416	1.633
	β_9	1.525	0.422	3.615	1.532	0.426	3.595
	β_{10}	1.383	0.419	3.302	1.388	0.423	3.281

Table 8.7.2.3C.c: ML and REML estimates of parameters (Est), standard errors (SE), the ratio of estimates to their standard errors (z-v) for the model 8.7.1.

		ML			REML		
		Est	SE	Z-v	Est	SE	Z-v
Extreme Minimal	φ	0.678	0.136	4.968	0.722	0.146	4.948
	ρ	0.9	0.106	8.518	0.9	0.103	8.765
	θ_{11}	0.818	0.145	5.649	0.821	0.145	5.647
	θ_{12}	0.675	0.154	4.391	0.678	0.154	4.392
	θ_{13}	0.47	0.124	3.805	0.473	0.124	3.805
	θ_{14}	0.88	0.144	6.118	0.885	0.145	6.118
	θ_{15}	0.897	0.189	4.74	0.902	0.19	4.743
	θ_{16}	0.46	0.116	3.952	0.462	0.117	3.952
	θ_{17}	0.768	0.168	4.571	0.774	0.169	4.573
	θ_{18}	0.896	0.161	5.551	0.901	0.162	5.551
	θ_{19}	0.87	0.169	5.141	0.875	0.17	5.143
	θ_{110}	0.525	0.126	4.18	0.528	0.126	4.181
	θ_{21}	1.313	0.17	7.706	1.319	0.171	7.702
	θ_{22}	0.876	0.167	5.241	0.881	0.168	5.242
	θ_{23}	0.793	0.147	5.397	0.797	0.148	5.398
	θ_{24}	1.268	0.162	7.837	1.274	0.163	7.838
	θ_{25}	1.223	0.206	5.94	1.231	0.207	5.944
	θ_{26}	0.682	0.134	5.104	0.685	0.134	5.104
	θ_{27}	0.969	0.186	5.218	0.977	0.187	5.22
	θ_{28}	1.354	0.193	7.025	1.36	0.194	7.023
	θ_{29}	1.253	0.188	6.669	1.261	0.189	6.673
	θ_{210}	0.853	0.15	5.699	0.858	0.15	5.701
	β_0	0.32	0.133	2.399	0.321	0.137	2.348
	β_1	2.178	0.361	6.031	2.189	0.364	6.011
	β_2	1.844	0.378	4.874	1.853	0.381	4.86
	β_3	1.255	0.327	3.843	1.263	0.33	3.828
	β_4	1.456	0.313	4.65	1.465	0.317	4.628
	β_5	0.94	0.311	3.021	0.946	0.315	3.004
	β_6	0.881	0.313	2.813	0.885	0.317	2.796
	β_7	-0.359	0.28	-1.281	-0.363	0.284	-1.276
	β_8	0.548	0.289	1.896	0.552	0.293	1.884
	β_9	0.926	0.304	3.048	0.931	0.307	3.03
	β_{10}	0.893	0.307	2.905	0.898	0.311	2.889

Table 8.7.2.3C.d: ML and REML estimates of parameters (Est), standard errors (SE), the ratio of estimates to their standard errors (z-v) for the model 8.7.1.

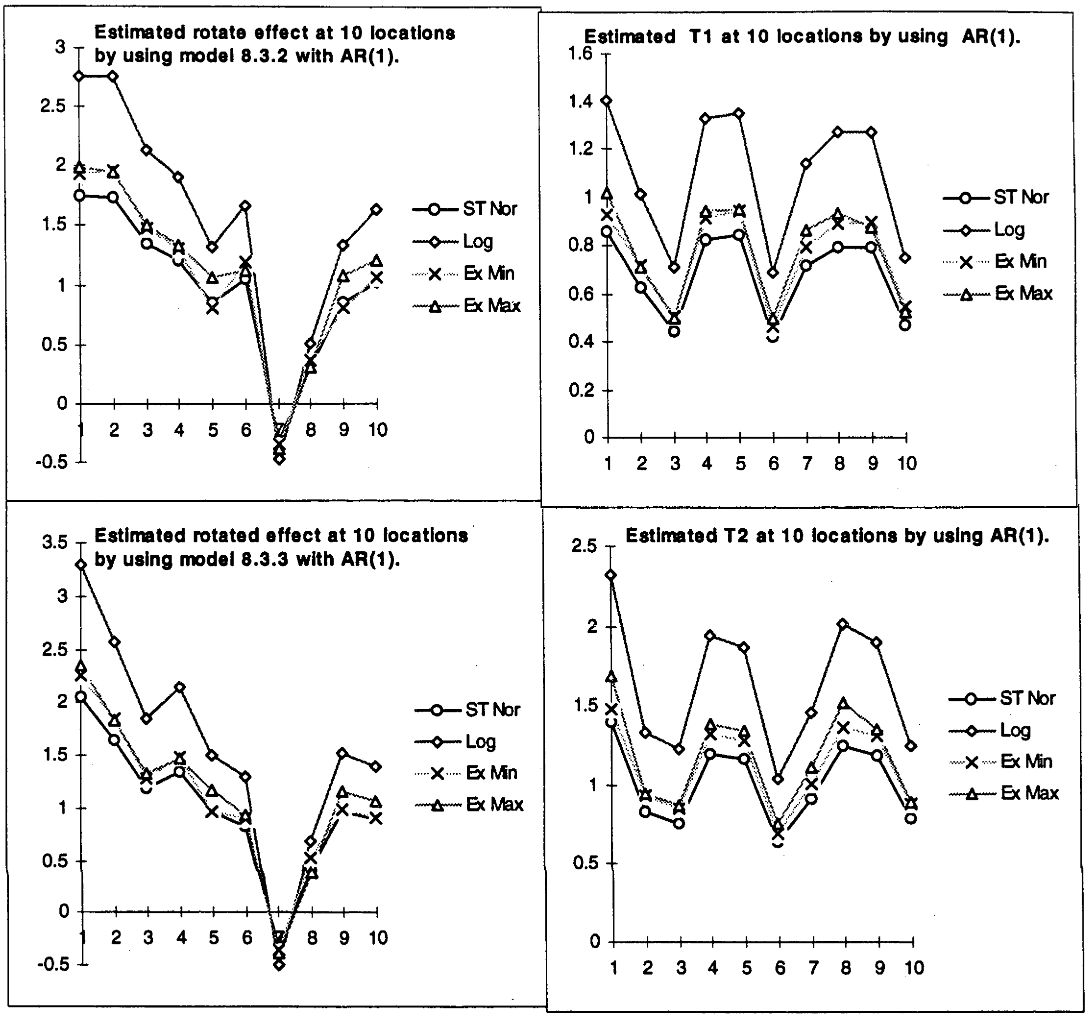
		ML			REML		
		Est	SE	Z-v	Est	SE	Z-v
Extreme Maximal	φ	0.655	0.14	4.688	0.695	0.149	4.668
	ρ	0.9	0.12	7.487	0.9	0.118	7.638
	θ_{11}	0.969	0.193	5.021	0.974	0.194	5.023
	θ_{12}	0.659	0.164	4.032	0.663	0.164	4.034
	θ_{13}	0.473	0.131	3.6	0.475	0.132	3.601
	θ_{14}	0.905	0.169	5.361	0.909	0.17	5.362
	θ_{15}	0.919	0.206	4.464	0.924	0.207	4.467
	θ_{16}	0.483	0.128	3.78	0.485	0.128	3.782
	θ_{17}	0.846	0.207	4.093	0.85	0.207	4.096
	θ_{18}	0.92	0.185	4.979	0.923	0.185	4.983
	θ_{19}	0.849	0.181	4.698	0.854	0.182	4.701
	θ_{110}	0.499	0.128	3.899	0.501	0.128	3.9
	θ_{21}	1.594	0.238	6.684	1.602	0.24	6.687
	θ_{22}	0.88	0.185	4.759	0.885	0.186	4.762
	θ_{23}	0.827	0.167	4.959	0.831	0.167	4.962
	θ_{24}	1.338	0.201	6.66	1.344	0.202	6.664
	θ_{25}	1.302	0.237	5.49	1.309	0.238	5.496
	θ_{26}	0.731	0.153	4.77	0.735	0.154	4.773
	θ_{27}	1.094	0.241	4.534	1.098	0.242	4.539
	θ_{28}	1.497	0.251	5.967	1.501	0.251	5.972
	θ_{29}	1.306	0.22	5.925	1.313	0.221	5.931
	θ_{210}	0.844	0.164	5.164	0.848	0.164	5.166
	β_0	-0.436	0.135	-3.226	-0.437	0.138	-3.162
	β_1	2.203	0.309	7.133	2.213	0.313	7.081
	β_2	1.798	0.295	6.087	1.808	0.299	6.043
	β_3	1.306	0.279	4.688	1.312	0.282	4.647
	β_4	1.463	0.28	5.23	1.468	0.283	5.182
	β_5	1.193	0.284	4.207	1.199	0.287	4.175
	β_6	0.946	0.276	3.427	0.949	0.28	3.395
	β_7	-0.351	0.322	-1.092	-0.351	0.325	-1.083
	β_8	0.365	0.281	1.3	0.365	0.284	1.283
	β_9	1.139	0.278	4.097	1.145	0.282	4.064
	β_{10}	0.971	0.276	3.52	0.974	0.279	3.488

Table 8.7.2.4: ML and REML estimates of treatment effect, standard errors and their z-v for the model 8.7.1 by AR(1) and constant correlation.

		ML			REML		
Model		Est	SE	z-v	Est	SE	z-v
AR(1) 8.3.2	Standard Nor	0.977	0.16	6.089	0.981	0.163	6.011
	Logistic	1.548	0.253	6.121	1.553	0.257	6.045
	Extreme Min	1.052	0.18	5.859	1.058	0.183	5.784
	Extreme Max	1.111	0.182	6.115	1.117	0.185	6.033
AR(1) 8.3.3	Standard Nor	0.99	0.162	6.12	0.995	0.165	6.034
	Logistic	1.569	0.256	6.137	1.575	0.26	6.052
	Extreme Min	1.068	0.182	5.87	1.075	0.186	5.769
	Extreme Max	1.123	0.183	6.127	1.129	0.187	6.04
Const. 8.3.2	Standard Nor	0.971	0.169	5.742	0.974	0.172	5.657
	Logistic	1.567	0.267	5.876	1.572	0.272	5.789
	Extreme Min	1.038	0.191	5.443	1.043	0.195	5.356
	Extreme Max	1.093	0.19	5.752	1.098	0.194	5.655
Const. 8.3.3	Standard Nor	0.983	0.17	5.794	0.986	0.173	5.701
	Logistic	1.588	0.269	5.91	1.594	0.274	5.817
	Extreme Min	1.056	0.192	5.491	1.062	0.197	5.387
	Extreme Max	1.103	0.191	5.781	1.108	0.195	5.678

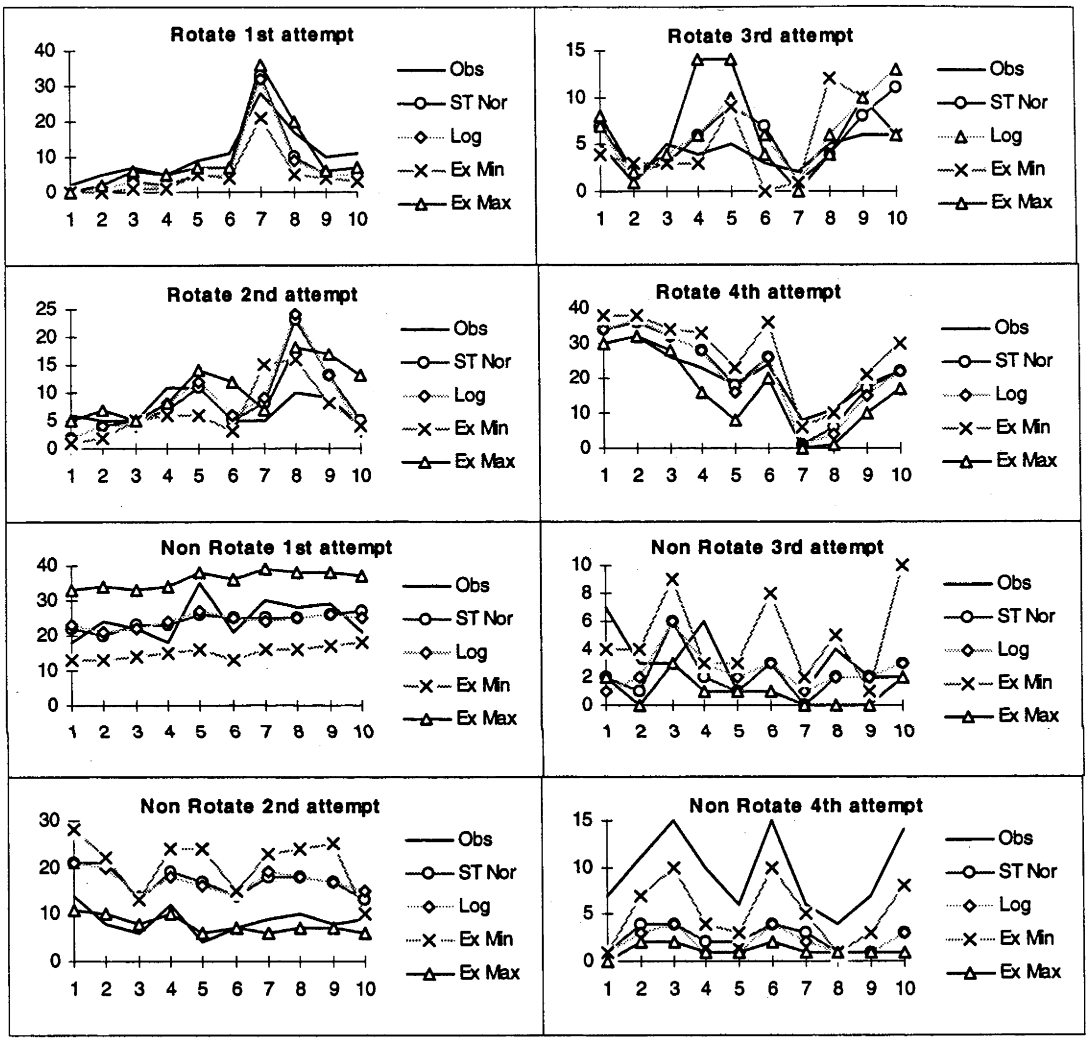
* Nor = Normal, Min =Minimal, Max =Maximal, Const.= Constant correlation.

Figure 8.7.1: REML estimates for rotate effect and threshold parameters at different locations. Vertical axis shows estimate, horizontal axis gives location.



* ST= Standard, Nor=Normal, Ex=Extreme, Min=Minimal and Max=Maximal, T1=θ_1 and T2=θ_2.

Figure 8.7.2: REML predicted and observed frequecies for map data for the model 8.3.3 by AR(1). Vertical axis represents frequency, horizontal shows 10 locations.



* Obs=Observed, ST= Standard, Nor=Normal, Ex=Extreme, Min=Minimal and Max=Maximal.

CHAPTER NINE

RANDOM THRESHOLD MODELS FOR INFLATED ZERO CLASS DATA

9.1 INTRODUCTION

In the chapters 5-8, various mixed threshold models involving different structures of variance component matrices have been introduced for ordinal response variables. Estimation equations of parameters and variance components and their asymptotic variance-covariance matrices have been developed by both ML and REML methods and applied to the various ordinal data. The approach demonstrates a great potential to analyse ordinal response data. However, in some applications, the data are presented in the form of frequencies, ie., the variation in some levels is taken to be zero. This chapter summarises all different structures of variance-covariance matrices in the previous chapters for the data that are recorded in the frequency form. Estimation procedures are set out in terms of composite link functions (Thompson and Baker 1981).

The motivating example is discrete data for which there is high probability of observing a zero response. These data are often modelled by zero inflated or zero added Poisson models (Heilborn, 1989 and Lambert 1992). However, these models presuppose that the nonzero part of the data can be adequately modelled by a Poisson distribution. Of course, the Poisson model for nonzero observations can be replaced by a more versatile distribution such as the negative binomial, but the inference problems associated with such distributions are more difficult and become especially so when the parameters of the distribution are required to incorporate a random component. The purpose of this chapter is to show that, when the number of different nonzero observations is not large or they can be grouped into classes, a random component threshold model can provide very good fits to the data.

The method is appropriate for modelling the annual frequency of use of different medical procedures recorded for each county in Washington State. The data for chemotherapy use, during 1987-1992, is given in Table 8 in appendix B and shows that, for each of the 39 counties of Washington State, the frequency of zero use is high. However, the remainder of the distribution is not close to having a Poisson distribution in that it has a *fat middle*. We show how a relatively simple threshold model incorporating a random county term, is very effective in modelling such data. Sections 9.2 and 9.3 develop the general estimation procedure. This is then applied to modelling the *medical procedure use* data. Section 9.4 extends the method to model such frequency data collected over successive years and allowing for possible dependence of the random county effects in different years. In the section 9.5, the county random effects are modelled as a time series process and ML and REML estimators are given for autoregressive AR(1) models.

9.2 THRESHOLD MODELS AND ESTIMATION

The random component threshold models have been given in the previous section. For the data under consideration, the observations y_k (k=0,1,...,M) are frequencies of the categories 0, 1, ...,M where the last category

M may be the accumulation of all observations $\geq M$. The vector $\mathbf{y} = [y_0, y_1, \ldots, y_M]'$ follows a multinomial distribution with corresponding probability $\mathbf{P} = [P_0, P_2, \ldots, P_M]'$. A threshold model is defined as

9.2.1 $P_k = G(\theta_k) - G(\theta_{k-1})$

where k=0, 1, 2,...,M and four different forms of G(.) have been given in section 5.2 of chapter 5.

This model is generalised to incorporate fixed and random regression components by altering it to

9.2.3 $P_k = G(\theta_k - \eta) - G(\theta_{k-1} - \eta)$,

where η is a linear combination of fixed and random effects. In general η the can be expressed as

9.2.1 $$\eta = \mathbf{X}\beta + \mathbf{Z}\mathbf{u}$$

where $\mathbf{X}$ is known matrix of regression variables, $\mathbf{Z}$ is incidence matrix, β is a vector of unknown fixed regression parameters and $\mathbf{u}$ is a vector of random effects taken here to be normally distributed with zero mean and $\mathbf{A}(\varphi,\rho)$ as variance-covariace matrix, where φ and ρ are vectors parameterising the variance matrix $\mathbf{A}$. In general $\mathbf{u}$ may be partitioned into independent vectors $\mathbf{u} = [\mathbf{u}_1', \mathbf{u}_2', \ldots, \mathbf{u}_q']'$ and $\mathbf{u}_j$ is taken to be distributed $N(0, \varphi_j\mathbf{A}_j(\rho))$.

Following discussion in the previous chapters, θ_0 is set to zero, θ_{-1}, θ_M taken to be at the lower/upper bounds of the distribution G and the remaining $[\theta_1, \theta_2, \ldots, \theta_{M-1}]$ are collected into a parameter vector θ .

Estimation and inference techniques are the same as previous chapters although a new form is presented for the log-likelihood function of the observations conditional on fixed random component. Let l_1 be the log-likelihood of the observations conditional on the random component vector $\mathbf{u}$ taken to be fixed and l_2 be the logarithm of the probability density function of $\mathbf{u}$. In what follows, the conditional log-likelihood l_1 is expressed in terms of τ which is related to the parameter $\alpha = [\theta', \beta', \mathbf{u}']'$ by the linear equation $\tau = \mathbf{S}\alpha = [\mathbf{X}^*, \mathbf{Z}^*]\alpha$, where $\mathbf{S}$ is a known matrix and matrices $\mathbf{X}^*$ and $\mathbf{Z}^*$ are a partition of the matrix $\mathbf{S}$ corresponding to the fixed parameters (θ and β) and random component $\mathbf{u}$.

As in previous chapters, for given initial value $\alpha_0 = [\theta_0', \beta_0', \mathbf{u}_0']'$ let $\tau_0 = \mathbf{S}\alpha_0$ and $\Delta\alpha$ be changes given by a Newton-Raphson iteration from α_0 to a value closer to the penalised likelihood (or BLUP) estimator $\tilde{\alpha}$. The quantity $\alpha_0 + \Delta\alpha$ is used as the initial value for the next iteration. The equation for $\Delta\alpha$ is

$$9.2.5 \qquad \mathbf{V}\Delta\alpha = \mathbf{S}'\partial l_1 / \partial\tau_0 - \begin{bmatrix} 0 \\ 0 \\ \mathbf{A}_0^{-1}\mathbf{u}_0 \end{bmatrix}, \quad \mathbf{V} = \mathbf{S}'(-\partial^2 l_1 / \partial\tau_0 \partial\tau_0')\mathbf{S} + \begin{bmatrix} 0 & 0 & 0 \\ 0 & 0 & 0 \\ 0 & 0 & \mathbf{A}_0^{-1} \end{bmatrix}$$

where $\mathbf{A}_0$ is an initial value of

$$9.2.6 \qquad \mathbf{A} = \begin{bmatrix} \varphi_1\mathbf{A}_1(\rho) & & & \\ & \varphi_2\mathbf{A}_2(\rho) & & \\ & & \cdot & \\ & & & \cdot \\ & & & & \varphi_q\mathbf{A}_q(\rho) \end{bmatrix}$$

corresponding to initial values φ_{j0} for φ_j and ρ_0 for ρ. Corresponding to the partition of α into θ, β, $\mathbf{u}$ we let

9.2.7 $$\mathbf{V}^{-1} = \begin{bmatrix} \mathbf{V}_{11} & \mathbf{V}_{12} & \mathbf{V}_{13} \\ \mathbf{V}_{21} & \mathbf{V}_{22} & \mathbf{V}_{23} \\ \mathbf{V}_{31} & \mathbf{V}_{32} & \mathbf{V}_{33} \end{bmatrix}^{-1} = \left[\begin{array}{ccc|c} \cdot & \cdot & & \cdot \\ \cdot & \cdot & & \cdot \\ \hline \cdot & \cdot & & \cdot \end{array}\right] = \begin{bmatrix} \Omega & \cdot \\ \cdot & \mathbf{T} \end{bmatrix}, \quad \mathbf{V}_{33}^{-1} = \mathbf{T}^*$$

and further $\mathbf{T} = [\mathbf{T}_{jj'}]$, $\mathbf{T}^* = [\mathbf{T}^*_{jj'}]$ are partitions of $\mathbf{T}$ and $\mathbf{T}^*$ confomally to the partition of $\mathbf{u}$ into its q components.

Once convergence is obtained for $\tilde{\alpha}$, approximate ML estimates of φ_j for any initial ρ_0, are obtained from

9.2.8 $$\hat{\varphi}_{j(ML)} = v_j^{-1}[\tilde{\mathbf{u}}_j' \mathbf{A}_j^{-1}(\rho_0)\tilde{\mathbf{u}}_j + \mathrm{tr}\,\mathbf{T}^*_{jj'}\mathbf{A}_j^{-1}(\rho_0)], \quad v_j = \text{dimension of } \mathbf{u}_j .$$

A third cycle of iteration is used for estimating ρ. After convergence of the first two cycles, the estimating equation for the ML estimator of ρ

9.2.9 $$\mathrm{tr}(\partial \mathbf{A}^{-1}/\partial\rho)\mathbf{A}(\rho_0) = [\mathrm{tr}(\partial \mathbf{A}^{-1}/\partial\rho)\mathbf{T}^* + \tilde{\mathbf{u}}'(\partial \mathbf{A}^{-1}/\partial\rho)\tilde{\mathbf{u}}].$$

These estimates of φ and ρ may be used as initial values of φ and ρ in further iterations and whole process repeated from 9.2.3 until convergence in all estimates is obtained.

Once convergence is obtained in the whole process, the asymptotic variance-covariance matrix of the approximate maximum likelihood estimators $\hat{\varphi}_{(ML)}$ and $\hat{\rho}_{(ML)}$, is given by

9.2.10

$$\mathrm{Var}\begin{bmatrix}\hat{\varphi}_{(ML)}\\ \hat{\rho}_{(ML)}\end{bmatrix} \cong 2\begin{bmatrix}\mathrm{tr}\Sigma^{-1}(\partial\Sigma/\partial\varphi)\Sigma^{-1}\partial\Sigma/\partial\varphi & \mathrm{tr}\Sigma^{-1}(\partial\Sigma/\partial\varphi)\Sigma^{-1}\partial\Sigma/\partial\rho \\ . & \mathrm{tr}\Sigma^{-1}(\partial\Sigma/\partial\rho)\Sigma^{-1}\partial\Sigma/\partial\rho\end{bmatrix}^{-1}_{\varphi=\hat{\varphi}_{(ML)},\rho=\hat{\rho}_{(ML)}}$$

where $\Sigma = \mathbf{B}^{-1} + \mathbf{Z}^{*}\mathbf{A}\mathbf{Z}^{*\prime}$ and $\mathbf{B} = -\partial^{2}l_{1} / \partial\tau\partial\tau'$.

The penalised likelihood (or BLUP) estimators of θ, β corresponding to $\varphi = \hat{\varphi}_{ML}$ and $\rho = \hat{\rho}_{ML}$ are also approximate maximum likelihood estimators with approximate variance-covariance given by

9.2.11 $$\mathrm{Var}\begin{bmatrix}\hat{\theta}_{ML}\\ \hat{\beta}_{ML}\end{bmatrix} \cong \Omega$$

where Ω is given by 9.2.5.

The REML estimates of the parameters are obtained by replacing $\mathbf{T}^{*}$ with $\mathbf{T}$ in the all above three steps. The approximate variance-covariance matrix for the approximate residual maximum likelihood estimators $\hat{\varphi}_{(REML)}$ and $\hat{\rho}_{(REML)}$ is given by

9.2.12

$$\mathrm{Var}\begin{bmatrix}\hat{\varphi}\\ \hat{\rho}\end{bmatrix}_{(REML)} \cong 2\begin{bmatrix}\mathrm{tr}\mathbf{Q}(\partial\Sigma/\partial\varphi)\mathbf{Q}\partial\Sigma/\partial\varphi & \mathrm{tr}\mathbf{Q}(\partial\Sigma/\partial\varphi)\mathbf{Q}\partial\Sigma/\partial\rho \\ . & \mathrm{tr}\mathbf{Q}(\partial\Sigma/\partial\rho)\mathbf{Q}\partial\Sigma/\partial\rho\end{bmatrix}^{-1}_{\varphi=\hat{\varphi}_{(REML)},\rho=\hat{\rho}_{(REML)}}$$

where $\mathbf{Q} = \Sigma^{-1} - \Sigma^{-1}(\mathbf{X}^{*\prime}\Sigma^{-1}\mathbf{X}^{*})^{-}\mathbf{X}^{*\prime}\Sigma^{-1}$. The 9.2.10 and 9.2.12 are analogous to the corresponding expressions for the normal response variables given in chapter 4. In the applications of section 9.3, 9.4 there is no parameter ρ in the model so that, in the above estimating equation, the third cycle of iteration is not required. In those sections, the approximate variance-covariance of ML and REML estimators $\hat{\varphi}_{ML}$ and $\hat{\varphi}_{REML}$ are inverses of north-west of 9.2.10 and 9.2.12 respectively.

It is in section 9.5, where autoregressive dependence between variance component terms is included in the model, that estimation of ρ is considered. In that section the above estimating equations are further simplified.

9.3 APPLICATION TO FREQUENCY OF USE OF MEDICAL PROCEDURES

The observed data consist of numbers of different occasions *injection of chemotherapy for cancer* (ICD-9-CM code 99.25) is used during a given year for each person aged 20 or over in Washington State. The observed frequencies for usage during 1987-1992 are reported in table 8 in appendix B. Frequencies for four or more usages are grouped, but this is largely to minimise tabulation rather than a restriction of the model and its fitting procedure.

The analysis of such data has been considered in health services research, where it is typically called small area analysis. Many studies focus on calculation of the utilisation rate for a particular diagnosis (or procedure) in each of several geographic areas or counties and compute a statistic such as coefficient of variation to show how much rates vary over regions. Glover (1938) showed considerable variation for a particular procedure over regions in England; Lewis (1969) and Wennberg and Gettelson (1973, 1975) showed significant variation in surgical rates for all common procedures between small areas in the United States. McPherson et al (1981, 1982) introduced a term corresponding to an area effect into the expected values. Diehr and

Grembowski (1990) described a simulation of the distributions of various test statistics under the null hypothesis of no area variation as a means of computing appropriate percentage points. The distribution of test statistics was also examined in Cain and Diehr (1992) when the number of admissions per individual were taken to have one of four theoretical distributions, viz. Bernoulli (binomial), Poisson, Poisson-Bernoulli and negative binomial. In the cases of multiple admissions per individual, they showed that the variance of observations in counties is probably larger than would occur under a Poisson model. Diehr et al (1992) showed that, for back surgery admissions in 1989 for Washington State, hypothesis tests for variation among counties, based on different statistics, gave different results. They investigated the power of several tests to detect excess variation.

Our aim here is somewhat different in that we are attempting to find a model which incorporates a random county (small area) effect and is capable of reproducing the general shape of the distribution of multiple admissions per patient. It is shown that comparatively simple threshold models fit surprisingly well.

We now use the estimation method given in section 9.2 to develop ML and REML estimates of parameters for application to the type of frequency data recorded in Table 8 at each year. For each data set (data set at different years), apart from threshold parameters $\boldsymbol{\theta}$ and fixed parameters $\boldsymbol{\beta}$ the random components $\mathbf{u}$ are included in the model through $\eta = \mathbf{x}'\boldsymbol{\beta} + \mathbf{z}'\mathbf{u}$ for known $\mathbf{x}$, $\mathbf{z}$. We assume that $\mathbf{x} = \mathbf{x}_i$, $\mathbf{z} = \mathbf{z}_i$ for all the observations in county i and let $\eta_i = \mathbf{x}_i'\boldsymbol{\beta} + \mathbf{z}_i'\mathbf{u}$.

The observation vector in the county i, $\mathbf{y}_i = [\mathbf{y}_{i0}, \mathbf{y}_{i1}, \ldots, \mathbf{y}_{ik}, \ldots, \mathbf{y}_{iM}]'$ follows a multinomial distribution. For observation vector $\mathbf{y} = [\mathbf{y}_1', \mathbf{y}_2', \ldots, \mathbf{y}_N']$, the log-likelihood function conditional on the given random component $\mathbf{u}$, is given by

9.3.1 $$l_1 = \text{constant} + \sum_{i=1}^{N} \sum_{k=0}^{M} y_{ik} \ln P_{ik}$$

with probabilities P_{ik} related to θ_k, η_i. Letting $\theta_0 = 0$,

9.3.2 $$\tau_{ik} = \begin{cases} -\eta_i & , \quad k = 0 \\ \theta_k - \eta_i & , \quad 1 \le k < M, \\ \theta_{k-1} - \eta_i & , \quad k = M \end{cases}$$

$\tau_i = [\tau_{i0}, \tau_{i1}, \ldots \tau_{iM}]'$ and $\tau_i = [\tau_{i1}', \tau_{i2}', \ldots, \tau_{iN}']'$

then

9.3.3 $$P_{ik} = \begin{cases} G(\tau_{ik}) & , \quad k = 0 \\ G(\tau_{ik}) - G(\tau_{i,k-1}) & , \quad 1 \le k < M. \\ 1 - G(\tau_{ik}) & , \quad k = M \end{cases}$$

Further if

$\mathbf{G}_i = [G(\tau_{i0}), G(\tau_{i1}), \ldots G(\tau_{i(M-1)}), 1 - G(\tau_{i(M-1)})]'$, $\mathbf{G} = [\mathbf{G}_1', \mathbf{G}_2, \ldots \mathbf{G}_N']'$,

$\mathbf{P}_i = [P_{i0}, P_{i1}, \ldots P_{iM}]'$, $\mathbf{P} = [\mathbf{P}_1', \mathbf{P}_2', \mathbf{P}_3', \ldots, \mathbf{P}_N']'$ then

$\mu_i = E(\mathbf{y}_i | \mathbf{u}_i) = y_{i.} \mathbf{P}_i = \mathbf{C}_i \mathbf{G}_i$ where $\mu_i = [\mu_{i0}, \mu_{i1}, \ldots \mu_{iM}]'$, $y_{i.} = 1'\mathbf{y}_i$ and for M=4 the matrix $\mathbf{C}_i$ is given by

9.3.4 $$\mathbf{C}_i = \mathbf{y}_{i.} \begin{bmatrix} 1 & 0 & 0 & 0 & 0 \\ -1 & 1 & 0 & 0 & 0 \\ 0 & -1 & 1 & 0 & 0 \\ 0 & 0 & -1 & 1 & 0 \\ 0 & 0 & 0 & 0 & 1 \end{bmatrix}.$$

The $\mu = [\mu_1', \mu_2', \ldots, \mu_N']' = \mathbf{CG}$, where $\mathbf{C}$ is block diagonal matrix with blocks $(\mathbf{C}_1, \mathbf{C}_2, \ldots, \mathbf{C}_N)$. The matrix $\mathbf{C}$ gives a composite link function described generally in Thompson and Baker (1981) and further developed in Jansen (1990, 1992, 1993).

First and second order derivatives of 9.2.3 (1_1) with respect to τ, for use in the general estimation procedure, are easily derivable from the above expression.

If $\mathbf{J}_{M-2} = [0'_{M-2}, 1]'$, $\mathbf{U} = [0_{M-1}, \mathbf{I}_{M-1}, \mathbf{J}_{M-2}]'$, $\mathbf{S}_i = [\mathbf{U}, -1_{M+1} \otimes (\mathbf{x}_i', \mathbf{z}_i')]$, $\mathbf{S} = [\mathbf{S}_1', \mathbf{S}_2', \ldots, \mathbf{S}_N']'$, $\alpha = [\theta', \beta', \mathbf{u}']'$ then $\tau = \mathbf{S}\alpha = [\mathbf{X}^*, \mathbf{Z}^*]\alpha$ and $\mathbf{S} = [1_N \otimes \mathbf{U}, -(\mathbf{X}, \mathbf{Z}) \otimes 1_{M+1}]$. Here the random component vector $\mathbf{u}$, corresponding to the county effects, consists of only one subvector of random components and is distributed as $\mathbf{N(0,A)}$.

A simple additive model for the i^{th} county at each year is

$$9.3.5 \quad \eta_i = \beta + u_i$$

where β is an overall mean effect and u_i is a random effect which is taken to be an independent selection, for each county, from an $N(0, \varphi)$ distribution. Thus for the model 9.3.5 $\mathbf{x}_i = 1$ and z_i is a vector with a 1 at position $i(i=1,2,\ldots 39)$ and remaining elements zero. All the four threshold models of chapter 5 are fitted. Both fixed effect β and the random county effects u_i can be estimated with a view to predicting the probability distribution of procedure use in subsequent years.

The estimates of parameters, standard errors and the ratio of estimates to the standard errors with both ML and REML methods for all four threshold models listed in section 5.2 of chapter 5 are given in Tables 9.3.1a, 9.3b, 9.3c and 9.3d. These tables give only the estimates of the fixed effects θ, β and variance component φ. All are significantly different from zero. A glance at the cut-points (threshold) parameter estimates indicates no clear pattern of variation over years and the same can be said for the mean parameter β. There may be a drift down in the threshold parameter. This variation over years is re-examined when a simultaneous model is fitted to all years of data. From the fitted model expected frequencies may be generated and these are given in fitted frequency columns of Table 8 in appendix B. Figure 9.3 shows REML predicted values of the unknown county random effects at different years. Bearing in mind the simplicity of the model, which contains only the parameters: β = overall mean, with $\theta_0 = 0$ and θ_1, θ_2, θ_3=cut-point parameters, φ =var(random county effects) , the agreement between the observed and expected frequencies is remarkable.

Note that predicted values of county random effects indicate differences between counties in relative use of this chemotherapy procedure. There appears to be possible shifts of the random county effects over the years and the next section is concerned with modelling those shifts.

Table 9.3a: Estimates of parameters (Est), standard errors (SE) and the ratio of Est to SE (z-v) by ML and REML methods in fitting model 9.3.1 to chemotherapy data from Washington State over several years.

		ML			REML		
Standard		Est	SE	z-v	Est	SE	z-v
Normal	φ	0.059	0.014	4.21	0.061	0.014	4.36
1987	θ_1	0.758	0.004	189.50	0.758	0.004	189.50
	θ_2	1.169	0.007	167.00	1.169	0.007	167.00
	θ_3	1.422	0.01	142.20	1.422	0.01	142.20
	β	-2.224	0.039	-57.03	-2.224	0.04	-55.60
	φ	0.03	0.007	4.29	0.031	0.007	4.43
	θ_1	0.751	0.004	187.75	0.751	0.004	187.75
1988	θ_2	1.173	0.007	167.57	1.173	0.007	167.57
	θ_3	1.419	0.01	141.90	1.419	0.01	141.90
	β	-2.164	0.028	-77.29	-2.164	0.029	-74.62
	φ	0.032	0.007	4.57	0.031	0.007	4.43
	θ_1	0.745	0.004	186.25	0.745	0.004	186.25
1989	θ_2	1.17	0.007	167.14	1.17	0.007	167.14
	θ_3	1.433	0.01	143.30	1.433	0.01	143.30
	β	-2.156	0.028	-77.00	-2.156	0.029	-74.34
	φ	0.032	0.008	4.00	0.033	0.008	4.13
	θ_1	0.719	0.003	239.67	0.719	0.003	239.67
1990	θ_2	1.149	0.006	191.50	1.149	0.006	191.50
	θ_3	1.426	0.01	142.60	1.426	0.01	142.60
	β	-2.183	0.029	-75.28	-2.183	0.03	-72.77
	φ	0.038	0.009	4.22	0.033	0.008	4.13
	θ_1	0.7	0.003	233.33	0.7	0.003	233.33
1991	θ_2	1.122	0.006	187.00	1.122	0.006	187.00
	θ_3	1.39	0.009	154.44	1.39	0.009	154.44
	β	-2.148	0.029	-74.07	-2.149	0.03	-71.63
	φ	0.059	0.014	4.21	0.039	0.009	4.33
	θ_1	0.697	0.003	232.33	0.697	0.003	232.33
1992	θ_2	1.103	0.006	183.83	1.103	0.006	183.83
	θ_3	1.346	0.009	149.56	1.346	0.009	149.56
	β	-2.171	0.031	-70.03	-2.171	0.032	-67.84

Table 9.3b: Estimates of parameters (Est), standard errors (SE) and the ratio of Est to SE (z-v) by ML and REML methods in fitting model 9.3.1 to chemotherapy data from Washington State over several years.

		ML			REML		
Logistic		Est	SE	z-v	Est	SE	z-v
1987	φ	0.42	0.1	4.20	0.431	0.101	4.27
	θ_1	2.147	0.012	178.92	2.147	0.012	178.92
	θ_2	3.521	0.025	140.84	3.521	0.025	140.84
	θ_3	4.446	0.039	114.00	4.446	0.039	114.00
	β	-4.348	0.105	-41.41	-4.348	0.106	-41.02
1988	φ	0.199	0.046	4.33	0.204	0.048	4.25
	θ_1	2.11	0.011	191.82	2.11	0.011	191.82
	θ_2	3.512	0.024	146.33	3.512	0.024	146.33
	θ_3	4.405	0.037	119.05	4.405	0.037	119.05
	β	-4.182	0.073	-57.29	-4.182	0.074	-56.51
1989	φ	0.196	0.046	4.26	0.202	0.048	4.21
	θ_1	2.093	0.011	190.27	2.093	0.011	190.27
	θ_2	3.503	0.023	152.30	3.503	0.023	152.30
	θ_3	4.461	0.038	117.39	4.461	0.038	117.39
	β	-4.159	0.072	-57.76	-4.159	0.073	-56.97
1990	φ	0.213	0.05	4.26	0.218	0.052	4.19
	θ_1	2.017	0.011	183.36	2.017	0.011	183.36
	θ_2	3.445	0.023	149.78	3.445	0.023	149.78
	θ_3	4.458	0.038	117.32	4.458	0.038	117.32
	β	-4.228	0.075	-56.37	-4.228	0.076	-55.63
1991	φ	0.214	0.05	4.28	0.22	0.052	4.23
	θ_1	1.959	0.01	195.90	1.959	0.01	195.90
	θ_2	3.347	0.021	159.38	3.347	0.021	159.38
	θ_3	4.317	0.035	123.34	4.317	0.035	123.34
	β	-4.14	0.075	-55.20	-4.141	0.076	-54.49
1992	φ	0.251	0.058	4.33	0.258	0.061	4.23
	θ_1	1.958	0.01	195.80	1.958	0.01	195.80
	θ_2	3.3	0.021	157.14	3.3	0.021	157.14
	θ_3	4.176	0.033	126.55	4.176	0.033	126.55
	β	-4.197	0.081	-51.81	-4.198	0.082	-51.20

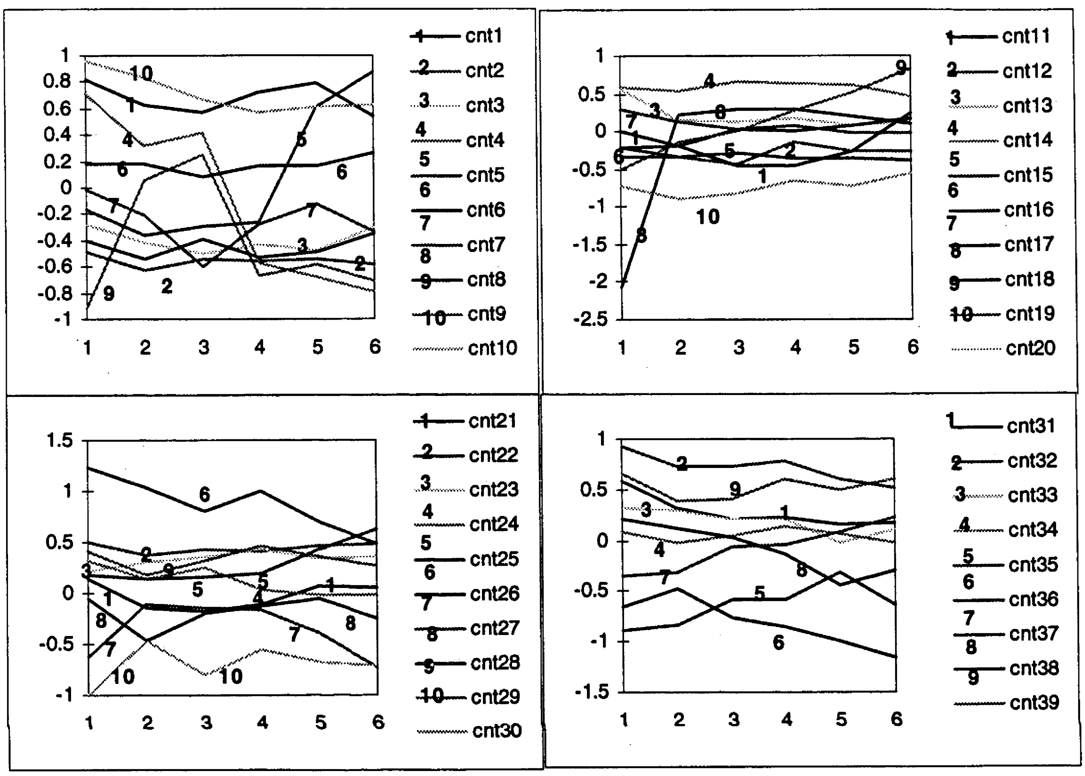
Table 9.3c: Estimates of parameters (Est), standard errors (SE) and the ratio of Est to SE (z-v) by ML and REML methods in fitting model 9.3.1 to chemotherapy data from Washington State over several years.

		ML			REML		
Extreme							
Minimal	φ	0.02	0.005	4.00	0.02	0.005	4.00
1987	θ_1	0.423	0.002	211.50	0.423	0.002	211.50
	θ_2	0.624	0.003	208.00	0.624	0.003	208.00
	θ_3	0.739	0.005	147.80	0.739	0.005	147.80
	β	-1.462	0.023	-63.57	-1.462	0.023	-63.57
	φ	0.01	0.002	5.00	0.011	0.003	3.67
	θ_1	0.422	0.002	211.00	0.422	0.002	211.00
1988	θ_2	0.63	0.003	210.00	0.63	0.003	210.00
	θ_3	0.743	0.004	185.75	0.743	0.004	185.75
	β	-1.428	0.017	-84.00	-1.428	0.017	-84.00
	φ	0.011	0.002	5.50	0.011	0.003	3.67
	θ_1	0.419	0.002	209.50	0.419	0.002	209.50
1989	θ_2	0.628	0.003	209.33	0.628	0.003	209.33
	θ_3	0.749	0.005	149.80	0.749	0.005	149.80
	β	-1.425	0.017	-83.82	-1.425	0.018	-79.17
	φ	0.011	0.003	3.67	0.011	0.003	3.67
	θ_1	0.404	0.002	202.00	0.404	0.002	202.00
1990	θ_2	0.616	0.003	205.33	0.616	0.003	205.33
	θ_3	0.742	0.004	185.50	0.742	0.004	185.50
	β	-1.44	0.018	-80.00	-1.44	0.018	-80.00
	φ	0.011	0.003	3.67	0.012	0.003	4.00
	θ_1	0.394	0.002	197.00	0.394	0.002	197.00
1991	θ_2	0.604	0.003	201.33	0.604	0.003	201.33
	θ_3	0.727	0.004	181.75	0.727	0.004	181.75
	β	-1.42	0.018	-78.89	-1.42	0.018	-78.89
	φ	0.013	0.003	4.33	0.013	0.003	4.33
	θ_1	0.391	0.002	195.50	0.391	0.002	195.50
1992	θ_2	0.592	0.003	197.33	0.592	0.003	197.33
	θ_3	0.704	0.004	176.00	0.704	0.004	176.00
	β	-1.433	0.019	-75.42	-1.433	0.019	-75.42

Table 9.3d: Estimates of parameters (Est), standard errors (SE) and the ratio of Est to SE (z-v) by ML and REML methods in fitting model 9.3.1 to chemotherapy data from Washington State over several years.

		ML			REML		
Extreme							
Maximal	φ	0.414	0.096	4.31	0.425	0.099	4.29
1987	θ_1	2.138	0.012	178.17	2.138	0.012	178.17
	θ_2	3.511	0.025	140.44	3.511	0.025	140.44
	θ_3	4.436	0.039	113.74	4.436	0.039	113.74
	β	-4.355	0.104	-41.88	-4.355	0.105	-41.48
	φ	0.195	0.046	4.24	0.201	0.047	4.28
	θ_1	2.101	0.011	191.00	2.101	0.011	191.00
1988	θ_2	3.503	0.024	145.96	3.503	0.024	145.96
	θ_3	4.396	0.037	118.81	4.396	0.037	118.81
	β	-4.19	0.072	-58.19	-4.191	0.073	-57.41
	φ	0.193	0.045	4.29	0.198	0.047	4.21
	θ_1	2.085	0.011	189.55	2.085	0.011	189.55
1989	θ_2	3.494	0.023	151.91	3.494	0.023	151.91
	θ_3	4.451	0.038	117.13	4.451	0.038	117.13
	β	-4.167	0.071	-58.69	-4.168	0.073	-57.10
	φ	0.209	0.049	4.27	0.215	0.051	4.22
	θ_1	2.009	0.011	182.64	2.009	0.011	182.64
1990	θ_2	3.436	0.023	149.39	3.436	0.023	149.39
	θ_3	4.448	0.038	117.05	4.448	0.038	117.05
	β	-4.236	0.074	-57.24	-4.236	0.075	-56.48
	φ	0.211	0.049	4.31	0.217	0.051	4.25
	θ_1	1.951	0.01	195.10	1.951	0.01	195.10
1991	θ_2	3.337	0.021	158.90	3.337	0.021	158.90
	θ_3	4.307	0.035	123.06	4.307	0.035	123.06
	β	-4.149	0.075	-55.32	-4.149	0.076	-54.59
	φ	0.247	0.057	4.33	0.254	0.06	4.23
	θ_1	1.951	0.01	195.10	1.951	0.01	195.10
1992	θ_2	3.291	0.021	156.71	3.291	0.021	156.71
	θ_3	4.167	0.033	126.27	4.167	0.033	126.27
	β	-4.206	0.081	-51.93	-4.206	0.082	-51.29

Figure 9.3: REML predicted value of county random effects for six years 1987-1992. Vertical axis is the county effect, horizontal shows year of record.



9.4 RANDOM COMPONENT THRESHOLD MODELS VARYING OVER TIME

We now combine all six data sets at different years and develop various models to such data to evaluate changes over time.

From tables 9.3a-9.3d we see that there is a possible small drift downwards in the estimates of the threshold (cut-point) parameters, but no dramatic changes, while the β estimates do not change significantly over years.

The estimate of variance of the random county effects is larger in 1987 than in subsequent years. From Figure 9.3 it is readily apparent that there are some relatively large shifts in these county estimates from 1987 to 1988 but the picture is comparatively stable from 1988 onwards. On the basis of these predictions a sequence of models for the combined data is proposed.

The observations in county i at year t are denoted by $y_{it0}, y_{it1}, \ldots, y_{itM}$, the frequencies of usages in categories 0,1,...,M for i=1,2...,N and t=1,2,...n. For $\mathbf{y}_{it} = [y_{it0}, y_{it1}, \ldots, y_{itk}, \ldots, y_{itM}]'$ following a multinomial distribution, the log-likelihood function conditional on the given random component $\mathbf{u}$, is given by

9.4.1 $\quad l_1 = \text{constant} + \sum_{i=1}^{N} \sum_{t=1}^{n} \sum_{k=0}^{M} y_{itk} \ln p_{itk}$

where, if

$$9.4.2 \qquad \tau_{itk} = \begin{cases} -\eta_{it} & , \quad k = 0 \\ \theta_k - \eta_{it} & , \quad 1 \le k < M, \\ \theta_{k-1} - \eta_{it} & , \quad k = M \end{cases}$$

$\tau_{it} = [\tau_{it0}, \tau_{it1}, \ldots \tau_{itM}]$, $\tau_i = [\tau'_{i1}, \tau'_{i2}, \ldots, \tau'_{in}]'$, $\tau = [\tau'_1, \tau'_2, \ldots, \tau'_N]'$

then

$$9.4.3 \qquad P_{itk} = \begin{cases} G(\tau_{itk}) & , \quad k = 0 \\ G(\tau_{itk}) - G(\tau_{it,k-1}) & , \quad 1 \le k < M. \\ 1 - G(\tau_{itk}) & , \quad k = M \end{cases}$$

For each threshold model of chapter 5, different models for the observed values are specified through different expressions for $\eta_{it} = \mathbf{x}'_{it}\beta + \mathbf{z}'_{it}\mathbf{u}$. The set of equations given above can be expressed in terms of composite link functions in much the same way as the single time period problem (section 9.3) by putting together the results for each time period. As in the previous section, if $\mathbf{S}_{it} = [\mathbf{U}, -1_{M+1} \otimes (\mathbf{x}'_{it}, \mathbf{z}'_{it})]$, $\mathbf{S}_i = [\mathbf{S}'_{i1}, \mathbf{S}'_{i2}, \ldots, \mathbf{S}'_{in}]'$, $\mathbf{S} = [\mathbf{S}'_1, \mathbf{S}'_2, \ldots, \mathbf{S}'_N]'$ and $\alpha = [\theta', \beta', \mathbf{u}']'$ then $\tau = \mathbf{S}\alpha$ and $\mathbf{S} = [1_{Nn} \otimes \mathbf{U}, -(\mathbf{X}, \mathbf{Z}) \otimes 1_{M+1}]$. Matrices $\mathbf{X}$ and $\mathbf{Z}$ are constructed from the $\mathbf{x}_{it}$ and $\mathbf{z}_{it}$ vectors. Here the random component vector $\mathbf{u}$ may have several component subvectors, depending on the model chosen for η.

The following models are considered. In models 1 and 2, the random county effects are taken to be constant over time.

Model 1: $\eta_{it} = \beta + u_i$, i=1,2,...,39 and t=1,2,...6.

For this model the mean parameter β as well as all the random county effects are considered to be constant over time. The ML and REML estimates of parameters, standard errors and the ratio of estimates to their standard errors are given in Table 9.4.1.

Model 2: $\eta_{it} = \beta_t + u_i$

In this case the mean parameter β is allowed to vary over years. Table 9.4.2a and 9.4.2b provide the ML and REML estimates of parameters, standard errors and the ratio of estimates to their standard errors. The results show that estimates β_t differ little from one another in model 2 and the estimates of the other parameters are identical (to two decimal places) to those obtained for model 1.

Table 9.4.1: Estimates of parameters (Est), standard errors (SE) and the ratio of Est to SE (z-v) by ML and REML methods in fitting model 1 to chemotherapy data from Washington State over several years.

		ML			REML		
Logistic	φ	0.202	0.046	4.39	0.21	0.048	4.38
	θ_1	2.042	0.004	510.50	2.042	0.004	510.50
	θ_2	3.432	0.009	381.33	3.432	0.009	381.33
	θ_3	4.37	0.015	291.33	4.37	0.015	291.33
	β	-4.205	0.072	-58.40	-4.205	0.073	-57.60
Standard Normal	φ	0.0304	0.0069	4.41	0.0312	0.0072	4.33
	θ_1	0.724	0.001	724.00	0.724	0.001	724.00
	θ_2	1.142	0.003	380.67	1.142	0.003	380.67
	θ_3	1.399	0.004	349.75	1.399	0.004	349.75
	β	-2.174	0.028	-77.64	-2.174	0.029	-74.97
Extreme Minimal	φ	0.011	0.002	5.50	0.0108	0.0025	4.32
	θ_1	0.405	0.001	405.00	0.405	0.001	405.00
	θ_2	0.611	0.001	611.00	0.611	0.001	611.00
	θ_3	0.729	0.002	364.50	0.729	0.002	364.50
	β	-1.435	0.017	-84.41	-1.435	0.017	-84.41
Extreme Maximal	φ	0.195	0.046	4.24	0.2037	0.047	4.33
	θ_1	2.101	0.011	191.00	2.034	0.004	508.50
	θ_2	3.503	0.024	145.96	3.423	0.009	380.33
	θ_3	4.396	0.037	118.81	4.361	0.015	290.73
	β	-4.19	0.072	-58.19	-4.214	0.073	-57.73

Table 9.4.2a: Estimates of parameters (Est), standard errors (SE) and the ratio of Est to SE (z-v) by ML and REML methods in fitting model 2 to chemotherapy data from Washington State over several years.

		ML			REML		
		Est	SE	z-v	Est	SE	z-v
Standard Normal	φ	0.0301	0.0068	4.43	0.0309	0.0071	4.35
	θ_1	0.724	0.001	724.00	0.724	0.001	724.00
	θ_2	1.142	0.003	380.67	1.142	0.003	380.67
	θ_3	1.4	0.004	350.00	1.4	0.004	350.00
	β_{11}	-2.236	0.028	-79.86	-2.236	0.029	-77.10
	β_{12}	-2.148	0.028	-76.71	-2.148	0.029	-74.07
	β_{13}	-2.151	0.028	-76.82	-2.151	0.029	-74.17
	β_{14}	-2.164	0.028	-77.29	-2.164	0.029	-74.62
	β_{15}	-2.159	0.028	-77.11	-2.159	0.029	-74.45
	β_{16}	-2.186	0.028	-78.07	-2.186	0.029	-75.38
Logistic	φ	0.2	0.05	4.00	0.21	0.05	4.20
	θ_1	2.042	0.004	510.50	2.042	0.004	510.50
	θ_2	3.432	0.009	381.33	3.432	0.009	381.33
	θ_3	4.37	0.015	291.33	4.37	0.015	291.33
	β_{11}	-4.347	0.072	-60.38	-4.347	0.073	-59.55
	β_{12}	-4.141	0.072	-57.51	-4.141	0.073	-56.73
	β_{13}	-4.149	0.072	-57.63	-4.149	0.073	-56.84
	β_{14}	-4.183	0.072	-58.10	-4.183	0.073	-57.30
	β_{15}	-4.173	0.072	-57.96	-4.173	0.073	-57.16
	β_{16}	-4.243	0.072	-58.93	-4.243	0.073	-58.12

Table 9.4.2b: Estimates of parameters (Est), standard errors (SE) and the ratio of Est to SE (z-v) by ML and REML methods in fitting model 2 to chemotherapy data from Washington State over several years.

	φ	0.0104	0.0024	4.33	0.0107	0.0025	4.28
	θ_1	0.405	0.001	405.00	0.405	0.001	405.00
	θ_2	0.611	0.001	611.00	0.611	0.001	611.00
Extreme Minimal	θ_3	0.729	0.002	364.50	0.729	0.002	364.50
	β_{11}	-1.475	0.017	-86.76	-1.475	0.017	-86.76
	β_{12}	-1.419	0.017	-83.47	-1.419	0.017	-83.47
	β_{13}	-1.421	0.017	-83.59	-1.421	0.017	-83.59
	β_{14}	-1.428	0.017	-84.00	-1.428	0.017	-84.00
	β_{15}	-1.425	0.017	-83.82	-1.425	0.017	-83.82
	β_{16}	-1.441	0.017	-84.76	-1.441	0.017	-84.76
	φ	0.196	0.045	4.36	0.2011	0.0464	4.33
	θ_1	2.034	0.004	508.50	2.034	0.004	508.50
Extreme Maximal	θ_2	3.423	0.009	380.33	3.423	0.009	380.33
	θ_3	4.361	0.015	290.73	4.361	0.015	290.73
	β_{11}	-4.353	0.071	-61.31	-4.353	0.072	-60.46
	β_{12}	-4.15	0.071	-58.45	-4.15	0.072	-57.64
	β_{13}	-4.158	0.071	-58.56	-4.158	0.072	-57.75
	β_{14}	-4.191	0.071	-59.03	-4.191	0.072	-58.21
	β_{15}	-4.182	0.071	-58.90	-4.182	0.072	-58.08
	β_{16}	-4.251	0.071	-59.87	-4.251	0.072	-59.04

For models 3 and 4 , the county effects are allowed to vary over time. The notion, inspired by Figure 9.3, is that the county effect is often fairly constant over time, but that changes do occur from year to year. For county i , the initial county effect (1987) is u_{i1} and subsequent changes to that initial county effect are given by adding to it successively u_{i2}, u_{i3}, u_{i4}, u_{i5}, u_{i6} according to the following models.

Model 3: $\eta_{it} = \beta + \sum_{j=1}^{t} u_{ij}$, where u_{ij} are independent $N(0,\varphi_j)$.

Model 4: $\eta_{it} = \beta_t + \sum_{j=1}^{t} u_{ij}$, where u_{ij} are independent $N(0, \varphi_j)$.

The difference between models 3, 4 is whether or not β is taken to be the same or different for the six years of record. The results of fitting models 3 and 4 are given in Table 9.4.3 and 9.4.4a, 9.4.4b respectively where the data has been grouped into categories 0, 1, ≥2 so that only one threshold parameter is estimated. The results in Table 9.4.4a and 9.4.4b indicate that the estimates of the β parameters are little different and again all other estimates of corresponding parameters in the two models are essentially the same.

Table 9.4.3: Estimates of parameters (Est), standard errors (SE) and the ratio of Est to SE (z-v) by ML and REML methods in fitting model 3 to chemotherapy data from Washington State over several years.

		ML			REML		
		Est	SE	z-v	Est	SE	z-v
Standard Normal	φ_1	0.0577	0.0133	4.34	0.0593	0.0138	4.30
	φ_2	0.0293	0.007	4.19	0.0294	0.007	4.20
	φ_3	0.0025	0.0008	3.13	0.0025	0.0008	3.13
	φ_4	0.0087	0.0022	3.95	0.0087	0.0022	3.95
	φ_5	0.007	0.0018	3.89	0.007	0.0018	3.89
	φ_6	0.0043	0.0012	3.58	0.0043	0.0012	3.58
	θ_1	0.727	0.001	727.00	0.727	0.001	727.00
	β	-2.223	0.039	-57.00	-2.223	0.04	-55.58
Logistic	φ_1	0.409	0.094	4.35	0.4204	0.098	4.29
	φ_2	0.231	0.055	4.20	0.2314	0.0547	4.23
	φ_3	0.014	0.0044	3.18	0.014	0.0043	3.26
	φ_4	0.06	0.015	4.00	0.0599	0.0152	3.94
	φ_5	0.045	0.012	3.75	0.0447	0.0117	3.82
	φ_6	0.03	0.01	3.00	0.0265	0.0074	3.58
	θ_1	2.043	0.004	510.75	2.043	0.004	510.75
	β	-4.343	0.103	-42.17	-4.343	0.105	-41.36
Extreme Minimal	φ_1	0.0194	0.0045	4.31	0.02	0.0046	4.35
	φ_2	0.0091	0.0022	4.14	0.0092	0.0022	4.18
	φ_3	0.0009	0.0003	3.00	0.0009	0.0003	3.00
	φ_4	0.0029	0.0007	4.14	0.0029	0.0007	4.14
	φ_5	0.0025	0.0007	3.57	0.0025	0.0007	3.57
	φ_6	0.0015	0.0004	3.75	0.0015	0.0004	3.75
	θ_1	0.408	0.001	408.00	0.408	0.001	408.00
	β	-1.463	0.023	-63.61	-1.463	0.023	-63.61
Extreme Maximal	φ_1	0.404	0.093	4.34	0.4149	0.0968	4.29
	φ_2	0.2293	0.0542	4.23	0.2294	0.0543	4.22
	φ_3	0.0137	0.0043	3.19	0.0137	0.0043	3.19
	φ_4	0.0591	0.015	3.94	0.0591	0.015	3.94
	φ_5	0.0439	0.0115	3.82	0.0439	0.0115	3.82
	φ_6	0.0261	0.0073	3.58	0.0261	0.0073	3.58
	θ_1	2.034	0.004	508.50	2.034	0.004	508.50
	β	-4.35	0.103	-42.23	-4.35	0.104	-41.83

Table 9.4.4a: Estimates of parameters (Est), standard errors (SE) and the ratio of Est to SE (z-v) by ML and REML methods in fitting model 4 to chemotherapy data from Washington State over several years.

		ML			REML		
		Est	SE	z-v	Est	SE	z-v
Standard Normal	φ_1	0.0581	0.0134	4.34	0.0597	0.0139	4.29
	φ_2	0.0262	0.0063	4.16	0.0269	0.0065	4.14
	φ_3	0.0024	0.0007	3.43	0.0023	0.0007	3.29
	φ_4	0.008	0.0021	3.81	0.0082	0.0021	3.90
	φ_5	0.0062	0.0016	3.88	0.0064	0.0017	3.76
	φ_6	0.0041	0.0011	3.73	0.0042	0.0012	3.50
	θ_1	0.727	0.001	727.00	0.727	0.001	727.00
	β_{11}	-2.225	0.039	-57.05	-2.225	0.039	-57.05
	β_{12}	-2.169	0.047	-46.15	-2.169	0.047	-46.15
	β_{13}	-2.157	0.048	-44.94	-2.157	0.048	-44.94
	β_{14}	-2.185	0.05	-43.70	-2.185	0.05	-43.70
	β_{15}	-2.152	0.051	-42.20	-2.152	0.052	-41.38
	β_{16}	-2.169	0.053	-40.92	-2.169	0.053	-40.92
Logistic	φ_1	0.4123	0.0949	4.34	0.424	0.099	4.28
	φ_2	0.2073	0.0492	4.21	0.213	0.051	4.18
	φ_3	0.0128	0.0041	3.12	0.014	0.004	3.50
	φ_4	0.0544	0.0139	3.91	0.056	0.014	4.00
	φ_5	0.0401	0.0106	3.78	0.041	0.011	3.73
	φ_6	0.0255	0.0071	3.59	0.026	0.007	3.71
	θ_1	2.043	0.004	510.75	2.043	0.004	510.75
	β_{11}	-4.347	0.104	-41.80	-4.347	0.105	-41.40
	β_{12}	-4.192	0.127	-33.01	-4.192	0.128	-32.75
	β_{13}	-4.16	0.128	-32.50	-4.16	0.13	-32.00
	β_{14}	-4.237	0.133	-31.86	-4.237	0.135	-31.39
	β_{15}	-4.154	0.137	-30.32	-4.154	0.139	-29.88
	β_{16}	-4.198	0.139	-30.20	-4.198	0.141	-29.77

Table 9.4.4b: Estimates of parameters (Est), standard errors (SE) and the ratio of Est to SE (z-v) by ML and REML methods in fitting model 4 to chemotherapy data from Washington State over several years.

		ML			REML		
		Est	SE	z-v	Est	SE	z-v
	φ_1	0.0195	0.0045	4.33	0.0201	0.0047	4.28
	φ_2	0.0081	0.002	4.05	0.0084	0.002	4.20
	φ_3	0.0008	0.0003	2.67	0.001	0.0003	3.33
	φ_4	0.0027	0.0007	3.86	0.0029	0.0008	3.63
	φ_5	0.0022	0.0006	3.67	0.0023	0.0006	3.83
Extreme	φ_6	0.0015	0.0004	3.75	0.0016	0.0005	3.20
Minimal	θ_1	0.408	0.001	408.00	0.408	0.001	408.00
	β_{11}	-1.464	0.023	-63.65	-1.464	0.023	-63.65
	β_{12}	-1.432	0.027	-53.04	-1.432	0.028	-51.14
	β_{13}	-1.425	0.027	-52.78	-1.425	0.028	-50.89
	β_{14}	-1.441	0.029	-49.69	-1.441	0.03	-48.03
	β_{15}	-1.421	0.03	-47.37	-1.421	0.031	-45.84
	β_{16}	-1.431	0.03	-47.70	-1.431	0.032	-44.72
	φ_1	0.4069	0.0937	4.34	0.418	0.097	4.31
	φ_2	0.2056	0.0488	4.21	0.211	0.051	4.14
	φ_3	0.0126	0.004	3.15	0.013	0.004	3.25
	φ_4	0.0537	0.0137	3.92	0.055	0.014	3.93
Extreme	φ_5	0.0393	0.0104	3.78	0.04	0.011	3.64
Maximal	φ_6	0.025	0.007	3.57	0.026	0.007	3.71
	θ_1	2.034	0.004	508.50	2.034	0.004	508.50
	β_{11}	-4.355	0.103	-42.28	-4.355	0.104	-41.88
	β_{12}	-4.2	0.126	-33.33	-4.2	0.127	-33.07
	β_{13}	-4.168	0.127	-32.82	-4.169	0.129	-32.32
	β_{14}	-4.245	0.132	-32.16	-4.245	0.134	-31.68
	β_{15}	-4.163	0.136	-30.61	-4.163	0.138	-30.17
	β_{16}	-4.207	0.139	-30.27	-4.207	0.141	-29.84

Note that the change in the county effects from 1987 to 1988 , viz. u_{i2} for county i , has the highest variance of any yearly change and that subsequent yearly changes have quite small variances estimated as 0.01, 0.06, 0.04, 0.03 . This leads us to consider also models in which say all u_{i6} are taken to be zero, indicating that county effects remained the same in 1992 as they were in 1991. Extending this notion backwards in time leads to the consideration of the models

9.4.4

Model	3a	3b	3c	3d	3e
$\eta_{it} = \beta_t +$	$\sum_{j=1}^{2} u_{ij}$	$\sum_{j=1}^{3} u_{ij}$	$\sum_{j=1}^{4} u_{ij}$	$\sum_{j=1}^{5} u_{ij}$	$\sum_{j=1}^{6} u_{ij}$

in which successive yearly changes are considered to be zero. A disadvantage of such models is that variance is additive over time, whereas from 1987 to 1988 the estimate of variance decreased. Subsequent changes to the estimates were increases.

Instead of reproducing the estimates for all of the above models, we take a measure of the goodness of fit of the data to be

9.4.2 $$Q^* = \sum (y_{itk} - e_{itk})^2 / e_{itk}$$

where e_{itk} is the expected frequency for cell i,t,k predicted by the model. Values of Q^* for the models are given in Table 9.4. The substantial reduction in the value of Q^* in going from model 1 to the simplest model 3(a) is partly illusory because the data is grouped differently for fitting models 3. Further reductions occur as more random components are added in going from model 3(a) to 3(e). When models 3 are fitted there are 3×6×39 cells in the frequency table so that there is a noticeable gain in the precision obtained by adding the extra components of variation.

9.5 AUTOREGRESSIVE MODEL

Although the addition of a yearly random component is shown in section 9.4 to reduce the goodness of fit statistic Q^*, a disadvantage is that the variance components are assumed independent whereas they may be correlated over time. In this section the random components for any one county are modelled by an autoregressive process of order one, AR(1). The model is denoted by:

Model 5: $\eta_{it} = \beta + u_{it}$, u_{it} is AR(1) for $t = 1,2,\ldots,6$

or a time varying mean model

Model 6: $\eta_{it} = \beta_t + u_{it}$, u_{it} as above.

For the AR(1) model the county effects are independent for different counties but the variance matrix for the random components within each county is of the form

9.5.1 $$\varphi A = \varphi \begin{bmatrix} 1 & \rho & . & . & \rho^5 \\ \rho & 1 & . & . & \rho^4 \\ . & . & . & . & . \\ \rho^4 & . & . & . & \rho \\ \rho^5 & . & . & \rho & 1 \end{bmatrix}.$$

The estimating equation for the maximum likelihood estimator of ρ has been given in section 8.5 of chapter by

9.5.2 $$f(\rho)=a\rho^3 + b\rho^2 + c\rho + d=0 ,$$

where, for general N=number of counties (39 here) and n_i =number of years of record for county i (n_i=n=6 here for all i),

$$a = 2\sum_{i=1}^{N}(n_i - 1),\ \ b = \hat{\varphi}_{(ML)}^{-1}[\sum_{i=1}^{N}(\mathrm{tr}\Gamma_i T_i + \tilde{u}_i' T_i \tilde{u}_i)]$$

$c = \sum_{i=1}^{N}\{\hat{\varphi}_{(ML)}^{-1}[tr(\mathbf{K}_i + 2\Lambda_i)\mathbf{T}_i^{*} + \tilde{\mathbf{u}}_i'(\mathbf{K}_i + 2\Lambda_i)\tilde{\mathbf{u}}_i] - (n_i - 1)\}$ and d=b. The matrices $\mathbf{K}_i$, Λ_i and Γ_i have been given in section 8.5 of chapter 8. The equation for $\hat{\rho}_{ML}$ can be solved by appropriate convergence techniques such as Newton-Raphson. Replacing $\mathbf{T}^{*}$ by $\mathbf{T}$ gives approximate REML estimates. The approximate variance for ML and REML estimators are given in section 9.2.

Estimates of parameters, standard errors and the ratio of estimates to their standard errors with ML and REML methods for the autoregressive models 5 and 6 are shown in Tables 9.5 and 9.6 . It can be seen that the time varying parameter estimates of model 6 are little different to those of the time invariant model 5 and the fit, as judged by the Q^{*} values in table 9.4.3a are practically the same. Note that the autoregressive parameter ρ is significantly high at $\hat{\rho}_{REML} = 0.87$, 0.88 , 0.89 , 0.87 corresponding to the four threshold models in section 5.2 of chapter 5 for the model 5 is almost identical in model 6. Because model 5 contains far fewer parameters, it must be considered to provide the more parsimonious fit. Apart from threshold parameters, only β, φ, ρ are required.

It is also notable that the goodness of fit statistic Q^{*} is larger for the all fitted models with threshold model 3 than 3 others in section 5.2 of chapter 5. Based on the goodness of fit statistic Q^{*}, model 5 is a suitable model with the threshold model 1 in section 5.2 of chapter 5.

Of course $Q^{*}=1191$ is a high value for a goodness of fit statistic of th-is type but, given the size of the data and simplicity of the model, the fit must be regarded as quite remarkable.

Table 9.4: Goodness of fit statistic Q^{*} for different models fitted to 1987-1992 data.

	MODEL							
Distribution	1	3a	3b	3c	3d	3e	5	6
ST Normal	25478	6955	5692	3113	1862	1201	1191	1191
Logistic	25339	6928	5616	3149	1887	1236	1222	1222
Ex. Minimal	26584	8129	6950	3993	2672	2004	1992	1992
Ex. Maximal	25352	6944	5632	3164	1902	1253	1237	1237

* ST= Standard, Ex. Minimal= Extreme minimal value and Ex. Maximal= Extreme maximal value.

Table 9.5 : Estimates of parameters (Est), standard errors (SE) and the ratio of Est to SE (z-v) by ML and REML methods in fitting model 5 to chemotherapy data from Washington State over several years.

AR(1)		ML			REML		
Dist.		Est.	SE	Ratio	Est.	SE	
	φ_1	0.044	0.008	5.649	0.044	0.080	0.555
	ρ	0.876	0.025	35.614	0.880	0.024	36.066
Standard	θ_1	0.727	0.001	727.00	0.727	0.001	727.00
Normal	β	-2.189	0.029	-75.48	-2.189	0.029	-75.483
	φ_1	0.295	0.052	5.725	0.302	0.054	5.593
	ρ	0.865	0.026	33.031	0.870	0.0260	33.46
	θ_1	2.043	0.004	510.75	2.043	0.004	510.75
Logistic	β	-4.25	0.075	-56.67	-4.251	0.076	-55.934
	φ_1	0.015	0.003	5.000	0.015	0.003	5.276
	ρ	0.883	0.024	36.792	0.885	0.023	37.983
Extreme	θ_1	0.408	0.001	408.00	0.408	0.001	408.00
Minimal	β	-1.443	0.017	-84.88	-1.443	0.017	-84.882
	φ_1	0.291	0.051	5.740	0.296	0.052	5.649
	ρ	0.865	0.026	33.011	0.867	0.026	33.354
Extreme	θ_1	2.034	0.004	508.50	2.034	0.004	508.50
Maximal	β	-4.258	0.074	-57.54	-4.259	0.075	-56.787

Table 9.6 : Estimates of parameters (Est), standard errors (SE) and the ratio of Est to SE (z-v) by ML and REML methods in fitting model 6 to chemotherapy data from Washington State over several years.

AR(1)		ML			REML		
Dist		Est.	SE	Ratio	Est.	SE	Ratio
Standard Normal	φ_1	0.043	0.008	5.522	0.044	0.008	5.453
	ρ	0.887	0.023	39.004	0.887	0.023	38.464
	θ_1	0.727	0.001	515.26	0.727	0.001	515.26
	β_{11}	-2.225	0.033	-66.68	-2.226	0.034	-65.88
	β_{12}	-2.168	0.033	-65.06	-2.168	0.034	-64.28
	β_{13}	-2.158	0.033	-64.77	-2.158	0.034	-63.99
	β_{14}	-2.185	0.033	-65.59	-2.185	0.034	-64.80
	β_{15}	-2.151	0.033	-64.61	-2.151	0.034	-63.83
	β_{16}	-2.169	0.033	-65.08	-2.169	0.034	-64.30
Logistic	φ_1	0.292	0.052	5.612	0.302	0.054	5.543
	ρ	0.877	0.024	36.12	0.878	0.025	35.63
	θ_1	2.043	0.004	465.97	2.043	0.004	465.97
	β_{11}	-4.349	0.088	-49.7	-4.349	0.089	-48.91
	β_{12}	-4.19	0.087	-47.99	-4.191	0.089	-47.23
	β_{13}	-4.162	0.087	-47.68	-4.163	0.089	-46.92
	β_{14}	-4.237	0.087	-48.52	-4.237	0.089	-47.75
	β_{15}	-4.151	0.087	-47.58	-4.151	0.089	-46.82
	β_{16}	-4.198	0.087	-48.06	-4.198	0.089	-47.3
Extreme Minimal	φ_1	0.015	0.003	5.465	0.015	0.003	5.397
	ρ	0.893	0.022	41.02	0.893	0.022	40.45
	θ_1	0.408	0.001	551.83	0.408	0.001	551.83
	β_{11}	-1.464	0.02	-74.98	-1.464	0.02	-74.08
	β_{12}	-1.431	0.019	-73.41	-1.431	0.02	-72.52
	β_{13}	-1.426	0.019	-73.13	-1.426	0.02	-72.24
	β_{14}	-1.441	0.019	-73.92	-1.441	0.02	-73.03
	β_{15}	-1.421	0.019	-72.91	-1.421	0.02	-72.03
	β_{16}	-1.431	0.02	-73.38	-1.431	0.02	-72.5
Extreme Maximal	φ_1	0.288	0.051	5.616	0.297	0.054	5.547
	ρ	0.877	0.024	35.999	0.877	0.025	35.51
	θ_1	2.034	0.004	508.5	2.034	0.004	508.5
	β_{11}	-4.356	0.087	-50.07	-4.356	0.088	-49.5
	β_{12}	-4.199	0.087	-48.26	-4.199	0.088	-47.72
	β_{13}	-4.171	0.087	-47.94	-4.171	0.088	-47.4
	β_{14}	-4.245	0.087	-48.79	-4.245	0.088	-48.24
	β_{15}	-4.16	0.087	-47.82	-4.16	0.088	-47.27
	β_{16}	-4.206	0.087	-48.35	-4.206	0.088	-47.8

CHAPTER 10

SIMULATION

10.1 INTRODUCTION

The previous chapters have demonstrated various threshold models involving different structures of variance-covariance matrices. The maximum likelihood (ML) and residual maximum likelihood (REML) estimators have been developed. It has been shown that the inferences by ML and REML are in agreement for most applications. Nevertheless, there are also some applications for which the two methods give different results, eg see chapter 6.

Furthermore, for normal response variables, there are some cases in which the REML estimators for the components variance coincide with the ANOVA methods with well known properties. Also some simulation studies proved that the ML estimators are negatively biased for variance components. The bias increases by increasing the number of fixed parameters fitted. The REML method was introduced to reduce such a bias (Swallow, 1984) and (McGilchrist 1989). In this chapter, the performance of the approximate ML and REML methods for the threshold models are investigated through simulations for threshold models.

The simulation is carried out under three different variance-covariance structures of the random components; one component, two components, and AR(1). In the one component and two components models, 200 data set are generated, while in the AR(1) there are 100 sets generated using the same true parameters. Averages of the estimates give an indication of the bias of the estimates and the standard error of the 200 or 100 estimates for each parameter gives an indication of the spread of the estimated values. These standard errors denoted in the results given in the tables by SEOS. They may be compared to the average of the asymptotic standard errors produced one for each data set fitted; the average asymptotic standard error is denoted in corresponding tables by ASE. In the tables, M refers to the threshold model, 1=standard normal, 2=logistic, 3=extreme minimal, 4= extreme maximal as described in section 5.2 of chapter 5, TU=true value, AB= average bias over simulations and SE=standard error is the standard error of that average bias computed as SEOS/(square root of number simulations). ASE and SEOS are as described above.

10.2 THE ONE COMPONENT

The data are generated from the model $p(Y_{it} \le y) = G(\theta_y - \eta_{it})$, where four different forms for the $G(.)$ are given in section 5.2 of chapter 5. The model for the η_{it} is given by

10.2.1 $\eta_{it} = \beta_{j(i)t} + u_i$

where the u_i are independent N(0, φ), β_{jt} is j^{th} (j=1,2) treatment effect at time t (t=1,2...n) and j(i)=treatment received by subject i. For each of the threshold models given in section 5.2 of chapter 5, three different data sets are generated. In the first data set, it is assumed that the observations are 0,1, 2 (y=0,1,2). For fixed values of threshold parameters and φ, the observations at time t are obtained for i=1,2,...30 subjects allocated randomly to either the treatment active (j=1) or to the treatment placebo (j=2).

Following discussion in the previous chapters, $\theta_{-1} = -\infty$, $\theta_0 = 0$ and $\theta_2 = \infty$. Estimates of θ_1 and other parameters are obtained by both ML and REML methods and the process replicated 200 times. The process is carried out for n=1, n=3 and n=5, and then for a new value of φ, the whole process is repeated. Tables 10.2.1.1.ij show the results and true values of the parameters for φ=0.3 and φ=0.5, where first 1 refers to one component variance, next 1 indicates one threshold parameter, i shows time (number of observation for each subject) and j gives more results for those combinations.

n=1 (Table 10.1.1.a):

The results show that ML estimators of parameters are very negatively biased with REML having much improved bias properties for all four threshold models in section 5.2 of chapter 5. Such bias increases for large values of the variance component parameter φ. Similar biases occur in the ML estimators of φ. The biases of ML and REML estimators of φ are smaller for threshold model 3 (G is taken to be extreme minimal value) in section 5.2 of chapter 5. The results also indicate a very good agreement between the average asymptotic standard errors (ASE) of estimators of parameters and the standard errors over simulations (SEOS) in both ML and REML methods. However, both ML and REML methods yield ASE larger than SEOS of estimators φ for threshold models 1, 2 of section 5.2 of chapter 5, and a very good agreement between ASE and SEOS for the threshold models 3, 4 of section 5.2 of chapter 5.

n=3 (Table 10.2.1.1.3a,b):

The biases of ML and REML estimators of parameters and variance component φ significantly decrease when increasing the number of observations for each subject for all four threshold models in section 5.2 of chapter 5. Moreover, the REML estimators of the variance component φ are positively biased and the bias is not significant for threshold models 2,3 and 1 respectively. The ASE and SEOS are very close for the all four threshold models in section 5.2 of chapter 5.

n=5 (Table 10.2.1.15a,b,c):

A further improvement of the estimation approach is obtained by increasing the number of observations from 3 to 5 for both ML and REML methods. The average asymptotic standard error (ASE) and the standard error over simulations (SEOS) of estimators are almost the same for both ML and REML methods.

Table 10.2.1.1.1a: Estimated average biases and average standard error over 200 simulations for the mixed threshold models.

			ML φ=0.3				ML φ=0.5			
M		TU	AB	SE	ASE	SEOS	AB	SE	ASE	SEOS
1	φ		-0.2804	0.0001	0.0503	0.0014	-0.4802	0.0001	0.0514	0.0014
	θ_1	1.5	-0.1376	0.0242	0.3569	0.3376	-0.2452	0.0222	0.3352	0.3136
	β_1	2	-0.2172	0.0325	0.4532	0.4526	-0.4073	0.028	0.4231	0.3966
	β_2	0.5	-0.101	0.0275	0.3373	0.3834	-0.2335	0.0229	0.3346	0.3244
2	φ		-0.2324	0.0067	0.2562	0.0954	-0.4544	0.0049	0.1754	0.069
	θ_1	1.5	-0.0907	0.0378	0.4532	0.5341	-0.0676	0.0366	0.4529	0.5177
	β_1	2	-0.135	0.0599	0.6568	0.847	-0.1181	0.055	0.6618	0.7776
	β_2	0.5	-0.1398	0.0395	0.5491	0.5585	-0.1528	0.0365	0.5376	0.5166
3	φ		-0.1995	0.0101	0.1781	0.1422	-0.3767	0.0112	0.2203	0.1584
	θ_1	1.5	-0.1198	0.0283	0.3905	0.3997	-0.2009	0.0284	0.3699	0.401
	β_1	2	-0.2346	0.0425	0.5302	0.5993	-0.3668	0.0389	0.5125	0.5504
	β_2	0.5	-0.1289	0.0306	0.3807	0.4312	-0.166	0.0259	0.3771	0.3663
4	φ	0.3	-0.2582	0.0067	0.0714	0.0928	-0.4593	0.0063	0.0732	0.0886
	θ_1	1.5	-0.0352	0.0326	0.4437	0.4527	-0.1083	0.0302	0.4266	0.4233
	β_1	2	-0.239	0.0361	0.5075	0.5016	-0.2574	0.0397	0.495	0.5557
	β_2	0.5	-0.0987	0.0257	0.3516	0.3567	-0.1502	0.0248	0.3482	0.3471
			REML φ=0.3				REML φ=0.5			
1	φ		0.0515	0.0019	0.4877	0.0269	-0.1524	0.003	0.4907	0.0416
	θ_1	1.5	-0.1614	0.0237	0.3583	0.3337	-0.0876	0.0258	0.3739	0.3574
	β_1	2	-0.3492	0.0249	0.4461	0.3509	-0.2285	0.0327	0.4831	0.4537
	β_2	0.5	-0.2535	0.0259	0.3966	0.3646	-0.0978	0.0276	0.3797	0.3829
2	φ		0.3047	0.0101	1.1291	0.1431	0.1145	0.012	1.1085	0.1698
	θ_1	1.5	-0.0926	0.0328	0.4492	0.4645	-0.0451	0.0297	0.454	0.4198
	β_1	2	-0.2031	0.0416	0.6608	0.5888	-0.1954	0.0479	0.6665	0.6775
	β_2	0.5	-0.1225	0.0442	0.5828	0.6247	-0.0012	0.0411	0.5803	0.5815
3	φ		0.104	0.0185	0.4828	0.2598	-0.0861	0.0175	0.496	0.2466
	θ_1	1.5	0.0179	0.0292	0.4194	0.4105	-0.0867	0.0294	0.3996	0.4142
	β_1	2	-0.1332	0.0441	0.5704	0.6204	-0.2873	0.0394	0.5501	0.5556
	β_2	0.5	-0.1365	0.0305	0.4182	0.4294	-0.2286	0.0268	0.4086	0.3779
4	φ		-0.0781	0.0112	0.3968	0.1569	-0.2973	0.0086	0.3934	0.1216
	θ_1	1.5	-0.038	0.0306	0.4445	0.4283	-0.0408	0.0289	0.4576	0.4084
	β_1	2	-0.1027	0.0355	0.5332	0.4972	-0.0107	0.0347	0.5549	0.4911
	β_2	0.5	-0.0362	0.0286	0.3798	0.4001	-0.018	0.027	0.3778	0.3825

Table 10.2.1.1.3a: Estimated average biases and average standard error over 200 simulations for the mixed threshold models.

			ML φ=0.3				ML φ=0.5			
M		TU	AB	SE	ASE	SEOS	AB	SE	ASE	SEOS
1	φ		-0.0769	0.0149	0.1725	0.2016	-0.1486	0.0179	0.2203	0.2457
	θ_1	1.5	-0.0352	0.0186	0.2435	0.2515	-0.0114	0.0186	0.2506	0.2552
	β_{11}	2	-0.1179	0.0311	0.4144	0.4202	-0.0696	0.0341	0.4422	0.4669
	β_{12}	0.7	0.0536	0.0264	0.3462	0.3568	0.0743	0.026	0.3684	0.3567
	β_{13}	0.05	0.0229	0.0287	0.3425	0.3888	0.0369	0.0254	0.3624	0.3481
	β_{21}	2	-0.1372	0.0316	0.4177	0.4274	-0.1661	0.0309	0.4227	0.424
	β_{22}	2.5	-0.0973	0.0354	0.4822	0.4791	-0.0251	0.0329	0.496	0.4507
	β_{23}	2.2	-0.1441	0.03	0.4372	0.4064	-0.0759	0.0322	0.4517	0.4409
2	φ		0.0051	0.0238	0.3184	0.3354	-0.1252	0.0268	0.3564	0.3765
	θ_1	1.5	0.0056	0.0224	0.2866	0.3154	-0.0279	0.0199	0.2823	0.2799
	β_{11}	2	-0.0953	0.0402	0.602	0.565	-0.1907	0.0374	0.602	0.5249
	β_{12}	0.7	0.1172	0.0342	0.5283	0.4819	0.1753	0.0377	0.5417	0.5291
	β_{13}	0.05	0.0217	0.0392	0.5329	0.5521	-0.0203	0.0409	0.547	0.5735
	β_{21}	2	-0.1012	0.0371	0.5998	0.5221	-0.153	0.0386	0.6012	0.5421
	β_{22}	2.5	0.2087	0.0504	0.7143	0.709	-0.033	0.047	0.6744	0.6598
	β_{23}	2.2	0.0075	0.0506	0.6373	0.7114	0.054	0.0543	0.6501	0.7622
			REML φ=0.3				REML φ=0.5			
1	φ		0.0072	0.0166	0.2188	0.2282	-0.0269	0.0229	0.2775	0.3156
	θ_1	1.5	0.022	0.0184	0.2553	0.2531	0.0049	0.0209	0.253	0.2883
	β_{11}	2	-0.0464	0.0302	0.4341	0.4168	-0.0795	0.0314	0.4448	0.433
	β_{12}	0.7	0.1332	0.0262	0.3634	0.3614	0.1086	0.0256	0.3783	0.3525
	β_{13}	0.05	0.0505	0.0255	0.3542	0.3515	0.0497	0.0246	0.3723	0.3397
	β_{21}	2	-0.0747	0.0315	0.428	0.4342	-0.1127	0.0332	0.4397	0.4581
	β_{22}	2.5	0.0404	0.0328	0.5011	0.4521	-0.0403	0.0371	0.5054	0.5118
	β_{23}	2.2	-0.0169	0.0318	0.4558	0.4378	0.0089	0.0375	0.4723	0.5171
2	φ		0.1978	0.0378	0.4174	0.5275	0.1252	0.0426	0.4852	0.6016
	θ_1	1.5	0.0312	0.0224	0.2936	0.3129	-0.025	0.024	0.2852	0.3382
	β_{11}	2	-0.0323	0.046	0.6226	0.6426	-0.0744	0.0379	0.638	0.534
	β_{12}	0.7	0.157	0.0404	0.5489	0.5635	0.1673	0.0374	0.5699	0.528
	β_{13}	0.05	-0.0901	0.0394	0.552	0.5497	0.0061	0.0434	0.5739	0.6118
	β_{21}	2	-0.0993	0.0451	0.6125	0.6293	-0.0999	0.0425	0.6178	0.5991
	β_{22}	2.5	0.2915	0.0535	0.738	0.7474	-0.0394	0.058	0.6824	0.8178
	β_{23}	2.2	0.0507	0.0471	0.6479	0.6581	-0.0981	0.0495	0.6356	0.6979

Table 10.2.1.1.3b: Estimated average biases and average standard error over 200 simulations for the mixed threshold models.

			ML φ=0.3				ML φ=0.5			
M		TU	AB	SE	ASE	SEOS	AB	SE	ASE	SEOS
3	φ		-0.0319	0.019	0.1924	0.2694	-0.0943	0.0216	0.2621	0.3043
	θ_1	1.5	-0.0367	0.0214	0.2526	0.3023	0.024	0.0193	0.2572	0.2721
	β_{11}	2	-0.0651	0.0311	0.486	0.4394	-0.0826	0.0357	0.4915	0.5034
	β_{12}	0.7	0.0082	0.0265	0.378	0.3746	0.0107	0.029	0.3956	0.4089
	β_{13}	0.05	0.0094	0.0229	0.3565	0.3238	0.048	0.0273	0.3775	0.3857
	β_{21}	2	-0.184	0.0301	0.4696	0.4253	-0.2224	0.0356	0.4732	0.5029
	β_{22}	2.5	0.03	0.0452	0.5871	0.6395	0.0674	0.0459	0.589	0.6477
	β_{23}	2.2	0.0671	0.0365	0.5377	0.516	-0.0152	0.0383	0.5287	0.5403
4	φ		-0.1191	0.0172	0.1486	0.1927	-0.2696	0.015	0.1702	0.1846
	θ_1	1.5	-0.0185	0.0246	0.3004	0.2757	-0.1066	0.0246	0.2748	0.3029
	β_{11}	2	-0.0132	0.0354	0.4526	0.3975	-0.1825	0.0356	0.4326	0.4377
	β_{12}	0.7	0.137	0.0358	0.3628	0.402	0.0623	0.0324	0.3684	0.398
	β_{13}	0.05	0.0849	0.0303	0.3645	0.3398	0.087	0.0258	0.3717	0.3174
	β_{21}	2	-0.171	0.0384	0.434	0.4313	-0.2395	0.0365	0.4226	0.4484
	β_{22}	2.5	-0.1724	0.0404	0.4842	0.4535	-0.2458	0.0337	0.4736	0.4137
	β_{23}	2.2	-0.0789	0.0352	0.4618	0.3956	-0.2463	0.0311	0.4382	0.3816
			REML φ=0.3				REML φ=0.5			
3	φ		0.0648	0.0251	0.2474	0.3555	-0.0059	0.0224	0.31	0.3161
	θ_1	1.5	0.0127	0.0202	0.2589	0.2854	-0.0039	0.019	0.2568	0.2686
	β_{11}	2	-0.1085	0.0359	0.4878	0.5071	-0.1366	0.0323	0.4945	0.4566
	β_{12}	0.7	-0.0123	0.0262	0.389	0.3711	-0.0092	0.0279	0.4012	0.3951
	β_{13}	0.05	-0.0561	0.0272	0.3719	0.3843	-0.1115	0.0283	0.3866	0.4002
	β_{21}	2	-0.1585	0.0312	0.4829	0.4408	-0.2206	0.0329	0.4851	0.4653
	β_{22}	2.5	0.0893	0.0456	0.5935	0.6452	0.0381	0.0434	0.5937	0.6141
	β_{23}	2.2	-0.0026	0.038	0.5245	0.5373	-0.0664	0.0387	0.5296	0.5474
4	φ		-0.034	0.022	0.1989	0.2548	-0.1668	0.0169	0.2323	0.2079
	θ_1	1.5	0.0498	0.0255	0.3146	0.2948	-0.0346	0.0252	0.2937	0.3113
	β_{11}	2	-0.0003	0.0383	0.4679	0.4431	-0.0739	0.036	0.4642	0.4444
	β_{12}	0.7	0.2368	0.0342	0.3804	0.3957	0.1385	0.0295	0.3847	0.3639
	β_{13}	0.05	0.0766	0.0404	0.3847	0.4681	0.0552	0.0349	0.3984	0.4307
	β_{21}	2	-0.054	0.0418	0.4585	0.4843	-0.1067	0.0346	0.4491	0.4265
	β_{22}	2.5	-0.1038	0.0344	0.5025	0.3981	-0.1574	0.0383	0.5002	0.4717
	β_{23}	2.2	-0.0715	0.0372	0.4743	0.4301	-0.1318	0.0366	0.4656	0.4507

Table 10.2.1.1.5a: Estimated average biases and average standard error over 200 simulations for the mixed threshold models.

			ML φ=0.3				ML φ=0.5			
M		TU	AB	SE	ASE	SEOS	AB	SE	ASE	SEOS
	φ		-0.0215	0.0118	0.1534	0.1545	-0.0282	0.0185	0.211	0.2389
1	θ	1.5	0.04	0.0171	0.1946	0.2235	0.0476	0.0167	0.1953	0.2154
	β_{11}	2	-0.0863	0.0333	0.4022	0.4353	-0.0678	0.0366	0.4232	0.4717
	β_{12}	1.5	0.1131	0.0277	0.3789	0.3627	0.0015	0.0305	0.3933	0.3932
	β_{13}	1.2	0.0003	0.0314	0.3597	0.4111	0.0426	0.0305	0.3814	0.3929
	β_{14}	0.5	0.0445	0.0292	0.3437	0.3813	0.0751	0.0326	0.367	0.4196
	β_{15}	0.04	-0.0128	0.0268	0.3483	0.3509	0.0532	0.0308	0.3709	0.3972
	β_{21}	2	-0.0529	0.0282	0.4027	0.3693	-0.0656	0.0371	0.4247	0.4779
	β_{22}	2.5	-0.0477	0.0313	0.4568	0.4095	0.0453	0.0356	0.4924	0.4581
	β_{23}	2.2	0.0377	0.0317	0.4319	0.4147	-0.0246	0.0322	0.4458	0.4149
	β_{24}	2.8	-0.0356	0.0334	0.5085	0.4363	-0.0494	0.0367	0.5251	0.4725
	β_{25}	1.5	0.0374	0.0338	0.3765	0.442	-0.0007	0.0301	0.3948	0.3879
2	φ		-0.0526	0.0171	0.2195	0.2374	-0.1181	0.0212	0.2889	0.2914
	θ_1	1.5	0.0191	0.0171	0.2205	0.2373	-0.0303	0.0151	0.2173	0.2081
	β_{11}	2	-0.0988	0.0446	0.5846	0.6192	-0.0283	0.0393	0.5954	0.5404
	β_{12}	1.5	0.0867	0.041	0.5542	0.569	0.0426	0.0448	0.5632	0.6153
	β_{13}	1.2	-0.0129	0.0424	0.536	0.5886	-0.0827	0.0373	0.54	0.5125
	β_{14}	0.5	0.0861	0.0396	0.5192	0.5507	0.1185	0.04	0.5327	0.5497
	β_{15}	0.04	0.0613	0.0391	0.5281	0.5426	0.0291	0.0413	0.5397	0.5671
	β_{21}	2	-0.0529	0.0516	0.5965	0.7175	-0.1284	0.0465	0.596	0.6392
	β_{22}	2.5	0.0703	0.046	0.665	0.6393	0.0008	0.047	0.6688	0.6463
	β_{23}	2.2	-0.0636	0.0425	0.6019	0.5902	-0.004	0.0443	0.6236	0.6092
	β_{24}	2.8	0.0607	0.0493	0.7215	0.6847	0.0359	0.0468	0.7237	0.6429
	β_{25}	1.5	0.0942	0.0452	0.5571	0.6283	0.0306	0.0484	0.5639	0.666
			REML φ=0.3				REML φ=0.5			
	φ		0.0494	0.0164	0.1813	0.1952	0.0353	0.0177	0.2384	0.233
1	θ_1	1.5	0.0004	0.0159	0.1909	0.1895	0.0273	0.014	0.1952	0.185
	β_{11}	2	-0.1108	0.0314	0.4052	0.374	-0.0897	0.0328	0.4331	0.4324
	β_{12}	1.5	0.0295	0.0288	0.3813	0.3432	0.0781	0.0276	0.4086	0.3644
	β_{13}	1.2	-0.0066	0.0305	0.3653	0.3638	-0.0435	0.0278	0.3893	0.3672
	β_{14}	0.5	0.0327	0.0281	0.3504	0.3348	0.0909	0.0283	0.379	0.3736
	β_{15}	0.04	0.0188	0.0269	0.3535	0.3201	0.0281	0.033	0.3856	0.4351
	β_{21}	2	-0.1244	0.0329	0.4038	0.3921	-0.0784	0.0294	0.4221	0.3875
	β_{22}	2.5	0.064	0.0347	0.4835	0.4133	0.1011	0.0345	0.5026	0.4556
	β_{23}	2.2	0.0031	0.0349	0.4358	0.4158	0.0263	0.0351	0.4535	0.4635
	β_{24}	2.8	-0.087	0.0366	0.5091	0.4363	-0.0487	0.033	0.5243	0.4358
	β_{25}	1.5	0.0415	0.0351	0.3814	0.4185	0.0074	0.0309	0.3961	0.4073

Table 10.2.1.1.5b: Estimated average biases and average standard error over 200 simulations for the mixed threshold models.

			ML φ=0.3				ML φ=0.5			
M		TU	AB	SE	ASE	SEOS	AB	SE	ASE	SEOS
3	φ		-0.0071	0.0118	0.1742	0.1646	-0.0744	0.0164	0.2124	0.2287
	θ_1	1.5	0.0159	0.0155	0.1961	0.2159	-0.0191	0.0139	0.1937	0.1945
	β_{11}	2	-0.0944	0.0333	0.4547	0.4636	-0.1452	0.0366	0.4694	0.5104
	β_{12}	1.5	0.0187	0.029	0.4134	0.404	-0.1167	0.0307	0.4218	0.4285
	β_{13}	1.2	-0.0114	0.0291	0.3905	0.4059	-0.0688	0.0282	0.4041	0.3936
	β_{14}	0.5	0.0104	0.0258	0.36	0.3596	-0.0624	0.0252	0.3774	0.3516
	β_{15}	0.04	-0.0551	0.0259	0.3566	0.3614	-0.1043	0.029	0.3772	0.4053
	β_{21}	2	-0.0972	0.0339	0.4583	0.4718	-0.1243	0.0322	0.4708	0.4501
	β_{22}	2.5	0.0201	0.0366	0.5513	0.5096	0.0435	0.0383	0.5661	0.535
	β_{23}	2.2	-0.0812	0.0369	0.4865	0.5134	-0.1479	0.0349	0.4897	0.4879
	β_{24}	2.8	0.0493	0.0455	0.6205	0.6343	0.0065	0.0398	0.6155	0.5562
	β_{25}	1.5	-0.0294	0.0314	0.4143	0.4368	-0.1094	0.0323	0.424	0.4516
			REML φ=0.3				REML φ=0.5			
2	φ		0.0371	0.0215	0.2707	0.2953	0.0158	0.0222	0.3492	0.3046
	θ_1	1.5	0.0098	0.0171	0.2194	0.2345	0.0193	0.0185	0.2221	0.2538
	β_{11}	2	-0.0625	0.0422	0.6009	0.5805	-0.1193	0.05	0.6062	0.6879
	β_{12}	1.5	0.044	0.0394	0.5653	0.5419	0.02	0.0425	0.5692	0.5848
	β_{13}	1.2	-0.0371	0.0439	0.5499	0.6032	-0.0541	0.0444	0.5549	0.6098
	β_{14}	0.5	0.059	0.0423	0.5379	0.5812	-0.0106	0.0456	0.5484	0.6264
	β_{15}	0.04	0.0117	0.0404	0.5481	0.5547	0.0515	0.0459	0.5585	0.6314
	β_{21}	2	-0.1481	0.0481	0.5818	0.6616	-0.092	0.0459	0.6057	0.6306
	β_{22}	2.5	0.021	0.0445	0.6541	0.6114	0.0859	0.0492	0.6875	0.6764
	β_{23}	2.2	-0.0932	0.0435	0.6002	0.5986	-0.0652	0.0472	0.6287	0.649
	β_{24}	2.8	0.0092	0.0479	0.7078	0.659	0.0873	0.0515	0.7403	0.7074
	β_{25}	1.5	0.0389	0.0456	0.5559	0.6272	0.0356	0.0403	0.5762	0.5534
3	φ		0.053	0.014	0.2023	0.1935	0.0723	0.0195	0.2668	0.2694
	θ_1	1.5	0.0312	0.0138	0.1985	0.1908	0.0343	0.0153	0.2006	0.2113
	β_{11}	2	-0.0511	0.0331	0.4664	0.4591	-0.0609	0.0326	0.473	0.4502
	β_{12}	1.5	-0.0165	0.0315	0.4194	0.437	0.0256	0.0325	0.4334	0.4488
	β_{13}	1.2	-0.0431	0.0296	0.397	0.4096	-0.0613	0.0341	0.4095	0.4719
	β_{14}	0.5	-0.0186	0.0276	0.369	0.3823	-0.0111	0.0286	0.3843	0.3954
	β_{15}	0.04	-0.0913	0.0262	0.3673	0.3627	-0.1302	0.0319	0.3884	0.4406
	β_{21}	2	-0.0715	0.0347	0.4636	0.4814	-0.0524	0.0354	0.4986	0.4888
	β_{22}	2.5	0.0762	0.0396	0.565	0.5491	0.0707	0.0421	0.5901	0.5813
	β_{23}	2.2	-0.0417	0.0378	0.4937	0.5238	0.0113	0.0436	0.532	0.6025
	β_{24}	2.8	0.0656	0.0423	0.6194	0.586	0.1305	0.042	0.6507	0.5807
	β_{25}	1.5	-0.0187	0.0308	0.4193	0.4272	-0.0119	0.0329	0.452	0.4543

Table 10.2.1.1.5c: Estimated average biases and average standard error over 200 simulations for the mixed threshold models with true value $\varphi = 0.3$.

			ML $\varphi=0.3$				ML $\varphi=0.5$			
M		TU	AB	SE	ASE	SEOS	AB	SE	ASE	SEOS
4	φ		-0.0745	0.0158	0.1403	0.1433	-0.0878	0.0205	0.195	0.213
	θ_1	1.5	-0.0505	0.0228	0.2169	0.2067	-0.0421	0.0206	0.2136	0.2145
	β_{11}	2	-0.219	0.0456	0.4078	0.4125	-0.0497	0.0402	0.4348	0.4174
	β_{12}	1.5	0.0623	0.052	0.394	0.4705	0.0902	0.037	0.4071	0.3848
	β_{13}	1.2	-0.0777	0.0485	0.3733	0.4389	0.0551	0.0418	0.3916	0.4344
	β_{14}	0.5	0.0016	0.0473	0.3681	0.428	0.1736	0.0429	0.3834	0.4458
	β_{15}	0.04	-0.0315	0.0451	0.3891	0.408	0.081	0.0396	0.3963	0.4119
	β_{21}	2	-0.0514	0.0421	0.4024	0.3812	-0.1611	0.0304	0.4111	0.3161
	β_{22}	2.5	-0.0943	0.0385	0.4534	0.3486	-0.1716	0.0342	0.4699	0.355
	β_{23}	2.2	-0.1453	0.0396	0.411	0.3585	-0.1389	0.0394	0.4366	0.4097
	β_{24}	2.8	-0.301	0.035	0.4672	0.3167	-0.344	0.0352	0.4869	0.3653
	β_{25}	1.5	-0.0599	0.0417	0.3665	0.3774	0.014	0.0386	0.3912	0.4014
			REML $\varphi=0.3$				REML $\varphi=0.5$			
4	φ		0.0671	0.0232	0.1945	0.2052	0.0051	0.0254	0.2342	0.276
	θ_1	1.5	0.0767	0.0279	0.2346	0.246	-0.0222	0.0213	0.2145	0.2311
	β_{11}	2	-0.0395	0.054	0.4428	0.4765	-0.0114	0.0468	0.45	0.5087
	β_{12}	1.5	0.0727	0.0482	0.4165	0.4258	0.0543	0.0392	0.4141	0.4258
	β_{13}	1.2	0.1357	0.0476	0.4037	0.4206	0.008	0.0406	0.3984	0.4412
	β_{14}	0.5	0.1328	0.0413	0.3862	0.3649	0.1706	0.0359	0.3916	0.3905
	β_{15}	0.04	0.1167	0.0417	0.3998	0.368	0.1193	0.0376	0.4049	0.4084
	β_{21}	2	0.1178	0.0578	0.4416	0.51	-0.1606	0.0311	0.4231	0.3381
	β_{22}	2.5	0.0495	0.0466	0.4888	0.412	-0.058	0.0376	0.499	0.4087
	β_{23}	2.2	-0.0412	0.0402	0.4382	0.3551	-0.0727	0.0383	0.4552	0.4161
	β_{24}	2.8	-0.2306	0.0362	0.4889	0.3201	-0.2578	0.0346	0.5155	0.3759
	β_{25}	1.5	0.1116	0.0465	0.4011	0.4103	-0.0876	0.0314	0.3972	0.3411

In the second data set, y can be taken as values 0, 1, 2, 3. All steps of the process are the same as those for the first data set except that $\theta_{-1} = -\infty$, $\theta_0 = 0$ and $\theta_3 = \infty$, θ_1 and θ_2 are threshold parameters which need to be estimated in addition to the fixed and variance components parameters. The results are given in the Tables 10.2.1.2.ij.

n=1 (Table 10.2.1.2a,b):

The ML estimators of parameters and variance component φ are seriously biased whereas the biases of REML estimators of parameters are rarely significant and REML estimators of φ are positively biased for all four threshold models in section 5.2 of chapter 5. As in the previous section, the biases are increased by increasing φ. Although both ML and REML methods yield a very good agreement between the ASE and SEOS for parameters for all four threshold models in section 5.2 of chapter 5, the ASE and SEOS of estimators φ are quite different for threshold models 1, 2, especially the REML method.

The biases of ML and REML estimators of variance component φ are smaller than previous data set (y=0,1,2).

n=3 and **n=5 (Tables 10.2.1.2.3a,b** and **10.2.1.2.5a,b,c,d):**

A considerable bias reduction and very good agreement between ASE and SEOS of ML and REML estimators of parameters and variance component φ are obtained by increasing the number of observations for each subject.

Table 10.2.1.2.1a: Estimated average biases and average standard error over 200 simulations for the mixed threshold models.

			ML φ=0.3				ML φ=0.5			
M		TU	AB	SE	ASE	SEOS	AB	SE	ASE	SEOS
1	φ		-0.2766	0.0001	0.0653	0.0021	-0.4761	0.0001	0.0673	0.002
	θ_1	1.5	-0.1719	0.0264	0.3455	0.3686	-0.298	0.0217	0.3238	0.3041
	θ_2	2.2	-0.2373	0.0339	0.4064	0.4738	-0.4077	0.0269	0.3792	0.3778
	β_1	2	-0.2617	0.0392	0.4316	0.5468	-0.4362	0.0305	0.4099	0.4275
	β_2	0.5	-0.1219	0.0267	0.3358	0.3726	-0.1824	0.0232	0.3321	0.3253
2	φ		-0.2235	0.0076	0.2718	0.1075	-0.4147	0.008	0.3013	0.1124
	θ_1	1.5	-0.1438	0.0357	0.438	0.5034	-0.0986	0.0355	0.4451	0.5013
	θ_2	2.2	-0.1257	0.0411	0.5305	0.5795	-0.0715	0.0415	0.5383	0.5856
	β_1	2	-0.1737	0.0481	0.6368	0.6783	-0.1297	0.0529	0.6411	0.7464
	β_2	0.5	-0.1406	0.039	0.5372	0.5503	-0.1472	0.0382	0.5408	0.5395
			REML				REML			
1	φ		0.2374	0.0068	0.5057	0.095	0.0388	0.0069	0.5059	0.0968
	θ_1	1.5	0.047	0.0258	0.4036	0.3598	-0.0078	0.0234	0.3973	0.328
	θ_2	2.2	0.1107	0.03	0.4763	0.4182	0.004	0.0285	0.4626	0.4003
	β_1	2	0.0006	0.0354	0.512	0.493	-0.0539	0.0273	0.5017	0.3828
	β_2	0.5	-0.0308	0.0257	0.4037	0.3579	-0.0374	0.0265	0.408	0.3723
2	φ		0.5909	0.0164	1.1028	0.2326	0.3906	0.0177	1.1308	0.2509
	θ_1	1.5	0.0676	0.0349	0.4718	0.4936	-0.0342	0.0335	0.4698	0.4733
	θ_2	2.2	0.0811	0.0417	0.56	0.5901	0.0821	0.0443	0.5703	0.6262
	β_1	2	-0.1541	0.0521	0.6781	0.7363	-0.0142	0.055	0.6834	0.7779
	β_2	0.5	-0.012	0.0412	0.5823	0.582	-0.0642	0.0422	0.5943	0.5973

Table 10.2.1.2.1b: Estimated average biases and average standard error over 200 simulations for the mixed threshold models.

			ML φ=0.3				ML φ=0.5			
M		TU	AB	SE	ASE	SEOS	AB	SE	ASE	SEOS
3	φ		-0.1805	0.0132	0.1541	0.1848	-0.3826	0.011	0.1675	0.1539
	θ_1	1.5	-0.0811	0.0299	0.3989	0.419	-0.2288	0.0245	0.3533	0.3438
	θ_2	2.2	-0.0998	0.0358	0.4826	0.5026	-0.3103	0.033	0.4317	0.4638
	β_1	2	-0.1646	0.0418	0.5315	0.5871	-0.3248	0.0369	0.4951	0.518
	β_2	0.5	-0.1198	0.0289	0.3784	0.4052	-0.1263	0.0258	0.3729	0.3623
4	φ		-0.2177	0.01	0.1254	0.1402	-0.4159	0.0103	0.1241	0.1462
	θ_1	1.5	-0.0617	0.033	0.4438	0.464	-0.1555	0.0294	0.4147	0.4162
	θ_2	2.2	-0.0832	0.0367	0.5109	0.517	-0.2485	0.0361	0.4794	0.5109
	β_1	2	-0.1348	0.0424	0.5202	0.597	-0.2758	0.0414	0.4884	0.5851
	β_2	0.5	-0.1228	0.0243	0.3531	0.3421	-0.1907	0.024	0.3535	0.3399
			REML				REML			
3	φ		0.119	0.0214	0.416	0.303	-0.0538	0.019	0.4438	0.2662
	θ_1	1.5	0.0293	0.0285	0.4204	0.4031	-0.0602	0.028	0.3949	0.3916
	θ_2	2.2	0.0948	0.0357	0.5169	0.5047	-0.036	0.0377	0.4837	0.5274
	β_1	2	-0.0839	0.0426	0.5611	0.6019	-0.2509	0.0411	0.5362	0.5758
	β_2	0.5	-0.1824	0.0288	0.4104	0.4068	-0.1631	0.0331	0.4161	0.4641
4	φ		0.0751	0.0178	0.4169	0.2506	-0.0411	0.0176	0.4682	0.2489
	θ_1	1.5	0.0546	0.0316	0.4771	0.4447	-0.0666	0.0276	0.4297	0.3903
	θ_2	2.2	0.1129	0.0408	0.5473	0.5741	-0.0529	0.0316	0.5004	0.4473
	β_1	2	0.1547	0.0431	0.5767	0.6069	0.0046	0.0357	0.5367	0.5048
	β_2	0.5	0.0504	0.0286	0.4004	0.403	0.0209	0.027	0.4108	0.3816

Table 10.2.1.2.3a: Estimated average biases and average standard error over 200 simulations for the mixed threshold models.

			ML φ=0.3				ML φ=0.5			
M		TU	AB	SE	ASE	SEOS	AB	SE	ASE	SEOS
1	φ		0.0123	0.0158	0.1883	0.2222	-0.0598	0.0219	0.2317	0.3101
	θ_1	1.5	-0.0151	0.0188	0.2503	0.2657	-0.0002	0.0188	0.2558	0.2657
	θ_2	2.2	0.0458	0.0238	0.2831	0.3364	0.003	0.0237	0.2868	0.3348
	β_{11}	2	-0.1116	0.0312	0.4024	0.4394	-0.1142	0.0313	0.4153	0.4425
	β_{12}	0.7	0.0993	0.0266	0.3587	0.375	0.0556	0.025	0.3715	0.3539
	β_{13}	0.05	-0.0374	0.0224	0.358	0.3163	-0.0279	0.0267	0.373	0.3779
	β_{21}	2	-0.1244	0.0295	0.3944	0.4163	-0.0448	0.0325	0.4129	0.4592
	β_{22}	2.5	0.1148	0.0319	0.439	0.4505	0.0928	0.0368	0.4563	0.5206
	β_{23}	2.2	0.0103	0.0318	0.4126	0.4489	0.0484	0.0328	0.4313	0.4645
2	φ		0.0369	0.0237	0.2951	0.335	-0.0621	0.0288	0.3507	0.4063
	θ_1	1.5	0.0323	0.0221	0.2905	0.3122	-0.0223	0.0215	0.2853	0.3027
	θ_2	2.2	0.0479	0.0256	0.3339	0.3625	-0.0147	0.0266	0.3299	0.3745
	β_{11}	2	-0.1082	0.0421	0.5798	0.5958	-0.2656	0.039	0.576	0.5508
	β_{12}	0.7	0.1425	0.0355	0.5402	0.5019	0.0297	0.0366	0.543	0.5166
	β_{13}	0.05	-0.0196	0.0403	0.5462	0.5694	-0.1835	0.0412	0.5601	0.5806
	β_{21}	2	-0.0511	0.0432	0.5677	0.6115	-0.1413	0.0399	0.5678	0.5628
	β_{22}	2.5	0.1097	0.0495	0.6144	0.6999	0.1403	0.0469	0.63	0.6618
	β_{23}	2.2	0.0197	0.0436	0.5795	0.6168	0.0331	0.0434	0.5881	0.6126
			REML				REML			
1	φ		0.0647	0.0159	0.2168	0.2248	0.0678	0.0224	0.2786	0.3165
	θ_1	1.5	0.0071	0.0177	0.2534	0.25	0.0339	0.0226	0.2618	0.3189
	θ_2	2.2	0.0231	0.0232	0.2844	0.3273	0.066	0.0273	0.2938	0.3855
	β_{11}	2	-0.1273	0.0281	0.4052	0.3966	-0.0761	0.0341	0.435	0.4819
	β_{12}	0.7	0.0699	0.0256	0.3618	0.3617	0.0497	0.0295	0.39	0.4173
	β_{13}	0.05	-0.0456	0.0255	0.3624	0.3601	-0.0622	0.0299	0.394	0.423
	β_{21}	2	-0.0359	0.028	0.4065	0.3948	-0.0034	0.0336	0.4231	0.4757
	β_{22}	2.5	0.111	0.0352	0.4498	0.496	0.0972	0.037	0.4616	0.5234
	β_{23}	2.2	0.0268	0.0327	0.4216	0.4618	-0.0008	0.0339	0.435	0.4788
2	φ		0.2067	0.0318	0.3992	0.4493	0.1272	0.042	0.4384	0.5912
	θ_1	1.5	0.0483	0.0238	0.2964	0.3367	0.032	0.0207	0.2948	0.2911
	θ_2	2.2	0.0754	0.0276	0.3406	0.39	0.0631	0.0232	0.3405	0.327
	β_{11}	2	-0.0599	0.0439	0.5947	0.6203	-0.0409	0.0442	0.5994	0.6225
	β_{12}	0.7	0.1777	0.0393	0.555	0.5564	0.2081	0.0373	0.5571	0.5242
	β_{13}	0.05	-0.0142	0.044	0.5577	0.6218	-0.1007	0.0419	0.5684	0.5894
	β_{21}	2	0.0492	0.0384	0.5794	0.5424	-0.0344	0.0439	0.5874	0.6177
	β_{22}	2.5	0.201	0.0493	0.6375	0.6977	0.2638	0.0548	0.657	0.7712
	β_{23}	2.2	0.1169	0.0443	0.5994	0.627	0.0543	0.0486	0.6051	0.684

Table 10.2.1.2.3b: Estimated average biases and average standard error over 200 simulations for the mixed threshold models.

			ML φ=0.3				ML φ=0.5			
M		TU	AB	SE	ASE	SEOS	AB	SE	ASE	SEOS
3	φ		-0.0586	0.0143	0.168	0.2013	-0.1278	0.0178	0.2192	0.2522
	θ_1	1.5	-0.0104	0.0211	0.256	0.2968	-0.0303	0.0192	0.2534	0.271
	θ_2	2.2	0.0066	0.0235	0.2961	0.3307	-0.0376	0.0218	0.2923	0.3082
	β_{11}	2	-0.1713	0.0337	0.4326	0.4748	-0.2087	0.0282	0.446	0.3992
	β_{12}	0.7	-0.0452	0.0264	0.3692	0.3711	-0.0235	0.027	0.3859	0.3819
	β_{13}	0.05	-0.1135	0.0243	0.3562	0.3421	-0.1269	0.0266	0.3774	0.3765
	β_{21}	2	-0.1465	0.0348	0.4284	0.4895	-0.1312	0.0335	0.4384	0.4741
	β_{22}	2.5	0.0097	0.0345	0.4825	0.4853	-0.0715	0.0394	0.4862	0.5565
	β_{23}	2.2	-0.0731	0.0369	0.4459	0.5187	-0.1287	0.035	0.4524	0.4955
4	φ		-0.0536	0.0162	0.162	0.2263	-0.1167	0.0157	0.2189	0.2195
	θ_1	1.5	-0.0015	0.0243	0.3045	0.3394	-0.0002	0.023	0.2998	0.3221
	θ_2	2.2	0.004	0.0283	0.3351	0.3948	-0.0307	0.0254	0.3297	0.3557
	β_{11}	2	-0.0355	0.0308	0.442	0.4299	-0.0464	0.0277	0.4482	0.3871
	β_{12}	0.7	0.1701	0.0277	0.3768	0.3869	0.1571	0.0281	0.3939	0.3941
	β_{13}	0.05	0.0612	0.028	0.3834	0.3912	0.0398	0.026	0.397	0.3645
	β_{21}	2	-0.005	0.035	0.4311	0.4892	0.0067	0.0348	0.4405	0.4875
	β_{22}	2.5	0.1261	0.0379	0.4664	0.5286	0.0572	0.0373	0.4743	0.5215
	β_{23}	2.2	0.047	0.0346	0.4438	0.4833	0.053	0.0355	0.4529	0.4971
			REML				REML			
3	φ		0.0584	0.0204	0.2221	0.2883	0.0423	0.026	0.2851	0.3655
	θ_1	1.5	0.0154	0.0205	0.2599	0.2886	0.0075	0.0202	0.2601	0.2837
	θ_2	2.2	0.0488	0.0242	0.3009	0.3409	0.0649	0.024	0.304	0.337
	β_{11}	2	-0.1521	0.0315	0.4472	0.4439	-0.1547	0.0326	0.4573	0.4583
	β_{12}	0.7	0.0473	0.0256	0.3858	0.3615	0.0365	0.0293	0.3989	0.4127
	β_{13}	0.05	-0.1245	0.0265	0.3741	0.3736	-0.1747	0.0279	0.3923	0.3925
	β_{21}	2	-0.0816	0.0379	0.4441	0.5344	-0.1027	0.0342	0.4611	0.4815
	β_{22}	2.5	0.0498	0.0392	0.4926	0.5536	0.0279	0.0384	0.5105	0.54
	β_{23}	2.2	-0.0651	0.0356	0.4573	0.5024	-0.0559	0.0366	0.4764	0.5156
4	φ		0.0878	0.0234	0.2299	0.3263	-0.0121	0.0226	0.2623	0.3118
	θ_1	1.5	0.048	0.0236	0.3244	0.3297	-0.0024	0.0229	0.3058	0.3167
	θ_2	2.2	0.0845	0.0287	0.3564	0.4005	0.0284	0.0275	0.3386	0.3803
	β_{11}	2	0.0192	0.0318	0.4691	0.4446	-0.0398	0.0301	0.4666	0.4165
	β_{12}	0.7	0.143	0.0274	0.3971	0.3833	0.2063	0.0318	0.4135	0.439
	β_{13}	0.05	0.0369	0.0325	0.4073	0.4541	0.064	0.0336	0.4222	0.4649
	β_{21}	2	0.1758	0.0355	0.4608	0.4959	0.0631	0.0381	0.4496	0.5264
	β_{22}	2.5	0.2874	0.0406	0.4995	0.5675	0.1454	0.0424	0.4907	0.5854
	β_{23}	2.2	0.1487	0.0357	0.4706	0.498	0.0808	0.0351	0.4631	0.4853

Table 10.2.1.2.5a: Estimated average biases and average standard error over 200 simulations for the mixed threshold models.

			ML φ=0.3				ML φ=0.5			
M		TU	AB	SE	ASE	SEOS	AB	SE	ASE	SEOS
1	φ		-0.0279	0.0113	0.138	0.1593	-0.0474	0.0168	0.1887	0.2365
	θ_1	1.5	0.0324	0.0142	0.1944	0.2	0.0483	0.0142	0.1956	0.2003
	θ_2	2.2	0.0634	0.0161	0.2167	0.2267	0.0814	0.017	0.2198	0.2394
	β_{11}	2	-0.0377	0.0251	0.3728	0.3538	-0.0601	0.0312	0.3907	0.4389
	β_{12}	1.5	0.076	0.026	0.3587	0.3657	0.0159	0.0254	0.3754	0.3578
	β_{13}	1.2	0.0502	0.0265	0.35	0.3735	-0.0521	0.0271	0.3665	0.381
	β_{14}	0.5	0.0454	0.0241	0.3404	0.3398	0.0089	0.0232	0.3606	0.3269
	β_{15}	0.04	0.0284	0.0245	0.3466	0.3443	-0.0333	0.0265	0.3701	0.3734
	β_{21}	2	-0.041	0.0284	0.3682	0.3995	-0.0382	0.0287	0.3914	0.4033
	β_{22}	2.5	0.0606	0.0277	0.4008	0.3894	0.0992	0.0301	0.4252	0.4234
	β_{23}	2.2	0.0332	0.028	0.3813	0.3941	0.0455	0.0311	0.4038	0.4376
	β_{24}	2.8	0.0646	0.0292	0.4257	0.4102	0.0845	0.034	0.4507	0.479
	β_{25}	1.5	0.0356	0.028	0.3532	0.3934	0.0344	0.0277	0.3753	0.3893
			REML				REML			
1	φ		0.0382	0.0139	0.1631	0.1964	0.0384	0.016	0.2197	0.2233
	θ_1	1.5	0.0291	0.0163	0.1959	0.2306	0.0325	0.0144	0.1973	0.2016
	θ_2	2.2	0.0456	0.0182	0.2183	0.2574	0.074	0.0163	0.2214	0.2274
	β_{11}	2	-0.0304	0.0281	0.379	0.3969	-0.0203	0.0298	0.4003	0.4156
	β_{12}	1.5	0.084	0.0251	0.3644	0.354	0.0702	0.0279	0.385	0.39
	β_{13}	1.2	0.0113	0.0264	0.3545	0.3729	0.0433	0.0276	0.3769	0.3859
	β_{14}	0.5	0.0766	0.0255	0.3458	0.3592	0.0441	0.0262	0.3694	0.3661
	β_{15}	0.04	-0.0559	0.0269	0.3556	0.3796	-0.0217	0.0265	0.3788	0.3707
	β_{21}	2	-0.0192	0.0291	0.3804	0.4104	-0.0424	0.0271	0.3967	0.3786
	β_{22}	2.5	0.0985	0.0299	0.415	0.422	0.0782	0.0298	0.43	0.4158
	β_{23}	2.2	0.0255	0.0294	0.3918	0.4154	0.0241	0.0275	0.4093	0.3836
	β_{24}	2.8	0.1511	0.0335	0.4486	0.4723	0.0965	0.0344	0.4592	0.4804
	β_{25}	1.5	0.0711	0.0298	0.3647	0.4205	0.0916	0.0283	0.3839	0.3957

Table 10.2.1.2.5a: Estimated average biases and average standard error over 200 simulations for the mixed threshold models.

			ML φ=0.3				ML φ=0.5			
M		TU	AB	SE	ASE	SEOS	AB	SE	ASE	SEOS
2	φ		-0.0487	0.0168	0.2022	0.2369	-0.0559	0.0198	0.285	0.2796
	θ_1	1.5	0.0061	0.0163	0.2208	0.23	-0.0151	0.0152	0.2186	0.2156
	θ_2	2.2	0.0486	0.0181	0.2554	0.2554	0.0265	0.0179	0.2537	0.2525
	β_{11}	2	-0.1387	0.0413	0.5435	0.5831	-0.0723	0.0418	0.5534	0.5905
	β_{12}	1.5	0.1071	0.0369	0.5283	0.521	-0.0108	0.0379	0.5317	0.5363
	β_{13}	1.2	-0.0385	0.0417	0.5191	0.5885	-0.0002	0.0411	0.5251	0.5811
	β_{14}	0.5	0.0579	0.0359	0.5199	0.5068	0.0696	0.0381	0.5225	0.5386
	β_{15}	0.04	-0.0204	0.0421	0.5384	0.594	0.0197	0.0387	0.5338	0.5476
	β_{21}	2	-0.0316	0.0395	0.5456	0.5568	-0.0914	0.0372	0.5631	0.5257
	β_{22}	2.5	0.0894	0.0444	0.5825	0.626	0.0284	0.038	0.5959	0.5374
	β_{23}	2.2	0.1023	0.0463	0.5671	0.6536	-0.0428	0.0455	0.5741	0.6437
	β_{24}	2.8	0.1467	0.0458	0.6248	0.6456	0.1274	0.0437	0.6379	0.6183
	β_{25}	1.5	0.0343	0.0401	0.5265	0.5651	-0.0283	0.0359	0.5404	0.508
			REML				REML			
2	φ		0.0756	0.0204	0.2635	0.2882	0.0264	0.0227	0.3191	0.3195
	θ_1	1.5	0.0327	0.0121	0.224	0.1709	0.0164	0.0175	0.222	0.2465
	θ_2	2.2	0.0534	0.0156	0.2575	0.2205	0.0539	0.0186	0.257	0.2622
	β_{11}	2	0.0627	0.0417	0.5616	0.59	-0.006	0.0417	0.5643	0.587
	β_{12}	1.5	0.0973	0.0328	0.5339	0.4645	0.0505	0.0357	0.5418	0.5025
	β_{13}	1.2	-0.116	0.0446	0.5227	0.6313	-0.0232	0.036	0.5314	0.507
	β_{14}	0.5	0.0279	0.0443	0.5229	0.6266	0.0725	0.0377	0.5308	0.5306
	β_{15}	0.04	-0.0499	0.0458	0.5417	0.6482	-0.0603	0.045	0.553	0.6329
	β_{21}	2	-0.0672	0.0374	0.5573	0.5294	-0.0949	0.0408	0.5682	0.5739
	β_{22}	2.5	0.0999	0.0413	0.5981	0.5845	0.0288	0.0429	0.6049	0.6036
	β_{23}	2.2	0.1337	0.0483	0.5852	0.6834	0.0249	0.0462	0.579	0.6495
	β_{24}	2.8	0.1196	0.0423	0.632	0.5983	0.1489	0.0449	0.647	0.6314
	β_{25}	1.5	0.0851	0.0401	0.5349	0.5676	0.0885	0.0414	0.55	0.5822

Table 10.2.1.2.5b: Estimated average biases and average standard error over 200 simulations for the mixed threshold models.

			ML φ=0.3				ML φ=0.5			
M		TU	AB	SE	ASE	SEOS	AB	SE	ASE	SEOS
3	φ		-0.0094	0.0116	0.1478	0.1635	-0.0518	0.0159	0.1941	0.2243
	θ_1	1.5	0.0314	0.0128	0.1968	0.1808	-0.0004	0.0143	0.1948	0.2017
	θ_2	2.2	0.0669	0.0167	0.2267	0.2362	0.0225	0.0183	0.2254	0.2587
	β_{11}	2	-0.0206	0.0282	0.4115	0.3984	-0.0888	0.0309	0.4229	0.4371
	β_{12}	1.5	0.0573	0.0258	0.3858	0.3654	-0.0565	0.029	0.3958	0.4107
	β_{13}	1.2	-0.0199	0.0283	0.3716	0.4009	-0.0827	0.0269	0.3837	0.3801
	β_{14}	0.5	-0.0589	0.0253	0.355	0.3579	-0.0405	0.0261	0.3697	0.3687
	β_{15}	0.04	-0.0438	0.0222	0.3568	0.3138	-0.1101	0.0267	0.3767	0.3775
	β_{21}	2	-0.0991	0.0275	0.4015	0.3895	-0.1054	0.0289	0.4222	0.4092
	β_{22}	2.5	-0.0434	0.0284	0.444	0.4011	-0.0403	0.0281	0.462	0.3969
	β_{23}	2.2	-0.0763	0.0318	0.4162	0.4495	-0.0692	0.0323	0.4359	0.4567
	β_{24}	2.8	0.0687	0.0372	0.4948	0.5254	-0.0686	0.0341	0.4934	0.4828
	β_{25}	1.5	-0.0437	0.0279	0.3777	0.3939	-0.0915	0.0291	0.3948	0.4115
			REML				REML			
3	φ		0.0422	0.0127	0.1721	0.1792	0.0579	0.0185	0.2357	0.2608
	θ_1	1.5	0.032	0.013	0.1981	0.184	0.0495	0.0132	0.2011	0.1859
	θ_2	2.2	0.0519	0.0162	0.2281	0.2292	0.0968	0.0168	0.2325	0.2358
	β_{11}	2	-0.0418	0.028	0.412	0.3966	-0.1367	0.0305	0.4288	0.4285
	β_{12}	1.5	0.0057	0.0262	0.387	0.3703	-0.0433	0.0257	0.4091	0.3616
	β_{13}	1.2	-0.0543	0.0283	0.3723	0.4006	-0.009	0.0332	0.4013	0.4671
	β_{14}	0.5	0.0107	0.0248	0.3579	0.351	-0.0152	0.0279	0.3865	0.3928
	β_{15}	0.04	-0.1035	0.0241	0.3603	0.341	-0.0953	0.0288	0.3932	0.4055
	β_{21}	2	-0.0162	0.0295	0.416	0.4178	-0.0067	0.0281	0.4333	0.3953
	β_{22}	2.5	-0.0289	0.0314	0.4537	0.4434	0.0431	0.0318	0.4757	0.4476
	β_{23}	2.2	-0.005	0.0317	0.4292	0.4489	-0.0319	0.0307	0.443	0.4319
	β_{24}	2.8	0.1152	0.0393	0.509	0.5555	0.0383	0.0314	0.5047	0.4415
	β_{25}	1.5	-0.0063	0.0302	0.3884	0.4273	0.0011	0.0279	0.408	0.392

Table 10.2.1.2.5d: Estimated average biases and average standard error over 200 simulations for the mixed threshold models.

			ML φ=0.3				ML φ=0.5			
M		TU	AB	SE	ASE	SEOS	AB	SE	ASE	SEOS
4	φ		-0.0285	0.0117	0.1411	0.159	-0.0752	0.017	0.1833	0.2296
	θ_1	1.5	0.0376	0.019	0.2339	0.2583	-0.0461	0.0176	0.2181	0.2375
	θ_2	2.2	0.0482	0.0196	0.2577	0.2665	-0.0417	0.021	0.2432	0.2839
	β_{11}	2	0.0138	0.0329	0.406	0.4458	-0.0085	0.0296	0.4088	0.3989
	β_{12}	1.5	0.103	0.031	0.3906	0.42	0.1209	0.0323	0.3955	0.4361
	β_{13}	1.2	0.032	0.0286	0.3755	0.388	0.0761	0.0261	0.3828	0.3527
	β_{14}	0.5	0.0983	0.0279	0.3665	0.3781	0.1005	0.0314	0.3802	0.4233
	β_{15}	0.04	0.0751	0.0294	0.3818	0.399	0.1345	0.0274	0.3914	0.3693
	β_{21}	2	0.0048	0.0322	0.3982	0.4368	-0.089	0.0261	0.3985	0.3525
	β_{22}	2.5	0.0752	0.0318	0.4228	0.4319	0.0097	0.033	0.4291	0.4445
	β_{23}	2.2	0.083	0.0332	0.4081	0.4499	0.0408	0.0323	0.4138	0.4355
	β_{24}	2.8	0.0771	0.0322	0.4442	0.4362	0.0373	0.0362	0.4585	0.4882
	β_{25}	1.5	0.1048	0.0286	0.3831	0.3875	-0.0034	0.0315	0.3843	0.4246
			REML				REML			
4	φ		0.0526	0.0156	0.1728	0.2114	0.0476	0.0191	0.229	0.2619
	θ_1	1.5	0.0368	0.0192	0.2363	0.2606	0.0155	0.0156	0.2252	0.2127
	θ_2	2.2	0.0837	0.0214	0.2618	0.2907	0.0304	0.0181	0.2509	0.2481
	β_{11}	2	0.0696	0.0316	0.4133	0.4283	0.032	0.0259	0.421	0.3545
	β_{12}	1.5	0.0947	0.0295	0.3936	0.4001	0.1429	0.0254	0.4054	0.3468
	β_{13}	1.2	0.0845	0.0285	0.3834	0.3861	0.0995	0.0323	0.3973	0.4413
	β_{14}	0.5	0.1702	0.0276	0.3713	0.3743	0.1184	0.0256	0.3893	0.3495
	β_{15}	0.04	0.037	0.0286	0.3906	0.3879	0.1037	0.0323	0.4068	0.4412
	β_{21}	2	0.0735	0.0325	0.4107	0.4412	-0.0679	0.0303	0.4172	0.4142
	β_{22}	2.5	0.1839	0.0301	0.4385	0.4079	0.0603	0.0292	0.4479	0.3991
	β_{23}	2.2	0.1652	0.0348	0.421	0.4717	0.1232	0.0287	0.4343	0.3931
	β_{24}	2.8	0.2039	0.0354	0.4659	0.4798	0.0915	0.0336	0.4759	0.4592
	β_{25}	1.5	0.1693	0.0331	0.3936	0.4492	0.1624	0.0287	0.4059	0.3921

In the third data set, observations are values of 0, 1, 2, 3 and 4. Again all steps of the process are exactly the same as those for the first data set except that $\theta_{-1} = -\infty$, $\theta_0 = 0$ and $\theta_4 = \infty$, leaving θ_1, θ_2 and θ_3 threshold parameters which need to be estimated. The results are provided in the Tables 10.2.1.3.ij.

n=1, n=3 and n=5 (Tables 10.2.1.3.1a,b, 10.2.1.3.3a,b,c and 10.2.1.3.5a,b,c,d):

The conclusion is more or less the same as in the previous data set (y=0,1,2,3). Moreover, both ML and REML estimators of variance component φ are improved for all four threshold models in section 5.2 of chapter 5.

Table 10.2.1.3.1a: Estimated average biases and average standard error over 200 simulations for the mixed threshold models.

			ML φ=0.3				ML φ=0.5			
M		TU	AB	SE	ASE	SEOS	AB	SE	ASE	SEOS
1	φ		-0.2732	0.0002	0.0794	0.0025	-0.2732	0.0002	0.0795	0.0028
	θ_1	1.5	-0.242	0.0235	0.3395	0.3258	-0.2186	0.0242	0.3531	0.3259
	θ_2	2.2	-0.3201	0.0249	0.3969	0.3462	-0.2979	0.0273	0.4076	0.3677
	θ_3	3.8	-0.6541	0.0282	0.5729	0.3923	-0.5996	0.0315	0.5839	0.4238
	β_1	2	-0.323	0.0273	0.42	0.3792	-0.2787	0.0314	0.429	0.4221
	β_2	0.5	-0.1725	0.0225	0.3375	0.3124	-0.2154	0.0239	0.3418	0.3221
2	φ		-0.1293	0.0151	0.4418	0.2019	-0.0997	0.0179	0.4722	0.2273
	θ_1	1.5	-0.1074	0.0339	0.4458	0.4521	-0.006	0.0366	0.4643	0.4664
	θ_2	2.2	-0.1306	0.0406	0.5297	0.542	-0.04	0.0464	0.5465	0.5903
	θ_3	3.8	0.0928	0.0556	0.8415	0.7416	0.1454	0.0581	0.8529	0.7398
	β_1	2	-0.1327	0.0495	0.6379	0.6602	-0.1087	0.0617	0.6434	0.7851
	β_2	0.5	-0.081	0.0436	0.5477	0.5813	-0.116	0.0428	0.5509	0.5446
			REML				REML			
1	φ	0.3	0.4914	0.0114	0.5578	0.1566	0.3991	0.0098	0.542	0.1281
	θ_1	1.5	0.0336	0.0195	0.4044	0.2679	0.1163	0.0286	0.4331	0.3742
	θ_2	2.2	0.1168	0.0253	0.4807	0.3473	0.2037	0.0357	0.5084	0.4669
	θ_3	3.8	0.0455	0.0271	0.6935	0.3732	0.2289	0.033	0.7281	0.431
	β_1	2	-0.0502	0.0352	0.5162	0.4844	0.2153	0.0351	0.5451	0.4585
	β_2	0.5	-0.0095	0.0216	0.4289	0.2972	-0.092	0.0335	0.4305	0.4376
2	φ	0.3	1.1881	0.0368	1.2259	0.4855	1.1728	0.0362	1.2398	0.4835
	θ_1	1.5	0.1475	0.0399	0.5053	0.5263	0.1534	0.0368	0.507	0.4914
	θ_2	2.2	0.2334	0.0502	0.599	0.6621	0.2426	0.0459	0.6018	0.6121
	θ_3	3.8	0.6307	0.0639	0.9058	0.8432	0.6145	0.059	0.9071	0.7873
	β_1	2	0.1887	0.0591	0.7254	0.7794	0.1158	0.0635	0.7193	0.8466
	β_2	0.5	0.003	0.0463	0.6291	0.6114	0.0641	0.0479	0.6299	0.6386

Table 10.2.1.3.1b: Estimated average biases and average standard error over 200 simulations for the mixed threshold models.

			ML φ=0.3				ML φ=0.5			
M		TU	AB	SE	ASE	SEOS	AB	SE	ASE	SEOS
3	φ		-0.2272	0.0093	0.0877	0.1305	-0.2231	0.0115	0.0907	0.1627
	θ_1	1.5	0.0014	0.041	0.4242	0.5748	0.1025	0.0285	0.454	0.4028
	θ_2	2.2	-0.0592	0.0454	0.4969	0.6368	-0.0899	0.0365	0.5081	0.5158
	θ_3	3.8	-0.8317	0.048	0.6041	0.674	-0.8219	0.043	0.6151	0.6083
	β_1	2	-0.088	0.0492	0.548	0.6903	-0.0638	0.0434	0.5633	0.6136
	β_2	0.5	-0.1108	0.0328	0.3859	0.461	-0.114	0.0332	0.3758	0.47
4	φ		-0.1714	0.0163	0.1473	0.2215	-0.2025	0.0136	0.1316	0.1783
	θ_1	1.5	-0.0889	0.0272	0.4332	0.37	-0.0607	0.035	0.4451	0.4587
	θ_2	2.2	-0.1279	0.0321	0.4973	0.4369	-0.0898	0.0414	0.5104	0.5426
	θ_3	3.8	-0.037	0.0462	0.7612	0.6279	0.082	0.053	0.7911	0.695
	β_1	2	-0.0816	0.038	0.5156	0.5166	-0.0499	0.0509	0.5235	0.6669
	β_2	0.5	-0.0862	0.0259	0.3577	0.3517	-0.0905	0.0291	0.3623	0.3813
			REML				REML			
3	φ		0.1045	0.0245	0.4006	0.3384	0.0618	0.0179	0.3989	0.2528
	θ_1	1.5	0.1271	0.0329	0.4652	0.455	0.1632	0.0379	0.4907	0.5359
	θ_2	2.2	0.129	0.0403	0.5483	0.5572	0.1787	0.0398	0.5712	0.5631
	θ_3	3.8	-0.4126	0.0453	0.6837	0.6264	-0.4256	0.0445	0.6932	0.63
	β_1	2	0.078	0.0468	0.5983	0.6472	0.0231	0.0439	0.6063	0.6202
	β_2	0.5	-0.2122	0.0311	0.4099	0.4299	-0.2128	0.0307	0.4273	0.4345
4	φ	0.3	0.301	0.0298	0.4924	0.397	0.2057	0.0291	0.4492	0.3931
	θ_1	1.5	0.1361	0.0338	0.4955	0.45	0.0826	0.0343	0.4787	0.4637
	θ_2	2.2	0.1977	0.0412	0.5665	0.5484	0.137	0.0426	0.5513	0.5759
	θ_3	3.8	0.3709	0.0521	0.8162	0.6928	0.3938	0.0539	0.8262	0.7287
	β_1	2	0.2957	0.0473	0.6037	0.6289	0.2652	0.0449	0.5937	0.6077
	β_2	0.5	0.1029	0.0307	0.4308	0.4089	0.0915	0.033	0.4125	0.446

Table 10.2.1.3.3a: Estimated average biases and average standard error over 200 simulations for the mixed threshold models.

			ML φ=0.3				ML φ=0.5			
M		TU	AB	SE	ASE	SEOS	AB	SE	ASE	SEOS
1	φ		0.0015	0.0151	0.1762	0.2135	-0.0205	0.0166	0.1657	0.2349
	θ_1	1.5	0.0271	0.0202	0.2593	0.2863	0.0004	0.0211	0.2539	0.2984
	θ_2	2.2	0.0576	0.0249	0.2896	0.3524	0.0341	0.0261	0.2842	0.3688
	θ_3	3.8	0.0918	0.0351	0.398	0.4959	0.0397	0.0376	0.3942	0.5322
	β_{11}	2	-0.0816	0.0306	0.3994	0.4322	-0.076	0.0294	0.3914	0.4158
	β_{12}	0.7	0.0216	0.0252	0.3593	0.3557	0.0796	0.0249	0.352	0.3522
	β_{13}	0.05	-0.0099	0.0275	0.36	0.389	-0.0052	0.026	0.35	0.3682
	β_{21}	2	-0.0396	0.0302	0.3921	0.4267	-0.0206	0.0311	0.3939	0.4392
	β_{22}	2.5	0.1257	0.0357	0.4193	0.5054	0.054	0.0372	0.416	0.5258
	β_{23}	2.2	0.069	0.0333	0.4044	0.4708	-0.0788	0.0331	0.3995	0.4677
2	φ		0.0173	0.0251	0.276	0.3478	-0.0105	0.024	0.2572	0.3295
	θ_1	1.5	-0.0166	0.0236	0.2855	0.3272	0.0039	0.0193	0.2846	0.2647
	θ_2	2.2	-0.0301	0.0293	0.328	0.4061	-0.0205	0.023	0.3265	0.3155
	θ_3	3.8	0.0431	0.0396	0.4427	0.5486	0.0485	0.0317	0.444	0.435
	β_{11}	2	-0.0959	0.0427	0.5638	0.5923	-0.1678	0.0401	0.5526	0.5494
	β_{12}	0.7	0.066	0.0399	0.5319	0.5526	0.1452	0.0401	0.525	0.5503
	β_{13}	0.05	-0.0199	0.0404	0.5413	0.5592	-0.0491	0.0373	0.5327	0.5112
	β_{21}	2	-0.0221	0.045	0.5562	0.6233	-0.1767	0.0398	0.5489	0.546
	β_{22}	2.5	0.1613	0.0484	0.5854	0.6707	0.1498	0.0425	0.583	0.583
	β_{23}	2.2	0.0263	0.0481	0.5638	0.6659	0.0284	0.0436	0.5628	0.5979
			REML				REML			
1	φ	0.3	0.0918	0.018	0.2124	0.2546	0.0229	0.0156	0.1883	0.2212
	θ_1	1.5	0.0015	0.0194	0.2592	0.2747	-0.0138	0.0199	0.2558	0.282
	θ_2	2.2	0.0415	0.0242	0.2904	0.3428	0.0143	0.0232	0.2855	0.3277
	θ_3	3.8	0.1197	0.0331	0.3959	0.4686	0.0708	0.032	0.3908	0.4521
	β_{11}	2	-0.082	0.0316	0.4134	0.4476	-0.0137	0.0297	0.4	0.4205
	β_{12}	0.7	0.0376	0.0265	0.3756	0.3745	0.1572	0.0266	0.3614	0.3757
	β_{13}	0.05	-0.0743	0.0302	0.3813	0.4265	0.0336	0.0243	0.3562	0.3432
	β_{21}	2	0.0042	0.0299	0.3979	0.4224	0.0067	0.0336	0.3977	0.4749
	β_{22}	2.5	0.1456	0.0339	0.4246	0.4795	0.1166	0.0349	0.4223	0.494
	β_{23}	2.2	0.0784	0.0307	0.4088	0.4337	-0.0004	0.0326	0.4056	0.4604

Table 10.2.1.3.3b: Estimated average biases and average standard error over 200 simulations for the mixed threshold models.

			ML φ=0.3				ML φ=0.5			
M		TU	AB	SE	ASE	SEOS	AB	SE	ASE	SEOS
3	φ		-0.0353	0.0154	0.1637	0.2179	0.0056	0.0193	0.1752	0.2736
	θ_1	1.5	0.0014	0.0199	0.2615	0.2815	0.0304	0.0204	0.2609	0.289
	θ_2	2.2	0.025	0.0237	0.3018	0.3349	0.0852	0.0268	0.3028	0.3791
	θ_3	3.8	-0.0259	0.0329	0.4323	0.4658	0.0242	0.036	0.4423	0.5091
	β_{11}	2	-0.121	0.0314	0.4318	0.4437	-0.1463	0.0297	0.4224	0.4196
	β_{12}	0.7	-0.0303	0.0286	0.3769	0.4045	0.002	0.0262	0.3717	0.3706
	β_{13}	0.05	-0.0675	0.0281	0.3649	0.3968	-0.0772	0.0248	0.3585	0.3508
	β_{21}	2	-0.0472	0.032	0.4214	0.4524	-0.0861	0.0299	0.426	0.4234
	β_{22}	2.5	0.1124	0.0349	0.4578	0.4938	0.0585	0.0332	0.4593	0.4695
	β_{23}	2.2	-0.0104	0.0347	0.432	0.4911	0.0291	0.0343	0.4427	0.4855
			REML				REML			
2	φ		0.1028	0.0295	0.3257	0.4087	0.1339	0.0292	0.3497	0.3985
	θ_1	1.5	-0.033	0.0207	0.2855	0.2873	0.0001	0.022	0.2869	0.3003
	θ_2	2.2	-0.0166	0.0272	0.3302	0.3774	-0.0054	0.0266	0.3299	0.3623
	θ_3	3.8	0.0561	0.0349	0.4432	0.4832	0.0751	0.0337	0.4447	0.459
	β_{11}	2	-0.1317	0.0379	0.573	0.5248	-0.0775	0.0417	0.5597	0.5686
	β_{12}	0.7	-0.0201	0.0399	0.5515	0.5532	0.156	0.04	0.532	0.5455
	β_{13}	0.05	-0.0112	0.0419	0.5553	0.5803	-0.0061	0.046	0.543	0.6279
	β_{21}	2	-0.0716	0.0421	0.551	0.583	-0.0638	0.0417	0.5702	0.5682
	β_{22}	2.5	0.1102	0.0429	0.5791	0.5949	0.1467	0.0496	0.5965	0.6765
	β_{23}	2.2	0.0798	0.0463	0.5616	0.6418	0.0196	0.0421	0.5746	0.5746
3	φ	0.3	0.0325	0.0194	0.205	0.2734	0.0569	0.019	0.2109	0.2694
	θ_1	1.5	-0.0388	0.0196	0.2596	0.2771	-0.0323	0.0209	0.2542	0.295
	θ_2	2.2	-0.0039	0.0222	0.3015	0.3136	-0.0116	0.0222	0.2943	0.3133
	θ_3	3.8	0.0162	0.0356	0.4413	0.5027	0.033	0.0325	0.448	0.4599
	β_{11}	2	-0.1754	0.031	0.439	0.4378	-0.126	0.0303	0.4375	0.4291
	β_{12}	0.7	-0.1109	0.0279	0.3847	0.3932	0.0572	0.0264	0.3867	0.3734
	β_{13}	0.05	-0.1383	0.027	0.3775	0.3807	-0.0624	0.0261	0.3741	0.3688
	β_{21}	2	-0.102	0.0339	0.4248	0.4788	-0.1721	0.0273	0.4191	0.3858
	β_{22}	2.5	0.0828	0.0351	0.4618	0.4956	0.0595	0.0346	0.4606	0.4888
	β_{23}	2.2	0.016	0.0361	0.4397	0.5094	-0.111	0.0332	0.4317	0.4701

Table 10.2.1.3.3c: Estimated average biases and average standard error over 200 simulations for the mixed threshold models.

			ML φ=0.3				ML φ=0.5			
M		TU	AB	SE	ASE	SEOS	AB	SE	ASE	SEOS
4	φ		-0.0453	0.0161	0.1606	0.2232	-0.0787	0.0157	0.146	0.2174
	θ_1	1.5	-0.0301	0.0252	0.3054	0.3495	0.0214	0.0247	0.3163	0.3421
	θ_2	2.2	-0.0275	0.0269	0.336	0.3729	-0.0001	0.0285	0.345	0.3953
	θ_3	3.8	0.007	0.0349	0.4293	0.4837	0.0462	0.0361	0.4407	0.4995
	β_{11}	2	-0.0524	0.0344	0.4394	0.4766	0.0433	0.0343	0.4474	0.4759
	β_{12}	0.7	0.057	0.0293	0.3775	0.4053	0.1485	0.0318	0.3761	0.4403
	β_{13}	0.05	-0.0398	0.0343	0.3952	0.4755	0.0874	0.0346	0.3797	0.4794
	β_{21}	2	-0.0385	0.0318	0.4284	0.4407	-0.0493	0.0375	0.4391	0.5194
	β_{22}	2.5	0.1273	0.0404	0.4557	0.5602	0.0871	0.0437	0.4615	0.6058
	β_{23}	2.2	0.0432	0.0359	0.4412	0.4971	0.0402	0.0419	0.4512	0.5804
			REML				REML			
4	φ		0.0526	0.0176	0.2096	0.2469	0.0516	0.0177	0.204	0.2481
	θ_1	1.5	0.0553	0.0246	0.3243	0.3457	-0.0348	0.0217	0.3016	0.304
	θ_2	2.2	0.0832	0.0286	0.3562	0.4017	-0.0322	0.0269	0.3338	0.3768
	θ_3	3.8	0.1352	0.0348	0.4471	0.4879	0.0597	0.0357	0.434	0.5001
	β_{11}	2	0.0371	0.0343	0.4618	0.4815	0.0094	0.0355	0.4432	0.4965
	β_{12}	0.7	0.1302	0.0298	0.3918	0.4188	0.1527	0.0259	0.384	0.3623
	β_{13}	0.05	0.0209	0.0282	0.3982	0.3959	0.059	0.0282	0.3904	0.3943
	β_{21}	2	0.12	0.0334	0.456	0.4686	-0.0498	0.0349	0.4417	0.488
	β_{22}	2.5	0.3352	0.0398	0.4841	0.5583	0.1469	0.0423	0.468	0.5926
	β_{23}	2.2	0.2023	0.0355	0.4681	0.4988	0.0999	0.0378	0.455	0.5287

Table 10.2.1.3.5a: Estimated average biases and average standard error over 200 simulations for the mixed threshold models.

			ML φ=0.3				ML φ=0.5			
M		TU	AB	SE	ASE	SEOS	AB	SE	ASE	SEOS
1	φ		-0.024	0.0105	0.1331	0.1479	0.0023	0.0098	0.1407	0.138
	θ_1	1.5	0.0167	0.0146	0.1928	0.2059	0.0264	0.0145	0.1956	0.2054
	θ_2	2.2	0.0383	0.015	0.2148	0.2124	0.041	0.0172	0.2175	0.2438
	θ_3	3.8	0.0285	0.0217	0.295	0.3065	0.079	0.0235	0.3015	0.3323
	β_{11}	2	-0.0404	0.0263	0.3644	0.3725	-0.0247	0.0286	0.3687	0.4047
	β_{12}	1.5	0.0435	0.0263	0.3557	0.3717	0.0886	0.029	0.3599	0.4102
	β_{13}	1.2	-0.0083	0.0251	0.3486	0.3552	0.0429	0.0288	0.3532	0.407
	β_{14}	0.5	0.0524	0.0247	0.3425	0.3496	0.0563	0.0243	0.3457	0.3436
	β_{15}	0.04	-0.0052	0.0256	0.3514	0.3627	-0.0092	0.0266	0.3553	0.3761
	β_{21}	2	-0.0507	0.0242	0.3571	0.3421	0.0059	0.0288	0.3631	0.4073
	β_{22}	2.5	0.0153	0.0228	0.3727	0.323	0.0893	0.0271	0.379	0.3837
	β_{23}	2.2	0.0319	0.0281	0.3653	0.3968	0.0374	0.0297	0.3695	0.4197
	β_{24}	2.8	0.0755	0.0282	0.3854	0.3992	0.0893	0.0295	0.3893	0.417
	β_{25}	1.5	0.052	0.0257	0.3488	0.3635	0.0174	0.0274	0.352	0.3873
			REML				REML			
1	φ		0.0467	0.0144	0.1579	0.203	0.064	0.0116	0.163	0.1636
	θ_1	1.5	0.0219	0.0149	0.1942	0.2114	0.0319	0.0148	0.1942	0.2079
	θ_2	2.2	0.0525	0.0175	0.2168	0.2474	0.0517	0.0167	0.2165	0.235
	θ_3	3.8	0.078	0.0245	0.3011	0.3461	0.0784	0.0254	0.3028	0.3573
	β_{11}	2	-0.0263	0.0295	0.3706	0.4175	0.0144	0.0286	0.3695	0.4018
	β_{12}	1.5	0.053	0.0253	0.3611	0.3576	0.0906	0.023	0.3598	0.3241
	β_{13}	1.2	0.0422	0.0287	0.3555	0.4058	0.0253	0.0271	0.3533	0.3807
	β_{14}	0.5	0.0155	0.0255	0.3488	0.3606	0.0613	0.0253	0.3468	0.3566
	β_{15}	0.04	0.0089	0.0242	0.3569	0.3422	-0.0063	0.0255	0.3551	0.3583
	β_{21}	2	-0.0041	0.0261	0.367	0.3697	-0.0053	0.0288	0.3732	0.4048
	β_{22}	2.5	0.0515	0.0256	0.3823	0.3619	0.0947	0.0288	0.3897	0.4055
	β_{23}	2.2	0.0153	0.029	0.3731	0.4108	0.0081	0.0302	0.3791	0.4254
	β_{24}	2.8	0.0949	0.0301	0.394	0.4261	0.0604	0.0313	0.3989	0.4399
	β_{25}	1.5	0.0199	0.0257	0.3565	0.3629	0.0008	0.0273	0.3627	0.3841

Table 10.2.1.3.5b: Estimated average biases and average standard error over 200 simulations for the mixed threshold models.

			ML φ=0.3				ML φ=0.5			
M		TU	AB	SE	ASE	SEOS	AB	SE	ASE	SEOS
2	φ		0.0034	0.0185	0.2147	0.2607	0.0452	0.0198	0.2363	0.2799
	θ_1	1.5	0.0294	0.0159	0.2216	0.2236	0.028	0.0184	0.221	0.2602
	θ_2	2.2	0.0506	0.0188	0.2549	0.264	0.0514	0.0217	0.2542	0.3064
	θ_3	3.8	0.0423	0.0254	0.3397	0.3579	0.0767	0.029	0.3412	0.4085
	β_{11}	2	-0.1052	0.0419	0.5366	0.5893	-0.0645	0.0434	0.5373	0.6126
	β_{12}	1.5	0.0373	0.0333	0.5241	0.4684	0.1381	0.0362	0.5277	0.5111
	β_{13}	1.2	-0.0223	0.0439	0.5237	0.6173	-0.0529	0.0385	0.5196	0.5424
	β_{14}	0.5	0.0201	0.0364	0.5194	0.5123	0.0926	0.0354	0.5173	0.4998
	β_{15}	0.04	-0.034	0.0402	0.5357	0.5656	-0.0021	0.0377	0.5368	0.5313
	β_{21}	2	-0.0268	0.0432	0.5301	0.6083	-0.078	0.0374	0.5289	0.5276
	β_{22}	2.5	0.1278	0.0371	0.5448	0.5222	0.0848	0.0369	0.548	0.5204
	β_{23}	2.2	0.0363	0.0396	0.5334	0.5578	-0.0277	0.0393	0.5397	0.5549
	β_{24}	2.8	0.1202	0.0402	0.5576	0.5656	0.0748	0.0443	0.5609	0.6248
	β_{25}	1.5	-0.048	0.0352	0.5143	0.495	0.0891	0.0414	0.5217	0.5843
			REML				REML			
2	φ		0.0753	0.0217	0.2538	0.3045	0.086	0.0198	0.264	0.2778
	θ_1	1.5	0.0092	0.0165	0.2202	0.2318	0.0088	0.0146	0.2202	0.2044
	θ_2	2.2	0.0185	0.0186	0.2533	0.2606	0.0473	0.0187	0.2544	0.2615
	θ_3	3.8	0.0857	0.027	0.3423	0.3788	0.0648	0.0263	0.3398	0.3683
	β_{11}	2	-0.1292	0.0433	0.5397	0.6081	-0.0455	0.0398	0.5423	0.5567
	β_{12}	1.5	0.0891	0.038	0.5298	0.5333	0.0758	0.0417	0.5273	0.5842
	β_{13}	1.2	-0.0323	0.0393	0.5239	0.551	-0.0638	0.039	0.5285	0.5466
	β_{14}	0.5	0.1086	0.0411	0.5241	0.5772	0.096	0.0363	0.5224	0.5089
	β_{15}	0.04	-0.001	0.0392	0.5377	0.5497	0.0446	0.0394	0.5352	0.5522
	β_{21}	2	-0.0323	0.0389	0.5301	0.5466	-0.0508	0.041	0.5382	0.5737
	β_{22}	2.5	-0.0115	0.0374	0.5425	0.5245	0.0582	0.037	0.5485	0.5176
	β_{23}	2.2	0.0132	0.0397	0.5348	0.5578	0.0114	0.0389	0.5386	0.5444
	β_{24}	2.8	0.1502	0.0393	0.5596	0.552	0.1076	0.0406	0.5603	0.568
	β_{25}	1.5	0.0023	0.0369	0.5162	0.5185	0.0694	0.0388	0.5238	0.5426

Table 10.2.1.3.5c: Estimated average biases and average standard error over 200 simulations for the mixed threshold models.

			ML φ=0.3				ML φ=0.5			
		TU	AB	SE	ASE	SEOS	AB	SE	ASE	SEOS
3	φ		-0.0077	0.0136	0.141	0.1923	-0.0285	0.0113	0.1363	0.1601
	θ_1	1.5	-0.0008	0.0138	0.1952	0.1947	0.0082	0.0136	0.195	0.192
	θ_2	2.2	0.0225	0.0172	0.2248	0.2425	0.0254	0.0168	0.2241	0.2378
	θ_3	3.8	0.0416	0.03	0.3554	0.4235	0.0571	0.0274	0.3542	0.3868
	β_{11}	2	-0.0958	0.0281	0.3903	0.3959	-0.0709	0.0297	0.3919	0.4206
	β_{12}	1.5	-0.0195	0.0266	0.374	0.3749	-0.0313	0.0254	0.3728	0.3596
	β_{13}	1.2	-0.0831	0.0254	0.3654	0.3579	-0.0785	0.029	0.3644	0.4103
	β_{14}	0.5	-0.0672	0.0268	0.3532	0.3777	-0.0322	0.0243	0.3518	0.3441
	β_{15}	0.04	-0.1555	0.0243	0.3578	0.3432	-0.067	0.0237	0.3533	0.3357
	β_{21}	2	-0.0439	0.0281	0.3913	0.3958	-0.0824	0.0316	0.3886	0.4476
	β_{22}	2.5	-0.0518	0.0267	0.4109	0.377	0.0231	0.0239	0.4134	0.3387
	β_{23}	2.2	-0.0382	0.0305	0.3989	0.4307	-0.0294	0.0293	0.398	0.4147
	β_{24}	2.8	-0.0107	0.0318	0.4303	0.4485	0.0461	0.0301	0.4288	0.4257
	β_{25}	1.5	-0.0455	0.0277	0.3749	0.3911	-0.0033	0.0242	0.3726	0.3427
			REML				REML			
3	φ		0.0515	0.0143	0.1678	0.2022	0.0729	0.0129	0.1744	0.1816
	θ_1	1.5	0.0366	0.0142	0.1981	0.2007	0.0268	0.0149	0.1991	0.2106
	θ_2	2.2	0.0682	0.017	0.2286	0.2397	0.0577	0.018	0.2294	0.2533
	θ_3	3.8	0.146	0.0269	0.3715	0.3799	0.1236	0.0281	0.3611	0.3967
	β_{11}	2	-0.1076	0.0306	0.398	0.4315	-0.0044	0.0301	0.4022	0.4247
	β_{12}	1.5	-0.0061	0.0255	0.3827	0.3597	0.0273	0.0247	0.3854	0.3478
	β_{13}	1.2	-0.0669	0.0266	0.3733	0.3746	-0.0544	0.0297	0.3748	0.4196
	β_{14}	0.5	-0.0535	0.026	0.3605	0.3672	-0.0401	0.0244	0.3611	0.3447
	β_{15}	0.04	-0.0922	0.0262	0.3649	0.3699	-0.0984	0.0256	0.3656	0.3607
	β_{21}	2	-0.0601	0.0285	0.399	0.4016	0.0011	0.0297	0.4059	0.4192
	β_{22}	2.5	0.0657	0.0271	0.424	0.3824	0.0378	0.0292	0.4251	0.4116
	β_{23}	2.2	-0.0171	0.0289	0.4065	0.4082	0.0183	0.0327	0.4119	0.4616
	β_{24}	2.8	0.0673	0.0283	0.4395	0.3993	0.1126	0.0331	0.4452	0.4663
	β_{25}	1.5	-0.0469	0.0273	0.3811	0.3847	-0.0173	0.0252	0.3862	0.3554

Table 10.2.1.3.5d: Estimated average biases and average standard error over 200 simulations for the mixed threshold models.

			ML φ=0.3				ML φ=0.5			
M		TU	AB	SE	ASE	SEOS	AB	SE	ASE	SEOS
4	φ		-0.008	0.0129	0.1411	0.1821	-0.0051	0.011	0.1432	0.154
	θ_1	1.5	0.008	0.0171	0.2315	0.2408	0.023	0.0197	0.2296	0.2745
	θ_2	2.2	0.0208	0.0194	0.2555	0.2739	0.0774	0.0228	0.2557	0.3177
	θ_3	3.8	0.0336	0.0229	0.3266	0.3229	0.0754	0.0282	0.3286	0.3936
	β_{11}	2	-0.0095	0.0314	0.3997	0.4429	0.0697	0.0385	0.399	0.5379
	β_{12}	1.5	0.1301	0.0299	0.3882	0.4217	0.0742	0.0312	0.385	0.4356
	β_{13}	1.2	0.0383	0.0292	0.3759	0.4121	-0.0019	0.0319	0.3747	0.4458
	β_{14}	0.5	0.1244	0.0259	0.3655	0.3659	0.1003	0.0318	0.3654	0.444
	β_{15}	0.04	0.0626	0.0298	0.3856	0.4205	0.0666	0.0302	0.3831	0.4224
	β_{21}	2	0.0394	0.029	0.3962	0.4092	0.0037	0.0353	0.3963	0.4934
	β_{22}	2.5	0.1469	0.0284	0.4114	0.4013	0.2056	0.0357	0.4133	0.4988
	β_{23}	2.2	0.0945	0.0295	0.4016	0.4158	0.1335	0.0332	0.4042	0.4631
	β_{24}	2.8	0.1667	0.0321	0.4204	0.4522	0.1915	0.0344	0.4214	0.4806
	β_{25}	1.5	0.1181	0.0268	0.3813	0.3783	0.0721	0.03	0.3826	0.4183
			REML				REML			
4	φ	0.3	0.0546	0.0153	0.1684	0.2154	0.0662	0.0131	0.1723	0.1845
	θ_1	1.5	0.0234	0.0162	0.2318	0.2283	0.0632	0.018	0.244	0.2537
	θ_2	2.2	0.0697	0.019	0.2571	0.2686	0.1047	0.0199	0.2689	0.2808
	θ_3	3.8	0.0775	0.0229	0.3289	0.3236	0.1571	0.0248	0.3417	0.3491
	β_{11}	2	0.037	0.0284	0.403	0.4008	0.1032	0.0356	0.4134	0.5022
	β_{12}	1.5	0.1804	0.0291	0.392	0.4109	0.1937	0.029	0.4008	0.4093
	β_{13}	1.2	0.0828	0.0288	0.3789	0.4056	0.1889	0.0335	0.391	0.4719
	β_{14}	0.5	0.1216	0.0274	0.3685	0.3863	0.1086	0.0279	0.3761	0.3939
	β_{15}	0.04	0.0977	0.0281	0.3842	0.3959	0.0596	0.0276	0.3883	0.3889
	β_{21}	2	0.0659	0.0307	0.4027	0.4333	0.1168	0.032	0.4153	0.4517
	β_{22}	2.5	0.1548	0.0301	0.417	0.4248	0.2159	0.0324	0.4295	0.4565
	β_{23}	2.2	0.1294	0.03	0.4096	0.423	0.1819	0.0327	0.4212	0.4618
	β_{24}	2.8	0.1622	0.0327	0.4254	0.4607	0.1693	0.0313	0.4371	0.4415
	β_{25}	1.5	0.0973	0.0287	0.3874	0.4043	0.1578	0.0282	0.4	0.3975

10.3 THE TWO COMPONENTS

For longitudinal models in section 7, a second random component is introduced to allow for a possible increase in variance. Now, this model is investigated in detail through simulation results. The model for the η_{it} is given by

10.3.1 $\eta_{it} = \beta_{j(i)t} + u_{1i} + z_t u_{2i}$

where u_{1i}, u_{2i} are independent normal variables with zero means and variances φ_1, φ_2 respectively and $z_t = 0$, t=1 ; $z_t = 1$, t=2,3,...,n. For n=3, n=5, and for each of the threshold models given in section 5.2 of chapter 5, again three different data sets are generated. The simulation results are presented in the tables 10.3.2.1.ij for $\varphi_1 = 0.5$, $\varphi_2 = 0.3$ and $\varphi_1 = 1$, $\varphi_2 = 0.3$.

n=3 and **n=5** for y=0,1,2 **(Tables 10.3.2.1.3a,b and 10.3.2.1.5a,b,c,d):**

The results of the simulations show that the ML estimators of parameters and variance components φ_1, φ_2 are negatively biased. The REML method reduces such biases and the biases of REML estimators are often individually not significant and the relative magnitudes of the parameters are preserved in the estimates. As the variances, φ_1 and φ_2, of variance components increases, the biases of estimators of parameters and variance components φ_1, φ_2 tends to increase in both ML and REML methods. The average of asymptotic standard error of estimators (ASE) agree quite closely with the standard error over simulations in both ML and REML methods for all four threshold models in section 5.2 of chapter 5. The biases of ML and REML estimators of variance components φ_1 and φ_2 are reduced by increasing the number of observations for each subject. Indeed the biases of estimators φ_1 and φ_2 are not significant for some threshold models.

Table 10.3.2.1.3a: Estimated average biases and average standard error over 200 simulations for the mixed threshold models.

			ML $\varphi_1 = 0.5$, $\varphi_2 = 0.3$				ML $\varphi_1 = 1$, $\varphi_2 = 0.3$			
M		TU	AB	SE	ASE	SEOS	AB	SE	ASE	SEOS
1	φ_1		-0.152	0.018	0.245	0.252	-0.386	0.028	0.339	0.394
	φ_2		-0.115	0.018	0.201	0.255	-0.103	0.02	0.228	0.284
	θ_1	1.5	-0.051	0.018	0.242	0.253	-0.07	0.017	0.243	0.236
	β_{11}	2	-0.215	0.027	0.42	0.373	-0.268	0.029	0.445	0.406
	β_{12}	.7	0.055	0.027	0.383	0.369	0.015	0.027	0.414	0.38
	β_{13}	0.05	0.025	0.023	0.38	0.326	0.032	0.028	0.413	0.391
	β_{21}	2	-0.17	0.027	0.423	0.379	-0.24	0.032	0.444	0.443
	β_{22}	2.5	-0.163	0.035	0.497	0.493	-0.217	0.033	0.514	0.453
	β_{23}	2.2	-0.187	0.034	0.459	0.467	-0.212	0.039	0.486	0.537
2	φ_1		-0.116	0.031	0.377	0.424	-0.324	0.038	0.537	0.53
	φ_2		0.05	0.037	0.418	0.51	0.016	0.037	0.384	0.511
	θ_1	1.5	-0.074	0.021	0.278	0.29	-0.079	0.02	0.279	0.274
	β_{11}	2	-0.209	0.044	0.609	0.608	-0.275	0.038	0.606	0.534
	β_{12}	.7	0.09	0.041	0.57	0.558	0.066	0.038	0.575	0.533
	β_{13}	0.05	-0.035	0.05	0.58	0.685	0.009	0.041	0.577	0.568
	β_{21}	2	-0.185	0.047	0.602	0.64	-0.204	0.048	0.629	0.671
	β_{22}	2.5	-0.131	0.048	0.679	0.658	-0.082	0.046	0.708	0.637
	β_{23}	2.2	-0.138	0.048	0.642	0.663	-0.201	0.047	0.659	0.649
			REML				REML			
1	φ_1		-0.098	0.023	0.288	0.31	-0.222	0.03	0.41	0.419
	φ_2		0.029	0.026	0.325	0.353	-0.041	0.024	0.284	0.339
	θ_1	1.5	0.004	0.021	0.255	0.282	-0.033	0.018	0.251	0.254
	β_{11}	2	-0.055	0.031	0.44	0.428	-0.159	0.032	0.47	0.447
	β_{12}	.7	0.106	0.026	0.404	0.362	0.014	0.029	0.437	0.408
	β_{13}	0.05	0.022	0.027	0.4	0.366	0.017	0.031	0.439	0.438
	β_{21}	2	-0.1	0.034	0.439	0.461	-0.197	0.031	0.464	0.428
	β_{22}	2.5	-0.033	0.037	0.531	0.508	-0.135	0.036	0.545	0.503
	β_{23}	2.2	-0.077	0.035	0.489	0.482	-0.192	0.038	0.506	0.531
2	φ_1		0.005	0.037	0.463	0.511	-0.09	0.05	0.665	0.706
	φ_2		0.125	0.043	0.527	0.594	0.18	0.047	0.596	0.663
	θ_1	1.5	0.031	0.023	0.291	0.31	0.009	0.021	0.293	0.295
	β_{11}	2	-0.135	0.044	0.604	0.603	-0.159	0.049	0.643	0.692
	β_{12}	.7	0.197	0.038	0.571	0.519	0.163	0.042	0.615	0.587
	β_{13}	0.05	-0.05	0.039	0.573	0.535	-0.027	0.047	0.621	0.668
	β_{21}	2	-0.083	0.046	0.625	0.63	-0.155	0.042	0.628	0.584
	β_{22}	2.5	0.033	0.05	0.719	0.686	0.043	0.051	0.729	0.719
	β_{23}	2.2	-0.029	0.054	0.676	0.739	-0.136	0.045	0.673	0.628

Table 10.3.2.1.3b: Estimated average biases and average standard error over 200 simulations for the mixed threshold models.

			ML $\varphi_1 = 0.5$, $\varphi_2 = 0.3$				ML $\varphi_1 = 1$, $\varphi_2 = 0.3$			
M		TU	AB	SE	ASE	SEOS	AB	SE	ASE	SEOS
3	φ_1		-0.119	0.023	0.277	0.323	-0.332	0.029	0.377	0.416
	φ_2		-0.089	0.023	0.224	0.325	-0.104	0.021	0.238	0.291
	θ_1	1.5	-0.061	0.019	0.248	0.262	-0.095	0.019	0.245	0.262
	β_{11}	2	-0.187	0.037	0.484	0.517	-0.32	0.033	0.494	0.469
	β_{12}	.7	0	0.029	0.411	0.405	-0.115	0.029	0.433	0.415
	β_{13}	0.05	-0.103	0.03	0.398	0.416	-0.066	0.034	0.431	0.474
	β_{21}	2	-0.241	0.036	0.479	0.502	-0.347	0.037	0.493	0.528
	β_{22}	2.5	-0.178	0.038	0.567	0.525	-0.21	0.046	0.592	0.649
	β_{23}	2.2	-0.196	0.041	0.525	0.571	-0.329	0.04	0.532	0.572
4	φ_1		-0.247	0.017	0.194	0.218	-0.521	0.019	0.28	0.263
	φ_2		-0.149	0.017	0.176	0.219	-0.222	0.011	0.118	0.151
	θ_1	1.5	-0.147	0.018	0.264	0.238	-0.22	0.018	0.24	0.249
	β_{11}	2	-0.197	0.028	0.43	0.369	-0.282	0.031	0.433	0.417
	β_{12}	.7	0.064	0.03	0.386	0.387	0.043	0.027	0.396	0.367
	β_{13}	0.05	0.082	0.031	0.398	0.403	0.112	0.03	0.406	0.399
	β_{21}	2	-0.236	0.032	0.42	0.423	-0.416	0.031	0.42	0.412
	β_{22}	2.5	-0.34	0.028	0.476	0.37	-0.438	0.03	0.485	0.405
	β_{23}	2.2	-0.29	0.03	0.445	0.395	-0.405	0.032	0.448	0.43
			REML				REML			
3	φ_1		0.1	0.036	0.374	0.507	-0.153	0.039	0.477	0.554
	φ_2		-0.003	0.029	0.302	0.407	0.032	0.029	0.384	0.415
	θ_1	1.5	0.023	0.019	0.259	0.267	-0.008	0.021	0.258	0.291
	β_{11}	2	-0.185	0.034	0.491	0.474	-0.212	0.034	0.518	0.479
	β_{12}	.7	-0.021	0.032	0.436	0.445	-0.013	0.034	0.469	0.48
	β_{13}	0.05	-0.045	0.028	0.426	0.39	-0.073	0.03	0.463	0.422
	β_{21}	2	-0.182	0.035	0.5	0.497	-0.271	0.037	0.507	0.519
	β_{22}	2.5	-0.085	0.043	0.591	0.601	-0.123	0.048	0.613	0.67
	β_{23}	2.2	-0.213	0.037	0.538	0.525	-0.271	0.043	0.556	0.603
4	φ_1		-0.145	0.019	0.262	0.248	-0.437	0.029	0.341	0.376
	φ_2		-0.095	0.022	0.232	0.276	-0.069	0.026	0.27	0.343
	θ_1	1.5	-0.054	0.021	0.278	0.263	-0.121	0.022	0.262	0.287
	β_{11}	2	-0.101	0.032	0.451	0.415	-0.19	0.036	0.461	0.471
	β_{12}	.7	0.112	0.031	0.403	0.4	0.094	0.029	0.429	0.383
	β_{13}	0.05	0.102	0.032	0.411	0.413	0.098	0.032	0.438	0.417
	β_{21}	2	-0.153	0.031	0.442	0.395	-0.262	0.032	0.444	0.41
	β_{22}	2.5	-0.184	0.035	0.518	0.444	-0.323	0.032	0.519	0.412
	β_{23}	2.2	-0.151	0.035	0.481	0.448	-0.282	0.033	0.483	0.434

Table 10.3.2.1.5a: Estimated average biases and average standard error over 200 simulations for the mixed threshold models.

			ML $\varphi_1 = 0.5$, $\varphi_2 = 0.3$				ML $\varphi_1 = 1$, $\varphi_2 = 0.3$			
M		TU	AB	SE	ASE	SEOS	AB	SE	ASE	SEOS
1	φ_1		-0.094	0.023	0.25	0.307	-0.209	0.031	0.368	0.421
	φ_2		0.049	0.025	0.275	0.327	0.024	0.026	0.278	0.343
	θ_1	1.5	-0.003	0.015	0.194	0.194	0.01	0.015	0.201	0.206
	β_{11}	2	-0.145	0.032	0.416	0.432	-0.135	0.037	0.461	0.494
	β_{12}	1.5	-0.011	0.029	0.429	0.384	0.025	0.038	0.471	0.505
	β_{13}	1.2	-0.039	0.03	0.416	0.4	-0.028	0.035	0.456	0.473
	β_{14}	0.5	0.052	0.029	0.404	0.389	0.049	0.036	0.445	0.477
	β_{15}	0.04	0.061	0.029	0.408	0.389	-0.001	0.035	0.451	0.468
	β_{21}	2	-0.13	0.029	0.408	0.394	-0.145	0.035	0.447	0.465
	β_{22}	2.5	-0.045	0.033	0.504	0.434	-0.122	0.039	0.528	0.526
	β_{23}	2.2	-0.102	0.034	0.463	0.455	-0.144	0.041	0.495	0.547
	β_{24}	2.8	-0.111	0.035	0.541	0.466	-0.139	0.04	0.565	0.536
	β_{25}	1.5	-0.035	0.03	0.416	0.406	-0.073	0.034	0.451	0.46
			REML				REML			
1	φ_1		-0.012	0.024	0.299	0.322	-0.104	0.037	0.422	0.504
	φ_2		0.026	0.022	0.288	0.294	0.067	0.028	0.326	0.379
	θ_1	1.5	0.013	0.015	0.197	0.196	0.011	0.014	0.202	0.193
	β_{11}	2	-0.067	0.032	0.43	0.418	-0.08	0.031	0.474	0.419
	β_{12}	1.5	0.068	0.033	0.438	0.437	0.053	0.033	0.486	0.444
	β_{13}	1.2	-0.034	0.032	0.421	0.418	-0.03	0.03	0.469	0.403
	β_{14}	0.5	0.035	0.03	0.41	0.4	0.041	0.033	0.459	0.456
	β_{15}	0.04	0.012	0.034	0.416	0.445	0.028	0.031	0.463	0.425
	β_{21}	2	-0.049	0.036	0.427	0.476	-0.161	0.033	0.452	0.448
	β_{22}	2.5	-0.006	0.037	0.514	0.489	-0.04	0.036	0.545	0.492
	β_{23}	2.2	-0.04	0.035	0.473	0.457	-0.085	0.039	0.507	0.529
	β_{24}	2.8	-0.026	0.035	0.554	0.465	-0.133	0.035	0.569	0.48
	β_{25}	1.5	-0.01	0.032	0.423	0.422	-0.022	0.032	0.462	0.443

Table 10.3.2.1.5b: Estimated average biases and average standard error over 200 simulations for the mixed threshold models.

			ML $\varphi_1 = 0.5$, $\varphi_2 = 0.3$				ML $\varphi_1 = 1$, $\varphi_2 = 0.3$			
M		TU	AB	SE	ASE	SEOS	AB	SE	ASE	SEOS
2	φ_1		-0.139	0.026	0.317	0.359	-0.262	0.038	0.495	0.524
	φ_2		0.04	0.027	0.348	0.385	0.105	0.038	0.401	0.523
	θ_1	1.5	0.013	0.015	0.223	0.215	-0.019	0.016	0.224	0.223
	β_{11}	2	-0.102	0.042	0.598	0.588	-0.161	0.047	0.62	0.649
	β_{12}	1.5	-0.045	0.04	0.583	0.568	0.031	0.039	0.615	0.533
	β_{13}	1.2	-0.062	0.043	0.571	0.608	-0.017	0.041	0.603	0.565
	β_{14}	0.5	0.027	0.043	0.566	0.603	0.121	0.043	0.592	0.592
	β_{15}	0.04	-0.058	0.044	0.574	0.616	0.04	0.046	0.601	0.634
	β_{21}	2	-0.09	0.041	0.582	0.582	-0.144	0.046	0.615	0.635
	β_{22}	2.5	0.022	0.049	0.679	0.691	-0.036	0.057	0.705	0.788
	β_{23}	2.2	0.019	0.047	0.639	0.659	-0.106	0.048	0.659	0.658
	β_{24}	2.8	-0.006	0.045	0.715	0.635	-0.063	0.055	0.741	0.754
	β_{25}	1.5	-0.001	0.043	0.572	0.598	-0.018	0.048	0.613	0.67
			REML				REML			
2	φ_1		-0.03	0.032	0.371	0.451	-0.186	0.039	0.556	0.546
	φ_2		0.046	0.03	0.361	0.41	0.165	0.037	0.48	0.513
	θ_1	1.5	0.054	0.015	0.228	0.205	0.02	0.016	0.229	0.228
	β_{11}	2	-0.061	0.049	0.613	0.674	-0.096	0.047	0.629	0.649
	β_{12}	1.5	0.162	0.041	0.603	0.573	0.089	0.042	0.632	0.585
	β_{13}	1.2	-0.047	0.039	0.579	0.546	-0.033	0.045	0.613	0.631
	β_{14}	0.5	0.143	0.038	0.569	0.525	0.117	0.042	0.602	0.589
	β_{15}	0.04	0.099	0.042	0.578	0.584	0.028	0.043	0.61	0.6
	β_{21}	2	-0.029	0.045	0.597	0.631	-0.115	0.047	0.621	0.651
	β_{22}	2.5	0.114	0.048	0.696	0.665	-0.002	0.047	0.706	0.658
	β_{23}	2.2	-0.005	0.049	0.638	0.678	-0.017	0.05	0.674	0.699
	β_{24}	2.8	0.095	0.047	0.733	0.657	0.147	0.06	0.786	0.834
	β_{25}	1.5	0.037	0.044	0.583	0.616	0.036	0.041	0.618	0.573

Table 10.3.2.1.5c: Estimated average biases and average standard error over 200 simulations for the mixed threshold models.

			ML $\varphi_1 = 0.5$, $\varphi_2 = 0.3$				ML $\varphi_1 = 1$, $\varphi_2 = 0.3$			
M		TU	AB	SE	ASE	SEOS	AB	SE	ASE	SEOS
3	φ_1		-0.068	0.024	0.28	0.334	-0.211	0.032	0.392	0.448
	φ_2		0.016	0.022	0.274	0.312	0	0.024	0.294	0.337
	θ_1	1.5	-0.003	0.014	0.197	0.199	-0.024	0.015	0.2	0.208
	β_{11}	2	-0.212	0.034	0.458	0.47	-0.198	0.039	0.499	0.542
	β_{12}	1.5	-0.065	0.029	0.454	0.403	-0.071	0.038	0.489	0.527
	β_{13}	1.2	-0.117	0.031	0.434	0.438	-0.121	0.038	0.47	0.534
	β_{14}	0.5	0.007	0.028	0.412	0.397	-0.013	0.034	0.454	0.47
	β_{15}	0.04	-0.083	0.032	0.417	0.454	-0.072	0.036	0.461	0.504
	β_{21}	2	-0.156	0.035	0.466	0.491	-0.24	0.035	0.49	0.492
	β_{22}	2.5	-0.09	0.04	0.563	0.553	-0.141	0.041	0.577	0.568
	β_{23}	2.2	-0.14	0.04	0.517	0.557	-0.248	0.042	0.531	0.581
	β_{24}	2.8	-0.063	0.046	0.62	0.639	-0.122	0.042	0.625	0.59
	β_{25}	1.5	-0.139	0.029	0.451	0.403	-0.159	0.035	0.482	0.488
			REML				REML			
3	φ_1		-0.052	0.023	0.318	0.325	-0.112	0.035	0.457	0.481
	φ_2		0.128	0.027	0.354	0.384	0.089	0.028	0.37	0.394
	θ_1	1.5	0.008	0.015	0.2	0.208	-0.022	0.014	0.203	0.188
	β_{11}	2	-0.163	0.033	0.469	0.467	-0.226	0.038	0.505	0.52
	β_{12}	1.5	-0.015	0.03	0.471	0.416	-0.102	0.035	0.504	0.491
	β_{13}	1.2	-0.105	0.031	0.449	0.438	-0.137	0.035	0.485	0.483
	β_{14}	0.5	-0.03	0.03	0.429	0.416	-0.053	0.032	0.47	0.436
	β_{15}	0.04	-0.055	0.035	0.433	0.485	-0.134	0.034	0.477	0.469
	β_{21}	2	-0.056	0.033	0.479	0.467	-0.173	0.041	0.506	0.563
	β_{22}	2.5	-0.004	0.044	0.585	0.621	-0.061	0.043	0.604	0.6
	β_{23}	2.2	-0.11	0.042	0.53	0.588	-0.213	0.04	0.544	0.558
	β_{24}	2.8	0.077	0.045	0.649	0.631	-0.068	0.042	0.641	0.58
	β_{25}	1.5	-0.131	0.037	0.465	0.522	-0.069	0.032	0.499	0.447

Table 10.3.2.1.5d: Estimated average biases and average standard error over 200 simulations for the mixed threshold models.

			ML $\varphi_1 = 0.5$, $\varphi_2 = 0.3$				ML $\varphi_1 = 1$, $\varphi_2 = 0.3$			
M		TU	AB	SE	ASE	SEOS	AB	SE	ASE	SEOS
4	φ_1		-0.183	0.021	0.215	0.245	-0.409	0.028	0.296	0.34
	φ_2		-0.043	0.022	0.22	0.257	-0.067	0.023	0.214	0.282
	θ_1	1.5	-0.068	0.021	0.215	0.247	-0.088	0.018	0.206	0.216
	β_{11}	2	-0.122	0.032	0.426	0.369	-0.18	0.034	0.441	0.414
	β_{12}	1.5	0.044	0.038	0.431	0.438	0.012	0.032	0.446	0.393
	β_{13}	1.2	0.051	0.044	0.421	0.512	0.023	0.034	0.433	0.414
	β_{14}	0.5	0.133	0.039	0.408	0.45	0.073	0.034	0.428	0.415
	β_{15}	0.04	0.123	0.038	0.423	0.439	0.178	0.038	0.435	0.458
	β_{21}	2	-0.152	0.038	0.405	0.437	-0.188	0.04	0.441	0.481
	β_{22}	2.5	-0.202	0.034	0.485	0.389	-0.256	0.032	0.512	0.392
	β_{23}	2.2	-0.158	0.037	0.449	0.426	-0.284	0.033	0.468	0.403
	β_{24}	2.8	-0.237	0.032	0.527	0.372	-0.413	0.036	0.536	0.437
	β_{25}	1.5	-0.056	0.031	0.402	0.362	-0.111	0.033	0.432	0.407
			REML				REML			
4	φ_1		-0.144	0.028	0.245	0.322	-0.232	0.033	0.386	0.406
	φ_2		0.065	0.028	0.284	0.313	0.013	0.029	0.293	0.354
	θ_1	1.5	0.041	0.022	0.228	0.247	-0.042	0.019	0.217	0.234
	β_{11}	2	-0.067	0.037	0.434	0.415	-0.094	0.036	0.474	0.441
	β_{12}	1.5	0.175	0.036	0.454	0.406	0.088	0.042	0.487	0.504
	β_{13}	1.2	0.081	0.038	0.436	0.432	0.044	0.037	0.468	0.446
	β_{14}	0.5	0.185	0.042	0.425	0.472	0.149	0.039	0.458	0.473
	β_{15}	0.04	0.139	0.038	0.435	0.433	0.096	0.043	0.471	0.52
	β_{21}	2	-0.061	0.041	0.416	0.464	-0.114	0.038	0.458	0.465
	β_{22}	2.5	-0.046	0.038	0.516	0.427	-0.168	0.043	0.547	0.527
	β_{23}	2.2	-0.089	0.038	0.467	0.428	-0.172	0.043	0.509	0.517
	β_{24}	2.8	-0.183	0.036	0.542	0.404	-0.276	0.044	0.577	0.53
	β_{25}	1.5	-0.004	0.037	0.422	0.424	-0.069	0.036	0.454	0.435

n=3 and **n=5** for y=0,1,2,3 (**Tables 10.3.2.2.3a,b,c**) and y=0,1,2,3,4 (**Tables 10.3.2.3.3a,b,c,** and **10.3.2.3.5a,b,c,d**):

The results of simulations support the conclusions in the previous section (y=0,1,2). Furthermore, the estimation of variance components φ_1 and φ_2 are improved in both ML and REML methods for all four threshold models in section 5.2 of chapter 5. The biases of ML and REML estimatores of φ_1, φ_2 are smaller than previous section.

We also developed simulation for model 10.3.1 for all four threshold models of section 5.2 of chapter 5 for $\varphi_1 = 1$ and $\varphi_2 = 0.5$. The results of simulations for φ_1 and φ_2 are summarised in Figures 10.3a, 10.3b, 10.3c and 10.3d, 10.3e, 10.3f for ML and REML respectively.

Table 10.3.2.2.3a: Estimated average biases and average standard error over 200 simulations for the mixed threshold models.

			ML $\varphi_1 = 0.5$, $\varphi_2 = 0.3$				ML $\varphi_1 = 1$, $\varphi_2 = 0.3$			
M		TU	AB	SE	ASE	SEOS	AB	SE	ASE	SEOS
1	φ_1		-0.089	0.021	0.251	0.288	-0.277	0.03	0.344	0.416
	φ_2		-0.061	0.021	0.228	0.293	-0.074	0.022	0.228	0.309
	θ_1	1.5	-0.038	0.02	0.243	0.283	-0.085	0.017	0.241	0.235
	θ_2	2.2	-0.028	0.023	0.277	0.325	-0.097	0.019	0.276	0.261
	β_{11}	2	-0.092	0.033	0.405	0.463	-0.197	0.031	0.431	0.441
	β_{12}	.7	0.052	0.027	0.386	0.38	0.024	0.028	0.418	0.393
	β_{13}	0.05	0.025	0.026	0.387	0.361	-0.031	0.029	0.424	0.41
	β_{21}	2	-0.12	0.03	0.418	0.422	-0.23	0.028	0.436	0.397
	β_{22}	2.5	-0.059	0.038	0.489	0.531	-0.144	0.037	0.506	0.515
	β_{23}	2.2	-0.061	0.029	0.408	0.412	-0.136	0.029	0.428	0.408
2	φ_1		-0.039	0.034	0.384	0.465	-0.331	0.039	0.467	0.551
	φ_2		0.042	0.039	0.363	0.535	0.046	0.04	0.386	0.562
	θ_1	1.5	-0.026	0.021	0.282	0.284	-0.069	0.021	0.278	0.288
	θ_2	2.2	-0.036	0.025	0.327	0.347	-0.079	0.026	0.323	0.359
	β_{11}	2	-0.082	0.046	0.582	0.624	-0.216	0.04	0.576	0.555
	β_{12}	.7	0.13	0.046	0.56	0.623	0.118	0.038	0.563	0.532
	β_{13}	0.05	-0.058	0.042	0.567	0.574	0.014	0.038	0.57	0.533
	β_{21}	2	-0.214	0.041	0.583	0.563	-0.234	0.042	0.599	0.584
	β_{22}	2.5	0.01	0.051	0.672	0.704	-0.06	0.053	0.681	0.736
	β_{23}	2.2	-0.082	0.043	0.574	0.592	-0.098	0.042	0.589	0.583
			REML				REML			
1	φ_1		-0.015	0.022	0.297	0.307	-0.059	0.036	0.429	0.515
	φ_2		0.066	0.03	0.315	0.418	0.015	0.026	0.306	0.369
	θ_1	1.5	-0.002	0.019	0.251	0.261	-0.004	0.02	0.255	0.29
	θ_2	2.2	0.018	0.023	0.285	0.327	0.014	0.025	0.291	0.358
	β_{11}	2	-0.107	0.032	0.414	0.452	-0.095	0.032	0.462	0.456
	β_{12}	.7	0.07	0.028	0.406	0.391	0.107	0.028	0.45	0.391
	β_{13}	0.05	-0.083	0.028	0.412	0.395	0.02	0.029	0.455	0.407
	β_{21}	2	-0.12	0.032	0.426	0.45	-0.122	0.035	0.463	0.493
	β_{22}	2.5	0.038	0.039	0.514	0.557	-0.005	0.042	0.541	0.591
	β_{23}	2.2	-0.024	0.032	0.428	0.446	0.01	0.032	0.461	0.45

Table 10.3.2.2.3b: Estimated average biases and average standard error over 200 simulations for the mixed threshold models.

			ML $\varphi_1 = 0.5$, $\varphi_2 = 0.3$				ML $\varphi_1 = 1$, $\varphi_2 = 0.3$			
M		TU	AB	SE	ASE	SEOS	AB	SE	ASE	SEOS
3	φ_1		-0.056	0.025	0.266	0.354	-0.299	0.029	0.348	0.405
	φ_2		-0.106	0.019	0.213	0.268	-0.106	0.019	0.215	0.275
	θ_1	1.5	-0.031	0.019	0.248	0.262	-0.086	0.018	0.243	0.249
	θ_2	2.2	-0.032	0.023	0.289	0.317	-0.114	0.022	0.285	0.309
	β_{11}	2	-0.171	0.037	0.446	0.522	-0.294	0.034	0.463	0.481
	β_{12}	.7	-0.024	0.03	0.404	0.423	-0.103	0.029	0.427	0.415
	β_{13}	0.05	-0.046	0.028	0.397	0.395	-0.107	0.028	0.429	0.391
	β_{21}	2	-0.256	0.033	0.455	0.468	-0.372	0.032	0.468	0.45
	β_{22}	2.5	-0.109	0.038	0.539	0.527	-0.308	0.042	0.536	0.588
	β_{23}	2.2	-0.122	0.033	0.436	0.461	-0.294	0.032	0.447	0.456
4	φ_1		-0.197	0.017	0.214	0.234	-0.451	0.025	0.294	0.347
	φ_2		-0.076	0.02	0.216	0.285	-0.082	0.023	0.213	0.322
	θ_1	1.5	-0.137	0.021	0.262	0.288	-0.162	0.018	0.251	0.251
	θ_2	2.2	-0.177	0.024	0.294	0.338	-0.214	0.022	0.286	0.315
	β_{11}	2	-0.137	0.031	0.415	0.431	-0.171	0.032	0.429	0.449
	β_{12}	.7	0.108	0.028	0.396	0.397	0.094	0.032	0.417	0.445
	β_{13}	0.05	0.089	0.031	0.41	0.434	0.126	0.031	0.43	0.442
	β_{21}	2	-0.217	0.033	0.415	0.465	-0.232	0.03	0.436	0.415
	β_{22}	2.5	-0.158	0.036	0.486	0.507	-0.264	0.037	0.505	0.52
	β_{23}	2.2	-0.031	0.032	0.408	0.446	-0.107	0.027	0.427	0.385
			REML							
2	φ_1		-0.01	0.034	0.422	0.478	-0.132	0.042	0.613	0.584
	φ_2		0.375	0.061	0.587	0.849	0.229	0.047	0.626	0.656
	θ_1	1.5	0.036	0.023	0.293	0.317	-0.043	0.02	0.285	0.287
	θ_2	2.2	0.064	0.028	0.339	0.384	-0.01	0.025	0.334	0.353
	β_{11}	2	-0.003	0.045	0.59	0.63	-0.192	0.041	0.596	0.575
	β_{12}	.7	0.15	0.038	0.584	0.526	0.119	0.042	0.594	0.588
	β_{13}	0.05	-0.052	0.044	0.595	0.612	-0.03	0.04	0.604	0.565
	β_{21}	2	-0.17	0.042	0.583	0.583	-0.206	0.042	0.61	0.586
	β_{22}	2.5	0.16	0.06	0.699	0.836	-0.004	0.052	0.698	0.726
	β_{23}	2.2	-0.022	0.045	0.589	0.619	0.002	0.048	0.613	0.674

Table 10.3.2.2.3c: Estimated average biases and average standard error over 200 simulations for the mixed threshold models.

			REML $\varphi_1 = 0.5$, $\varphi_2 = 0.3$				REML $\varphi_1 = 0.5$, $\varphi_2 = 0.3$			
M		TU	AB	SE	ASE	SEOS	AB	SE	ASE	SEOS
3	φ_1		-0.035	0.025	0.304	0.357	-0.045	0.038	0.461	0.543
	φ_2		0.051	0.028	0.325	0.395	0.063	0.033	0.352	0.467
	θ_1	1.5	-0.018	0.018	0.252	0.258	-0.019	0.018	0.257	0.26
	θ_2	2.2	-0.007	0.023	0.294	0.324	0.01	0.025	0.303	0.357
	β_{11}	2	-0.141	0.032	0.447	0.45	-0.24	0.032	0.484	0.46
	β_{12}	.7	-0.011	0.024	0.418	0.34	-0.025	0.03	0.464	0.429
	β_{13}	0.05	-0.135	0.026	0.415	0.364	-0.036	0.032	0.468	0.446
	β_{21}	2	-0.167	0.033	0.466	0.47	-0.211	0.037	0.502	0.524
	β_{22}	2.5	-0.105	0.042	0.554	0.588	-0.107	0.038	0.585	0.542
	β_{23}	2.2	-0.199	0.032	0.449	0.451	-0.212	0.035	0.488	0.494
4	φ_1		-0.092	0.022	0.283	0.31	-0.19	0.035	0.4	0.488
	φ_2		0.078	0.029	0.348	0.402	-0.016	0.026	0.289	0.371
	θ_1	1.5	-0.016	0.023	0.288	0.328	-0.07	0.02	0.271	0.276
	θ_2	2.2	-0.016	0.028	0.321	0.387	-0.061	0.025	0.308	0.352
	β_{11}	2	-0.012	0.034	0.441	0.472	-0.03	0.031	0.459	0.443
	β_{12}	.7	0.225	0.035	0.43	0.491	0.197	0.03	0.447	0.425
	β_{13}	0.05	0.097	0.033	0.436	0.46	0.168	0.032	0.456	0.45
	β_{21}	2	-0.02	0.033	0.45	0.456	-0.094	0.031	0.471	0.436
	β_{22}	2.5	0.091	0.039	0.544	0.541	-0.046	0.04	0.555	0.57
	β_{23}	2.2	0.109	0.035	0.448	0.49	0.034	0.034	0.467	0.474

Table 10.3.2.2.5a: Estimated average biases and average standard error over 200 simulations for the mixed threshold models.

			ML $\varphi_1 = 0.5$, $\varphi_2 = 0.3$				ML $\varphi_1 = 1$, $\varphi_2 = 0.3$			
M		TU	AB	SE	ASE	SEOS	AB	SE	ASE	SEOS
1	φ_1		-0.091	0.016	0.235	0.228	-0.172	0.028	0.351	0.398
	φ_2		0.024	0.021	0.238	0.301	0.018	0.025	0.263	0.347
	θ_1	1.5	-0.014	0.014	0.195	0.192	-0.011	0.015	0.198	0.214
	θ_2	2.2	-0.005	0.015	0.219	0.206	0.005	0.019	0.224	0.266
	β_{11}	2	-0.07	0.027	0.39	0.384	-0.091	0.032	0.427	0.455
	β_{12}	1.5	0.036	0.027	0.406	0.379	0.039	0.032	0.443	0.444
	β_{13}	1.2	-0.017	0.027	0.398	0.377	-0.038	0.03	0.434	0.423
	β_{14}	0.5	0.066	0.027	0.393	0.381	0.051	0.037	0.432	0.514
	β_{15}	0.04	0.018	0.03	0.402	0.424	0.007	0.029	0.439	0.405
	β_{21}	2	-0.08	0.027	0.382	0.381	-0.102	0.029	0.426	0.411
	β_{22}	2.5	0.022	0.034	0.45	0.474	-0.075	0.034	0.484	0.482
	β_{23}	2.2	-0.015	0.032	0.428	0.456	-0.057	0.034	0.466	0.473
	β_{24}	2.8	0.102	0.035	0.484	0.499	-0.012	0.039	0.513	0.541
	β_{25}	1.5	0.047	0.031	0.4	0.432	-0.027	0.031	0.441	0.437
			REML				REML			
1	φ_1		0.024	0.023	0.289	0.314	-0.03	0.031	0.414	0.443
	φ_2		0.115	0.025	0.304	0.353	0.099	0.028	0.324	0.396
	θ_1	1.5	0.032	0.014	0.199	0.198	0.025	0.015	0.205	0.212
	θ_2	2.2	0.045	0.017	0.224	0.242	0.068	0.018	0.233	0.254
	β_{11}	2	-0.009	0.032	0.406	0.446	-0.106	0.031	0.442	0.436
	β_{12}	1.5	0.068	0.028	0.429	0.397	0.054	0.037	0.465	0.526
	β_{13}	1.2	0.005	0.029	0.42	0.402	-0.001	0.036	0.458	0.513
	β_{14}	0.5	0.054	0.029	0.415	0.406	-0.023	0.035	0.455	0.495
	β_{15}	0.04	-0.009	0.027	0.425	0.382	-0.051	0.036	0.466	0.506
	β_{21}	2	0.004	0.033	0.395	0.456	0.014	0.032	0.438	0.453
	β_{22}	2.5	0.079	0.03	0.463	0.425	0.054	0.032	0.502	0.451
	β_{23}	2.2	-0.024	0.03	0.44	0.418	0.064	0.037	0.486	0.519
	β_{24}	2.8	0.063	0.034	0.489	0.476	0.126	0.039	0.533	0.553
	β_{25}	1.5	0.005	0.027	0.414	0.382	0.031	0.029	0.454	0.408

Table 10.3.2.2.5b: Estimated average biases and average standard error over 200 simulations for the mixed threshold models.

			ML $\varphi_1 = 0.5$, $\varphi_2 = 0.3$				ML $\varphi_1 = 1$, $\varphi_2 = 0.3$			
M		TU	AB	SE	ASE	SEOS	AB	SE	ASE	SEOS
2	φ_1		-0.118	0.026	0.327	0.361	-0.224	0.042	0.452	0.588
	φ_2		0.047	0.027	0.341	0.382	0.052	0.03	0.352	0.426
	θ_1	1.5	-0.017	0.017	0.22	0.234	-0.053	0.015	0.221	0.207
	θ_2	2.2	-0.009	0.019	0.254	0.27	-0.046	0.018	0.256	0.256
	β_{11}	2	-0.083	0.038	0.55	0.541	-0.19	0.045	0.586	0.625
	β_{12}	1.5	0.077	0.037	0.557	0.518	0.026	0.038	0.592	0.538
	β_{13}	1.2	-0.042	0.038	0.547	0.534	-0.027	0.042	0.583	0.589
	β_{14}	0.5	0.028	0.038	0.545	0.536	0.005	0.04	0.585	0.566
	β_{15}	0.04	-0.026	0.041	0.561	0.572	-0.032	0.044	0.605	0.618
	β_{21}	2	-0.039	0.043	0.561	0.608	-0.219	0.039	0.569	0.546
	β_{22}	2.5	-0.02	0.041	0.608	0.579	0.009	0.043	0.636	0.604
	β_{23}	2.2	-0.071	0.043	0.583	0.604	-0.096	0.046	0.61	0.644
	β_{24}	2.8	0	0.046	0.639	0.648	-0.053	0.048	0.66	0.668
	β_{25}	1.5	0.031	0.041	0.559	0.581	0.018	0.042	0.583	0.594
			REML				REML			
2	φ_1		0.045	0.035	0.395	0.489	-0.094	0.041	0.576	0.583
	φ_2		0.154	0.033	0.42	0.462	0.236	0.039	0.52	0.552
	θ_1	1.5	0.011	0.017	0.224	0.24	0.012	0.016	0.228	0.224
	θ_2	2.2	0.052	0.02	0.259	0.286	0.031	0.02	0.264	0.285
	β_{11}	2	-0.111	0.038	0.564	0.539	-0.168	0.043	0.59	0.608
	β_{12}	1.5	0.082	0.038	0.576	0.531	0.082	0.04	0.611	0.567
	β_{13}	1.2	-0.062	0.04	0.566	0.568	-0.033	0.042	0.601	0.587
	β_{14}	0.5	0.145	0.042	0.566	0.585	0.038	0.042	0.602	0.591
	β_{15}	0.04	-0.021	0.04	0.58	0.557	-0.043	0.05	0.622	0.713
	β_{21}	2	-0.084	0.042	0.562	0.596	-0.121	0.047	0.586	0.667
	β_{22}	2.5	0.01	0.044	0.622	0.62	0.011	0.047	0.656	0.665
	β_{23}	2.2	-0.057	0.043	0.599	0.601	-0.038	0.051	0.634	0.721
	β_{24}	2.8	0.093	0.052	0.666	0.738	0.089	0.048	0.692	0.683
	β_{25}	1.5	0.021	0.04	0.571	0.56	-0.03	0.045	0.603	0.63

Table 10.3.2.2.5c: Estimated average biases and average standard error over 200 simulations for the mixed threshold models.

			ML $\varphi_1 = 0.5$, $\varphi_2 = 0.3$				ML $\varphi_1 = 1$, $\varphi_2 = 0.3$			
M		TU	AB	SE	ASE	SEOS	AB	SE	ASE	SEOS
3	φ_1		-0.033	0.018	0.263	0.257	-0.166	0.029	0.373	0.417
	φ_2		0.004	0.022	0.247	0.307	0.054	0.027	0.291	0.385
	θ_1	1.5	-0.002	0.015	0.197	0.206	-0.029	0.015	0.202	0.216
	θ_2	2.2	0.015	0.017	0.229	0.246	0.005	0.017	0.236	0.247
	β_{11}	2	-0.159	0.03	0.425	0.42	-0.218	0.029	0.46	0.412
	β_{12}	1.5	-0.004	0.03	0.434	0.418	-0.067	0.032	0.472	0.446
	β_{13}	1.2	-0.096	0.03	0.419	0.426	-0.137	0.035	0.461	0.501
	β_{14}	0.5	-0.023	0.029	0.408	0.404	-0.034	0.03	0.453	0.425
	β_{15}	0.04	-0.064	0.027	0.415	0.386	-0.117	0.032	0.464	0.449
	β_{21}	2	-0.132	0.032	0.421	0.458	-0.155	0.033	0.454	0.473
	β_{22}	2.5	-0.011	0.035	0.495	0.497	-0.039	0.039	0.527	0.553
	β_{23}	2.2	-0.118	0.035	0.462	0.493	-0.083	0.035	0.497	0.501
	β_{24}	2.8	-0.056	0.04	0.522	0.57	-0.07	0.043	0.55	0.611
	β_{25}	1.5	-0.061	0.031	0.427	0.435	-0.017	0.036	0.464	0.514
			REML				REML			
3	φ_1		0.016	0.023	0.302	0.327	-0.014	0.032	0.438	0.456
	φ_2		0.079	0.026	0.304	0.373	0.085	0.031	0.335	0.437
	θ_1	1.5	-0.018	0.014	0.198	0.2	0.044	0.014	0.208	0.201
	θ_2	2.2	0.012	0.018	0.23	0.253	0.079	0.016	0.242	0.233
	β_{11}	2	-0.139	0.03	0.434	0.429	-0.133	0.033	0.479	0.473
	β_{12}	1.5	-0.044	0.032	0.446	0.447	-0.002	0.03	0.489	0.423
	β_{13}	1.2	-0.064	0.033	0.435	0.468	-0.073	0.037	0.479	0.527
	β_{14}	0.5	-0.081	0.028	0.422	0.39	-0.013	0.034	0.471	0.481
	β_{15}	0.04	-0.079	0.032	0.432	0.455	-0.08	0.036	0.483	0.507
	β_{21}	2	-0.106	0.032	0.427	0.451	-0.071	0.037	0.472	0.517
	β_{22}	2.5	-0.016	0.038	0.503	0.529	0.031	0.039	0.541	0.554
	β_{23}	2.2	-0.129	0.035	0.471	0.489	-0.09	0.041	0.509	0.577
	β_{24}	2.8	-0.009	0.042	0.536	0.591	0.041	0.039	0.568	0.553
	β_{25}	1.5	-0.07	0.032	0.436	0.449	-0.032	0.037	0.48	0.517

Table 10.3.2.2.5d: Estimated average biases and average standard error over 200 simulations for the mixed threshold models.

			ML $\varphi_1 = 0.5$, $\varphi_2 = 0.3$				ML $\varphi_1 = 1$, $\varphi_2 = 0.3$			
M		TU	AB	SE	ASE	SEOS	AB	SE	ASE	SEOS
4	φ_1		-0.089	0.022	0.223	0.299	-0.225	0.028	0.333	0.384
	φ_2		-0.042	0.021	0.199	0.284	-0.02	0.026	0.229	0.36
	θ_1	1.5	-0.089	0.017	0.215	0.229	-0.073	0.016	0.216	0.219
	θ_2	2.2	-0.091	0.02	0.241	0.27	-0.063	0.019	0.244	0.266
	β_{11}	2	-0.05	0.032	0.414	0.445	-0.031	0.032	0.446	0.447
	β_{12}	1.5	0.103	0.031	0.424	0.433	0.113	0.034	0.46	0.468
	β_{13}	1.2	0.017	0.032	0.415	0.444	0.069	0.035	0.451	0.482
	β_{14}	0.5	0.094	0.031	0.417	0.429	0.103	0.033	0.451	0.464
	β_{15}	0.04	0.04	0.034	0.435	0.47	0.087	0.036	0.467	0.498
	β_{21}	2	-0.12	0.035	0.391	0.487	-0.063	0.029	0.43	0.406
	β_{22}	2.5	-0.018	0.034	0.447	0.467	0.034	0.037	0.498	0.512
	β_{23}	2.2	-0.046	0.032	0.426	0.441	-0.034	0.034	0.469	0.472
	β_{24}	2.8	0.008	0.034	0.48	0.466	-0.018	0.04	0.522	0.554
	β_{25}	1.5	-0.013	0.028	0.398	0.386	-0.021	0.03	0.438	0.421
			REML				REML			
4	φ_1		-0.051	0.021	0.268	0.293	-0.134	0.035	0.39	0.488
	φ_2		0.073	0.024	0.289	0.332	0.066	0.026	0.302	0.369
	θ_1	1.5	0.003	0.016	0.226	0.222	-0.029	0.017	0.223	0.237
	θ_2	2.2	0.013	0.019	0.252	0.265	0.002	0.021	0.253	0.291
	β_{11}	2	0.017	0.03	0.418	0.413	0.034	0.035	0.456	0.481
	β_{12}	1.5	0.097	0.032	0.437	0.44	0.124	0.034	0.476	0.468
	β_{13}	1.2	0.101	0.036	0.432	0.495	0.089	0.031	0.465	0.435
	β_{14}	0.5	0.149	0.032	0.426	0.442	0.169	0.034	0.466	0.467
	β_{15}	0.04	0.123	0.035	0.444	0.481	0.115	0.034	0.477	0.467
	β_{21}	2	0.034	0.03	0.408	0.42	-0.025	0.032	0.444	0.449
	β_{22}	2.5	0.101	0.036	0.477	0.499	0.075	0.036	0.514	0.495
	β_{23}	2.2	0.007	0.031	0.449	0.427	0.037	0.04	0.489	0.561
	β_{24}	2.8	0.113	0.034	0.506	0.471	0.08	0.04	0.547	0.56
	β_{25}	1.5	0.118	0.029	0.425	0.398	0.066	0.032	0.459	0.453

Table 10.3.2.3.3a: Estimated average biases and average standard error over 200 simulations for the mixed threshold models.

			ML $\varphi_1 = 0.5$, $\varphi_2 = 0.3$				ML $\varphi_1 = 1$, $\varphi_2 = 0.3$			
M		TU	AB	SE	ASE	SEOS	AB	SE	ASE	SEOS
1	φ_1		-0.066	0.021	0.246	0.304	-0.129	0.033	0.366	0.468
	φ_2		-0.025	0.023	0.24	0.327	-0.054	0.023	0.234	0.319
	θ_1	1.5	-0.037	0.019	0.247	0.263	-0.04	0.02	0.254	0.288
	θ_2	2.2	-0.032	0.022	0.278	0.306	-0.043	0.024	0.288	0.337
	θ_3	3.8	-0.075	0.03	0.377	0.422	-0.03	0.033	0.389	0.465
	β_{11}	2	-0.091	0.03	0.396	0.42	-0.132	0.036	0.437	0.505
	β_{12}	.7	0.049	0.026	0.387	0.363	0.06	0.032	0.433	0.451
	β_{13}	0.05	0.044	0.026	0.39	0.366	0.011	0.032	0.439	0.459
	β_{21}	2	-0.102	0.029	0.403	0.416	-0.064	0.03	0.438	0.42
	β_{22}	2.5	0	0.032	0.447	0.45	0.05	0.035	0.479	0.49
	β_{23}	2.2	-0.077	0.03	0.433	0.422	-0.036	0.036	0.464	0.503
2	φ_1		-0.085	0.032	0.348	0.44	-0.203	0.046	0.502	0.647
	φ_2		0.119	0.04	0.436	0.548	0.117	0.044	0.419	0.621
	θ_1	1.5	-0.038	0.018	0.283	0.251	-0.033	0.023	0.286	0.323
	θ_2	2.2	-0.014	0.022	0.329	0.309	-0.034	0.027	0.331	0.378
	θ_3	3.8	-0.003	0.031	0.438	0.429	-0.066	0.036	0.434	0.513
	β_{11}	2	-0.012	0.038	0.555	0.524	-0.088	0.041	0.58	0.571
	β_{12}	.7	0.181	0.036	0.546	0.498	0.18	0.04	0.581	0.566
	β_{13}	0.05	-0.001	0.044	0.56	0.611	0.083	0.04	0.588	0.556
	β_{21}	2	-0.146	0.041	0.562	0.563	-0.122	0.04	0.577	0.556
	β_{22}	2.5	0.095	0.047	0.609	0.643	0.087	0.044	0.625	0.614
	β_{23}	2.2	-0.02	0.045	0.592	0.626	-0.095	0.047	0.604	0.663
			REML				REML			
1	φ_1		0.068	0.026	0.311	0.361	-0.033	0.034	0.423	0.482
	φ_2		0.14	0.03	0.347	0.427	0.131	0.031	0.366	0.441
	θ_1	1.5	0.027	0.02	0.261	0.288	0.01	0.019	0.261	0.262
	θ_2	2.2	0.061	0.025	0.294	0.355	0.035	0.024	0.295	0.334
	θ_3	3.8	0.11	0.032	0.399	0.45	0.03	0.032	0.395	0.458
	β_{11}	2	-0.006	0.029	0.421	0.413	-0.038	0.032	0.447	0.454
	β_{12}	.7	0.127	0.027	0.423	0.381	0.083	0.032	0.455	0.451
	β_{13}	0.05	-0.055	0.028	0.429	0.391	0	0.031	0.462	0.445
	β_{21}	2	-0.025	0.032	0.417	0.448	-0.065	0.032	0.447	0.446
	β_{22}	2.5	0.155	0.034	0.475	0.485	0.087	0.031	0.502	0.444
	β_{23}	2.2	0.032	0.033	0.458	0.468	0.006	0.03	0.487	0.422

Table 10.3.2.3.3b: Estimated average biases and average standard error over 200 simulations for the mixed threshold models.

			ML $\varphi_1 = 0.5$, $\varphi_2 = 0.3$				ML $\varphi_1 = 1$, $\varphi_2 = 0.3$			
M		TU	AB	SE	ASE	SEOS	AB	SE	ASE	SEOS
3	φ_1		-0.101	0.025	0.228	0.348	-0.231	0.035	0.344	0.493
	φ_2		-0.061	0.022	0.221	0.306	-0.101	0.02	0.203	0.277
	θ_1	1.5	-0.069	0.02	0.249	0.279	-0.073	0.019	0.247	0.271
	θ_2	2.2	-0.076	0.025	0.289	0.344	-0.11	0.022	0.287	0.313
	θ_3	3.8	-0.159	0.036	0.419	0.509	-0.246	0.032	0.405	0.455
	β_{11}	2	-0.174	0.032	0.43	0.453	-0.275	0.033	0.447	0.463
	β_{12}	0.7	-0.082	0.032	0.404	0.442	-0.058	0.027	0.428	0.382
	β_{13}	0.05	-0.13	0.027	0.4	0.38	-0.071	0.031	0.432	0.442
	β_{21}	2	-0.185	0.033	0.424	0.46	-0.281	0.03	0.451	0.43
	β_{22}	2.5	-0.113	0.035	0.472	0.485	-0.212	0.035	0.49	0.497
	β_{23}	2.2	-0.18	0.032	0.452	0.449	-0.289	0.034	0.473	0.486
4	φ_1		-0.111	0.023	0.234	0.324	-0.273	0.032	0.338	0.445
	φ_2		0.025	0.028	0.256	0.399	-0.02	0.029	0.244	0.412
	θ_1	1.5	-0.065	0.021	0.286	0.298	-0.135	0.021	0.268	0.289
	θ_2	2.2	-0.058	0.025	0.319	0.352	-0.173	0.025	0.301	0.345
	θ_3	3.8	-0.111	0.034	0.407	0.476	-0.218	0.031	0.391	0.432
	β_{11}	2	-0.055	0.034	0.428	0.487	-0.101	0.034	0.45	0.482
	β_{12}	.7	0.199	0.028	0.413	0.402	0.214	0.033	0.447	0.467
	β_{13}	0.05	0.086	0.032	0.424	0.446	0.202	0.035	0.458	0.488
	β_{21}	2	-0.022	0.035	0.431	0.491	-0.12	0.03	0.443	0.428
	β_{22}	2.5	0.109	0.038	0.479	0.532	-0.018	0.035	0.486	0.495
	β_{23}	2.2	0.073	0.037	0.465	0.521	-0.027	0.033	0.474	0.464
			REML				REML			
2	φ_1		0.123	0.039	0.471	0.547	0.02	0.057	0.624	0.799
	φ_2		0.316	0.059	0.533	0.82	0.238	0.05	0.56	0.702
	θ_1	1.5	0.032	0.021	0.297	0.297	-0.01	0.022	0.292	0.311
	θ_2	2.2	0.048	0.025	0.342	0.348	-0.01	0.027	0.337	0.379
	θ_3	3.8	0.131	0.035	0.454	0.486	0.003	0.036	0.445	0.504
	β_{11}	2	-0.039	0.044	0.576	0.61	-0.161	0.045	0.6	0.641
	β_{12}	.7	0.091	0.035	0.579	0.482	0.143	0.043	0.609	0.603
	β_{13}	0.05	-0.092	0.046	0.6	0.638	0.038	0.041	0.62	0.576
	β_{21}	2	-0.058	0.049	0.577	0.672	-0.088	0.041	0.591	0.582
	β_{22}	2.5	0.236	0.045	0.635	0.628	0.104	0.044	0.638	0.615
	β_{23}	2.2	0.034	0.041	0.612	0.562	-0.013	0.047	0.625	0.661

Table 10.3.2.3.3c: Estimated average biases and average standard error over 200 simulations for the mixed threshold models.

			REML $\varphi_1 = 0.5$, $\varphi_2 = 0.3$				REML $\varphi_1 = 0.5$, $\varphi_2 = 0.3$			
M		TU	AB	SE	ASE	SEOS	AB	SE	ASE	SEOS
3	φ_1		0.002	0.029	0.293	0.403	-0.106	0.033	0.414	0.465
	φ_2		-0.002	0.024	0.266	0.34	0.052	0.028	0.313	0.402
	θ_1	1.5	-0.005	0.019	0.257	0.268	-0.064	0.016	0.252	0.233
	θ_2	2.2	0.001	0.024	0.298	0.34	-0.057	0.02	0.295	0.289
	θ_3	3.8	-0.017	0.038	0.444	0.534	-0.156	0.032	0.422	0.45
	β_{11}	2	-0.189	0.031	0.434	0.434	-0.279	0.032	0.459	0.45
	β_{12}	.7	-0.062	0.027	0.412	0.385	-0.105	0.029	0.45	0.412
	β_{13}	0.05	-0.15	0.028	0.412	0.39	-0.119	0.029	0.457	0.408
	β_{21}	2	-0.149	0.032	0.441	0.451	-0.292	0.032	0.464	0.46
	β_{22}	2.5	-0.015	0.035	0.495	0.496	-0.111	0.034	0.518	0.482
	β_{23}	2.2	-0.155	0.038	0.472	0.529	-0.256	0.033	0.497	0.464
4	φ_1		0.015	0.025	0.296	0.35	-0.035	0.038	0.444	0.535
	φ_2		0.082	0.031	0.326	0.438	0.172	0.039	0.401	0.547
	θ_1	1.5	-0.01	0.021	0.293	0.3	-0.023	0.02	0.286	0.288
	θ_2	2.2	0.003	0.026	0.326	0.369	0.022	0.027	0.324	0.384
	θ_3	3.8	0.021	0.032	0.419	0.45	0.001	0.037	0.416	0.518
	β_{11}	2	0.021	0.034	0.446	0.483	0.072	0.033	0.478	0.472
	β_{12}	.7	0.266	0.031	0.437	0.437	0.265	0.033	0.486	0.463
	β_{13}	0.05	0.208	0.032	0.44	0.448	0.152	0.033	0.494	0.465
	β_{21}	2	0.017	0.034	0.448	0.485	-0.02	0.037	0.469	0.521
	β_{22}	2.5	0.216	0.037	0.503	0.524	0.197	0.043	0.529	0.614
	β_{23}	2.2	0.112	0.035	0.486	0.498	0.107	0.039	0.513	0.556

Table 10.3.2.3.5a: Estimated average biases and average standard error over 200 simulations for the mixed threshold models.

			ML $\varphi_1 = 0.5$, $\varphi_2 = 0.3$				ML $\varphi_1 = 1$, $\varphi_2 = 0.3$			
M		TU	AB	SE	ASE	SEOS	AB	SE	ASE	SEOS
1	φ_1		-0.015	0.022	0.245	0.308	-0.114	0.027	0.35	0.376
	φ_2		0.045	0.021	0.241	0.301	0.025	0.022	0.253	0.318
	θ_1	1.5	0.024	0.014	0.198	0.202	-0.002	0.016	0.202	0.221
	θ_2	2.2	0.032	0.018	0.222	0.249	0.025	0.019	0.229	0.267
	θ_3	3.8	0.042	0.025	0.302	0.358	0.033	0.024	0.306	0.342
	β_{11}	2	-0.031	0.028	0.389	0.402	-0.079	0.031	0.418	0.435
	β_{12}	1.5	0.019	0.029	0.412	0.415	0.002	0.033	0.437	0.467
	β_{13}	1.2	-0.034	0.031	0.407	0.434	-0.016	0.034	0.434	0.479
	β_{14}	0.5	-0.002	0.029	0.408	0.417	0.028	0.032	0.435	0.452
	β_{15}	0.04	-0.008	0.029	0.418	0.404	-0.012	0.032	0.445	0.446
	β_{21}	2	-0.073	0.024	0.374	0.335	0.023	0.03	0.419	0.428
	β_{22}	2.5	0.056	0.028	0.419	0.398	0.097	0.033	0.46	0.466
	β_{23}	2.2	0.008	0.028	0.41	0.402	0.072	0.035	0.451	0.494
	β_{24}	2.8	0.071	0.031	0.43	0.435	0.115	0.036	0.471	0.503
	β_{25}	1.5	0.014	0.03	0.395	0.421	0.078	0.035	0.437	0.49
			REML							
1	φ_1		0.061	0.022	0.283	0.318	0.024	0.034	0.414	0.48
	φ_2		0.098	0.024	0.282	0.34	0.139	0.027	0.321	0.387
	θ_1	1.5	0.041	0.015	0.2	0.208	0.03	0.015	0.206	0.206
	θ_2	2.2	0.074	0.017	0.225	0.243	0.076	0.017	0.234	0.24
	θ_3	3.8	0.146	0.027	0.313	0.381	0.111	0.025	0.314	0.36
	β_{11}	2	0.023	0.028	0.39	0.394	0.018	0.031	0.436	0.432
	β_{12}	1.5	0.126	0.028	0.415	0.4	0.04	0.032	0.462	0.447
	β_{13}	1.2	0.037	0.028	0.409	0.4	-0.035	0.034	0.458	0.474
	β_{14}	0.5	0.037	0.026	0.406	0.364	0.034	0.036	0.461	0.503
	β_{15}	0.04	0.004	0.031	0.418	0.443	-0.015	0.033	0.472	0.473
	β_{21}	2	-0.032	0.03	0.388	0.422	0.053	0.035	0.428	0.488
	β_{22}	2.5	0.114	0.03	0.439	0.419	0.102	0.034	0.476	0.474
	β_{23}	2.2	0.023	0.03	0.428	0.424	0.102	0.034	0.467	0.484
	β_{24}	2.8	0.171	0.034	0.451	0.481	0.147	0.036	0.487	0.515
	β_{25}	1.5	0.05	0.03	0.414	0.422	0.09	0.033	0.453	0.467

Table 10.3.2.3.5b: Estimated average biases and average standard error over 200 simulations for the mixed threshold models.

			ML $\varphi_1 = 0.5$, $\varphi_2 = 0.3$				ML $\varphi_1 = 1$, $\varphi_2 = 0.3$			
M		TU	AB	SE	ASE	SEOS	AB	SE	ASE	SEOS
2	φ_1		-0.08	0.027	0.326	0.383	-0.166	0.036	0.476	0.505
	φ_2		0.128	0.027	0.388	0.386	0.107	0.031	0.389	0.437
	θ_1	1.5	-0.017	0.016	0.221	0.223	-0.019	0.015	0.225	0.212
	θ_2	2.2	-0.002	0.019	0.255	0.265	0.002	0.017	0.261	0.247
	θ_3	3.8	0.025	0.026	0.34	0.365	0.007	0.023	0.343	0.332
	β_{11}	2	-0.055	0.037	0.544	0.522	-0.135	0.043	0.57	0.603
	β_{12}	1.5	0.047	0.036	0.561	0.514	0.039	0.041	0.583	0.579
	β_{13}	1.2	-0.065	0.043	0.556	0.606	-0.003	0.042	0.582	0.592
	β_{14}	0.5	0.007	0.041	0.562	0.581	0.035	0.041	0.589	0.583
	β_{15}	0.04	0.07	0.041	0.575	0.582	-0.007	0.043	0.601	0.603
	β_{21}	2	-0.098	0.039	0.531	0.545	-0.031	0.038	0.557	0.541
	β_{22}	2.5	0.082	0.035	0.57	0.501	0.065	0.039	0.596	0.549
	β_{23}	2.2	0.002	0.037	0.56	0.518	-0.013	0.042	0.586	0.598
	β_{24}	2.8	0.056	0.039	0.58	0.558	0.056	0.045	0.608	0.632
	β_{25}	1.5	-0.002	0.039	0.543	0.558	0.033	0.043	0.575	0.61
			REML				REML			
2	φ_1		0.065	0.033	0.386	0.46	-0.054	0.041	0.549	0.585
	φ_2		0.164	0.035	0.378	0.496	0.282	0.04	0.519	0.566
	θ_1	1.5	0.03	0.016	0.226	0.228	-0.026	0.017	0.224	0.247
	θ_2	2.2	0.065	0.02	0.261	0.283	-0.004	0.019	0.261	0.27
	θ_3	3.8	0.106	0.028	0.347	0.394	0.034	0.028	0.348	0.399
	β_{11}	2	-0.024	0.042	0.549	0.588	-0.071	0.038	0.567	0.543
	β_{12}	1.5	0.101	0.039	0.567	0.553	0.071	0.04	0.593	0.568
	β_{13}	1.2	-0.03	0.042	0.562	0.592	-0.055	0.045	0.595	0.639
	β_{14}	0.5	0.178	0.046	0.57	0.651	0.088	0.044	0.596	0.621
	β_{15}	0.04	0.018	0.039	0.579	0.554	-0.05	0.049	0.617	0.699
	β_{21}	2	-0.094	0.043	0.549	0.601	-0.135	0.042	0.573	0.595
	β_{22}	2.5	0.07	0.043	0.589	0.606	-0.037	0.04	0.616	0.564
	β_{23}	2.2	0.024	0.04	0.578	0.564	-0.122	0.045	0.61	0.634
	β_{24}	2.8	0.172	0.045	0.604	0.642	0.062	0.051	0.632	0.715
	β_{25}	1.5	0.057	0.037	0.566	0.523	-0.008	0.041	0.598	0.586

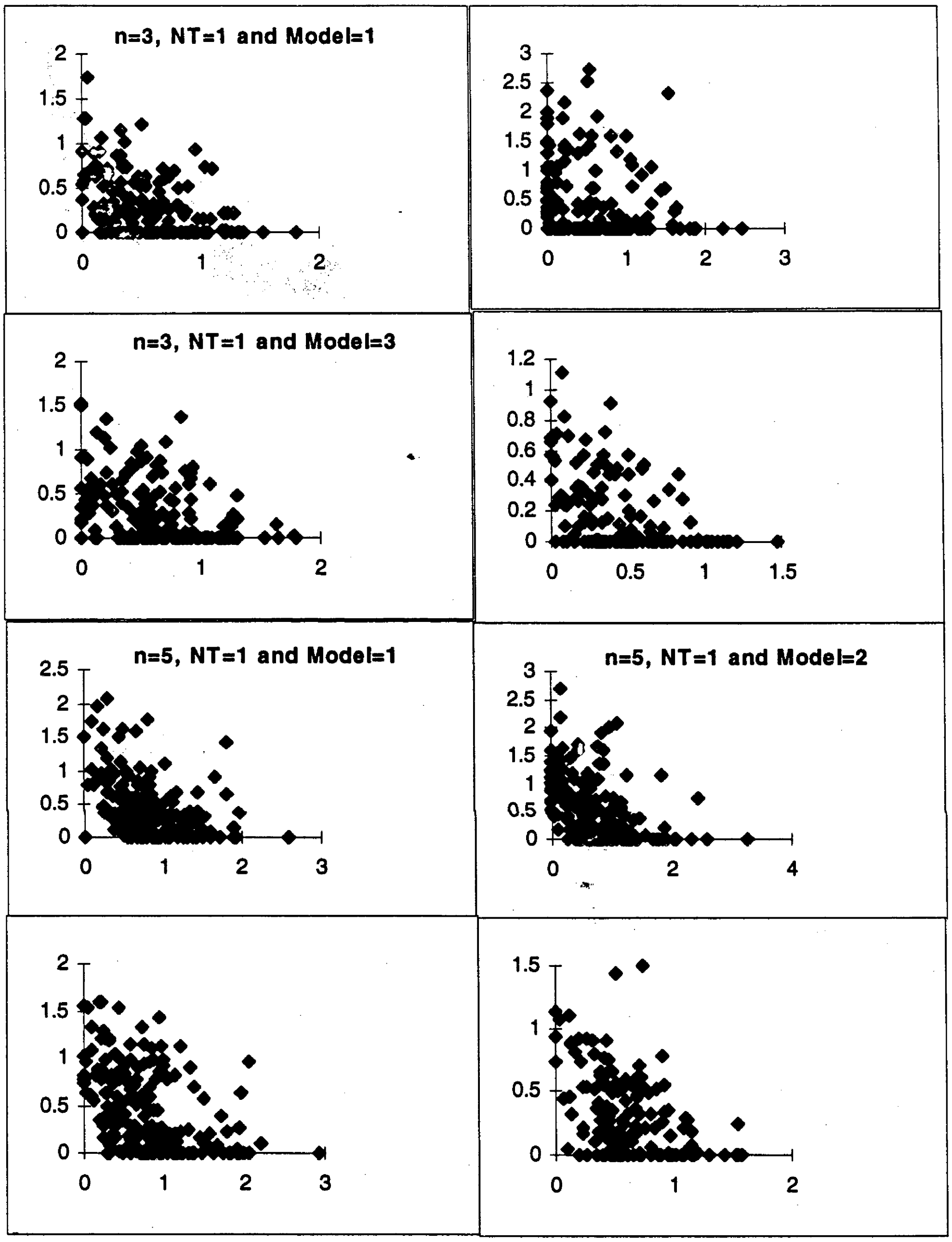
Table 10.3.2.3.5c: Estimated average biases and average standard error over 200 simulations for the mixed threshold models.

			ML $\varphi_1 = 0.5$, $\varphi_2 = 0.3$				ML $\varphi_1 = 1$, $\varphi_2 = 0.3$			
M		TU	AB	SE	ASE	SEOS	AB	SE	ASE	SEOS
3	φ_1		-0.028	0.021	0.243	0.292	-0.105	0.03	0.361	0.428
	φ_2		0.008	0.022	0.231	0.306	0.001	0.024	0.249	0.341
	θ_1	1.5	-0.001	0.015	0.197	0.208	-0.025	0.014	0.199	0.2
	θ_2	2.2	0.024	0.016	0.228	0.233	-0.026	0.018	0.232	0.256
	θ_3	3.8	0.015	0.026	0.346	0.363	-0.073	0.028	0.336	0.399
	β_{11}	2	-0.135	0.03	0.405	0.422	-0.224	0.029	0.442	0.412
	β_{12}	1.5	-0.021	0.027	0.417	0.384	-0.088	0.031	0.453	0.442
	β_{13}	1.2	-0.088	0.033	0.409	0.461	-0.156	0.033	0.448	0.46
	β_{14}	0.5	-0.007	0.027	0.401	0.377	-0.06	0.029	0.445	0.415
	β_{15}	0.04	-0.099	0.031	0.411	0.435	-0.036	0.03	0.456	0.426
	β_{21}	2	-0.112	0.031	0.407	0.432	-0.193	0.032	0.44	0.46
	β_{22}	2.5	-0.039	0.034	0.452	0.485	-0.104	0.033	0.481	0.468
	β_{23}	2.2	-0.099	0.038	0.44	0.54	-0.177	0.036	0.469	0.508
	β_{24}	2.8	-0.051	0.035	0.464	0.495	-0.097	0.034	0.493	0.486
	β_{25}	1.5	-0.089	0.031	0.419	0.442	-0.089	0.032	0.452	0.452
			REML				REML			
3	φ_1		0.058	0.023	0.302	0.324	-0.014	0.031	0.425	0.436
	φ_2		0.108	0.021	0.309	0.3	0.141	0.027	0.351	0.377
	θ_1	1.5	0.033	0.014	0.202	0.192	0.035	0.017	0.207	0.236
	θ_2	2.2	0.068	0.018	0.234	0.249	0.066	0.019	0.241	0.274
	θ_3	3.8	0.085	0.026	0.349	0.368	0.082	0.03	0.352	0.419
	β_{11}	2	-0.082	0.032	0.421	0.452	-0.136	0.032	0.452	0.451
	β_{12}	1.5	-0.026	0.031	0.439	0.434	0.009	0.031	0.472	0.439
	β_{13}	1.2	-0.067	0.032	0.432	0.46	-0.043	0.033	0.467	0.464
	β_{14}	0.5	-0.001	0.029	0.426	0.414	-0.014	0.032	0.464	0.453
	β_{15}	0.04	-0.07	0.032	0.437	0.455	-0.068	0.034	0.477	0.475
	β_{21}	2	-0.042	0.033	0.418	0.472	-0.074	0.035	0.454	0.491
	β_{22}	2.5	0.033	0.032	0.469	0.446	0.006	0.036	0.504	0.508
	β_{23}	2.2	-0.007	0.031	0.456	0.445	-0.035	0.041	0.493	0.577
	β_{24}	2.8	0.036	0.032	0.481	0.454	-0.01	0.036	0.516	0.511
	β_{25}	1.5	-0.011	0.03	0.434	0.425	-0.03	0.034	0.474	0.48

Table 10.3.2.3.5d: Estimated average biases and average standard error over 200 simulations for the mixed threshold models.

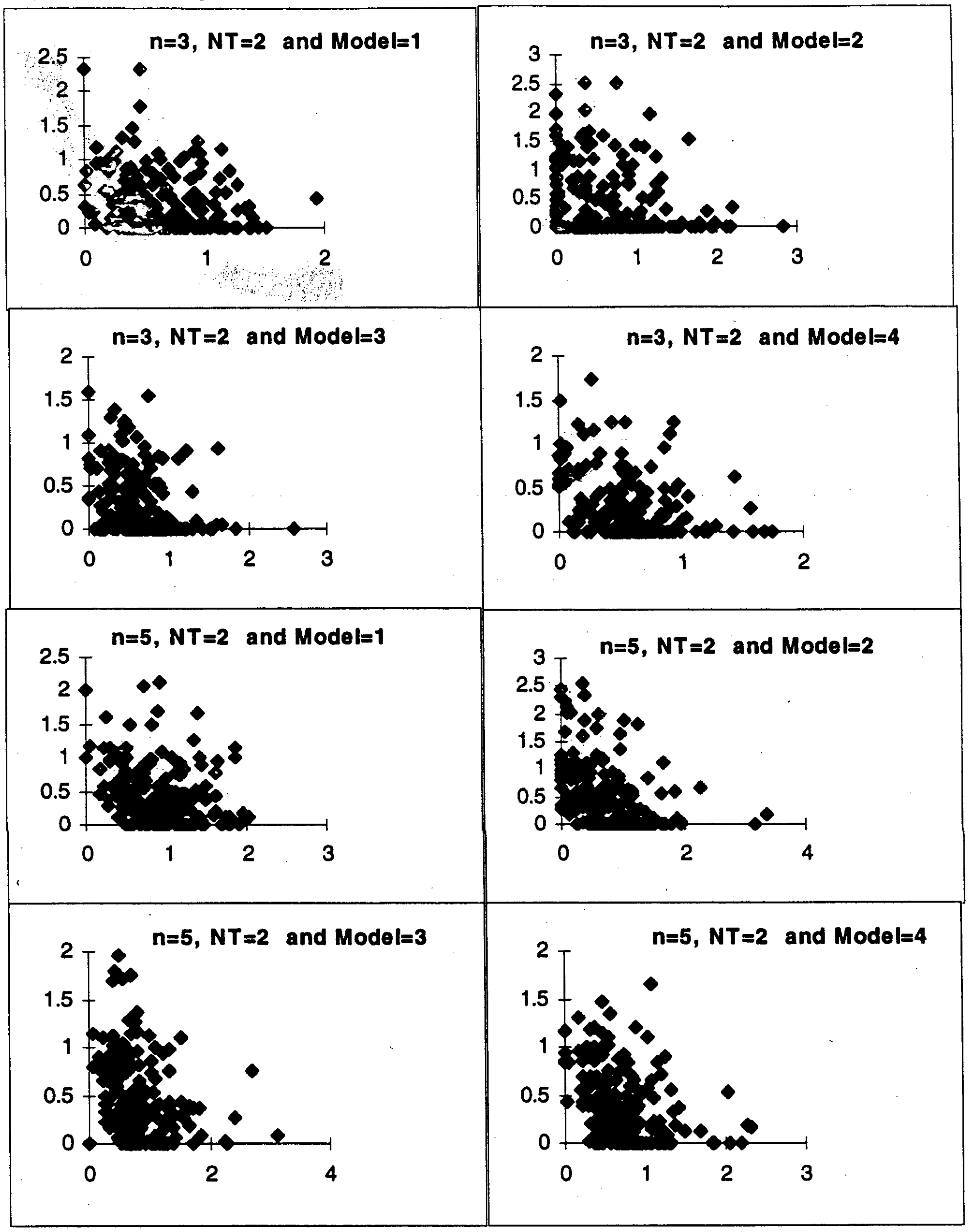
			ML $\varphi_1 = 0.5$, $\varphi_2 = 0.3$				ML $\varphi_1 = 1$, $\varphi_2 = 0.3$			
M		TU	AB	SE	ASE	SEOS	AB	SE	ASE	SEOS
4	φ_1		-0.065	0.021	0.232	0.297	-0.166	0.029	0.347	0.407
	φ_2		0.035	0.025	0.234	0.349	-0.002	0.021	0.251	0.297
	θ_1	1.5	-0.015	0.016	0.223	0.231	-0.056	0.016	0.219	0.224
	θ_2	2.2	-0.011	0.019	0.248	0.27	-0.064	0.019	0.247	0.274
	θ_3	3.8	-0.015	0.026	0.321	0.368	-0.05	0.026	0.322	0.365
	β_{11}	2	-0.031	0.031	0.407	0.438	-0.019	0.032	0.437	0.447
	β_{12}	1.5	0.121	0.028	0.427	0.396	0.141	0.034	0.453	0.482
	β_{13}	1.2	0.033	0.033	0.42	0.467	0.043	0.033	0.449	0.461
	β_{14}	0.5	0.154	0.031	0.42	0.445	0.145	0.032	0.453	0.45
	β_{15}	0.04	0.069	0.033	0.439	0.472	0.05	0.036	0.472	0.506
	β_{21}	2	0.004	0.033	0.399	0.461	0.011	0.032	0.433	0.459
	β_{22}	2.5	0.083	0.031	0.441	0.444	0.066	0.041	0.47	0.578
	β_{23}	2.2	0.006	0.03	0.43	0.429	0.053	0.038	0.462	0.541
	β_{24}	2.8	0.139	0.034	0.452	0.474	0.109	0.04	0.483	0.565
	β_{25}	1.5	0.089	0.029	0.413	0.408	0.103	0.036	0.448	0.502
			REML				REML			
4	φ_1		0.054	0.022	0.299	0.317	-0.008	0.03	0.428	0.428
	φ_2		0.14	0.029	0.311	0.405	0.182	0.031	0.362	0.435
	θ_1	1.5	0.054	0.018	0.236	0.252	0.016	0.017	0.23	0.235
	θ_2	2.2	0.084	0.021	0.263	0.299	0.036	0.019	0.259	0.27
	θ_3	3.8	0.121	0.028	0.336	0.391	0.038	0.026	0.331	0.361
	β_{11}	2	0.109	0.035	0.427	0.491	0.082	0.034	0.461	0.476
	β_{12}	1.5	0.192	0.037	0.45	0.526	0.211	0.033	0.49	0.472
	β_{13}	1.2	0.147	0.031	0.443	0.436	0.139	0.031	0.486	0.444
	β_{14}	0.5	0.174	0.029	0.44	0.413	0.135	0.031	0.487	0.44
	β_{15}	0.04	0.064	0.032	0.456	0.449	0.076	0.034	0.502	0.482
	β_{21}	2	0.157	0.033	0.423	0.468	0.109	0.036	0.446	0.515
	β_{22}	2.5	0.228	0.035	0.472	0.497	0.174	0.035	0.496	0.491
	β_{23}	2.2	0.175	0.037	0.461	0.516	0.115	0.038	0.486	0.533
	β_{24}	2.8	0.238	0.033	0.482	0.469	0.173	0.04	0.507	0.565
	β_{25}	1.5	0.164	0.033	0.443	0.474	0.159	0.035	0.471	0.493

Figure 10.3a: Distributions of ML estimates of φ_1, φ_2 obtained from 200 simulations for the threshold models 1,2,3 and 4 of chapter 5 with true of $\varphi_1 = 1$ and $\varphi_2 = 0.5$. Vertical axis is the φ_2 and horizontal gives φ_1.



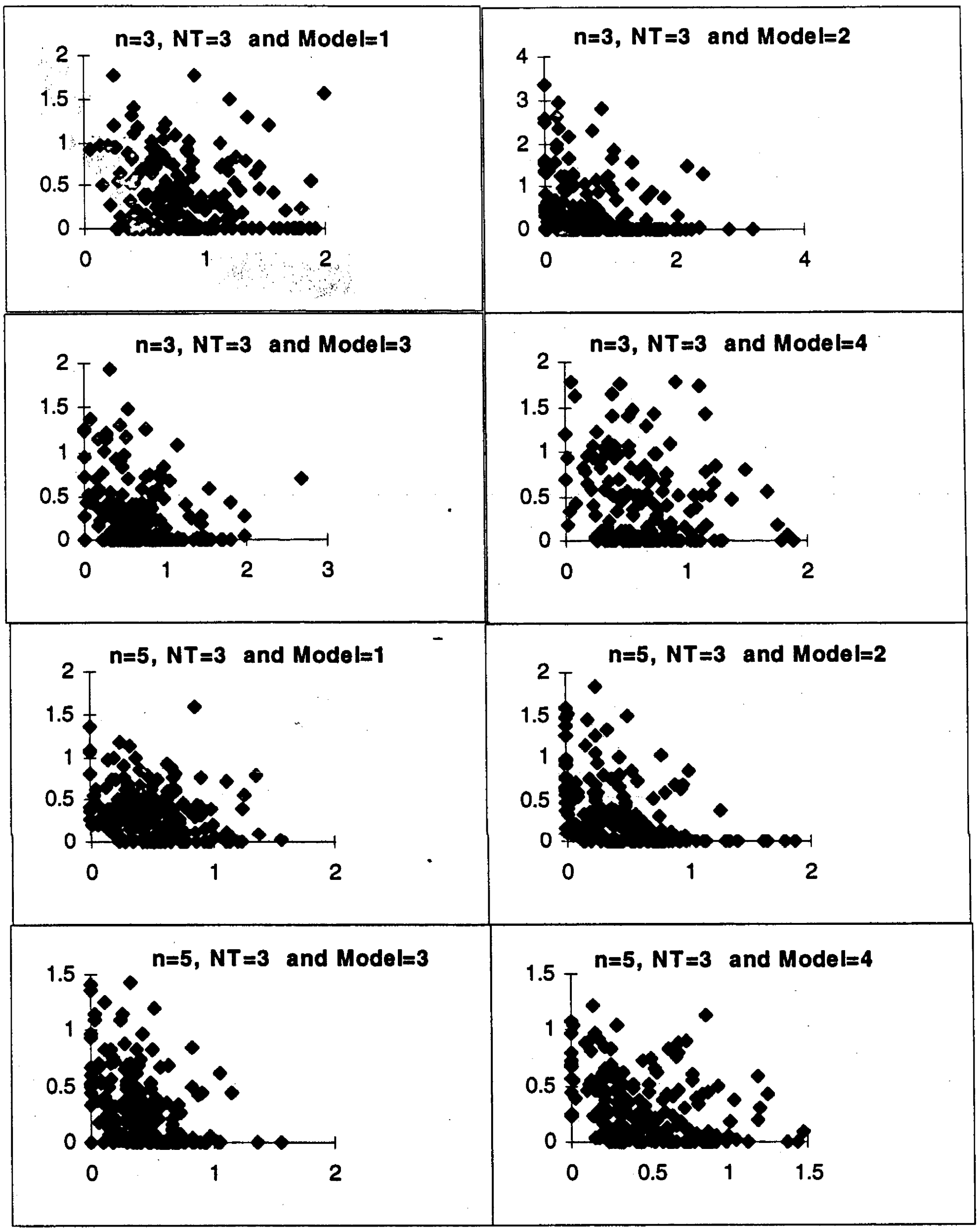
n=Number of observations for each subject; NT= Number of estimated threshold parameters.

Figure 10.3b: Distributions of ML estimates of φ_1, φ_2 obtained from 200 simulations for the threshold models 1,2,3 and 4 of chapter 5 with true of $\varphi_1 = 1$ and $\varphi_2 = 0.5$. Vertical axis is the φ_2 and horizontal gives φ_1.



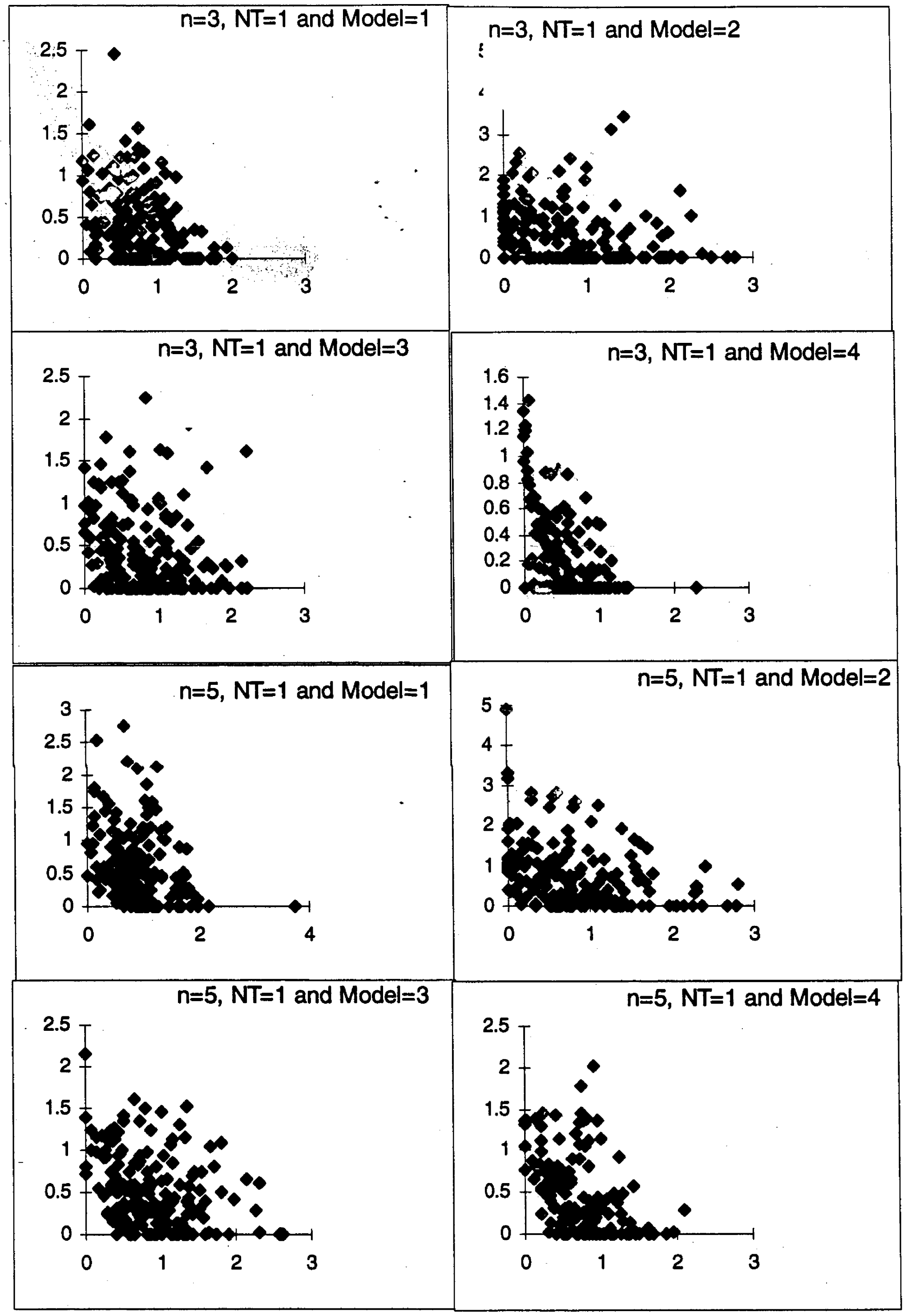
n=Number of observations for each subject; NT= Number of estimated threshold parameters.

Figure 10.3c: Distributions of ML estimates of φ_1, φ_2 obtained from 200 simulations for the threshold models 1,2,3 and 4 of chapter 5 with true of $\varphi_1 = 1$ and $\varphi_2 = 0.5$. Vertical axis is the φ_2 and horizontal gives φ_1.



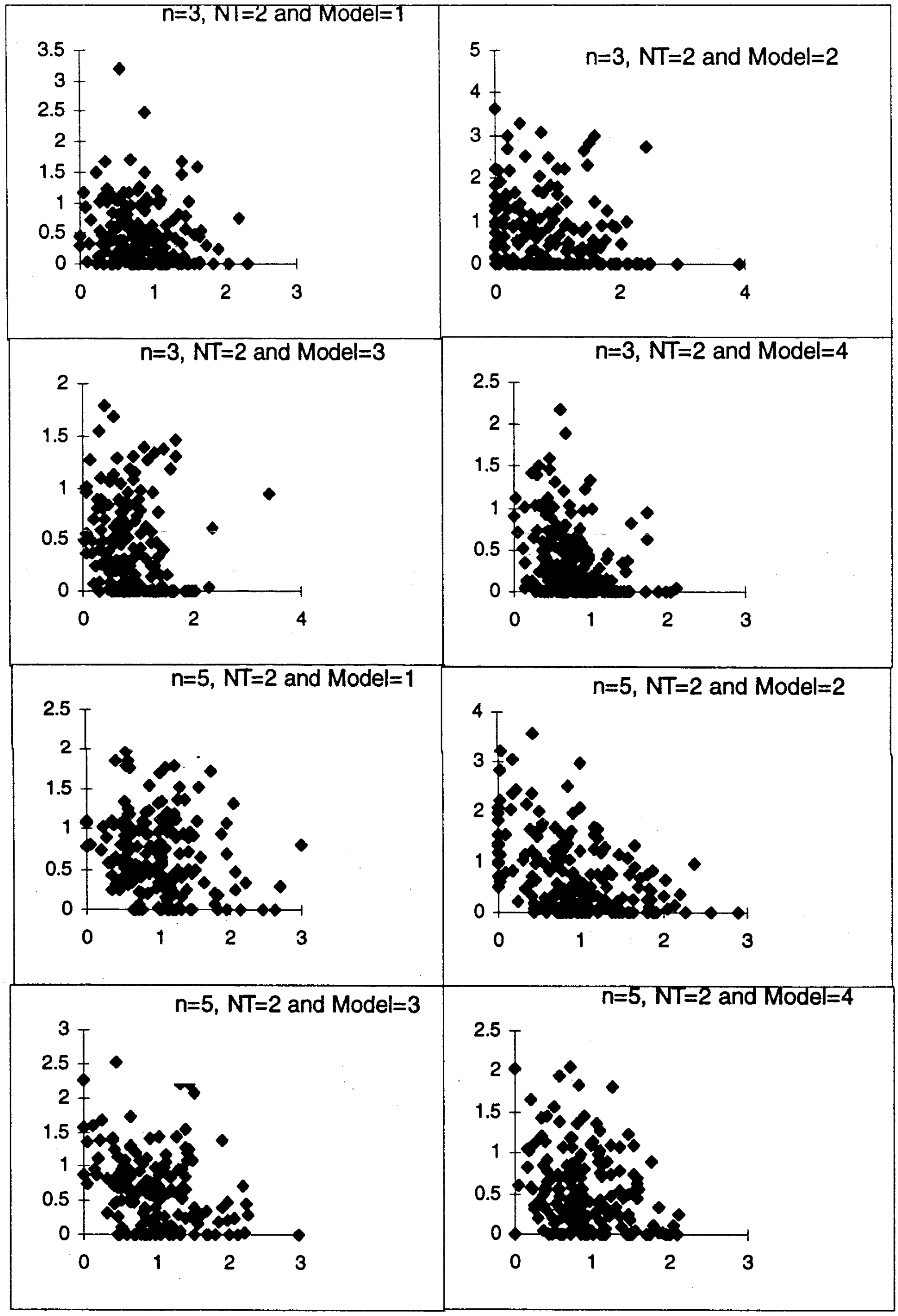
n=Number of observations for each subject; NT= Number of estimated threshold parameters.

Figure 10.3d: Distributions of REML estimates of φ_1, φ_2 obtained from 200 simulations for the threshold models 1,2,3 and 4 of chapter 5 with true of $\varphi_1 = 1$ and $\varphi_2 = 0.5$. Vertical axis is the φ_2 and horizontal gives φ_1.



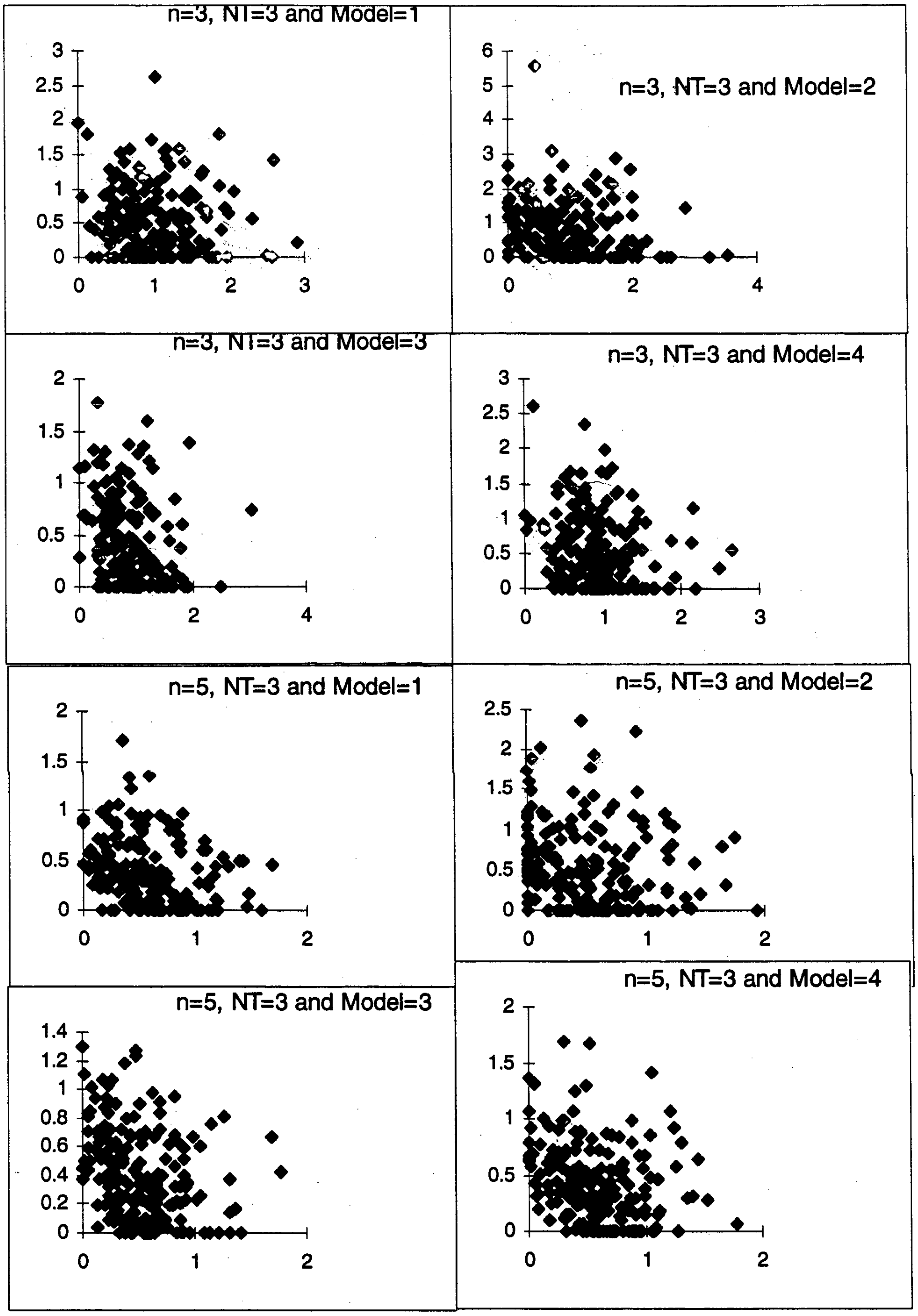
n=Number of observations for each subject; NT= Number of estimated threshold parameters.

Figure 10.3e: Distributions of REML estimates of φ_1, φ_2 obtained from 200 simulations for the threshold models 1,2,3 and 4 of chapter 5 with true of $\varphi_1 = 1$ and $\varphi_2 = 0.5$. Vertical axis is the φ_2 and horizontal gives φ_1.



n=Number of observations for each subject; NT= Number of estimated threshold parameters.

Figure 10.3f: Distributions of REML estimates of φ_1, φ_2 obtained from 200 simulations for the threshold models 1,2,3 and 4 of chapter 5 with true of $\varphi_1 = 1$ and $\varphi_2 = 0.5$. Vertical axis is the φ_2 and horizontal gives φ_1.



n=Number of observations for each subject; NT= Number of estimated threshold parameters.

10.4 AR(1)

In the models, for each subject, the random components are distributed as normal with variance covariance correponding to that of a first order autoregressive process, AR(1). For each of the threshold models in section 5.2 of chapter 5, response variables Y_{it} taking on values 0, 1, 2, 3 are generated according to the model $P(Y_{it} \le y) = G(\theta_y - \eta_{it})$,

10.4.1 $\eta_{it} = \beta_{j(i)} + u_{it}$,

where u_{it} is a normal random variable with zero mean and $\varphi\rho^{|t-s|}$ is the covariance between u_{it} and u_{is} (t,s=1,2,...5), β_j is the j^{th} treatment effect (active, j=1 and placebo, j=0) and j(i)= treatment received by subject i. We take $\theta_{-1} = -\infty$, $\theta_0 = 0$ and $\theta_3 = \infty$. For $\theta_1 = 1.5$, $\theta_2 = 2.2$, $\beta_1 = 2$ and $\beta_2 = 0.5$, 30 subjects are randomly assigned to either a treatment active (j=1) or a treatment placebo (j=2). The observations are obtained at time t=1,2,...5 for subjects i=1,2,...30. Estimates of parameters θ_1, θ_2 β_1, β_2, φ and ρ are obtained and process replicated 100 times. Tables 10.4.2.5j show the results by ML and REML methods for the different combinations of the parameters in the variances in which the φ and ρ are allowed to change. The threshold and fixed parameters are kept at the same values.

As in the one and two component models, results indicate that the ML estimators of parameters and variance components φ and ρ are negatively biased. The REML method reduces the biases of the estimators. The biases are increased by increasing the variance components φ and ρ for all four threshold models in section 5.2 of chapter 5. The average asymptotic standard error (ASE) of the parameter estimators are in agreement with the standard error over simulations (SEOS) in both ML and REML methods. However, the ASE of the ML and REML estimators of the variance components φ and ρ are greater than SEOS for all four threshold models in section 5.2 of chapter 5.

Table 10.4.2.5a: Estimated average biases and average standard error over 100 simulations for the mixed threshold models with random components following a AR(1) process.

			ML $\varphi = 0.51$ and $\rho = 0.1$				REML $\varphi = 0.51$ and $\rho = 0.1$			
M		TU	AB	SE	ASE	SEOS	AB	SE	ASE	SEOS
1	φ	0.51	-0.32	0.004	0.16	0.04	-0.27	0.01	0.17	0.05
	ρ	0.1	-0.17	0.04	0.65	0.42	-0.08	0.04	0.56	0.39
	θ_1	1.5	-0.2	0.01	0.15	0.14	-0.17	0.02	0.16	0.15
	θ_2	2.2	-0.26	0.02	0.18	0.16	-0.24	0.02	0.18	0.18
	β_1	2	-0.26	0.02	0.2	0.18	-0.22	0.02	0.2	0.19
	β_2	.5	-0.04	0.01	0.16	0.15	-0.05	0.02	0.16	0.16
2	φ	0.51	-0.15	0.01	0.4	0.14	-0.07	0.01	0.42	0.14
	ρ	0.1	-0.12	0.05	0.9	0.47	-0.07	0.04	0.76	0.44
	θ_1	1.5	-0.07	0.02	0.2	0.21	-0.07	0.02	0.2	0.2
	θ_2	2.2	-0.11	0.02	0.23	0.22	-0.09	0.02	0.23	0.23
	β_1	2	-0.16	0.03	0.28	0.26	-0.12	0.02	0.29	0.25
	β_2	.5	0.01	0.02	0.25	0.21	-0.01	0.02	0.25	0.21
3	φ	0.51	-0.263	0.011	0.169	0.105	-0.239	0.01	0.177	0.102
	ρ	0.1	-0.061	0.039	0.659	0.391	0.002	0.042	0.607	0.423
	θ_1	1.5	-0.154	0.015	0.164	0.154	-0.154	0.017	0.162	0.173
	θ_2	2.2	-0.194	0.019	0.195	0.189	-0.233	0.02	0.193	0.202
	β_1	2	-0.26	0.021	0.223	0.208	-0.276	0.023	0.227	0.23
	β_2	.5	-0.084	0.017	0.18	0.173	-0.082	0.017	0.178	0.17
4	φ	0.51	-0.279	0.009	0.164	0.09	-0.253	0.009	0.172	0.093
	ρ	0.1	-0.195	0.043	0.651	0.425	0.032	0.045	0.607	0.448
	θ_1	1.5	-0.191	0.019	0.173	0.187	-0.214	0.015	0.171	0.153
	θ_2	2.2	-0.268	0.022	0.199	0.224	-0.279	0.019	0.197	0.19
	β_1	2	-0.175	0.024	0.211	0.237	-0.208	0.02	0.215	0.205
	β_2	.5	-0.033	0.017	0.165	0.165	-0.016	0.015	0.172	0.154

Table 10.4.2.5b: Estimated average biases and average standard error over 100 simulations for the mixed threshold models with random components following a AR(1) process.

			ML $\varphi = 0.55$ and $\rho = 0.3$				REML $\varphi = 0.55$ and $\rho = 0.3$			
M		TU	AB	SE	ASE	SEOS	AB	SE	ASE	SEOS
1	φ	0.55	-0.35	0.01	0.17	0.07	-0.29	0.01	0.18	0.1
	ρ	0.3	-0.08	0.04	0.65	0.41	-0.01	0.04	0.51	0.39
	θ_1	1.5	-0.2	0.02	0.15	0.15	-0.15	0.02	0.16	0.17
	θ_2	2.2	-0.28	0.02	0.18	0.18	-0.19	0.02	0.18	0.19
	β_1	2	-0.25	0.02	0.2	0.19	-0.19	0.02	0.21	0.22
	β_2	.5	-0.04	0.02	0.16	0.16	-0.01	0.02	0.17	0.19
2	φ	0.55	-0.19	0.01	0.4	0.15	-0.09	0.02	0.42	0.22
	ρ	0.3	-0.13	0.05	0.95	0.45	-0.18	0.05	0.77	0.48
	θ_1	1.5	-0.09	0.02	0.2	0.21	-0.05	0.02	0.2	0.17
	θ_2	2.2	-0.12	0.03	0.23	0.26	-0.07	0.02	0.23	0.23
	β_1	2	-0.15	0.03	0.29	0.29	-0.1	0.03	0.29	0.28
	β_2	.5	0	0.02	0.25	0.25	0.05	0.03	0.26	0.27
3	φ	0.55	-0.098	0.008	0.161	0.083	-0.054	0.011	0.174	0.113
	ρ	0.3	-0.07	0.04	0.751	0.395	0.092	0.042	0.639	0.415
	θ_1	1.5	-0.092	0.016	0.166	0.158	-0.058	0.018	0.169	0.179
	θ_2	2.2	-0.14	0.019	0.198	0.195	-0.067	0.021	0.205	0.207
	β_1	2	-0.192	0.021	0.23	0.213	-0.147	0.022	0.238	0.223
	β_2	.5	-0.056	0.017	0.173	0.169	-0.065	0.016	0.178	0.165
4	φ	0.55	-0.118	0.008	0.158	0.077	-0.08	0.008	0.168	0.08
	ρ	0.3	-0.066	0.041	0.814	0.411	0.033	0.042	0.664	0.415
	θ_1	1.5	-0.119	0.019	0.183	0.186	-0.061	0.017	0.189	0.166
	θ_2	2.2	-0.149	0.023	0.21	0.231	-0.073	0.02	0.216	0.198
	β_1	2	-0.085	0.024	0.225	0.241	-0.02	0.022	0.232	0.224
	β_2	.5	0.005	0.017	0.163	0.167	0.097	0.016	0.17	0.164

Table 10.4.2.5c: Estimated average biases and average standard error over 100 simulations for the mixed threshold models with random components following a AR(1) process.

			ML $\varphi = 1.1$ and $\rho = 0.3$				REML $\varphi = 1.1$ and $\rho = 0.3$			
M		TU	AB	SE	ASE	SEOS	AB	SE	ASE	SEOS
1	φ	1.1	-0.81	0.02	0.25	0.17	-0.71	0.02	0.28	0.2
	ρ	0.3	-0.02	0.05	0.72	0.47	0.02	0.03	0.59	0.33
	θ_1	1.5	-0.33	0.02	0.2	0.2	-0.29	0.02	0.2	0.21
	θ_2	2.2	-0.45	0.02	0.23	0.25	-0.39	0.03	0.24	0.27
	β_1	2	-0.43	0.03	0.28	0.27	-0.35	0.03	0.3	0.3
	β_2	1	-0.13	0.02	0.24	0.24	-0.1	0.03	0.25	0.27
2	φ	1.1	-0.71	0.02	0.41	0.17	-0.62	0.02	0.43	0.2
	ρ	0.3	-0.13	0.05	0.88	0.48	-0.04	0.04	0.72	0.44
	θ_1	1.5	-0.18	0.02	0.19	0.17	-0.22	0.02	0.19	0.19
	θ_2	2.2	-0.26	0.02	0.22	0.21	-0.3	0.02	0.22	0.22
	β_1	2	-0.23	0.03	0.29	0.26	-0.3	0.03	0.29	0.29
	β_2	.5	-0.05	0.03	0.25	0.26	-0.1	0.03	0.26	0.28
3	φ	1.1	-0.849	0.009	0.165	0.092	-0.787	0.012	0.183	0.120
	ρ	0.3	0.072	0.034	0.560	0.343	0.065	0.031	0.508	0.308
	θ_1	1.5	-0.398	0.016	0.148	0.163	-0.350	0.015	0.154	0.154
	θ_2	2.2	-0.531	0.020	0.173	0.202	-0.495	0.018	0.179	0.177
	β_1	2	-0.498	0.022	0.195	0.222	-0.420	0.020	0.205	0.197
	β_2	.5	-0.053	0.018	0.176	0.182	-0.063	0.018	0.181	0.178
4	φ	1.1	-0.84	0.01	0.17	0.11	-0.77	0.01	0.19	0.1
	ρ	0.3	0.04	0.04	0.57	0.37	0.07	0.04	0.44	0.37
	θ_1	1.5	-0.39	0.01	0.15	0.15	-0.37	0.02	0.15	0.16
	θ_2	2.2	-0.54	0.02	0.17	0.18	-0.48	0.02	0.18	0.18
	β_1	2	-0.51	0.02	0.2	0.19	-0.41	0.02	0.21	0.19
	β_2	.5	-0.08	0.02	0.18	0.18	-0.07	0.02	0.18	0.19

Table 10.4.2.5d: Estimated average biases and average standard error over 100 simulations for the mixed threshold models with random components following a AR(1) process.

			ML $\varphi = 0.84$ and $\rho = 0.8$				REML $\varphi = 0.84$ and $\rho = 0.8$			
M		TU	AB	SE	ASE	SEOS	AB	SE	ASE	SEOS
1	φ	0.84	-0.51	0.02	0.18	0.16	-0.4	0.02	0.21	0.18
	ρ	0.8	-0.03	0.01	0.36	0.08	-0.03	0.01	0.27	0.1
	θ_1	1.5	-0.12	0.02	0.16	0.16	-0.09	0.02	0.16	0.16
	θ_2	2.2	-0.16	0.02	0.19	0.2	-0.11	0.02	0.19	0.2
	β_1	2	-0.18	0.03	0.23	0.26	-0.1	0.03	0.25	0.25
	β_2	.5	0.01	0.02	0.19	0.2	0.04	0.02	0.21	0.2
2	φ	0.84	-0.474	0.022	0.396	0.217	-0.391	0.025	0.416	0.251
	ρ	0.8	-0.103	0.023	1.059	0.228	-0.080	0.020	0.778	0.199
	θ_1	1.5	-0.077	0.022	0.196	0.222	-0.062	0.018	0.199	0.182
	θ_2	2.2	-0.126	0.024	0.230	0.238	-0.074	0.022	0.235	0.223
	β_1	2	-0.141	0.031	0.305	0.315	-0.123	0.030	0.311	0.304
	β_2	.5	-0.027	0.024	0.264	0.236	-0.008	0.027	0.276	0.275
3	φ	0.84	-0.517	0.015	0.18	0.152	-0.441	0.019	0.204	0.187
	ρ	0.8	-0.048	0.015	0.37	0.153	-0.073	0.023	0.341	0.234
	θ_1	1.5	-0.109	0.016	0.168	0.163	-0.109	0.015	0.168	0.146
	θ_2	2.2	-0.138	0.02	0.2	0.197	-0.197	0.019	0.198	0.188
	β_1	2	-0.196	0.027	0.252	0.267	-0.268	0.023	0.256	0.235
	β_2	.5	-0.014	0.022	0.205	0.216	-0.075	0.021	0.212	0.214
4	φ	0.84	-0.51	0.016	0.18	0.157	-0.477	0.016	0.195	0.163
	ρ	0.8	-0.048	0.012	0.372	0.123	-0.049	0.016	0.343	0.156
	θ_1	1.5	-0.167	0.018	0.175	0.181	-0.144	0.019	0.178	0.187
	θ_2	2.2	-0.227	0.021	0.202	0.206	-0.176	0.02	0.206	0.199
	β_1	2	-0.129	0.026	0.243	0.258	-0.098	0.025	0.25	0.252
	β_2	.5	0.057	0.015	0.195	0.153	0.04	0.019	0.198	0.188

Table 10.4.2.5e: Estimated average biases and average standard error over 100 simulations for the mixed threshold models with random components following a AR(1) process.

			ML $\varphi = 0.303$ and $\rho = 0.1$				REML $\varphi = 0.303$ and $\rho = 0.1$			
M		TU	AB	SE	ASE	SEOS	AB	SE	ASE	SEOS
1	φ	.303	-0.111	0.005	0.165	0.051	-0.063	0.005	0.175	0.052
	ρ	0.1	-0.115	0.043	0.643	0.431	-0.073	0.043	0.536	0.429
	θ_1	1.5	-0.099	0.014	0.16	0.139	-0.062	0.016	0.164	0.165
	θ_2	2.2	-0.124	0.017	0.186	0.17	-0.065	0.018	0.191	0.181
	β_1	2	-0.137	0.018	0.206	0.183	-0.099	0.018	0.211	0.182
	β_2	.5	-0.011	0.015	0.158	0.145	-0.007	0.016	0.162	0.156
2	φ	.303	0.02	0.011	0.396	0.115	0.054	0.012	0.41	0.118
	ρ	0.1	-0.167	0.046	0.965	0.463	0.034	0.039	0.923	0.394
	θ_1	1.5	-0.043	0.019	0.2	0.193	-0.028	0.02	0.201	0.204
	θ_2	2.2	-0.044	0.023	0.235	0.231	-0.016	0.024	0.237	0.243
	β_1	2	-0.075	0.028	0.284	0.281	-0.025	0.029	0.293	0.294
	β_2	.5	0.013	0.024	0.246	0.243	0.031	0.023	0.246	0.234
3	φ	.303	-0.105	0.008	0.161	0.076	-0.056	0.009	0.174	0.09
	ρ	0.1	-0.144	0.039	0.758	0.388	0.016	0.041	0.64	0.415
	θ_1	1.5	-0.109	0.016	0.165	0.163	-0.086	0.016	0.169	0.155
	θ_2	2.2	-0.159	0.02	0.198	0.196	-0.105	0.019	0.203	0.185
	β_1	2	-0.185	0.022	0.228	0.218	-0.161	0.024	0.233	0.241
	β_2	.5	-0.079	0.016	0.172	0.161	-0.1	0.017	0.181	0.175
4	φ	.303	-0.114	0.008	0.158	0.085	-0.085	0.007	0.168	0.075
	ρ	0.1	-0.116	0.04	0.801	0.403	-0.008	0.042	0.687	0.418
	θ_1	1.5	-0.136	0.017	0.181	0.174	-0.084	0.018	0.185	0.182
	θ_2	2.2	-0.176	0.021	0.208	0.213	-0.093	0.021	0.213	0.205
	β_1	2	-0.108	0.019	0.22	0.191	-0.035	0.023	0.232	0.226
	β_2	.5	0.008	0.014	0.164	0.145	0.072	0.014	0.165	0.141

CHAPTER ELEVEN

DISCUSSION

The GLMM is applied to various discrete response data through chapters 5-9. Essentially, the threshold models of McCullagh (1980) are generalised by including random components in the linear predictor and the GLMM allows general specification of the random components variance-covariance matrices. Both approximate ML and REML estimates of parameters and variance components are developed by assuming normality for random components.

It is shown that the GLMM has great potential to analyse discrete response data. The estimates of regression coefficients are shown to be consistent, though the method is an approximate approach. The results in ML and REML are closely in agreement in most applications. Moreover, the results of the applications also indicate that the choice of the threshold models listed in chapter 5 appear not to be very critical.

In terms of random components, the results of the applications shown that the variances of the random components are significant for most cases.

Furthermore, the GLMM approach gives the prediction of the random components. These estimates of random components (prediction) are very important, eg, in chapter 6, the estimated household random effects may be matched to household descriptors in an effort to delineate what is important in a household occupied by cohabiting drug users, or in section 7.8 of chapter 7, the predicted values of the second random component may be used to show the direction of patient effect change (increase or decrease over time) and identifying patients who show greatest changes over time. Consequently, it is important to include random components in the linear predictor of the threshold models.

In addition, chapters 6 and 9 introduce threshold models to analyse two important types of data that occur more frequently in practice. The GLMM approach allows the modelling of these data in addition to fixed regression parameters in terms of random components with more complicated variance-covariance structures.

For any particular threshold model (1, 2, 3 or 4 of chapter 5), the simulation studies show that the REML method reduces the biases of parameters and variance components estimators. The estimation approach is improved for increasing number of observations for each subject. It also minimises the difference between the two estimation approaches ML and

REML. Moreover, the simulation results also indicate that in both ML and REML methods the estimates of variance components are less biased for more categories of response data.

As in LMM (McGilchrist 1989), although the REML method reduces the bias, the variance component estimates are negatively biased in both ML and REML for correlated random component models.

11.1 GENERALIZATION

In the chapters 5-10, the threshold models are based on the assumption that the cut-points (threshold parameters) do not depend on the any regression variable. A generalization of those models is to model threshold parameters in terms of some regression variables as

11.1.1 $\theta_j = \mathbf{x}^* \alpha_j$

where $\mathbf{x}^*$ is a vector of regression variables and $\alpha_j = [\alpha_{j1}, \alpha_{j2}, \ldots, \alpha_{jp'}]'$ is called a category-specific parameters vector (Terza, 1985).

A special case of the model 11.1.1 is to model threshold parameters as a function of time in chapters 7 and 8.

The threshold models in this thesis can be modified to analyse bivariate or multivariate ordinal response data. For bivariate ordinal response data, the threshold model is given by

11.1.2 $$p(Y_1 \le y_1 , Y_2 \le y_2) = G(\theta_{y_1} - \eta_1 , \theta_{y_2} - \eta_2)$$

where $G(.,.)$ is some bivariate distribution, $\eta_1 = \mathbf{x}'\beta_1 + \mathbf{u}$ and $\eta_2 = \mathbf{x}'\beta_2 + \mathbf{u}$.

Application of the GLMM to continuous-ratio model; and the so called stereotype regression model (Anderson 1984) follows a similar direction to the threshold model in this thesis.

11.2 FURTHER RESEARCH DIRECTIONS

The parameters and variance components are tested by using their corresponding estimated standard errors. Moreover, in this thesis three types of selection of the best model among four threshold models listed in chapter 5 are given. In chapter 5, 6 and 7, 8 selections are based on the estimated values of conditional log-likelihood (l_1) and discriminate approach respectively. While in chapter 9, the selection of the best threshold model is based on the goodness of fit statistic Q. Hence, asymptotic theory that is needed to be able to test and select a more appropriate model.

In chapters 7 and 9, for multiple observation of the same subject, models involving further random components corresponding to changes of subject effects over time are used. These models will be more general if the estimation approach gives estimation equations for hyperparameters describing covariance between those random components.

For correlated models, eg, AR(1), simulation results indicate that both ML and REML estimators of variance components are negatively biased with REML having smaller bias. Further investigation to reduce the biases are of considerable interest.

Chapters 7, 8, 9 and 10 give models for the correlated random components. These models can be generalised to MA(p,q) and ARMA(p,d,q).

The incidence matrices $\mathbf{Z}$ associated with random components $\mathbf{u}$ are assumed to be known in this thesis. However, as Harville (1977) mentioned, these matrices in some applications are a function of unknown parameters. The motivating example is the kind of data set that have been discussed in chapter 9. We have applied the random component threshold models to analyse 45 diagnostics test in 39 counties in Washington State. The results and data sets are not reported in this thesis. The estimated variance for county random effects for threshold model 2 of chapter 5, are 1.24, 0.86, 3.11, 2.98, 1.8, 1.1, 1.3, 2.9, 1.43, 1.4, 2.64, 2.7, 1.41, 2.11, 2.5, 2.75, 5.32, 5.8, 2.9, 1.8, 1.41, 1.1, 3.5, 1.6, 1.42, 1.82, 4.03, 2.61, 2.41, 1.32, 3.8, 3.18, 3.2, 3.36, 1.62, 1.4, 2.11, 2.9, 3.25, 0.53, 1.4, 0.9, 0.84, 1.7 and 0.52 in the REML method. Then, attempts are made to combine all 45 data sets and analyse by fitting model

11.2.1 $$\boldsymbol{\eta} = \mathbf{X}\boldsymbol{\beta} + \mathbf{Z}(\boldsymbol{\gamma})\mathbf{u}$$

where $\mathbf{u}$ is $N(\mathbf{0}, \mathbf{A}(\varphi))$ and γ is an unknown parameters vector. However, these attempts have not been completed.

Furthermore, a limited simulation (not reported in thesis) for simple mixed normal error model is shown to have very good accuracy in estimating γ. This topic requires further efforts to be completed.

In chapter 9 a simple identity composite link function is used. This approach can be generalised for a more general composite link function.

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APPENDIX A

SOME USEFUL THEOREMS AND LEMMAS

Theorem 1: For given nonsingular matrices $\mathbf{D}$ and $\mathbf{A}$, the positive symmetric matrix $\boldsymbol{\Sigma} = \mathbf{D} + \mathbf{ZAZ'}$ has the following properties

A.1 $\quad \boldsymbol{\Sigma}^{-1} = \mathbf{D}^{-1} - \mathbf{D}^{-1}\mathbf{ZT^{*}Z'D}^{-1}, \quad \mathbf{T}^{*} = (\mathbf{A}^{-1} + \mathbf{Z'D}^{-1}\mathbf{Z})^{-1},$

A.2 $\quad |\boldsymbol{\Sigma}| = |\mathbf{T}^{-1}||\mathbf{D}||\mathbf{A}|,$

A.3 $\quad |\mathbf{A}^{-1} + \mathbf{Z'D}^{-1}\mathbf{Z}| \neq 0$, ie the $\mathbf{T}^{*}$ does exist.

Proof:

The proof of the A.1 has been given in chapter 4 provided A.3.

A.2 Using Searle (1982) page 258, we have

(1) $\quad \begin{vmatrix} \mathbf{T}^{-1} & \mathbf{Z'} \\ \mathbf{Z} & \mathbf{D} \end{vmatrix} = |\mathbf{T}^{-1}||\mathbf{D} - \mathbf{ZTZ'}| = |\mathbf{T}^{-1}||\boldsymbol{\Sigma}^{-1}||\mathbf{D}|^{2}, \; \mathbf{D} - \mathbf{ZTZ'} = \mathbf{D}\boldsymbol{\Sigma}^{-1}\mathbf{D}$

(2) $\quad \begin{vmatrix} \mathbf{T}^{-1} & \mathbf{Z'} \\ \mathbf{Z} & \mathbf{D} \end{vmatrix} = |\mathbf{D}||\mathbf{T}^{-1} - \mathbf{Z'D}^{-1}\mathbf{Z}| = |\mathbf{D}||\mathbf{A}^{-1}|, \quad \mathbf{T}^{-1} - \mathbf{Z'D}^{-1}\mathbf{Z} = \mathbf{A}^{-1}.$

Equating (1) to (2) gives

(3) $\quad |\mathbf{T}^{*-1}||\boldsymbol{\Sigma}^{-1}||\mathbf{D}|^{2} = |\mathbf{A}^{-1}||\mathbf{D}|^{1}$ which yields $|\boldsymbol{\Sigma}| = |\mathbf{T}^{*-1}||\mathbf{A}||\mathbf{D}|$.

Result A.3 follows from A.2.

Definition: For a m×n matrix $\mathbf{A}$, any matrix $\mathbf{A}^{-}$ that satisfies (4) is called a generalized inverse of the matrix $\mathbf{A}$,

(4) $\quad \mathbf{AA^{-}A} = \mathbf{A}$.

Definition: The Moore-Penrose inverse ($\mathbf{A}^+$) of the matrix $\mathbf{A}$ is a particular generalized inverse of the matrix $\mathbf{A}$ which satisfies the four following conditions,

(a) $\mathbf{AA^+A} = \mathbf{A}$, (b) $\mathbf{A^+AA^+} = \mathbf{A^+}$

(c) $(\mathbf{A^+A})' = \mathbf{A^+A}$, (d) $(\mathbf{AA^+})' = \mathbf{AA^+}$.

Corollary 1: (Searle 1982)

Let $\mathbf{A}^-$ be any particular generalized inverse of matrix $\mathbf{A}$. Marsaglia and Styan (1974) showed that with

(7) $\mathbf{S} = \mathbf{D} - \mathbf{CA^-B}$, the matrix $\mathbf{Q} = \begin{bmatrix} \mathbf{A} & \mathbf{B} \\ \mathbf{C} & \mathbf{D} \end{bmatrix}$ has,

(8) $$\dot{\mathbf{Q}} = \begin{bmatrix} \mathbf{A}^- & 0 \\ 0 & 0 \end{bmatrix} + \begin{bmatrix} -\mathbf{A^-B} \\ \mathbf{I} \end{bmatrix} \mathbf{S}^- [-\mathbf{CA}^- \quad \mathbf{I}]$$

as a generalized inverse *if and only if* $r_Q = r_A + r_S$, where $\mathbf{A}^-$ is a particular g-inverse and $\mathbf{S}^-$ is a g-inverse.

The proof is given in Marsaglia and Styan (1974) and a discussion is provided by Searle (1982) page 261.

Lemma 1: (Rao 1952)

For any positive definite matrix $\mathbf{A} = \begin{bmatrix} \mathbf{A}_{11} & \mathbf{A}_{12} \\ \mathbf{A}'_{12} & \mathbf{A}_{22} \end{bmatrix}$, there is a upper triangular matrix $\mathbf{B}$ that satisfies the following relationship

(9) $\mathbf{BAB}' = \mathbf{D}$,

where $\mathbf{D}$ is a diagonal matrix , $\mathbf{B} = \begin{bmatrix} \mathbf{I} & -\mathbf{A}_{12}\mathbf{A}_{22}^{-1} \\ 0 & \mathbf{I} \end{bmatrix}$ and

$$\mathbf{D} = \begin{bmatrix} \mathbf{A}_{11} - \mathbf{A}_{12}\mathbf{A}_{22}^{-1}\mathbf{A}_{21} & . \\ . & \mathbf{A}_{22} \end{bmatrix}.$$

Thus, we have

(10) $\quad \mathbf{A}^{-1} = \mathbf{B}'^{-1}\mathbf{D}^{-1}\mathbf{B}^{-1}.$

Replacing components in the right hand side of (10) gives following expression for the inverse of nonsingular matrix $\mathbf{A}$.

(11) $\quad \mathbf{A}^{-1} = \begin{bmatrix} 0 & 0 \\ 0 & \mathbf{A}_{22}^{-1} \end{bmatrix} + \begin{bmatrix} \mathbf{I} \\ -\mathbf{A}_{22}^{-1}\mathbf{A}_{21} \end{bmatrix} [\mathbf{A}_{11} - \mathbf{A}_{12}\mathbf{A}_{22}^{-1}\mathbf{A}_{21}]^{-1} [\mathbf{I} \quad -\mathbf{A}_{12}\mathbf{A}_{22}^{-1}].$

This is the equation 14 in Searle (1982), page 260.

Theorem 2:

Let $\mathbf{y}$ be a multivariate normally distributed vector of dimension n with μ as mean and Σ as variance-covariance matrix. Then

3.1 $\quad E(\mathbf{y}'\mathbf{A}\mathbf{y}) = tr(\mathbf{A}\Sigma) + \mu'\mathbf{A}\mu$, true also if $\mathbf{y}$ is not normal,

3.2 $\quad Var(\mathbf{y}'\mathbf{A}\mathbf{y}) = 2tr(\mathbf{A}\Sigma)^2 + 4\mu'\mathbf{A}\Sigma\mathbf{A}\mu$,

3.3 $\quad Cov(\mathbf{y}'\mathbf{A}\mathbf{y}, \mathbf{y}'\mathbf{B}\mathbf{y}) = 2tr(\mathbf{A}\Sigma\mathbf{B}\Sigma) + 4\mu'\mathbf{A}\Sigma\mathbf{B}\mu$, for $\mathbf{A}' = \mathbf{A}$, and $\mathbf{B} = \mathbf{B}'$,

3.4 $\quad k_r(\mathbf{y}'\mathbf{A}\mathbf{y}) = 2^{r-1}(r-1)![tr(\mathbf{A}\Sigma)^r + r\mu'(\mathbf{A}\Sigma)^{r-1}\mu$,

3.5 $\quad Var(\mathbf{Q}\mathbf{y}) = \mathbf{Q}\,var(\mathbf{y})\mathbf{Q}' = \mathbf{Q}\Sigma\mathbf{Q}'$

3.6 $\quad Cov(\mathbf{Q}\mathbf{y}, \mathbf{y}'\mathbf{P}') = \mathbf{Q}Var(\mathbf{y})\mathbf{P}' = \mathbf{Q}\Sigma\mathbf{P}'$

where $tr(\mathbf{A})$ indicates trace of matrix $\mathbf{A}$, and $k_r(.)$ represents r^{th} cumulant of the (.), $\mathbf{Q}$ and $\mathbf{P}$ are known matrices.

Proof is given in Searle (1971).

APPENDIX B

DATA SETS

This appendix represents the data sets that have been used in chapters 5-9. These data sets are dairy produce data, arthritis data, methadone program data, skin condition data, skin disorder data, respiratory disorder data, map data and chemotherapy data. These data sets are copied from journal and books except for methadone and chemotherapy data. Thus, the data sets are explained in detail in those journal and books in addition to the information that have been given in the corresponding chapters in this thesis.

Table 1: Dairy produce data.

S	BGBB					MB					MMGB					LSB				
	0.01	.1	1	2.5	5	0.01	.1	1	2.5	5	0.01	.1	1	2.5	5	0.01	.1	1	2.5	5
1	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1	0	0	0	0	1
2	0	0	0	0	1	0	0	0	0	1	0	0	1	1	1	0	0	0	0	1
3	0	0	0	2	1	0	0	0	0	0	0	0	0	2	2	0	0	0	0	0
4	0	0	0	1	1	0	0	0	0	1	0	0	0	1	1	0	0	0	1	1
5	1	1	2	2	2	1	1	1	2	2	1	1	1	2	2	1	1	2	2	2
6	0	0	0	0	2	0	0	1	0	0	0	0	0	1	1	0	0	0	2	2
7	0	0	0	0	1	0	0	0	2	2	0	0	0	1	1	0	0	1	1	2
8	0	0	1	2	2	0	1	1	2	2	0	0	1	1	1	0	0	0	1	1
9	1	2	2	2	2	1	2	2	2	2	0	2	2	2	2	0	2	2	2	2
10	0	0	1	2	1	0	0	1	2	2	0	0	2	2	2	0	0	1	1	1
11	2	2	2	2	2	2	2	1	2	2	0	0	1	1	2	2	2	1	1	2
12	0	0	1	1	1	0	0	1	1	1	0	0	0	1	1	0	0	0	1	1
13	0	0	1	1	1	0	0	1	2	2	0	0	0	1	1	0	0	0	0	0
14	1	1	2	1	1	1	2	2	2	2	0	2	2	1	1	1	2	1	1	1
15	0	0	2	2	2	0	2	2	2	2	0	1	1	2	2	0	0	1	2	2
16	0	0	1	2	2	0	0	0	2	2	0	0	0	2	1	0	0	1	2	2
17	0	0	0	0	0	0	0	1	0	1	0	0	1	0	0	0	0	0	0	0
18	0	0	0	2	2	0	0	0	1	1	0	0	0	0	0	0	0	0	0	0
19	0	2	2	2	2	0	0	2	2	2	0	2	2	2	2	1	0	1	2	2
20	0	1	2	1	2	1	1	2	1	1	1	2	2	2	2	1	1	2	2	2
21	0	0	0	0	1	0	0	0	1	2	0	0	0	1	2	0	0	1	1	1
22	2	2	2	2	2	2	2	2	2	2	2	2	2	1	2	2	2	2	2	2
23	0	1	1	1	1	0	1	1	1	1	0	0	1	1	1	0	0	1	1	2
24	0	0	0	1	1	0	0	1	1	1	0	0	1	2	1	0	0	0	1	1
25	0	0	1	2	2	0	2	1	2	1	0	1	2	2	1	0	0	0	2	2
26	2	2	2	1	1	2	2	2	2	2	2	2	2	2	2	1	2	2	1	1
27	0	0	0	2	2	0	0	0	2	1	0	0	0	2	0	0	0	0	2	2
28	0	0	1	0	2	0	0	0	0	1	0	0	0	0	2	0	0	0	2	2
29	0	2	2	2	2	2	1	2	2	2	0	0	2	2	2	0	2	2	2	2
30	0	0	0	0	1	0	1	1	1	1	0	0	0	1	1	0	0	0	0	0
31	1	2	2	2	2	0	2	2	2	2	0	0	2	2	2	0	1	2	2	2
32	0	1	1	0	2	0	0	0	0	0	0	0	0	1	2	0	0	0	1	2
33	0	0	0	0	1	0	0	0	2	2	0	0	0	1	1	0	0	0	1	1
34	2	2	2	2	2	2	2	2	2	2	2	2	2	1	2	0	2	2	2	2
35	0	1	2	0	1	0	0	2	1	0	0	2	2	0	2	0	2	2	2	2
36	1	1	1	2	2	0	0	2	2	2	0	0	1	1	2	0	1	1	2	2
37	0	0	0	1	2	0	0	0	0	0	0	0	0	1	1	0	0	0	1	0
38	0	1	1	1	1	0	0	0	0	1	0	0	1	1	1	0	0	1	1	2
39	0	0	0	2	2	0	0	0	2	2	0	0	1	1	2	0	0	1	2	2
40	0	0	0	1	1	0	0	0	1	1	0	0	0	1	1	0	0	0	0	0
41	0	0	0	0	1	0	0	1	1	1	0	0	0	1	1	0	0	0	0	0
42	0	0	0	1	1	0	0	1	0	1	0	0	0	1	1	0	0	0	0	1
43	0	0	0	0	0	0	0	0	0	0	0	0	0	0	2	0	0	0	0	0
44	0	0	0	0	2	0	0	0	2	0	0	0	0	0	2	0	0	0	0	0
45	2	2	2	2	2	0	2	2	2	2	2	2	2	2	2	0	0	2	2	2
46	0	0	0	0	2	0	0	0	2	1	0	0	0	2	2	0	0	0	1	2
47	0	0	0	2	0	0	0	2	2	0	0	0	0	2	2	0	0	0	0	0
48	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	1	1	0
49	0	0	0	0	1	0	0	0	0	1	0	0	0	0	1	0	0	0	0	2
50	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0
51	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1
52	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0
53	0	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
54	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
55	0	0	0	0	1	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0
56	0	0	2	2	2	0	2	2	2	2	0	2	2	2	2	0	0	2	2	2
57	0	2	2	2	2	0	2	2	2	2	0	0	2	2	2	0	2	1	2	2
58	0	2	2	2	2	0	2	2	2	2	0	1	2	2	2	0	0	2	2	2
59	0	2	2	2	2	1	2	2	2	2	0	2	2	2	2	0	2	2	2	2
60	0	2	2	2	2	0	0	0	2	2	0	0	0	2	2	0	1	2	2	2
61	0	0	0	2	2	0	1	1	2	2	0	0	0	2	2	0	0	0	2	2
62	0	0	2	2	2	0	0	2	2	2	0	0	2	2	2	0	2	0	2	2
63	0	0	0	0	0	0	0	0	1	2	0	0	1	0	0	0	0	0	0	0
64	0	0	0	2	2	0	0	2	2	2	0	2	2	2	2	0	2	0	1	1

Table 1: (continued).

65	0	0	0	0	2	0	0	0	0	0	0	1	1	0	0	0	0	0	1	1
66	0	0	0	2	2	0	0	0	1	2	1	1	1	2	2	0	0	0	1	1
67	0	0	0	1	2	0	0	0	0	1	0	0	0	0	0	0	0	0	1	0
68	1	1	2	2	2	1	1	2	2	2	0	1	2	2	2	1	1	2	1	2
69	0	2	2	2	2	0	0	0	0	1	0	2	0	0	0	0	0	0	0	0
70	0	0	2	2	2	0	0	1	1	2	0	0	0	1	1	0	0	2	1	2
71	1	1	1	1	2	1	2	2	1	2	0	0	1	1	1	0	1	1	2	2
72	2	2	2	2	2	0	2	2	2	2	2	2	2	2	2	0	2	2	2	2
73	0	2	2	2	2	2	2	2	2	2	0	0	2	2	2	0	0	1	2	2
74	1	1	0	1	1	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0
75	0	0	1	1	1	0	0	1	1	1	0	0	1	1	1	0	0	1	1	1
76	0	0	0	0	2	0	0	0	1	1	0	0	0	0	0	0	0	0	2	2
77	0	1	1	2	1	0	0	1	2	2	0	0	1	2	2	0	1	1	2	2
78	0	2	2	2	2	0	0	2	2	2	0	0	2	2	2	0	0	0	2	2
79	0	0	0	0	2	0	0	0	0	0	0	0	0	0	1	0	0	0	1	2
80	0	0	2	2	1	0	0	2	2	2	0	2	0	2	2	0	0	0	2	2
81	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
82	0	1	2	1	2	0	2	2	2	2	0	1	1	1	1	0	0	1	1	2
83	0	0	0	1	2	0	0	1	2	2	0	0	1	1	2	0	1	1	2	2
84	0	0	1	1	1	0	0	0	2	2	0	0	1	2	2	0	0	0	0	2
85	0	0	1	2	2	0	0	1	2	2	0	0	1	2	2	0	0	1	2	2
86	0	0	2	2	2	0	0	2	2	2	0	0	2	2	2	0	0	1	2	2
87	0	0	0	2	2	0	0	2	2	2	0	0	1	2	2	0	0	1	2	2
88	0	0	1	0	2	0	0	1	0	2	0	0	0	0	0	0	0	0	0	0
89	0	2	2	2	2	0	2	2	1	2	0	2	2	2	2	0	2	2	2	2
90	0	2	2	2	2	1	2	2	2	2	0	1	2	2	2	1	2	2	2	2
91	2	2	2	2	2	0	2	2	2	2	2	2	2	2	2	0	2	2	2	2
92	0	1	1	2	2	0	0	1	1	2	0	0	1	2	2	1	1	2	2	2
93	0	2	2	2	2	2	2	2	2	2	0	0	2	2	2	0	2	2	2	2
94	0	0	2	2	2	0	0	2	2	2	0	0	2	2	2	0	0	2	2	2
95	2	2	2	2	2	0	2	2	2	2	1	0	2	2	2	1	2	2	1	1
96	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	1	1	1	1
97	0	0	0	0	1	0	0	2	2	2	0	0	2	2	2	0	0	0	0	1
98	0	0	0	2	2	0	2	2	2	2	2	2	2	2	2	2	2	2	2	2
99	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1
100	0	0	0	0	1	0	0	0	0	0	0	0	0	0	1	0	0	2	2	2
101	0	0	0	2	2	0	0	0	2	2	0	0	0	2	2	0	0	1	1	1
102	0	0	0	2	2	0	0	0	2	2	0	2	0	2	2	2	2	2	2	2
103	0	0	0	2	2	0	0	0	2	0	0	0	0	2	2	0	0	0	1	0
104	0	0	2	2	2	0	0	0	2	2	0	2	0	2	2	1	2	2	2	2
105	0	2	0	2	2	0	2	0	2	2	0	0	0	2	2	0	0	1	2	2
106	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1
107	0	2	2	2	2	0	0	0	0	2	0	0	0	1	1	0	2	2	2	2
108	0	0	0	2	2	0	0	1	0	0	0	0	0	0	0	0	0	1	2	2
109	0	2	2	2	2	2	2	2	2	2	0	2	2	2	2	2	2	2	2	2
110	0	0	0	1	2	0	0	0	0	1	0	2	1	0	0	0	0	0	0	1
111	0	2	2	2	2	2	2	2	0	0	0	2	2	0	0	2	2	2	2	2
112	0	0	2	2	2	1	2	2	2	2	0	0	1	2	2	0	0	2	2	2
113	0	0	1	1	1	0	0	2	2	2	0	2	2	2	2	0	1	2	2	2
114	1	1	2	2	2	1	2	2	2	2	0	0	1	2	2	0	2	2	2	2
115	0	0	2	2	2	0	1	2	2	2	0	0	2	2	2	0	2	2	2	2
116	1	2	2	2	2	1	1	2	2	2	0	0	2	2	2	0	0	2	2	2
117	0	0	1	2	2	0	2	2	2	2	0	2	2	2	2	0	0	2	2	2
118	0	1	2	2	2	0	2	2	2	2	0	0	2	2	2	0	0	0	0	0
119	1	1	2	2	2	1	2	2	2	2	0	2	2	2	2	0	0	2	2	2
120	0	0	0	1	2	0	0	2	1	1	0	0	2	2	2	0	0	2	2	2
121	0	2	2	2	2	1	2	2	2	2	0	0	2	2	2	0	2	2	2	2
122	0	2	2	2	2	0	2	2	2	2	0	0	0	2	2	0	2	2	2	2
123	0	1	2	2	2	0	1	1	2	2	0	0	2	2	2	0	1	2	2	2
124	1	1	2	2	2	0	0	2	2	2	0	0	2	2	2	2	2	2	2	2
125	0	2	2	2	2	0	0	2	2	2	0	0	2	2	2	0	0	2	2	2

* S = Sample, Media type (BGBB, MB, MMGM, LSB),
Product incoulum sizes (0.01, .1, 2.5, 5)g
Response (0 = no gas production, 1 = gas production within 48h,
2 = gas production within 24h).

Table 2: Data from the arthritis trial.

Patient	Gen	Age	Tr	Self-assessment				
				w-0	w-1	w-5	w-9	w-13
1	1	48	1	1	1	1	1	1
2	1	29	1	1	1	1	1	1
3	1	59	2	1	1	1	1	1
4	2	56	2	1	1	1	1	1
5	1	33	2	1	1	1	1	1
6	1	61	2	1	1	0	1	1
7	1	63	1	0	0	1	9	9
8	1	57	2	1	0	1	1	1
9	1	47	2	1	1	1	0	1
10	2	42	1	0	0	1	9	0
11	1	62	1	1	1	1	1	1
12	1	42	2	1	1	1	1	1
13	1	50	1	1	1	1	1	1
14	2	47	1	1	1	9	9	9
15	1	45	2	0	0	0	1	1
16	1	55	1	1	1	1	1	1
17	1	56	1	1	1	1	1	1
18	1	57	2	1	1	1	1	1
19	2	57	2	1	1	1	0	9
20	1	45	1	1	0	1	0	1
21	1	29	1	1	1	0	9	9
22	2	51	1	0	0	1	1	0
23	2	65	2	1	1	0	1	0
24	2	50	1	1	1	1	0	1
25	1	65	1	1	1	1	1	1
26	2	58	2	1	1	0	0	0
27	2	62	1	0	1	1	1	1
28	2	35	1	1	1	1	1	1
29	1	28	1	1	1	1	1	1
30	1	41	1	1	1	1	9	9
31	1	40	2	1	0	1	0	1
32	1	33	2	0	0	0	0	0
33	2	60	2	0	0	0	0	0
34	1	62	1	1	0	1	1	1
35	1	45	2	1	1	0	1	1
36	1	64	2	0	0	0	0	0
37	1	55	2	0	0	0	1	1
38	1	57	1	1	1	1	1	9
39	1	51	2	1	1	0	1	1
40	2	57	1	1	1	1	1	1
41	1	37	2	1	0	1	9	1
42	1	52	1	0	1	1	1	9
43	1	52	2	1	1	9	1	1
44	1	46	1	1	1	1	1	1
45	1	63	1	0	0	1	0	9
46	1	60	2	1	1	0	0	0
47	1	63	1	0	1	9	0	0
48	2	33	2	1	0	0	1	9
49	1	60	1	0	0	1	1	1
50	1	58	1	1	1	1	1	1
51	1	37	2	0	0	0	1	0

* Gen = Gender, Tr =Treatment (1 = Auranofin, 2= Placebo),
W = Week, 0 =poor, 1= good and 9 = missing.

Table 3. Observation values of drug use and crime, values of covariates.

	Dep. Variables				Covariates													
P	H	Co	B	Cr	1	2	3	4	5	6	7	8	9	10	11	12	13	14
1	2	0	15	1	1	1	1	40	11	2	19	10	22	0	9	16	7	26
2	5	0	0	6	1	4.29	0	0	23	1	21	31	20	0	10	12	0	7
3	7.5	0	4	4	0	0	0	0	6	0	4	21	21	0	4	14	6	9
4	0	.04	0	0	1	8.71	1	100	7	9	4	21	23	0	8	11	6	36
5	1	5	1.6	5	1	8.29	1	80	10	5	1	28	29	1	9	21	11	15
6	1	0	0	0	0	11	1	50	14	5	3	22	21	0	10	16	0	0
7	1.5	0	1	4	0	0	0	0	4	2	6	23	29	0	9	10	10	18
8	.04	0	1.3	0	1	11.6	1	90	14	17	6	16	20	0	10	16	4	3
9	.04	0	0	3	1	12.6	1	90	8	9	15	19	17	1	10	17	0	0
10	.39	.25	.11	4	0	8	1	100	8	4	16	22	20	0	8	18	4	0
11	.04	.18	0	1	1	12.6	1	100	7	1	1	16	28	0	9	15	6	70
12	0	0	0	0	0	12	1	60	9	15	17	28	22	1	6	13	9	0
13	4	.07	0	1	0	4	0	0	2	3	13	20	20	1	12	99	1	0
14	0.8	0.5	0	1	0	0	0	0	1	0	3	9	25	0	9	9	5	12
15	.18	0	2	4	0	2	0	0	2	8	3	13	29	2	11	17	1	48
16	0	0	.04	7	0	0	0	0	9	13	8	21	16	0	10	16	1	1
17	0	.07	0	0	1	12.3	1	150	2	3	0	10	43	0	7	15	28	168
18	0	.07	0	0	1	10.7	1	55	0	8	0	22	20	0	9	16	4	0
19	.75	0	0	1	0	0	0	0	13	1	13	34	20	0	9	15	2	0
20	.04	3	0	0	0	12	1	40	3	4	2	27	17	0	8	14	2	0
21	.04	.33	0	0	1	12.6	1	90	0	2	0	23	34	0	10	22	17	96
22	.13	.57	0	0	1	12.6	1	90	3	10	1	19	34	1	7	23	17	0
23	0	0	2.5	3	0	12	1	110	2	3	7	14	31	1	8	22	13	0
24	2	.07	0	3	1	7.71	0	0	11	7	8	22	20	0	10	12	3	0
25	.07	0	0	0	1	0.57	0	0	0	13	0	16	30	1	10	24	13	0
26	.04	0	0	0	1	0.43	0	0	3	5	3	12	41	0	7	22	16	0
27	3	.04	0	0	1	2.71	0	0	0	3	0	23	16	1	8	12	1	0
28	1.5	2	6.5	1	1	2	0	0	14	2	20	27	17	0	8	12	2	0
29	3	.07	.07	1	0	0	0	0	7	2	2	21	25	1	7	23	2	4
30	.71	.04	0	0	1	9	1	100	6	6	9	20	30	1	8	16	14	0
31	.07	0	0	0	0	12	1	35	15	2	7	17	17	0	8	6	2	0
32	0.1	0	0	1	0	12	1	40	15	0	26	10	24	0	10	18	7	0
33	2	1.2	3.5	1	0	0	0	0	0	0	16	24	21	0	10	13	1	1.5
34	.04	4	17	3	1	10	1	140	18	8	22	23	19	1	9	51	6	60
35	.04	0	0	0	0	8	1	90	0	12	0	15	28	2	12	20	4	8
36	.11	.04	0	0	1	11.7	1	100	2	3	0	13	20	0	12	99	2	0
37	1.5	0	0	0	1	9.29	1	55	13	8	12	23	22	1	11	6	1	0
38	.14	1.5	0	1	1	11.4	1	90	3	0	0	14	37	0	8	16	16	6
39	3	0	0	0	1	12.9	1	20	0	0	1	17	28	0	9	17	9	0
40	2	0	0	2	0	4	0	0	17	4	22	29	24	0	7	13	7	48
41	3	.04	0	1	0	0	0	0	13	1	24	31	24	2	10	99	1	0
42	2.5	.14	.14	1	1	9.86	1	85	4	0	1	21	23	1	10	18	5	2
43	1	.25	0	0	1	3.57	1	40	0	2	0	19	25	0	9	19	5	14
44	0	.04	0	0	1	10.7	1	5	7	4	9	15	35	0	8	14	2	0
45	1	.07	0	0	0	8	0	0	1	10	0	15	23	1	10	99	4	0
46	2.5	0	.25	2	1	5.14	1	10	11	0	9	21	27	0	11	25	7	0
47	1.5	.04	5	1	0	2	0	0	15	2	19	21	26	1	10	99	3	0
48	0	.21	0	0	1	7	0	0	4	10	16	11	23	0	6	12	8	30
49	1.3	0	0	0	1	14.6	1	50	3	2	6	3	32	0	16	31	4	0
50	1.5	.04	.33	4	1	4.43	1	40	14	4	5	25	17	1	10	15	1	0
51	.07	.14	.67	0	1	12.7	1	50	1	9	4	12	37	0	11	18	21	0
52	.18	0	0	0	1	12.3	1	80	2	9	2	16	46	0	12	26	28	132

P=Patient, H =Heroin, Co = Cocaine, B = Benzodiazepine, Cr = Crime.

Table 4: Data from Clinical Trial.

p	Cl	T	I	Time			p	Cl	T	I	Time			p	Cl	T	I	Time		
				1	2	3					1	2	3					1	2	3
1	5	1	3	3	9	3	59	6	2	4	2	2	2	117	10	1	3	1	1	1
2	5	1	3	3	2	2	60	6	2	3	3	3	9	118	10	1	3	1	1	1
3	5	1	4	3	2	2	61	6	2	4	4	4	9	119	10	1	3	3	3	3
4	5	1	3	2	2	1	62	6	2	4	4	3	3	120	10	1	3	1	1	1
5	5	1	3	3	2	2	63	6	2	4	5	9	9	121	10	1	3	2	2	2
6	5	1	4	2	1	3	64	6	2	3	1	9	1	122	10	1	3	2	2	1
7	5	1	4	1	1	1	65	6	2	3	4	2	4	123	10	2	3	3	3	3
8	5	1	4	1	1	1	66	6	2	4	5	9	9	124	10	2	3	4	4	4
9	5	1	5	5	9	9	67	6	2	5	4	5	9	125	10	2	3	1	1	1
10	5	1	3	1	1	1	68	6	2	4	4	4	3	126	10	2	3	2	2	9
11	5	1	4	4	4	4	69	6	2	5	3	4	4	127	10	2	3	2	2	2
12	5	1	4	3	1	1	70	6	2	4	4	3	3	128	10	2	3	4	4	9
13	5	1	4	1	1	1	71	8	1	4	9	4	4	129	10	2	3	1	1	2
14	5	1	4	3	3	3	72	8	1	4	3	2	1	130	10	2	3	2	3	3
15	5	1	4	1	1	1	73	8	1	5	1	9	1	131	10	2	3	4	3	3
16	5	1	3	1	1	9	74	8	1	4	1	1	1	132	10	2	3	3	3	3
17	5	1	3	4	4	4	75	8	1	3	2	1	9	133	10	2	4	3	3	4
18	5	1	3	3	9	9	76	8	1	4	2	1	1	134	10	2	3	3	3	4
19	5	1	4	9	1	9	77	8	1	3	1	1	1	135	10	2	3	3	3	3
20	5	2	3	4	3	3	78	8	1	4	2	2	2	136	10	2	3	5	9	9
21	5	2	3	4	4	4	79	8	1	3	1	1	1	137	10	2	3	2	2	1
22	5	2	4	4	5	4	80	8	1	4	3	3	4	138	10	2	3	4	4	4
23	5	2	3	4	4	5	81	8	1	3	2	2	1	139	10	2	3	4	3	3
24	5	2	3	4	4	4	82	8	1	3	2	1	1	140	11	1	4	2	1	1
25	5	2	4	4	4	4	83	8	1	4	2	1	1	141	11	1	3	4	3	3
26	5	2	4	4	9	9	84	8	1	4	2	2	2	142	11	1	5	3	9	9
27	5	2	3	4	4	9	85	8	1	4	3	2	1	143	11	1	3	2	1	1
28	5	2	3	2	2	9	86	8	1	4	2	1	1	144	11	1	4	9	3	2
29	5	2	5	3	3	4	87	8	1	4	2	2	1	145	11	1	4	3	9	9
30	5	2	3	4	4	4	88	8	2	3	1	1	2	146	11	1	4	2	2	2
31	5	2	3	4	4	9	89	8	2	4	2	2	3	147	11	1	4	2	2	2
32	5	2	4	4	4	9	90	8	2	3	2	2	3	148	11	1	4	2	2	1
33	5	2	4	4	5	9	91	8	2	3	3	5	5	149	11	1	5	2	1	1
34	5	2	4	4	4	9	92	8	2	3	2	2	2	150	11	1	3	1	1	9
35	5	2	3	4	9	9	93	8	2	4	3	3	3	151	11	1	3	2	1	1
36	5	2	4	1	1	9	94	8	2	3	3	3	3	152	11	1	3	3	2	2
37	5	2	3	4	4	4	95	8	2	5	4	3	3	153	11	1	5	2	2	1
38	6	1	3	3	3	3	96	8	2	4	4	4	5	154	11	1	5	1	1	1
39	6	1	4	2	2	2	97	8	2	5	4	9	9	155	11	1	4	2	1	1
40	6	1	4	3	2	2	98	8	2	3	3	9	5	156	11	2	4	2	2	1
41	6	1	4	4	9	9	99	8	2	5	4	3	4	157	11	2	4	4	4	4
42	6	1	4	2	2	2	100	8	2	3	2	3	3	158	11	2	4	4	4	4
43	6	1	4	2	2	1	101	9	1	5	2	2	1	159	11	2	4	4	3	4
44	6	1	4	3	3	3	102	9	2	4	3	3	3	160	11	2	3	4	4	9
45	6	1	3	1	1	1	103	9	2	4	3	3	3	161	11	2	4	4	3	3
46	6	1	4	3	1	1	104	9	2	5	4	3	3	162	11	2	4	2	2	2
47	6	1	4	2	2	1	105	10	1	3	1	1	1	163	11	2	3	4	4	9
48	6	1	3	2	9	1	106	10	1	3	1	1	1	164	11	2	5	4	3	3
49	6	1	3	3	4	4	107	10	1	3	2	2	1	165	11	2	4	4	3	3
50	6	1	5	2	2	2	108	10	1	3	2	2	1	166	11	2	4	3	3	3
51	6	1	4	2	1	1	109	10	1	3	1	1	1	167	11	2	4	2	2	1
52	6	1	4	3	4	4	110	10	1	3	3	2	1	168	11	2	3	4	3	3
53	6	1	4	1	1	1	111	10	1	3	2	2	2	169	11	2	4	4	4	4
54	6	1	4	1	1	1	112	10	1	3	1	1	1	170	11	2	3	4	4	3
55	6	2	4	3	3	3	113	10	1	3	3	1	1	171	11	2	4	4	3	3
56	6	2	4	4	4	4	114	10	1	3	2	2	2	172	11	2	3	4	3	3
57	6	2	4	2	2	2	115	10	1	3	3	2	2							
58	6	2	4	4	4	9	116	10	1	3	3	3	2							

* p= Patient,
Cl = Clinic, T = Treatment (1 = Test Drug, 2 = Placebo),
I = Initial Stage of Disease (3 = Fair, 4= =Poor, 5=Exacerbation),
Response (1 = Rapidly Improving, 2 = Slowly Improving, 3 = Stable, 4 = Slowly Worsening, 5= Rapidly Worsening and 9 = Missing).

Table 5: Data from clinical trial to compare active and placebo treatments for skin disorder.

Subject	Tr	Day				Subject	Tr	Day			
		3	7	10	14			3	7	10	14
1	1	2	1	1	1	41	2	2	1	1	0
2	1	1	1	1	0	42	2	1	1	1	0
3	1	1	1	1	1	43	2	1	1	1	1
4	1	0	1	0	1	44	2	2	2	2	1
5	1	2	1	1	0	45	2	3	1	2	1
6	1	1	1	0	2	46	2	1	1	0	1
7	1	2	1	1	0	47	2	0	1	0	1
8	1	1	0	1	0	48	2	2	1	1	1
9	1	1	1	1	0	49	2	1	0	0	0
10	1	1	0	1	0	50	2	1	1	2	1
11	1	1	0	1	1	51	2	2	1	1	1
12	1	1	1	0	1	52	2	1	0	1	1
13	1	2	1	1	1	53	2	2	2	2	1
14	1	1	0	0	0	54	2	1	1	1	0
15	1	2	1	2	1	55	2	2	1	2	1
16	1	2	1	0	0	56	2	2	2	2	1
17	1	1	2	1	1	57	2	3	1	2	1
18	1	2	2	2	1	58	2	1	1	0	0
19	1	0	0	0	0	59	2	2	2	2	0
20	1	1	1	1	0	60	2	1	1	0	0
21	1	2	0	1	1	61	2	2	2	1	1
22	1	1	1	2	0	62	2	2	1	2	0
23	1	1	0	0	0	63	2	2	2	2	1
24	1	1	0	0	0	64	2	2	0	1	2
25	1	1	0	1	0	65	2	2	1	1	1
26	1	1	1	1	1	66	2	2	0	2	0
27	1	2	1	2	1	67	2	2	1	1	0
28	1	2	1	1	1	68	2	1	1	0	1
29	1	1	2	1	1	69	2	2	1	1	1
30	1	0	0	0	0	70	2	2	2	2	1
31	1	0	1	0	1	71	2	2	2	1	1
32	1	1	1	1	0	72	2	2	1	1	1
33	1	1	0	0	0						
34	1	0	0	0	0						
35	1	1	0	0	0						
36	1	1	2	1	1						
37	2	2	1	1	1						
38	2	1	1	0	0						
39	2	2	2	2	1						
40	2	1	1	0	1						

* Tr = Treatment (1 = Active treatment, 2 =Placebo treatment),
Response (0 = Excellent, 1 = Good, 2 = Fair, 3 = Poor).

Table 6: Data from Multicentre, Multivisit Clinical Trial to Compare Two Treatments for Patients with a Respiratory Disorder.

P	C	T	S	A	Visit					P	C	T	S	A	Visit				
					B	1	2	3	4						B	1	2	3	4
1	1	1	1	32	1	2	2	4	2	57	2	1	1	37	1	3	4	4	4
2	1	1	1	47	2	2	3	4	4	58	2	1	1	39	2	3	4	4	4
3	1	1	2	11	4	4	4	4	2	59	2	1	1	60	4	4	3	3	4
4	1	1	2	14	2	3	3	3	2	60	2	1	1	63	4	4	4	4	4
5	1	1	2	15	0	2	3	3	3	61	2	1	2	13	4	4	4	4	4
6	1	1	2	20	3	3	2	3	1	62	2	1	2	14	1	4	4	4	4
7	1	1	2	22	1	2	2	2	3	63	2	1	2	19	3	3	2	3	3
8	1	1	2	22	2	1	3	4	4	64	2	1	2	20	2	4	4	4	3
9	1	1	2	23	3	3	4	4	3	65	2	1	2	20	2	1	1	0	0
10	1	1	2	23	2	3	4	4	4	66	2	1	2	21	3	3	4	4	4
11	1	1	2	25	2	3	3	2	3	67	2	1	2	24	4	4	4	4	4
12	1	1	2	26	1	2	2	3	2	68	2	1	2	25	3	4	3	3	1
13	1	1	2	26	2	2	2	2	2	69	2	1	2	25	3	4	4	3	3
14	1	1	2	26	2	4	1	4	2	70	2	1	2	25	2	2	4	4	4
15	1	1	2	28	1	2	2	1	2	71	2	1	2	26	2	3	4	4	4
16	1	1	2	28	0	0	1	2	1	72	2	1	2	28	2	3	2	2	1
17	1	1	2	30	3	3	4	4	2	73	2	1	2	31	4	4	4	4	4
18	1	1	2	30	3	4	4	4	3	74	2	1	2	34	2	4	4	2	4
19	1	1	2	31	1	2	3	1	1	75	2	1	2	35	4	4	4	4	4
20	1	1	2	31	3	3	4	4	4	76	2	1	2	37	4	3	2	2	4
21	1	1	2	31	0	2	3	2	1	77	2	1	2	41	3	4	4	3	4
22	1	1	2	32	3	4	4	3	3	78	2	1	2	43	3	3	4	4	2
23	1	1	2	34	1	1	2	1	1	79	2	1	2	52	1	2	1	2	2
24	1	1	2	46	4	3	4	3	4	80	2	1	2	55	4	4	4	4	4
25	1	1	2	48	2	3	2	0	2	81	2	1	2	55	2	2	3	3	1
26	1	1	2	50	2	2	2	2	2	82	2	1	2	58	4	4	4	4	4
27	1	1	2	57	3	3	4	3	4	83	2	1	2	68	2	3	3	3	4
28	1	2	1	13	4	4	4	4	4	84	2	2	1	31	3	4	4	4	4
29	1	2	1	31	2	1	0	2	2	85	2	2	1	32	3	2	2	3	4
30	1	2	1	35	1	0	0	0	0	86	2	2	1	36	3	3	2	1	3
31	1	2	1	36	2	3	3	2	2	87	2	2	1	38	1	2	0	0	0
32	1	2	1	45	2	2	2	2	1	88	2	2	1	39	1	2	1	1	2
33	1	2	2	13	3	4	4	4	4	89	2	2	1	39	3	2	3	0	0
34	1	2	2	14	2	2	1	2	3	90	2	2	1	44	3	4	4	4	4
35	1	2	2	15	2	2	3	3	2	91	2	2	1	47	2	3	3	2	3
36	1	2	2	19	2	3	3	0	0	92	2	2	1	48	2	2	1	0	0
37	1	2	2	20	4	4	4	4	4	93	2	2	1	48	2	2	2	2	2
38	1	2	2	23	3	3	1	1	1	94	2	2	1	51	3	4	2	4	4
39	1	2	2	23	4	4	2	4	4	95	2	2	1	58	1	4	2	2	0
40	1	2	2	24	3	4	4	4	3	96	2	2	2	11	3	4	4	4	4
41	1	2	2	25	1	1	2	2	2	97	2	2	2	14	2	1	2	3	2
42	1	2	2	26	2	4	2	4	3	98	2	2	2	15	3	2	2	3	3
43	1	2	2	26	1	2	1	2	2	99	2	2	2	15	4	3	3	3	4
44	1	2	2	27	1	2	2	1	2	100	2	2	2	19	4	2	2	3	3
45	1	2	2	27	3	3	4	3	3	101	2	2	2	20	3	2	4	4	4
46	1	2	2	28	2	1	1	1	1	102	2	2	2	20	1	4	4	4	4
47	1	2	2	28	2	0	0	0	0	103	2	2	2	33	3	3	3	2	3
48	1	2	2	30	1	0	0	0	0	104	2	2	2	36	2	4	3	3	4
49	1	2	2	37	1	0	0	0	0	105	2	2	2	38	4	3	0	0	0
50	1	2	2	37	3	2	3	3	2	106	2	2	2	42	3	2	2	2	2
51	1	2	2	43	2	3	2	4	4	107	2	2	2	43	2	1	0	0	0
52	1	2	2	43	1	1	1	3	2	108	2	2	2	45	3	4	2	1	2
53	1	2	2	44	3	4	3	4	2	109	2	2	2	48	4	4	0	0	0
54	1	2	2	46	2	2	2	2	2	110	2	2	2	52	2	3	4	3	4
55	1	2	2	49	2	2	2	2	2	111	2	2	2	66	3	3	3	4	4
56	1	2	2	63	2	2	2	2	2										

* P = Patient, C = Centre, T = Treatment (1= Active, 2 = Placebo), S = Sex and B = Base.

Table 7: Map Data.

S	T	Location										S	T	Location									
		1	2	3	4	5	6	7	8	9	10			1	2	3	4	5	6	7	8	9	10
1	1	4	4	4	4	4	4	4	2	4	4	46	2	2	1	4	4	2	4	2	3	1	1
2	1	2	4	4	4	2	1	2	4	3	4	47	2	4	4	4	2	1	1	2	2	2	4
3	1	4	4	4	2	4	4	3	2	4	4	48	2	3	1	4	4	1	1	4	4	1	1
4	1	3	4	4	4	4	4	4	1	4	4	49	2	3	4	4	4	4	3	2	2	4	4
5	1	4	4	4	4	4	4	4	4	4	4	50	2	4	1	2	2	1	4	1	1	2	1
6	1	4	4	4	3	1	1	2	2	2	1	51	2	2	1	4	3	3	1	1	2	1	1
7	1	4	4	4	3	3	3	1	2	2	4	52	2	1	1	4	1	4	4	3	1	2	1
8	1	4	4	4	2	4	1	1	1	2	3	53	2	2	4	1	1	4	1	1	2	1	2
9	1	4	4	4	4	2	4	1	1	4	4	54	2	1	2	1	1	1	4	1	1	2	2
10	1	1	1	4	4	1	4	1	4	3	4	55	2	2	2	2	3	1	2	1	1	4	2
11	1	4	4	4	2	4	4	1	3	3	4	56	2	4	1	1	3	1	2	1	1	1	2
12	1	4	4	4	3	4	4	1	2	2	1	57	2	2	1	4	2	1	4	2	1	1	4
13	1	4	4	4	2	4	4	1	1	4	4	58	2	2	3	3	4	1	1	2	3	1	1
14	1	4	4	4	4	4	4	1	1	4	4	59	2	1	4	4	2	4	4	1	1	1	4
15	1	4	3	1	2	1	1	1	1	1	2	60	2	1	4	4	3	1	1	1	4	1	4
16	1	4	4	4	3	4	2	4	1	4	3	61	2	3	1	3	2	1	1	2	2	1	4
17	1	2	2	2	2	4	1	2	3	1	3	62	2	3	1	1	2	1	4	1	1	1	1
18	1	2	1	2	1	2	4	1	1	2	1	63	2	1	2	1	4	1	4	1	4	4	1
19	1	2	2	3	1	1	1	1	3	1	1	64	2	2	4	4	4	1	3	4	2	4	4
20	1	3	4	4	4	4	4	4	4	4	4	65	2	4	1	1	2	1	1	4	1	3	4
21	1	4	4	4	4	2	2	1	2	1	3	66	2	1	1	1	2	1	1	1	1	1	1
22	1	4	2	4	4	4	4	1	3	2	2	67	2	1	2	1	1	1	1	1	1	1	3
23	1	4	4	4	4	2	2	1	2	4	1	68	2	4	4	4	4	4	4	4	4	4	4
24	1	4	4	4	4	4	2	3	2	3	1	69	2	2	1	1	1	1	1	1	1	1	1
25	1	3	4	2	4	2	4	1	1	4	1	70	2	2	1	3	1	1	1	1	1	1	2
26	1	3	2	1	2	1	1	1	1	1	1	71	2	2	4	1	1	1	1	1	1	1	1
27	1	3	1	1	4	2	4	1	1	2	4	72	2	2	1	1	1	1	3	1	1	1	1
28	1	2	1	1	1	1	1	1	1	1	1	73	2	4	1	1	1	1	2	1	1	1	1
29	1	4	2	1	4	1	4	1	4	1	4	74	2	3	3	1	2	1	1	1	2	1	4
30	1	4	4	3	4	4	3	4	4	4	4	75	2	1	1	1	1	1	2	1	1	1	1
31	1	4	4	4	4	2	4	2	1	4	4	76	2	1	1	1	1	1	2	2	1	1	1
32	1	4	4	2	2	2	3	2	2	1	1	77	2	1	1	1	1	1	1	1	1	1	1
33	1	4	4	3	2	3	4	1	4	4	4	78	2	2	2	4	4	1	2	1	1	2	4
34	1	4	4	2	2	3	4	1	4	4	4	79	2	1	1	4	2	1	1	1	1	1	1
35	1	4	4	4	4	4	4	4	2	4	4	80	2	1	1	1	1	2	1	2	1	4	2
36	1	4	4	4	4	3	4	1	4	2	2	81	2	2	2	1	3	1	4	4	1	2	4
37	1	4	4	1	4	2	4	1	4	3	3	82	2	1	4	2	1	1	4	1	1	3	4
38	1	4	4	3	4	3	4	1	1	3	2	83	2	1	1	4	1	2	1	2	1	2	1
39	1	4	4	4	4	4	1	1	1	2	3	84	2	2	3	4	4	4	4	1	1	2	4
40	1	4	4	1	1	1	2	1	1	4	4	85	2	1	4	1	4	1	1	1	2	1	1
41	1	1	1	3	2	1	1	1	1	1	1	86	2	1	1	1	1	1	4	1	3	1	2
42	1	2	4	4	1	4	4	4	4	4	4	87	2	1	1	1	3	1	4	4	1	1	2
43	1	4	4	4	4	2	1	1	3	1	4	88	2	4	1	2	1	1	1	1	1	1	1
44	2	3	4	2	2	2	4	1	3	1	1	89	2	1	2	1	1	1	1	1	2	1	2
45	2	3	2	2	2	1	2	1	2	4	3												

* S = Subject and T = Treatment (1 = Rotated, 2 = Nonrotated).

Table 8: Fitted and observed frequency for use of chemotherapy (ICD-9-CM code 99.25) for those age 20 and over during 1987-1992, in each counties of Washington State, using model 2 of section 5.2 of chapter 5.

1987

C	Fitted frequency					Observed frequency				
	0	1	1	3	≥4	0	1	1	3	≥4
1	8786	227	23	5	3	8784	231	21	6	2
2	11999	85	8	2	1	12000	86	7	2	0
3	69937	601	60	12	8	69938	609	57	8	7
4	34866	802	81	17	11	34864	834	56	10	13
5	37996	365	36	7	5	37996	365	35	5	8
6	140285	1906	191	39	26	140285	1847	233	53	29
7	2981	34	3	1	0	2981	37	1	0	0
8	54184	412	41	8	6	54185	413	39	7	7
9	16242	74	7	2	1	16244	71	9	1	1
10	3776	112	11	2	2	3774	112	11	5	2
11	22762	261	26	5	4	22762	266	24	4	2
12	1726	14	1	0	0	1727	15	0	0	0
13	33771	682	69	14	9	33770	681	73	11	11
14	43432	886	90	18	12	43431	848	118	31	10
15	36410	334	33	7	4	36411	327	33	12	6
16	13450	124	12	3	2	13450	124	13	1	2
17	1011225	15419	1550	318	209	1011220	15686	1396	251	167
18	1182503	1732	172	35	23	1182508	1717	177	35	28
19	17919	124	12	3	2	17920	123	15	1	0
20	11311	63	6	1	1	11313	63	7	0	0
21	39015	516	52	11	7	39014	531	45	8	2
22	6899	129	13	3	2	6898	136	9	2	1
23	25543	362	36	7	5	25542	362	38	8	3
24	21655	340	34	7	5	21654	349	28	4	6
25	12624	173	17	4	2	12624	172	18	4	3
26	5773	224	23	5	3	5771	200	36	12	9
27	372120	2280	227	46	31	372121	2341	169	45	28
28	7126	77	8	2	1	7126	71	10	2	4
29	49034	848	85	18	12	49033	827	101	20	15
30	5317	22	2	0	0	5319	20	3	0	0
31	268034	5476	554	114	75	268034	5413	598	117	90
32	242679	6961	710	146	96	242682	6799	797	214	100
33	19571	305	31	6	4	19570	296	40	7	4
34	100022	1245	125	26	17	100021	1292	99	15	7
35	2473	12	1	0	0	2475	10	1	0	0
36	34727	204	20	4	3	34729	198	22	5	5
37	82625	663	66	14	9	82626	683	46	6	16
38	27494	389	39	8	5	27494	374	51	12	5
39	122843	2696	273	56	37	122843	2649	316	50	47

Table 8 (Continued)

1988

1	8826	220	24	5	3	8823	217	27	7	3
2	12172	87	9	2	1	12175	84	7	3	2
3	70077	621	65	13	9	70079	630	53	11	12
4	35827	657	70	13	9	35825	666	60	13	12
5	38777	362	38	7	5	38779	348	44	9	10
6	143278	2294	243	47	33	143278	2245	285	52	35
7	2990	33	3	1	0	2991	30	6	0	0
8	55178	429	45	9	6	55181	420	47	10	9
9	16526	234	25	5	3	16526	231	31	3	2
10	3841	119	13	2	2	3837	129	9	0	2
11	22810	254	27	5	4	22811	249	32	3	5
12	1732	16	2	0	0	1734	13	3	1	0
13	34344	537	57	11	8	34343	523	70	8	12
14	43664	1009	108	21	14	43661	1002	120	27	6
15	37357	354	37	7	5	37359	346	36	10	9
16	13815	153	16	3	2	13816	150	16	4	3
17	1034753	15538	1644	317	220	1034748	15780	1504	252	188
18	122501	2032	215	42	29	122500	2008	208	57	45
19	17792	204	22	4	3	17793	206	22	2	2
20	11413	62	6	1	1	11418	60	5	1	0
21	39377	457	48	9	6	39378	469	41	5	5
22	6916	134	14	3	2	6914	135	15	4	1
23	26035	476	51	10	7	26034	458	67	16	3
24	21783	334	35	7	5	21782	335	38	8	1
25	12828	199	21	4	3	12827	208	15	2	3
26	5736	216	23	5	3	5731	215	30	1	6
27	377077	4546	479	92	64	377076	4647	433	72	31
28	7468	63	7	1	1	7470	60	8	1	1
29	50113	803	85	16	11	50112	781	100	21	14
30	5438	46	5	1	1	5440	47	2	1	0
31	280104	5145	546	105	73	280104	5054	587	133	96
32	242089	6756	725	140	97	242090	6619	808	182	109
33	19562	352	37	7	5	19560	358	32	8	5
34	102798	1335	141	27	19	102798	1373	124	14	11
35	2407	14	1	0	0	2411	9	1	1	1
36	34693	292	31	6	4	34695	293	26	5	6
37	83917	829	87	17	12	83918	863	56	10	15
38	27367	410	43	8	6	27367	395	54	12	7
39	124713	2450	261	50	35	124712	2414	288	56	39

Table 8 (Continued)

1989

1	8477	204	22	4	3	8474	193	30	7	6
2	12320	99	11	2	1	12323	99	8	3	0
3	70306	586	63	13	8	70308	596	50	13	8
4	35042	723	79	16	10	35040	739	67	17	7
5	39389	401	43	9	5	39391	397	47	5	8
6	147775	2189	237	47	29	147776	2121	297	60	23
7	3007	23	2	0	0	3010	23	0	0	0
8	56320	522	56	11	7	56322	506	67	12	9
9	17389	304	33	7	4	17388	309	35	2	3
10	3870	103	11	2	1	3867	102	19	0	0
11	22079	191	21	4	3	22081	193	18	2	3
12	1667	15	2	0	0	1669	14	1	0	0
13	33989	531	57	11	7	33988	531	51	14	12
14	43746	1152	126	25	16	43743	1135	150	27	10
15	38719	394	42	8	5	38721	386	41	14	8
16	14232	202	22	4	3	14232	203	21	5	2
17	1061925	14829	1601	319	199	1061923	14968	1518	281	183
18	125457	2287	248	49	31	125456	2258	240	69	49
19	18078	247	27	5	3	18078	264	15	3	1
20	11496	68	7	1	1	11500	71	2	1	0
21	39912	453	49	10	6	39913	471	34	7	5
22	6274	132	14	3	2	6272	138	13	1	1
23	26551	517	56	11	7	26549	519	57	10	7
24	21784	380	41	8	5	21783	386	33	8	9
25	12926	207	22	4	3	12925	207	25	4	2
26	5863	178	20	4	2	5859	172	29	3	4
27	391511	4636	499	100	62	391510	4733	431	90	43
28	7525	85	9	2	1	7526	88	5	1	2
29	51212	962	104	21	13	51211	940	111	29	21
30	5534	34	4	1	0	5538	31	2	1	1
31	295645	4992	541	108	67	295645	4919	583	114	91
32	245297	6904	757	151	94	245296	6801	842	162	102
33	19831	332	36	7	4	19830	328	40	7	5
34	106909	1521	164	33	20	106908	1554	136	38	11
35	2411	18	2	0	0	2414	15	2	1	0
36	35229	223	24	5	3	35233	228	16	5	2
37	85994	1111	120	24	15	85994	1129	106	18	16
38	26493	372	40	8	5	26493	375	42	5	3
39	125925	2595	282	56	35	125923	2577	310	57	26

Table 8 (Continued)
1990

1	8338	217	26	5	3	8335	222	29	2	2
2	12202	89	10	2	1	12205	92	8	0	0
3	74975	620	73	15	8	74977	622	68	13	11
4	36595	262	31	6	4	36598	255	30	8	7
5	41040	397	47	9	5	41041	394	48	9	6
6	160815	2393	284	57	33	160815	2333	326	70	37
7	2901	28	3	1	0	2902	31	0	0	0
8	56759	425	50	10	6	56761	443	30	9	7
9	17747	115	14	3	2	17750	112	10	3	5
10	3984	89	11	2	1	3981	93	11	1	1
11	23052	185	22	4	3	23054	191	16	1	4
12	1622	18	2	0	0	1623	19	1	0	0
13	35289	531	63	13	7	35288	531	59	14	11
14	43983	1056	127	26	15	43981	1032	158	27	8
15	42729	374	44	9	5	42731	347	61	12	10
16	15018	190	23	5	3	15018	180	32	6	2
17	1108726	15112	1790	360	206	1108724	15228	1699	342	201
18	128306	2200	262	53	30	128305	2197	266	53	30
19	18805	309	37	7	4	18804	316	37	3	3
20	11283	74	9	2	1	11286	77	5	1	0
21	40279	457	54	11	6	40279	456	58	10	3
22	6232	118	14	3	2	6230	126	12	0	0
23	27182	521	62	13	7	27180	513	79	6	7
24	22611	293	35	7	4	22611	299	29	5	6
25	13684	208	25	5	3	13683	220	19	2	1
26	5857	199	24	5	3	5852	200	28	5	2
27	402522	4342	513	103	59	402522	4373	491	102	50
28	7749	87	10	2	1	7750	90	6	3	1
29	55236	1109	132	27	15	55235	1069	140	37	38
30	5565	40	5	1	1	5568	36	7	1	0
31	318466	5056	601	121	69	318467	4951	656	152	87
32	246293	6763	813	164	94	246289	6765	850	160	63
33	20103	311	37	7	4	20102	316	33	7	5
34	111182	1617	192	39	22	111180	1677	160	17	17
35	2398	17	2	0	0	2401	15	2	0	0
36	34073	184	22	4	2	34077	175	18	11	4
37	89717	1091	129	26	15	89717	1081	124	31	24
38	27415	304	36	7	4	27416	309	29	8	5
39	122211	2840	340	69	39	122208	2856	336	71	28

Table 8 (Continued)

1991

1	8421	254	32	7	4	8417	266	25	9	1
2	12336	98	12	3	2	12338	99	10	3	0
3	76504	647	80	17	10	76506	652	76	13	11
4	37294	259	32	7	4	37297	260	27	4	8
5	41791	1046	132	27	17	41789	1036	138	28	23
6	169012	2715	341	71	43	169012	2680	347	85	57
7	2877	35	4	1	1	2878	33	5	2	0
8	57700	487	61	13	8	57702	522	28	9	7
9	18614	142	18	4	2	18617	143	17	3	0
10	4109	103	13	3	2	4106	112	6	5	0
11	23692	246	31	6	4	23693	256	20	3	7
12	1661	17	2	0	0	1662	16	2	0	1
13	36375	536	67	14	8	36375	542	60	13	11
14	44583	1116	141	29	18	44581	1098	170	29	10
15	44457	427	53	11	7	44459	399	68	19	10
16	16069	239	30	6	4	16069	238	27	6	8
17	1135399	15289	1912	396	242	1135398	15356	1846	403	234
18	133047	2230	280	58	35	133046	2237	282	51	34
19	19185	442	56	12	7	19182	447	53	12	7
20	11417	75	9	2	1	11420	80	4	0	0
21	40927	603	76	16	10	40926	633	60	4	8
22	6240	134	17	4	2	6238	138	17	3	1
23	28293	542	68	14	9	28292	535	80	15	4
24	23055	309	39	8	5	23055	317	29	7	8
25	13829	289	36	8	5	13827	295	38	4	3
26	6089	168	21	4	3	6086	163	24	11	1
27	415566	3844	479	99	60	415567	3882	484	67	48
28	8251	107	13	3	2	8251	105	15	2	2
29	57567	1120	141	29	18	57566	1090	160	38	21
30	5714	40	5	1	1	5717	39	4	0	0
31	331123	5309	666	138	84	331125	5157	751	175	112
32	250362	6231	789	164	100	250360	6189	843	164	89
33	20537	271	34	7	4	20537	264	38	7	7
34	115974	1680	210	44	27	115972	1774	155	21	12
35	2374	24	3	1	0	2375	25	0	0	1
36	34737	176	22	5	3	34742	164	23	3	10
37	92637	1378	173	36	22	92637	1362	176	47	23
38	27396	239	30	6	4	27398	240	26	6	5
39	123505	2746	347	72	44	123502	2765	341	70	35

Table 8 (Continued)
1992

1	8670	192	24	5	4	8668	191	26	5	4
2	12470	89	11	2	2	12472	90	8	3	1
3	78763	748	92	19	14	78764	755	72	27	17
4	38277	224	27	6	4	38280	222	24	8	4
5	42533	1309	164	34	24	42531	1273	189	42	30
6	173536	2903	359	74	53	173535	2882	374	91	43
7	2885	27	3	1	0	2886	28	2	0	0
8	57979	532	65	13	10	57980	564	39	7	9
9	18890	121	15	3	2	18893	126	8	3	1
10	4236	101	13	3	2	4234	104	14	0	3
11	23836	393	49	10	7	23835	406	43	7	4
12	1660	16	2	0	0	1661	18	0	0	0
13	37477	546	67	14	10	37476	553	65	10	10
14	44956	930	115	24	17	44955	902	152	22	12
15	45890	402	49	10	7	45892	392	53	12	10
16	16718	254	31	6	5	16717	255	37	2	3
17	1151488	14461	1779	368	263	1151488	14472	1771	380	248
18	139412	1978	244	50	36	139412	1978	258	46	27
19	19294	573	72	15	11	19291	567	81	16	9
20	11597	86	11	2	2	11599	87	10	1	0
21	41617	561	69	14	10	41617	567	65	15	8
22	6313	131	16	3	2	6311	138	13	2	2
23	29201	537	66	14	10	29200	525	79	12	12
24	23324	295	36	8	5	23324	303	28	8	5
25	13910	332	41	9	6	13908	324	48	9	9
26	6265	130	16	3	2	6263	132	20	2	0
27	430220	2669	326	67	48	430222	2753	252	46	57
28	8736	88	11	2	2	8737	88	11	2	1
29	59552	1003	124	26	18	59551	974	144	26	27
30	5847	37	4	1	1	5850	38	1	1	0
31	337892	5215	644	133	95	337894	5058	722	170	135
32	256834	5554	690	143	102	256831	5587	679	129	97
33	20958	297	37	8	5	20957	310	26	7	4
34	120462	1512	186	39	27	120461	1589	132	25	19
35	2452	17	2	0	0	2455	14	2	0	1
36	35575	145	18	4	3	35580	142	13	7	2
37	95792	1548	191	40	28	95791	1545	192	42	29
38	27527	265	32	7	5	27528	273	27	1	7
39	125325	2949	367	76	54	125323	2942	389	71	47

* C = County.

APPENDIX C

DYALOG APL PROGRAMS

In chapters 5-9 various DYALOG APL programs have been written to analyse different ordinal data sets. However, the size of the programs is large and printing all of them will take considerable amount of space. Moreover, fitted models in some chapters are special cases of those in the others. Thus, instead of producing all programs in different chapters for different data sets, we provide the programs that are more general. The programs for the other data sets can be obtained easily from those given. This appendix represents a selection of DYALOG APL programs that have been used in this thesis. The programs given are the ones that have been used to analyse the respiratory data set by different models in chapter 7 and the AR(1) model in chapter 8.

RESPK1 fits model 1 in section 7.4 of chapter 7 to respiratory data.

```
RESPK1;T1;MPHI;MPHI2;A12;A2;DL8;FC;I2;I3;I4;NO;PHI2;RI1;RI2;TE7;TS;
X2;X3;X4;X5;GI;A1;B0;B1;B11;B12;B13;C1;C11;C12;D;MPHI;N;NB;PHI;RA0;
RA1;RC;TR;TRJ;VI;VINR;VMPHI;TE21;TE32;TE43;TE54;TE65;A;B;CDF4;CDF5;
CDF6;CDF7;DL4;DL5;DL6;DL7;ETTE31;ETTE4;ETTE41;ETTE5;ETTE51;ETTE6;ET
TE61;ETTE7;J;MEET4;MEET5;MEET6;MEET7;MET4;MET5;MET6;MET7;PDF4;PDF5;
PDF6;PDF7;PPDF4;PPDF5;PPDF6;PPDF7;T3;T4;T5;T6;TE4;TE5;TE6;TET211;TE
T23;TET312;TET32;TET34;TET4;TET423;TET43;RET45;TET534;TET54;TET56;T
ET6;TET645;TET65;TET7;G;E1;BLM;DL4;ETTE21;ETTE3;I;L;LSEF;MEET3;MET3
;T2;TE11;TET3;TE12;TE2;TE3;TET1;TET11;TET21;TET12;P0;PDF3;RI;RII;T;
TET2;V;V1;VBET;VCOM;VFIX;INF00;ALF1;ALF2;BET0;INF01;INF11;INF12;INF
13;INF21;INF22;INF23;IN;V0;DEL0;DEL;BLUP;E;NUP;DL1;DL2;DL3;CDF1;CDF
2;PPDF1;PPDF2;CDF3;PPDF3;PDF1;PDF2;EE;MET0;MEET0;MET1;MEET1;MET2;ME
ET2;ETTE1;ETTE2;TE1;T
 COUNT←0
 ML←1
 NT←3
 E←0 5↓RESPK
 ⎕TRAP←11 'E' '→LL1'
 N←¯1 ρE
 NB←1 ρE
 RP←N
 M←NB×N
 FNUM←1
 RESKD1
 RA←¯1 ρX1
 RB←¯1 ρZ
 MPH←1 0ρ0
 RPH←1 0ρ0
 TREAT←0 3ρ0
 VTREAT←(0,N)ρ0
 MTREAT←0 3ρ0
 MVTREAT←(0,N)ρ0
 VAC←(0,RA+NT)ρ0
 MLEF←((RA+NT),0)ρ0
 RLEF←((RA+NT),0)ρ0
 MPRD←(NB,0)ρ0
 RPROP←10 0ρ0
 RPRD←(NB,0)ρ0
 MPROP←10 0ρ0
AG:E←0 5↓RESPK
 ⎕TRAP←11 'E' '→LL1'
 N←¯1 ρE
 NB←1 ρE
 RP←N
 M←NB×N
 RA←¯1 ρX1
 RB←¯1 ρZ
 MPHI←1
 NO←1 ρZ
 E←(M,1)ρ,E
 RC←RB
```

RESPK1 (continued)

```
 FC←RA
 I←0
 PHI←MPHI
 BET0←RBρ0
 ALF1←RAρ0
 T1←0.2
 T2←0.4
 T3←1
 T4←1.5
 T5←2
 T6←2.4
 TS←NT (1 ,T1),(1 ,T2),1 ,T3
 →(NT≠1)/D1
 DL1 DL2 DL3←E∘=¨1 2 3
 →LP
D1:→(NT≠2)/D2
 DL1 DL2 DL3 DL8←E∘=¨0 1 2 3
 →LP
D2:DL1 DL2 DL3 DL4 DL8←E∘=¨0 1 2 3 4
LP:T←⍉(((NT,NT)ρ1,NTρ0),(NT,RA+RB)ρ0),[1]((M,NT)ρ0),X1,Z
LOOP:L←(Z+.×((RB),1)ρBET0)+X1+.×(RA,1)ρALF1
 →(FNUM≠1)/E1
 PRHAZAD4
 →E4
E1:→(FNUM≠2)/E2
 PRODDS
 →E4
E2:→(FNUM≠3)/E3
 PRHDS
 →E4
E3:PRXHDS
E4:→(NT≠1)/F1
 DERIV1
 →F3
F1:→(NT≠2)/F2
 DERIV31
 →F3
F2:DERIV43
F3:
 MEET2←(RB,1)ρ÷((+/(NB,N)ρ,MEET0)+÷MPHI)
⍝MEET3←((NB,N)ρ+/(((M,N) X1)×(,MEET0)∘.×Nρι1)),(NB,N)ρ+/((((M,N) (0,
N)↓X1)×(,MEET0)∘.×Nρι1)
 MEET3←(⍉Z)+.×X1×(,MEET0)∘.×RAρι1
 →(NT≠1)/N1
 ETTE2←(NB,1)ρ+/(NB,N)ρ(M,1) ETTE1
 MEET3←ETTE2,MEET3
 →N3
N1:→(NT≠2)/N2
 ETTE2←(NB,1)ρ+/(NB,N)ρ(M,1) ETTE1
 ETTE2←ETTE2,(NB,1)ρ+/(NB,N)ρ(M,1) 0 1↓ETTE1
 ETTE3←(NB,1)ρ+/0 1↓(NB,N)ρ(M,1) ETTE1
```

```
 ETTE3←ETTE3,(NB,1)⍴+/0 1↓(NB,N)⍴(M,1) 0 1↓ETTE1
 MEET3←(ETTE2,[1]ETTE3),MEET3
 →N3
N2:ETTE2←(NB,1)⍴+/(NB,N)⍴(M,1) ETTE1
 ETTE2←ETTE2,(NB,1)⍴+/(NB,N)⍴(M,1) 0 1↓ETTE1
 ETTE2←ETTE2,(NB,1)⍴+/(NB,N)⍴(M,1) 0 2↓ETTE1
 MEET3←ETTE2,MEET3
N3:DEL←T+.×TE1,[1]MET0

ETTE7←⍉(TET1,(⍉ETTE1)+.×X1),[1]((⍉X1)+.×ETTE1),(⍉X1)+.×((,MEET0)∘.×
RA⍴⍳1)×X1
 ETTE7←⌹ETTE7-(⍉MEET3)+.×((,MEET2)∘.×(RA+NT)⍴⍳1)×MEET3
 MET3←(NB,1)⍴(÷MPHI)×BET0
 MEET7←(⍉MEET3)+.×MEET2×((-NB),1) DEL
 MEET0←(⍉MEET3)+.×MEET2×MET3
 V←(((RA+NT),1)⍴TS,ALF1)+ETTE7+.×(((RA+NT),1) DEL)+MEET0-MEET7
 DEL0←MEET3+.×ETTE7+.×MEET7-(((RA+NT),1) DEL)+MEET0
 DEL0←((RB,1)⍴BET0)+MEET2×(((-RB),1) DEL)+DEL0-MET3
 BLUP←V,[1]DEL0
 BLM←((RB+RA+NT),1)⍴TS,ALF1,BET0
 I←I+1
 DEL←0
 DEL0←0
 ALF1←RA NT↓,BLUP
 T1←1 ,BLUP
 T2←1 1↓,BLUP
 T3←1 2↓,BLUP
 TS←NT ,BLUP
 BET0←(-RB) ,BLUP
 B0←((-RB),1) BLUP
 →(0.01>⌈/,|BLUP-BLM)/L1
 →(I≥26)/LL1
 V←0
 →LOOP
L1:
 I←0
 →(ML=1)/MAXL
 RI←(+/,MEET2)÷MPHI
 MEET3←((,MEET2)∘.×(RA+NT)⍴⍳1)×MEET3
 RI←RI+(+/DIAG MEET3+.×ETTE7+.×⍉MEET3)÷MPHI
 →RMAXL
MAXL:RI←(+/,MEET2)÷MPHI
RMAXL:MPHI←,((⍉B0)+.×B0)÷RB-RI
 →(0.0001≥|MPHI-PHI)/L2
 PHI←MPHI
 →LOOP
L2:
 →(ML=1)/MAXL1
 A1←(+/+/(,MEET2)×,MEET2)
 A1←A1+2×+/DIAG(MEET3+.×ETTE7+.×⍉MEET3)×((NB,NB)⍴0)MATDIAG,MEET2
 A1←A1++/DIAG(MEET3+.×ETTE7+.×⍉MEET3)+.×MEET3+.×ETTE7+.×⍉MEET3
 →RMAXL1
MAXL1:A1←(+/+/(,MEET2)×,MEET2)
```

```
RMAXL1:A1←A1÷2×MPHI*4
 A1←(÷A1+((÷MPHI*2)×(RB-2×RI))÷2)*0.5
 →(ML≠1)/PREM
 MLEF←MLEF,3 RND(((NT+RA),1)ρTS,ALF1),((((RA+NT),1)ρ(NT+RA) (DIAG
ETTE7)*0.5),((NT+RA),1)ρ(TS,ALF1)÷(NT+RA) (DIAG ETTE7)*0.5
 MPH←MPH,1 3ρMPHI,A1,MPHI÷A1
 ETA←L
 NT←3+RA-4
 V←(¯4 ¯4 ETTE7)
 V←(+/DIAG
V)+2×(+/,((ιN)∘.=1+ιN)×V)+(+/,((ιN)∘.=2+ιN)×V)+(+/,((ιN)∘.=3+ιN)×V)
 MTREAT←MTREAT,[1]1
3ρ((+/¯4 ,ALF1)÷4),((V*0.5)÷4),(+/¯4 ,ALF1)÷V*0.5
 Y1←(ETA≤0)
 Y2←((ETA>0)∧ETA≤T1)
 Y3←((ETA>T1)∧ETA≤T2)
 Y4←((ETA>T2)∧ETA≤T3)
 Y5←(ETA>T3)
 E←(NB,RP)ρ(0×Y1)+(1×Y2)+(2×Y3)+(3×Y4)+4×Y5
 DL1 DL2 DL3 DL4 DL8←E∘=¨0 1 2 3 4
 DL5←(,1∘=(NB,1) 0 1↓RESPK)∘.×RPρι1
MPO←((1,RP)ρ+/[1]DL5×DL1),[1]((1,RP)ρ+/[1]DL5×DL2),[1]((1,RP)ρ+/[1]
DL5×DL3),[1]((1,RP)ρ+/[1]DL5×DL4),[1]((1,RP)ρ+/[1]DL5×DL8)
 DL5←(,2∘=(NB,1) 0 1↓RESPK)∘.×RPρι1

MPO←MPO,[1]((1,RP)ρ+/[1]DL5×DL1),[1]((1,RP)ρ+/[1]DL5×DL2),[1]((1,RP
)ρ+/[1]DL5×DL3),[1]((1,RP)ρ+/[1]DL5×DL4),[1]((1,RP)ρ+/[1]DL5×DL8)
 MPROP←MPROP,MPO
 MPRD←MPRD,(0 5↓RESPK)=(NB,RP)ρ(0×Y1)+(1×Y2)+(2×Y3)+(3×Y4)+4×Y5
 →(FNUM=4)/PRE
 FNUM←FNUM+1
 NT←3
 →AG
 →LL2
PRE:ML←2
 FNUM←1
 NT←3
 →AG
PREM:RLEF←RLEF,3
RND(((NT+RA),1)ρTS,ALF1),((((RA+NT),1)ρ(NT+RA) (DIAG
ETTE7)*0.5),((NT+RA),1)ρ(TS,ALF1)÷(NT+RA) (DIAG ETTE7)*0.5
 RPH←RPH,1 3ρMPHI,A1,MPHI÷A1
 ETA←L
 NT←3+RA-8
 V←(¯4 ¯4 ETTE7)
 V←(+/DIAG
V)+2×(+/,((ιN)∘.=1+ιN)×V)+(+/,((ιN)∘.=2+ιN)×V)+(+/,((ιN)∘.=3+ιN)×V)
 TREAT←TREAT,[1]1 3ρ((+/¯4 ,ALF1)÷4),((V*0.5)÷4),(+/¯4 ,ALF1)÷V*0.5
 VTREAT←VTREAT,[1]¯4 ¯4 ETTE7
 Y1←(ETA≤0)
 Y2←((ETA>0)∧ETA≤T1)
 Y3←((ETA>T1)∧ETA≤T2)
 Y4←((ETA>T2)∧ETA≤T3)
```

```
 Y5←(ETA>T3)
 E←(NB,RP)ρ(0×Y1)+(1×Y2)+(2×Y3)+(3×Y4)+4×Y5
 DL1 DL2 DL3 DL4 DL8←E∘=¨0 1 2 3 4
 DL5←(,1∘=(NB,1) 0 1↓RESPK)∘.×RPρι1

RPO←((1,RP)ρ+/[1]DL5×DL1),[1]((1,RP)ρ+/[1]DL5×DL2),[1]((1,RP)ρ+/[1]
DL5×DL3),[1]((1,RP)ρ+/[1]DL5×DL4),[1]((1,RP)ρ+/[1]DL5×DL8)
 DL5←(,2∘=(NB,1) 0 1↓RESPK)∘.×RPρι1

RPO←RPO,[1]((1,RP)ρ+/[1]DL5×DL1),[1]((1,RP)ρ+/[1]DL5×DL2),[1]((1,RP
)ρ+/[1]DL5×DL3),[1]((1,RP)ρ+/[1]DL5×DL4),[1]((1,RP)ρ+/[1]DL5×DL8)
 RPROP←RPROP,RPO
 RPRD←RPRD,(0 5↓RESPK)=(NB,RP)ρ(0×Y1)+(1×Y2)+(2×Y3)+(3×Y4)+4×Y5
 →(FNUM=4)/LL2
 FNUM←FNUM+1
 NT←3
 →AG
 →LL2
LL1:COUNT←1
LL2:MLEF←MPH,[1]MLEF
 RLEF←RPH,[1]RLEF
```

RESPK2 fits models 2 and 3 in section 7.4 of chapter 7 to respiratory data.

```
RESPK2;T1;RP;Y2;Y3;Y4;Y5;Z;TET45;TET5;V11;V2;VAC;VIN;X1;Y1;RPO;SZ;N
B;NT;PHI1;RA;RB;DL5;DL8;E;ETA;FNUM;M;ML;MPO;A;B2;COUNT;DL1;DL2;DL3;
DL4;MPHI1;MPHI2;A12;A2;DL8;FC;I2;I3;I4;NO;PHI2;RI1;RI2;TE7;TS;X2;X3
;X4;X5;GI;A1;B0;B1;B11;B12;B13;C1;C11;C12;D;MPHI;N;NB;PHI;RA0;RA1;R
C;TR;TRJ;VI;VINR;VMPHI;TE21;TE32;TE43;TE54;TE65;A;B;CDF4;CDF5;CDF6;
CDF7;DL4;DL5;DL6;DL7;ETTE31;ETTE4;ETTE41;ETTE5;ETTE51;ETTE6;ETTE61;
ETTE7;J;MEET4;MEET5;MEET6;MEET7;MET4;MET5;MET6;MET7;PDF4;PDF5;PDF6;
PDF7;PPDF4;PPDF5;PPDF6;PPDF7;T3;T4;T5;T6;TE4;TE5;TE6;TET211;TET23;T
ET312;TET32;TET34;TET4;TET423;TET43;RET45;TET534;TET54;TET56;TET6;T
ET645;TET65;TET7;G;E1;BLM;DL4;ETTE21;ETTE3;I;L;LSEF;MEET3;MET3;T2;T
E11;TET3;TE12;TE2;TE3;TET1;TET11;TET21;TET12;P0;PDF3;RI;RII;T;TET2;
V;V1;VBET;VCOM;VFIX;INF00;ALF1;ALF2;BET0;INF01;INF11;INF12;INF13;IN
F21;INF22;INF23;IN;V0;DEL0;DEL;BLUP;E;NUP;DL1;DL2;DL3;CDF1;CDF2;PPD
F1;PPDF2;CDF3;PPDF3;PDF1;PDF2;EE;MET0;MEET0;MET1;MEET1;MET2;MEET2;E
TTE1;ETTE2;TE1;T
 COUNT←0
 ML←1
 NT←3
 E←0 5↓RESPK
⍝ ⎕TRAP←11 'E' '→LL1'
 N←¯1 ρE
 NB←1 ρE
 RP←N
 M←NB×N
 FNUM←2
 RESK2
```

```
 RA←¯1 ρX1
 RB←¯1 ρZ
 MPH←2 0ρ0
 RPH←2 0ρ0
 TREAT←0 3ρ0
 VTREAT←(0,N+1)ρ0
 MTREAT←0 3ρ0
 MVTREAT←111 0ρ0
 VAC←(0,RA+NT)ρ0
 MLEF←((RA+NT),0)ρ0
 RLEF←((RA+NT),0)ρ0
 MPRD←(NB,0)ρ0
 RPROP←10 0ρ0
 RPRD←(NB,0)ρ0
 MPROP←10 0ρ0
AG:E←0 5↓RESPK
⍝ ⎕TRAP←11 'E' '→LL1'
 N←¯1 ρE
 NB←1 ρE
 RP←N
 M←NB×N
 RA←¯1 ρX1
 RB←¯1 ρZ
 MPHI1←1
 MPHI2←0.5
 NO←1 ρZ
 E←(M,1)ρ,E
 RC←RB
 FC←RA
 I←0
 PHI1←MPHI1
 PHI2←MPHI2
 BET0←RBρ0
 ALF1←RAρ0
 T1←0.2
 T2←0.4
 T3←1
 T4←1.5
 T5←2
 T6←2.5
 TS←NT (1 ,T1),(1 ,T2),1 ,T3
 →(NT≠1)/D1
 DL1 DL2 DL3←E∘=¨1 2 3
 →LP
D1:→(NT≠2)/D2
 DL1 DL2 DL3 DL8←E∘=¨0 1 2 3
 →LP
D2:DL1 DL2 DL3 DL4 DL8←E∘=¨0 1 2 3 4
LP:T←⍉(((NT,NT)ρ1,NTρ0),(NT,RA+RB)ρ0),[1]((M,NT)ρ0),X1,Z
LOOP:L←(Z+.×((RB),1)ρBET0)+X1+.×(RA,1)ρALF1
 →(FNUM≠1)/E1
 PRHAZAD4
 →E4
```

RESPK2 (continued)

```
E1:→(FNUM≠2)/E2
 PRODDS
 →E4
E2:→(FNUM≠3)/E3
 PRHDS
 →E4
E3:PRXHDS
E4:→(NT≠1)/F1
 DERIV1
 →F3
F1:→(NT≠2)/F2
 DERIV31
 →F3
F2:DERIV43
F3:MET2←((M,1)ρ0,(RP-1)ρ1)×MEET0
 MEET2←(RB,1)ρ÷((+/(NB,N)ρ,MEET0)+÷MPHI1),(+/0
1↓(NB,N)ρ,MEET0)+÷MPHI2
 MEET3←(⍉Z)+.×X1×(,MEET0)∘.×RAρι1
 →(NT≠1)/N1
 ETTE2←(NB,1)ρ+/(NB,N)ρ(M,1) ETTE1
 ETTE3←(NB,1)ρ+/0 1↓(NB,N)ρ(M,1) ETTE1
 MEET3←(ETTE2,[1]ETTE3),MEET3
 →N3
N1:→(NT≠2)/N2
 ETTE2←(NB,1)ρ+/(NB,N)ρ(M,1) ETTE1
 ETTE2←ETTE2,(NB,1)ρ+/(NB,N)ρ(M,1) 0 1↓ETTE1
 ETTE3←(NB,1)ρ+/0 1↓(NB,N)ρ(M,1) ETTE1
 ETTE3←ETTE3,(NB,1)ρ+/0 1↓(NB,N)ρ(M,1) 0 1↓ETTE1
 MEET3←(ETTE2,[1]ETTE3),MEET3

→N3
N2:ETTE2←(NB,1)ρ+/(NB,N)ρ(M,1) ETTE1
 ETTE2←ETTE2,(NB,1)ρ+/(NB,N)ρ(M,1) 0 1↓ETTE1
 ETTE2←ETTE2,(NB,1)ρ+/(NB,N)ρ(M,1) 0 2↓ETTE1
 ETTE3←(NB,1)ρ+/0 1↓(NB,N)ρ(M,1) ETTE1
 ETTE3←ETTE3,(NB,1)ρ+/0 1↓(NB,N)ρ(M,1) 0 1↓ETTE1
 ETTE3←ETTE3,(NB,1)ρ+/0 1↓(NB,N)ρ(M,1) 0 2↓ETTE1
 MEET3←(ETTE2,[1]ETTE3),MEET3
N3:DEL←T+.×TE1,[1]MET0

ETTE7←⍉(TET1,(⍉ETTE1)+.×X1),[1]((⍉X1)+.×ETTE1),(⍉X1)+.×((,MEET0)∘.×
RAρι1)×X1
 ETTE3←(((-NB),1) MEET2)×(÷((-NB),1) MEET2)-÷MPHI2
 ETTE2←÷((NB,1) MEET2)×((-NB),1) MEET2
 ETTE2←ETTE2-((÷((-NB),1) MEET2)-÷MPHI2)*2
 ETTE2←(÷((-NB),1) MEET2)÷ETTE2
 MEET1←((,ETTE2)∘.×(NT+RA)ρι1)×(NB,NT+RA) MEET3
 MET3←((,ETTE2×ETTE3)∘.×(NT+RA)ρι1)×(NB,0)↓MEET3
 TE2←((,(((-NB),1) MEET2)×ETTE2÷(NB,1) MEET2)∘.×(NT+RA)ρι1)×((-
NB),RA+NT) MEET3
 TE3←((,ETTE2×ETTE3)∘.×(NT+RA)ρι1)×(NB,NT+RA) MEET3
```

```
 ETTE7←⌹ETTE7-((⍉(NB,NT+RA) MEET3)+.×MEET1-MET3)+(⍉((-
NB),NT+RA) MEET3)+.×TE2-TE3
 TE2←⍉(MEET1-MET3),[1]TE2-TE3
 TE3←(RB,1)⍴((÷MPHI1)×NB BET0),(÷MPHI2)×(-NB) BET0
 MEET7←TE2+.×((-RB),1) DEL
 MEET0←TE2+.×TE3
 V←(((NT+RA),1)⍴TS,ALF1)+ETTE7+.×(((NT+RA),1) DEL)+MEET0-MEET7
 DEL0←MEET3+.×ETTE7+.×MEET7-(((RA+NT),1) DEL)+MEET0
 DEL0←(((-RB),1) DEL)+DEL0-TE3
 DEL0←((RB,1)⍴BET0)+((ETTE2×(NB,1) DEL0)-ETTE2×ETTE3×((-
NB),1) DEL0),[1](-
ETTE2×ETTE3×(NB,1) DEL0)+((ETTE2÷(NB,1) MEET2)×((-NB),1) MEET2)×((-
NB),1) DEL0
 BLUP←V,[1]DEL0
 BLM←((NT+RA+RB),1)⍴TS,ALF1,BET0
 I←I+1
 ALF1←RA NT↓,BLUP
 T1←1 ,BLUP
 T2←1 1↓,BLUP
 T3←1 2↓,BLUP
 TS←NT ,BLUP
 BET0←(-RB) ,BLUP
 →(0.01>⌈/,|BLUP-BLM)/L1
 →(I≥26)/LL1
 V←0
 →LOOP
L1:
 I←0
 B0←(NB,1) ((RA+NT),0)↓BLUP
 B1←(NB,1) ((RA+NT+NB),0)↓BLUP
 →(ML=1)/MAXL1
 RI1←(+/DIAG(NB,NB) (⍉TE2)+.×ETTE7+.×TE2)÷MPHI1
 RI1←RI1+(+/,ETTE2)÷MPHI1
 RI2←(+/DIAG((-NB),(-NB)) (⍉TE2)+.×ETTE7+.×TE2)÷MPHI2
 RI2←RI2+(+/,(ETTE2÷(NB,1) MEET2)×(NB,0)↓MEET2)÷MPHI2
 →RMAXL1
MAXL1:RI1←(+/,ETTE2)÷MPHI1
 RI2←(+/,(ETTE2÷(NB,1) MEET2)×(NB,0)↓MEET2)÷MPHI2
RMAXL1:MPHI1←,((⍉B0)+.×B0)÷NB-RI1
 MPHI2←,((⍉B1)+.×B1)÷NB-RI2
 →((0.0001≥|MPHI1-PHI1)∧0.0001≥|MPHI2-PHI2)/L2
 PHI1←MPHI1
 PHI2←MPHI2

 →LOOP
L2:
 →(ML=1)/MAXL2
 A1←+/+/ETTE2×ETTE2
 A1←A1+2×+/,ETTE2×(NB,1)⍴,DIAG(NB,NB) (⍉TE2)+.×ETTE7+.×TE2

A1←A1++/DIAG((NB,NB) (⍉TE2)+.×ETTE7+.×TE2)+.×(NB,NB) (⍉TE2)+.×ETTE7
+.×TE2
```

```
 A3←(ETTE2÷(NB,1) MEET2)×((-NB),1) MEET2
 A2←(+/,A3×A3)+2×+/,A3×(NB,1)ρDIAG((-NB),(-
NB)) (⍉TE2)+.×ETTE7+.×TE2
 A2←A2++/DIAG(((-NB),(-NB)) (⍉TE2)+.×ETTE7+.×TE2)+.×((-NB),(-
NB)) (⍉TE2)+.×ETTE7+.×TE2
 A3←ETTE2×ETTE3
 A12←(+/,A3×A3)-
2×+/,A3×(NB,1)ρDIAG(NB,NB) (0,NB)↓(⍉TE2)+.×ETTE7+.×TE2

A12←A12++/DIAG((NB,NB) (NB,0)↓(⍉TE2)+.×ETTE7+.×TE2)+.×(NB,NB) (0,NB
)↓(⍉TE2)+.×ETTE7+.×TE2
 →RMAXL2
MAXL2:
 A1←+/+/ETTE2×ETTE2
 A2←(ETTE2÷(NB,1) MEET2)×((-NB),1) MEET2
 A2←(+/,A2×A2)
 A12←ETTE2×ETTE3
 A12←+/,A12×A12
RMAXL2:
 A1←A1÷2×MPHI1*4
 A1←A1+((÷MPHI1*2)×(NB-2×RI1))÷2
 A2←A2÷2×MPHI2*4
 A2←A2+((÷MPHI2*2)×(NB-2×RI2))÷2
 A12←A12÷2×(MPHI1*2)×MPHI2*2
 A1←(DIAG⌹(2 2ρA1,A12,A12,A2))*0.5
 →(ML≠1)/PREM
 MLEF←MLEF,3 RND(((NT+RA),1)ρTS,ALF1),(((RA+NT),1)ρ(NT+RA) (DIAG
ETTE7)*0.5),((NT+RA),1)ρ(TS,ALF1)÷(NT+RA) (DIAG ETTE7)*0.5
 MPH←MPH,2
3ρMPHI1,(1 ,A1),(MPHI1÷(1 ,A1)),MPHI2,(¯1 A1),MPHI2÷¯1 A1
 ETA←L
 V←(¯4 ¯4 8 8 ETTE7)
 V←(+/DIAG
V)+2×(+/,((⍳N)∘.=1+⍳N)×V)+(+/,((⍳N)∘.=2+⍳N)×V)+(+/,((⍳N)∘.=3+⍳N)×V)
 MTREAT←MTREAT,[1]1
3ρ((+/4 1↓,ALF1)÷4),((V*0.5)÷4),(+/4 1↓,ALF1)÷V*0.5
 Y1←(ETA≤0)
 Y2←((ETA>0)∧ETA≤T1)
 Y3←((ETA>T1)∧ETA≤T2)
 Y4←((ETA>T2)∧ETA≤T3)
 Y5←(ETA>T3)
 E←(NB,RP)ρ(0×Y1)+(1×Y2)+(2×Y3)+(3×Y4)+4×Y5
 DL1 DL2 DL3 DL4 DL8←E∘=¨0 1 2 3 4
 DL5←(,1∘=(NB,1) 0 1↓RESPK)∘.×RPρ⍳1
 RCOM←B0,B1

MP0←((1,RP)ρ+/[1]DL5×DL1),[1]((1,RP)ρ+/[1]DL5×DL2),[1]((1,RP)ρ+/[1]
DL5×DL3),[1]((1,RP)ρ+/[1]DL5×DL4),[1]((1,RP)ρ+/[1]DL5×DL8)
 DL5←(,2∘=(NB,1) 0 1↓RESPK)∘.×RPρ⍳1
```

RESPK2 (continued)

```
MPO←MPO,[1]((1,RP)ρ+/[1]DL5×DL1),[1]((1,RP)ρ+/[1]DL5×DL2),[1]((1,RP
)ρ+/[1]DL5×DL3),[1]((1,RP)ρ+/[1]DL5×DL4),[1]((1,RP)ρ+/[1]DL5×DL8)
 MPROP←MPROP,MPO
 MPRD←MPRD,(0 5↓RESPK)=(NB,RP)ρ(0×Y1)+(1×Y2)+(2×Y3)+(3×Y4)+4×Y5
 →(FNUM=4)/PRE
 FNUM←FNUM+1
 NT←3
 →AG
PRE:ML←2
 FNUM←1
 NT←3
 →AG
PREM:RLEF←RLEF,3
RND(((NT+RA),1)ρTS,ALF1),(((RA+NT),1)ρ(NT+RA) (DIAG
ETTE7)*0.5),((NT+RA),1)ρ(TS,ALF1)÷(NT+RA) (DIAG ETTE7)*0.5
 RPH←RPH,2
3ρMPHI1,(1 ,A1),(MPHI1÷(1 ,A1)),MPHI2,(¯1 A1),MPHI2÷¯1 A1
 ETA←L
 MVTREAT←MVTREAT,B0,B1
 →LL2
 NT←3+RA-8
 V←(¯4 ¯4 8 8 ETTE7)
 V←(+/DIAG
V)+2×(+/,((ιN)∘.=1+ιN)×V)+(+/,((ιN)∘.=2+ιN)×V)+(+/,((ιN)∘.=3+ιN)×V)
 TREAT←TREAT,[1]1
3ρ((+/4 1↓,ALF1)÷4),((V*0.5)÷4),(+/4 1↓,ALF1)÷V*0.5
 VTREAT←VTREAT,[1](¯4 ¯4 8 8 ETTE7),4 1ρ4 1↓,ALF1
 Y1←(ETA≤0)
 Y2←((ETA>0)∧ETA≤T1)
 Y3←((ETA>T1)∧ETA≤T2)
 Y4←((ETA>T2)∧ETA≤T3)
 Y5←(ETA>T3)
 E←(NB,RP)ρ(0×Y1)+(1×Y2)+(2×Y3)+(3×Y4)+4×Y5
 DL1 DL2 DL3 DL4 DL8←E∘=¨0 1 2 3 4
 DL5←(,1∘=(NB,1) 0 1↓RESPK)∘.×RPρι1

RPO←((1,RP)ρ+/[1]DL5×DL1),[1]((1,RP)ρ+/[1]DL5×DL2),[1]((1,RP)ρ+/[1]
DL5×DL3),[1]((1,RP)ρ+/[1]DL5×DL4),[1]((1,RP)ρ+/[1]DL5×DL8)
 DL5←(,2∘=(NB,1) 0 1↓RESPK)∘.×RPρι1

RPO←RPO,[1]((1,RP)ρ+/[1]DL5×DL1),[1]((1,RP)ρ+/[1]DL5×DL2),[1]((1,RP
)ρ+/[1]DL5×DL3),[1]((1,RP)ρ+/[1]DL5×DL4),[1]((1,RP)ρ+/[1]DL5×DL8)
 RPROP←RPROP,RPO
 RPRD←RPRD,(0 5↓RESPK)=(NB,RP)ρ(0×Y1)+(1×Y2)+(2×Y3)+(3×Y4)+4×Y5
 →(FNUM=4)/LL2
 FNUM←FNUM+1
 NT←3
 →AG
 →LL2
LL1:COUNT←1
LL2:MLEF←MPH,[1]MLEF
 RLEF←RPH,[1]RLEF
```

RESPK2 (continued)

```
RESK2;X2;X4;I2;I3;I4;X5
 X3←1∘=(NB,1) RESPK
 X3←X3,(NB,1) 0 3↓RESPK
 X3←X3,2∘=(NB,1) 0 2↓RESPK
 X3←X3,0∘=(NB,1) 0 4↓RESPK
 X3←X3,1∘=(NB,1) 0 4↓RESPK
 X3←X3,2∘=(NB,1) 0 4↓RESPK
 X3←X3,3∘=(NB,1) 0 4↓RESPK
 X1←((M,1)ρ1),((M,RP)ρ,(RP,RP)ρ1,RPρ0)×(,(,1∘=(NB,1) 0
1↓RESPK)∘.×RPρι1)∘.×RPρι1
 Z←⍉(NB,M)ρ(RPρ1),Mρ0
 Z←Z,⍉(NB,M)ρ(0,(RP-1)ρ1),Mρ0
⍝ →END
 I←0
⍝ X4←(4 2ρ1 0 1 1 1 1 1 1)+.×⍉14 2ρ4 2 3 1⍉(1 7 I 0↓X3)∘.×2 2ρ1,2ρ0
 I←1
⍝LP:X4←X4,[1](4 2ρ1 0 1 1 1 1 1 1)+.×⍉14 2ρ4 2 3 1⍉(1 7 I 0↓X3)∘.×2
2ρ1,2ρ0
⍝ →(I=NB-1)/ED
 I←I+1
⍝ →LP
⍝ED:X1←X1,X4
```

PRHAZAD4

```
 CDF1←⍉((¯1 ρE),(1 ρE))ρ(-L)NORMALCUMX 0 1
 CDF2←⍉((¯1 ρE),(1 ρE))ρ(T1-L)NORMALCUMX 0 1
 CDF3←⍉((¯1 ρE),(1 ρE))ρ(T2-L)NORMALCUMX 0 1
 CDF4←⍉((¯1 ρE),(1 ρE))ρ(T3-L)NORMALCUMX 0 1
 CDF5←⍉((¯1 ρE),(1 ρE))ρ(T4-L)NORMALCUMX 0 1
 CDF6←⍉((¯1 ρE),(1 ρE))ρ(T5-L)NORMALCUMX 0 1
 PDF1←⍉((¯1 ρE),(1 ρE))ρ(-L)NORMAL 0 1
 PDF2←⍉((¯1 ρE),(1 ρE))ρ(T1-L)NORMAL 0 1
 PDF3←⍉((¯1 ρE),(1 ρE))ρ(T2-L)NORMAL 0 1
 PDF4←⍉((¯1 ρE),(1 ρE))ρ(T3-L)NORMAL 0 1
 PDF5←⍉((¯1 ρE),(1 ρE))ρ(T4-L)NORMAL 0 1
 PDF6←⍉((¯1 ρE),(1 ρE))ρ(T5-L)NORMAL 0 1
 PPDF1←⍉((¯1 ρE),(1 ρE))ρ(L)×(-L)NORMAL 0 1
 PPDF2←⍉((¯1 ρE),(1 ρE))ρ(L-T1)×(T1-L)NORMAL 0 1
 PPDF3←⍉((¯1 ρE),(1 ρE))ρ(L-T2)×(T2-L)NORMAL 0 1
 PPDF4←⍉((¯1 ρE),(1 ρE))ρ(L-T3)×(T3-L)NORMAL 0 1
 PPDF5←⍉((¯1 ρE),(1 ρE))ρ(L-T4)×(T4-L)NORMAL 0 1
 PPDF6←⍉((¯1 ρE),(1 ρE))ρ(L-T5)×(T5-L)NORMAL 0 1
```

PRODDS

```
CDF1←⍉((¯1 ρE),(1 ρE))ρ(*-L)÷1+*-L
CDF2←⍉((¯1 ρE),(1 ρE))ρ(*T1-L)÷1+*T1-L
CDF3←⍉((¯1 ρE),(1 ρE))ρ(*T2-L)÷1+*T2-L
CDF4←⍉((¯1 ρE),(1 ρE))ρ(*T3-L)÷1+*T3-L
PDF1←⍉((¯1 ρE),(1 ρE))ρ(*-L)÷(1+*-L)*2
PDF2←⍉((¯1 ρE),(1 ρE))ρ(*T1-L)÷(1+*T1-L)*2
PDF3←⍉((¯1 ρE),(1 ρE))ρ(*T2-L)÷(1+*T2-L)*2
PDF4←⍉((¯1 ρE),(1 ρE))ρ(*T3-L)÷(1+*T3-L)*2
PPDF1←⍉((¯1 ρE),(1 ρE))ρ((*-L)-(*-2×L))÷(1+*-L)*3
PPDF2←⍉((¯1 ρE),(1 ρE))ρ((*T1-L)-(*2×T1-L))÷(1+*T1-L)*3
PPDF3←⍉((¯1 ρE),(1 ρE))ρ((*T2-L)-(*2×T2-L))÷(1+*T2-L)*3
PPDF4←⍉((¯1 ρE),(1 ρE))ρ((*T3-L)-(*2×T3-L))÷(1+*T3-L)*3
```

PRHDS

```
CDF1←⍉((¯1 ρE),(1 ρE))ρ1-*-*-L
CDF2←⍉((¯1 ρE),(1 ρE))ρ1-*-*T1-L
CDF3←⍉((¯1 ρE),(1 ρE))ρ1-*-*T2-L
CDF4←⍉((¯1 ρE),(1 ρE))ρ1-*-*T3-L
PDF1←⍉((¯1 ρE),(1 ρE))ρ*-L+*-L
PDF2←⍉((¯1 ρE),(1 ρE))ρ*(T1-L)-*T1-L
PDF3←⍉((¯1 ρE),(1 ρE))ρ*(T2-L)-*T2-L
PDF4←⍉((¯1 ρE),(1 ρE))ρ*(T3-L)-*T3-L
PPDF1←⍉((¯1 ρE),(1 ρE))ρ(1-*-L)×(*-L+*-L)
PPDF2←⍉((¯1 ρE),(1 ρE))ρ(1-*T1-L)××(T1-L)-*T1-L
PPDF3←⍉((¯1 ρE),(1 ρE))ρ(1-*T2-L)××(T2-L)-*T2-L
PPDF4←⍉((¯1 ρE),(1 ρE))ρ(1-*T3-L)××(T3-L)-*T3-L
```

PRXHDS

```
CDF1←⍉((¯1 ρE),(1 ρE))ρ*-*L
CDF2←⍉((¯1 ρE),(1 ρE))ρ*-*-T1-L
CDF3←⍉((¯1 ρE),(1 ρE))ρ*-*-T2-L
CDF4←⍉((¯1 ρE),(1 ρE))ρ*-*-T3-L
PDF1←⍉((¯1 ρE),(1 ρE))ρ*L-*L
PDF2←⍉((¯1 ρE),(1 ρE))ρ*-(T1-L)+*-T1-L
PDF3←⍉((¯1 ρE),(1 ρE))ρ*-(T2-L)+*-T2-L
PDF4←⍉((¯1 ρE),(1 ρE))ρ*-(T3-L)+*-T3-L
PPDF1←⍉((¯1 ρE),(1 ρE))ρ-(1-*L)×(*L-*L)
PPDF2←⍉((¯1 ρE),(1 ρE))ρ-(1-*-T1-L)××-(T1-L)+*-T1-L
PPDF3←⍉((¯1 ρE),(1 ρE))ρ-(1-*-T2-L)××-(T2-L)+*-T2-L
PPDF4←⍉((¯1 ρE),(1 ρE))ρ-(1-*-T3-L)××-(T3-L)+*-T3-L
```

DERIV43

```
 COUNT←0
⍝ ⎕TRAP←11 'E' '→D11'
 MET0←DL1×-PDF1÷CDF1
 MEET0←DL1×(-(PDF1÷CDF1)*2)+PPDF1÷CDF1

 MET1←DL2×(PDF1-PDF2)÷CDF2-CDF1
 MEET1←DL2×(-((PDF1-PDF2)÷(CDF2-CDF1))*2)+(PPDF2-PPDF1)÷CDF2-CDF1
 ETTE1←DL2×-((PDF2÷CDF2-CDF1)×((PDF1-PDF2)÷(CDF2-
CDF1)))+PPDF2÷CDF2-CDF1
 TE1←DL2×PDF2÷CDF2-CDF1
 TET1←DL2×(-(PDF2÷CDF2-CDF1)*2)+PPDF2÷CDF2-CDF1
 MET2←DL3×(PDF2-PDF3)÷CDF3-CDF2
 MEET2←DL3×(-((PDF2-PDF3)÷(CDF3-CDF2))*2)+(PPDF3-PPDF2)÷CDF3-CDF2
 ETTE21←DL3×((PDF2÷CDF3-CDF2)×((PDF2-PDF3)÷(CDF3-
CDF2)))+PPDF2÷CDF3-CDF2
 ETTE2←DL3×-((PDF3÷CDF3-CDF2)×((PDF2-PDF3)÷(CDF3-
CDF2)))+PPDF3÷CDF3-CDF2
 TE2←DL3×PDF3÷CDF3-CDF2
 TE21←DL3×PDF2÷CDF3-CDF2
 TET12←DL3×(PDF3×PDF2)÷(CDF3-CDF2)*2
 TET2←DL3×(-(PDF3÷CDF3-CDF2)*2)+PPDF3÷CDF3-CDF2
 TET211←DL3×-((PDF2÷CDF3-CDF2)*2)+PPDF2÷CDF3-CDF2
 TET21←DL3×(PDF3×PDF2)÷(CDF3-CDF2)*2
 MET3←DL4×(PDF3-PDF4)÷CDF4-CDF3
 MEET3←DL4×(-((PDF3-PDF4)÷(CDF4-CDF3))*2)+(PPDF4-PPDF3)÷CDF4-CDF3
 ETTE31←DL4×((PDF3÷CDF4-CDF3)×((PDF3-PDF4)÷(CDF4-
CDF3)))+PPDF3÷CDF4-CDF3
 ETTE3←DL4×-((PDF4÷CDF4-CDF3)×((PDF3-PDF4)÷(CDF4-
CDF3)))+PPDF4÷CDF4-CDF3
 TE3←DL4×PDF4÷CDF4-CDF3
 TE32←DL4×PDF3÷CDF4-CDF3
 TET23←DL4×(PDF3×PDF4)÷(CDF4-CDF3)*2
 TET3←DL4×(-(PDF4÷CDF4-CDF3)*2)+PPDF4÷CDF4-CDF3
 TET312←DL4×-((PDF3÷CDF4-CDF3)*2)+PPDF3÷CDF4-CDF3
 TET32←DL4×(PDF4×PDF3)÷(CDF4-CDF3)*2
⍝ MET4←DL5×(PDF4-PDF5)÷CDF5-CDF4
⍝ MEET4←DL5×(-((PDF4-PDF5)÷(CDF5-CDF4))*2)+(PPDF5-PPDF4)÷CDF5-CDF4
⍝ ETTE41←DL5×((PDF4÷CDF5-CDF4)×((PDF4-PDF5)÷(CDF5-
CDF4)))+PPDF4÷CDF5-CDF4
⍝ ETTE4←DL5×-((PDF5÷CDF5-CDF4)×((PDF4-PDF5)÷(CDF5-
CDF4)))+PPDF5÷CDF5-CDF4
⍝ TE4←DL5×PDF5÷CDF5-CDF4
⍝ TE43←DL5×PDF4÷CDF5-CDF4
⍝ TET34←DL5×(PDF4×PDF5)÷(CDF5-CDF4)*2
⍝ TET4←DL5×(-(PDF5÷CDF5-CDF4)*2)+PPDF5÷CDF5-CDF4
⍝ TET423←DL5×-((PDF4÷CDF5-CDF4)*2)+PPDF4÷CDF5-CDF4
⍝ TET43←DL5×(PDF5×PDF4)÷(CDF5-CDF4)*2
 MET7←DL8×PDF4÷1-CDF4
 MEET7←DL8×-((PDF4÷1-CDF4)*2)+PPDF4÷1-CDF4
 ETTE7←DL8×((PDF4÷1-CDF4)*2)+PPDF4÷1-CDF4
 TET7←DL8×-((PDF4÷1-CDF4)*2)+PPDF4÷1-CDF4
```

DERIV43 (continued)

```
 TE7←DL8×PDF4÷1-CDF4
 ETTE1←-(ETTE1+ETTE21),(ETTE2+ETTE31),ETTE3+ETTE7
 TE1←(+/+/TE1)-+/+/TE21
 TE2←(+/+/TE2)-+/+/TE32
 TE3←(+/+/TE3)-+/+/TE7
⍝TE6←(+/+/TE4)-+/+/TE7
 MET0←MET0+MET1+MET2+MET3+MET7
 MEET0←-MEET0+MEET1+MEET2+MEET3+MEET7
 TET1←-((1 1⍴+/+/TET1+TET211),(1 1⍴+/,TET12)),1 1⍴0
 TET2←-(1 1⍴+/,TET21),((1 1⍴+/+/TET2+TET312),(1 1⍴+/,TET23))
 TET3←-(1 1⍴0),(1 1⍴+/,TET32),(1 1⍴+/+/TET3+TET7)
⍝ TET6←-(1 2⍴0),(1 1⍴+/,TET43),(1 1⍴+/+/TET4+TET7)
 TET1←TET1,[1]TET2,[1]TET3
 TE1←3 1⍴TE1,TE2,TE3
⍝ →D12
⍝D11:COUNT←1
⍝D12:
```

RESPVTK1 fits model 4 in section 7.4 of chapter 7 to respiratory data.

```
RESPVTK1;T1;RP;Y2;Y3;Y4;Y5;Z;TET45;TET5;V11;V2;VAC;VIN;X1;Y1;RPO;SZ
;NB;NT;PHI1;RA;RB;DL5;DL8;E;ETA;FNUM;M;ML;MPO;A;B2;COUNT;DL1;DL2;DL
3;DL4;MPHI;MPHI2;A12;A2;DL8;FC;I2;I3;I4;NO;PHI2;RI1;RI2;TE7;TS;X2;X
3;X4;X5;GI;A1;B0;B1;B11;B12;B13;C1;C11;C12;D;MPHI;N;NB;PHI;RA0;RA1;
RC;TR;TRJ;VI;VINR;VMPHI;TE21;TE32;TE43;TE54;TE65;A;B;CDF4;CDF5;CDF6
;CDF7;DL4;DL5;DL6;DL7;ETTE31;ETTE4;ETTE41;ETTE5;ETTE51;ETTE6;ETTE61
;ETTE7;J;MEET4;MEET5;MEET6;MEET7;MET4;MET5;MET6;MET7;PDF4;PDF5;PDF6
;PDF7;PPDF4;PPDF5;PPDF6;PPDF7;T3;T4;T5;T6;TE4;TE5;TE6;TET211;TET23;
TET312;TET32;TET34;TET4;TET423;TET43;RET45;TET534;TET54;TET56;TET6;
TET645;TET65;TET7;G;E1;BLM;DL4;ETTE21;ETTE3;I;L;LSEF;MEET3;MET3;T2;
TE11;TET3;TE12;TE2;TE3;TET1;TET11;TET21;TET12;P0;PDF3;RI;RII;T;TET2
;V;V1;VBET;VCOM;VFIX;INF00;A
LF1;ALF2;BET0;INF01;INF11;INF12;INF13;INF21;INF22;INF23;IN;V0;DEL0;
DEL;BLUP;E;NUP;DL1;DL2;DL3;CDF1;CDF2;PPDF1;PPDF2;CDF3;PPDF3;PDF1;PD
F2;EE;MET0;MEET0;MET1;MEET1;MET2;MEET2;ETTE1;ETTE2;TE1;T
 COUNT←0
 ML←1
 NT←12
 E←0 5↓RESPK
 ⎕TRAP←11 'E' '→LL1'
 N←¯1 ⍴E
 NB←1 ⍴E
 RP←N
 M←NB×N
 FNUM←1
 RESKD1
 RA←¯1 ⍴X1
 RB←¯1 ⍴Z
```

RESPVTK1 (continued)

```
 MPH←1 0⍴0
 RPH←1 0⍴0
 TREAT←0 3⍴0
 VTREAT←(0,N+1)⍴0
 MTREAT←0 3⍴0
 MVTREAT←(0,N)⍴0
 VAC←(0,RA+NT)⍴0
 MLEF←((RA+NT),0)⍴0
 RLEF←((RA+NT),0)⍴0
 MPRD←(NB,0)⍴0
 RPROP←10 0⍴0
 RPRD←(NB,0)⍴0
 MPROP←10 0⍴0
AG:E←0 5↓RESPK
 ⎕TRAP←11 'E' '→LL1'
 N←¯1 ⍴E
 NB←1 ⍴E
 RP←N
 M←NB×N
 RA←¯1 ⍴X1
 RB←¯1 ⍴Z
 MPHI←1
 NO←1 ⍴Z
 E←(M,1)⍴,E
 RC←RB
 FC←RA
 I←0
 PHI←MPHI
 BET0←RB⍴0
 ALF1←RA⍴0
 T1←0.2
 T2←0.4
 T3←1
 T4←1.5
 T5←2
 T6←2.4
 TS←(4⍴T1),(4⍴T2),4⍴T3
 DL1 DL2 DL3 DL4 DL8←E∘=¨0 1 2 3 4
 T←⍉(((NT,NT)⍴1,NT⍴0),(NT,RA+RB)⍴0),[1]((M,NT)⍴0),X1,Z
LOOP:L←(Z+.×((RB),1)⍴BET0)+X1+.×(RA,1)⍴ALF1
 →(FNUM≠1)/E1
 PRHAZAD4
 →E4
E1:→(FNUM≠2)/E2
 PRODDS
 →E4
E2:→(FNUM≠3)/E3
 PRHDS
 →E4
E3:PRXHDS
E4:
```

RESPVTK1 (continued)

```
 DERMVT
 MEET2←(RB,1)⍴÷((+/(NB,N)⍴,MEET0)+÷MPHI)

 MEET3←+/[2](NB,N,RA)⍴,X1×(,MEET0)∘.×RA⍴⍳1
 ETTE2←(NB,1)⍴+/(NB,N)⍴(M,1) ETTE1
 ETTE2←ETTE2,(NB,1)⍴+/(NB,N)⍴(M,1) 0 1↓ETTE1
 ETTE2←ETTE2,(NB,1)⍴+/(NB,N)⍴(M,1) 0 2↓ETTE1
 ETTE2←ETTE2,(NB,1)⍴+/(NB,N)⍴(M,1) 0 3↓ETTE1
 ETTE2←ETTE2,(NB,1)⍴+/(NB,N)⍴(M,1) 0 4↓ETTE1
 ETTE2←ETTE2,(NB,1)⍴+/(NB,N)⍴(M,1) 0 5↓ETTE1
 ETTE2←ETTE2,(NB,1)⍴+/(NB,N)⍴(M,1) 0 6↓ETTE1
 ETTE2←ETTE2,(NB,1)⍴+/(NB,N)⍴(M,1) 0 7↓ETTE1
 ETTE2←ETTE2,(NB,1)⍴+/(NB,N)⍴(M,1) 0 8↓ETTE1
 ETTE2←ETTE2,(NB,1)⍴+/(NB,N)⍴(M,1) 0 9↓ETTE1
 ETTE2←ETTE2,(NB,1)⍴+/(NB,N)⍴(M,1) 0 10↓ETTE1
 ETTE2←ETTE2,(NB,1)⍴+/(NB,N)⍴(M,1) 0 11↓ETTE1
 MEET3←ETTE2,MEET3
 DEL←T+.×TE1,[1]MET0

ETTE7←⍉(TET1,(⍉ETTE1)+.×X1),[1]((⍉X1)+.×ETTE1),(⍉X1)+.×((,MEET0)∘.×
RA⍴⍳1)×X1
 ETTE7←⌹ETTE7-(⍉MEET3)+.×((,MEET2)∘.×(RA+NT)⍴⍳1)×MEET3
 MET3←(NB,1)⍴(÷MPHI)×BET0
 MEET7←(⍉MEET3)+.×MEET2×((-NB),1) DEL
 MEET0←(⍉MEET3)+.×MEET2×MET3
 V←(((RA+NT),1)⍴TS,ALF1)+ETTE7+.×(((RA+NT),1) DEL)+MEET0-MEET7
 DEL0←MEET3+.×ETTE7+.×MEET7-(((RA+NT),1) DEL)+MEET0
 DEL0←((RB,1)⍴BET0)+MEET2×(((-RB),1) DEL)+DEL0-MET3
 BLUP←V,[1]DEL0
 BLM←((RB+RA+NT),1)⍴TS,ALF1,BET0
 I←I+1
 DEL←0
 DEL0←0
 ALF1←RA NT↓,BLUP
 T1←(M,1)⍴RP ,BLUP
 T2←(M,1)⍴RP RP↓,BLUP
 T3←(M,1)⍴RP (2×RP)↓,BLUP
 TS←NT ,BLUP
 BET0←(-RB) ,BLUP
 B0←((-RB),1) BLUP
 →(0.01>⌈/,|BLUP-BLM)/L1
 V←0
 →LOOP
L1:
 I←0
 →(ML=1)/MAXL
 RI←(+/,MEET2)÷MPHI
 MEET3←((,MEET2)∘.×(RA+NT)⍴⍳1)×MEET3
 RI←RI+(+/DIAG MEET3+.×ETTE7+.×⍉MEET3)÷MPHI
 →RMAXL
MAXL:RI←(+/,MEET2)÷MPHI
```

```
RMAXL:MPHI←,((⍉B0)+.×B0)÷RB-RI
 →(0.0001≥|MPHI-PHI)/L2
 PHI←MPHI
 →LOOP
L2:
 →(ML=1)/MAXL1
 A1←(+/+/(,MEET2)×,MEET2)
 A1←A1+2×+/DIAG(MEET3+.×ETTE7+.×⍉MEET3)×((NB,NB)⍴0)MATDIAG,MEET2
 A1←A1++/DIAG(MEET3+.×ETTE7+.×⍉MEET3)+.×MEET3+.×ETTE7+.×⍉MEET3
 →RMAXL1
MAXL1:A1←(+/+/(,MEET2)×,MEET2)
RMAXL1:A1←A1÷2×MPHI*4
 A1←(÷A1+((÷MPHI*2)×(RB-2×RI))÷2)*0.5
 →(ML≠1)/PREM
 MLEF←MLEF,3 RND(((NT+RA),1)⍴TS,ALF1),((((RA+NT),1)⍴(NT+RA) (DIAG
ETTE7)*0.5),((NT+RA),1)⍴(TS,ALF1)÷(NT+RA) (DIAG ETTE7)*0.5
 MPH←MPH,1 3⍴MPHI,A1,MPHI÷A1
 ETA←L
 V←(¯4 ¯4 ETTE7)
 V←(+/DIAG
V)+2×(+/,((⍳N)∘.=1+⍳N)×V)+(+/,((⍳N)∘.=2+⍳N)×V)+(+/,((⍳N)∘.=3+⍳N)×V)
 MTREAT←MTREAT,[1]1
3⍴((+/¯4 ,ALF1)÷4),((V*0.5)÷4),(+/¯4 ,ALF1)÷V*0.5
 Y1←(ETA≤0)
 Y2←((ETA>0)∧ETA≤T1)
 Y3←((ETA>T1)∧ETA≤T2)
 Y4←((ETA>T2)∧ETA≤T3)
 Y5←(ETA>T3)
 E←(NB,RP)⍴(0×Y1)+(1×Y2)+(2×Y3)+(3×Y4)+4×Y5
 DL1 DL2 DL3 DL4 DL8←E∘=¨0 1 2 3 4
 DL5←(,1∘=(NB,1) 0 1↓RESPK)∘.×RP⍴⍳1

MPO←((1,RP)⍴+/[1]DL5×DL1),[1]((1,RP)⍴+/[1]DL5×DL2),[1]((1,RP)⍴+/[1]
DL5×DL3),[1]((1,RP)⍴+/[1]DL5×DL4),[1]((1,RP)⍴+/[1]DL5×DL8)
 DL5←(,2∘=(NB,1) 0 1↓RESPK)∘.×RP⍴⍳1

MPO←MPO,[1]((1,RP)⍴+/[1]DL5×DL1),[1]((1,RP)⍴+/[1]DL5×DL2),[1]((1,RP
)⍴+/[1]DL5×DL3),[1]((1,RP)⍴+/[1]DL5×DL4),[1]((1,RP)⍴+/[1]DL5×DL8)
 MPROP←MPROP,MPO
 MPRD←MPRD,(0 5↓RESPK)=(NB,RP)⍴(0×Y1)+(1×Y2)+(2×Y3)+(3×Y4)+4×Y5
 →(FNUM=4)/PRE
 FNUM←FNUM+1
 NT←12
 →AG
PRE:ML←2
 FNUM←1
 NT←12
 →AG
PREM:RLEF←RLEF,3
RND(((NT+RA),1)⍴TS,ALF1),((((RA+NT),1)⍴(NT+RA) (DIAG
ETTE7)*0.5),((NT+RA),1)⍴(TS,ALF1)÷(NT+RA) (DIAG ETTE7)*0.5
```

```
 RPH←RPH,1 3ρMPHI,A1,MPHI÷A1
 ETA←L
 V←(¯4 ¯4 ETTE7)
 V←(+/DIAG
V)+2×(+/,((ιN)∘.=1+ιN)×V)+(+/,((ιN)∘.=2+ιN)×V)+(+/,((ιN)∘.=3+ιN)×V)
 TREAT←TREAT,[1]1 3ρ((+/¯4 ,ALF1)÷4),((V*0.5)÷4),(+/¯4 ,ALF1)÷V*0.5
 VTREAT←VTREAT,[1](¯4 ¯4 ETTE7),4 1ρ¯4 ALF1
 Y1←(ETA≤0)
 Y2←((ETA>0)∧ETA≤T1)
 Y3←((ETA>T1)∧ETA≤T2)
 Y4←((ETA>T2)∧ETA≤T3)
 Y5←(ETA>T3)
 E←(NB,RP)ρ(0×Y1)+(1×Y2)+(2×Y3)+(3×Y4)+4×Y5
 DL1 DL2 DL3 DL4 DL8←E∘=¨0 1 2 3 4
 DL5←(,1∘=(NB,1) 0 1↓RESPK)∘.×RPρι1

RPO←((1,RP)ρ+/[1]DL5×DL1),[1]((1,RP)ρ+/[1]DL5×DL2),[1]((1,RP)ρ+/[1]
DL5×DL3),[1]((1,RP)ρ+/[1]DL5×DL4),[1]((1,RP)ρ+/[1]DL5×DL8)
 DL5←(,2∘=(NB,1) 0 1↓RESPK)∘.×RPρι1

RPO←RPO,[1]((1,RP)ρ+/[1]DL5×DL1),[1]((1,RP)ρ+/[1]DL5×DL2),[1]((1,RP
)ρ+/[1]DL5×DL3),[1]((1,RP)ρ+/[1]DL5×DL4),[1]((1,RP)ρ+/[1]DL5×DL8)
 RPROP←RPROP,RPO
 RPRD←RPRD,(0 5↓RESPK)=(NB,RP)ρ(0×Y1)+(1×Y2)+(2×Y3)+(3×Y4)+4×Y5
 →(FNUM=4)/LL2
 FNUM←FNUM+1
 NT←12
 →AG
 →LL2
LL1:COUNT←1
LL2:MLEF←MPH,[1]MLEF
 RLEF←RPH,[1]RLEF
```

RESPVTK2 fits models 5 and 6 in section 7.4 of chapter 7 to respiratory data.

```
RESPVTK2;T1;RP;Y2;Y3;Y4;Y5;Z;TET45;TET5;V11;V2;VAC;VIN;X1;Y1;RPO;SZ
;NB;NT;PHI1;RA;RB;DL5;DL8;E;ETA;FNUM;M;ML;MPO;A;B2;COUNT;DL1;DL2;DL
3;DL4;MPHI1;MPHI2;A12;A2;DL8;FC;I2;I3;I4;NO;PHI2;RI1;RI2;TE7;TS;X2;
X3;X4;X5;GI;A1;B0;B1;B11;B12;B13;C1;C11;C12;D;MPHI;N;NB;PHI;RA0;RA1
;RC;TR;TRJ;VI;VINR;VMPHI;TE21;TE32;TE43;TE54;TE65;A;B;CDF4;CDF5;CDF
6;CDF7;DL4;DL5;DL6;DL7;ETTE31;ETTE4;ETTE41;ETTE5;ETTE51;ETTE6;ETTE6
1;ETTE7;J;MEET4;MEET5;MEET6;MEET7;MET4;MET5;MET6;MET7;PDF4;PDF5;PDF
6;PDF7;PPDF4;PPDF5;PPDF6;PPDF7;T3;T4;T5;T6;TE4;TE5;TE6;TET211;TET23
;TET312;TET32;TET34;TET4;TET423;TET43;RET45;TET534;TET54;TET56;TET6
;TET645;TET65;TET7;G;E1;BLM;DL4;ETTE21;ETTE3;I;L;LSEF;MEET3;MET3;T2
;TE11;TET3;TE12;TE2;TE3;TET1;TET11;TET21;TET12;P0;PDF3;RI;RII;T;TET
2;V;V1;VBET;VCOM;VFIX;INF00;ALF1;ALF2;BET0;INF01;INF11;INF12;INF13;
INF21;INF22;INF23;IN;V0;DEL0;DEL;BLUP;E;NUP;DL1;DL2;DL3;CDF1;CDF2;P
PDF1;PPDF2;CDF3;PPDF3;PDF1;PDF2;EE;MET0;MEET0;MET1;MEET1;MET2;MEET2
;ETTE1;ETTE2;TE1;T
 COUNT←0
 ML←2
 NT←12
 E←0 5↓RESPK
⍝ ⎕TRAP←11 'E' '→LL1'
 N←¯1 ρE
 NB←1 ρE
 RP←N
 M←NB×N
 FNUM←1
 RESK2
 RA←¯1 ρX1
 RB←¯1 ρZ
 MPH←2 0ρ0
 RPH←2 0ρ0
 TREAT←0 3ρ0
 VTREAT←(0,N+1)ρ0
 MTREAT←0 3ρ0
 MVTREAT←111 0ρ0
 VAC←(0,RA+NT)ρ0
 MLEF←((RA+NT),0)ρ0
 RLEF←((RA+NT),0)ρ0
 MPRD←(NB,0)ρ0
 RPROP←10 0ρ0
 RPRD←(NB,0)ρ0
 MPROP←10 0ρ0
AG:E←0 5↓RESPK
⍝ ⎕TRAP←11 'E' '→LL1'
 N←¯1 ρE
 NB←1 ρE
 RP←N
 M←NB×N
 RA←¯1 ρX1
 RB←¯1 ρZ
```

RESPVTK2 (continued)

```
 MPHI1←1
 MPHI2←0.5
 NO←1 ρZ
 E←(M,1)ρ,E
 RC←RB
 FC←RA
 I←0
 PHI1←MPHI1
 PHI2←MPHI2
 BET0←RBρ0
 ALF1←RAρ0
 T1←0.2
 T2←0.8
 T3←1.5
 T4←2
 T5←2.3
 T6←2.6
 T4←2
 TS←(4ρT1),(4ρT2),4ρT3
 DL1 DL2 DL3 DL4 DL8←E∘=¨0 1 2 3 4
 T←⍉(((NT,NT)ρ1,NTρ0),(NT,RA+RB)ρ0),[1]((M,NT)ρ0),X1,Z
LOOP:L←(Z+.×((RB),1)ρBET0)+X1+.×(RA,1)ρALF1
 →(FNUM≠1)/E1
 PRHAZAD4
 →E4
E1:→(FNUM≠2)/E2
 PRODDS
 →E4
E2:→(FNUM≠3)/E3
 PRHDS
 →E4
E3:PRXHDS
E4:
 DERMVT
 MET2←((M,1)ρ0,(RP-1)ρ1)×MEET0
 MEET2←(RB,1)ρ÷((+/(NB,N)ρ,MEET0)+÷MPHI1),(+/0
1↓(NB,N)ρ,MEET0)+÷MPHI2
 MEET3←+/[2](NB,N,RA)ρ,X1×(,MEET0)∘.×RAρι1
 MEET3←MEET3,[1]+/[2](NB,N,RA)ρ,X1×(,MET2)∘.×RAρι1
 ETTE2←(NB,1)ρ+/(NB,N)ρ(M,1) ETTE1
 ETTE2←ETTE2,(NB,1)ρ+/(NB,N)ρ(M,1) 0 1↓ETTE1
 ETTE2←ETTE2,(NB,1)ρ+/(NB,N)ρ(M,1) 0 2↓ETTE1
 ETTE2←ETTE2,(NB,1)ρ+/(NB,N)ρ(M,1) 0 3↓ETTE1
 ETTE2←ETTE2,(NB,1)ρ+/(NB,N)ρ(M,1) 0 4↓ETTE1
 ETTE2←ETTE2,(NB,1)ρ+/(NB,N)ρ(M,1) 0 5↓ETTE1
 ETTE2←ETTE2,(NB,1)ρ+/(NB,N)ρ(M,1) 0 6↓ETTE1
 ETTE2←ETTE2,(NB,1)ρ+/(NB,N)ρ(M,1) 0 7↓ETTE1
 ETTE2←ETTE2,(NB,1)ρ+/(NB,N)ρ(M,1) 0 8↓ETTE1
 ETTE2←ETTE2,(NB,1)ρ+/(NB,N)ρ(M,1) 0 9↓ETTE1
 ETTE2←ETTE2,(NB,1)ρ+/(NB,N)ρ(M,1) 0 10↓ETTE1
 ETTE2←ETTE2,(NB,1)ρ+/(NB,N)ρ(M,1) 0 11↓ETTE1
```

RESPVTK2 (continued)

```
 ETTE3←(NB,1)ρ+/0 1↓(NB,N)ρ(M,1) ETTE1
 ETTE3←ETTE3,(NB,1)ρ+/0 1↓(NB,N)ρ(M,1) 0 1↓ETTE1
 ETTE3←ETTE3,(NB,1)ρ+/0 1↓(NB,N)ρ(M,1) 0 2↓ETTE1
 ETTE3←ETTE3,(NB,1)ρ+/0 1↓(NB,N)ρ(M,1) 0 3↓ETTE1
 ETTE3←ETTE3,(NB,1)ρ+/0 1↓(NB,N)ρ(M,1) 0 4↓ETTE1
 ETTE3←ETTE3,(NB,1)ρ+/0 1↓(NB,N)ρ(M,1) 0 5↓ETTE1
 ETTE3←ETTE3,(NB,1)ρ+/0 1↓(NB,N)ρ(M,1) 0 6↓ETTE1
 ETTE3←ETTE3,(NB,1)ρ+/0 1↓(NB,N)ρ(M,1) 0 7↓ETTE1
 ETTE3←ETTE3,(NB,1)ρ+/0 1↓(NB,N)ρ(M,1) 0 8↓ETTE1
 ETTE3←ETTE3,(NB,1)ρ+/0 1↓(NB,N)ρ(M,1) 0 9↓ETTE1
 ETTE3←ETTE3,(NB,1)ρ+/0 1↓(NB,N)ρ(M,1) 0 10↓ETTE1
 ETTE3←ETTE3,(NB,1)ρ+/0 1↓(NB,N)ρ(M,1) 0 11↓ETTE1
 MEET3←(ETTE2,[1]ETTE3),MEET3
 DEL←T+.×TE1,[1]MET0

ETTE7←⍉(TET1,(⍉ETTE1)+.×X1),[1]((⍉X1)+.×ETTE1),(⍉X1)+.×((,MEET0)∘.×
RAρι1)×X1
 ETTE3←(((-NB),1) MEET2)×(÷((-NB),1) MEET2)-÷MPHI2
 ETTE2←÷((NB,1) MEET2)×((-NB),1) MEET2
 ETTE2←ETTE2-((÷((-NB),1) MEET2)-÷MPHI2)*2
 ETTE2←(÷((-NB),1) MEET2)÷ETTE2
 MEET1←((,ETTE2)∘.×(RA+NT)ρι1)×(NB,NT+RA) MEET3
 MET3←((,ETTE2×ETTE3)∘.×(RA+NT)ρι1)×(NB,0)↓MEET3
 TE2←((,(((-NB),1) MEET2)×ETTE2÷(NB,1) MEET2)∘.×(RA+NT)ρι1)×((-
NB),RA+NT) MEET3
 TE3←((,ETTE2×ETTE3)∘.×(RA+NT)ρι1)×(NB,RA+NT) MEET3
 ETTE7←⌹ETTE7-((⍉(NB,RA+NT) MEET3)+.×MEET1-MET3)+(⍉((-
NB),RA+NT) MEET3)+.×TE2-TE3
 TE2←⍉(MEET1-MET3),[1]TE2-TE3
 TE3←(RB,1)ρ((÷MPHI1)×NB BET0),(÷MPHI2)×(-NB) BET0
 MEET7←TE2+.×((-RB),1) DEL
 MEET0←TE2+.×TE3
 2 RND,V←(((RA+NT),1)ρTS,ALF1)+ETTE7+.×(((RA+NT),1) DEL)+MEET0-
MEET7
 DEL0←MEET3+.×ETTE7+.×MEET7-(((RA+NT),1) DEL)+MEET0
 DEL0←(((-RB),1) DEL)+DEL0-TE3
 DEL0←((RB,1)ρBET0)+((ETTE2×(NB,1) DEL0)-ETTE2×ETTE3×((-
NB),1) DEL0),[1](-
ETTE2×ETTE3×(NB,1) DEL0)+((ETTE2÷(NB,1) MEET2)×((-NB),1) MEET2)×((-
NB),1) DEL0
 BLUP←V,[1]DEL0
 BLM←((NT+RA+RB),1)ρTS,ALF1,BET0
 I←I+1
 ALF1←RA NT↓,BLUP
 T1←(M,1)ρRP ,BLUP
 T2←(M,1)ρRP RP↓,BLUP
 T3←(M,1)ρRP (2×RP)↓,BLUP
 TS←NT ,BLUP
 BET0←(-RB) ,BLUP
 →(0.01>⌈/,|BLUP-BLM)/L1
 V←0
```

```
 →LOOP
L1:
 B0←(NB,1) ((RA+NT),0)↓BLUP
 B1←(NB,1) ((RA+NT+NB),0)↓BLUP
 →(ML=1)/MAXL1
 RI1←(+/DIAG(NB,NB) (⍉TE2)+.×ETTE7+.×TE2)÷MPHI1
 RI1←RI1+(+/,ETTE2)÷MPHI1
 RI2←(+/DIAG((-NB),(-NB)) (⍉TE2)+.×ETTE7+.×TE2)÷MPHI2
 RI2←RI2+(+/,(ETTE2÷(NB,1) MEET2)×(NB,0)↓MEET2)÷MPHI2
 →RMAXL1
MAXL1:
 RI1←(+/,ETTE2)÷MPHI1
 RI2←(+/,(ETTE2÷(NB,1) MEET2)×(NB,0)↓MEET2)÷MPHI2
RMAXL1:
 MPHI1←,((⍉B0)+.×B0)÷NB-RI1
 MPHI2←,((⍉B1)+.×B1)÷NB-RI2
 →((0.0001≥|MPHI1-PHI1)∧0.0001≥|MPHI2-PHI2)/L2
 PHI1←MPHI1
 PHI2←MPHI2
 →LOOP
L2:
 →(ML=1)/MAXL2
 A1←+/+/ETTE2×ETTE2
 A1←A1+2×+/,ETTE2×(NB,1)ρ,DIAG(NB,NB) (⍉TE2)+.×ETTE7+.×TE2

A1←A1++/DIAG((NB,NB) (⍉TE2)+.×ETTE7+.×TE2)+.×(NB,NB) (⍉TE2)+.×ETTE7
+.×TE2
 A3←(ETTE2÷(NB,1) MEET2)×((-NB),1) MEET2
 A2←(+/,A3×A3)+2×+/,A3×(NB,1)ρDIAG((-NB),(-
NB)) (⍉TE2)+.×ETTE7+.×TE2
 A2←A2++/DIAG(((-NB),(-NB)) (⍉TE2)+.×ETTE7+.×TE2)+.×((-NB),(-
NB)) (⍉TE2)+.×ETTE7+.×TE2
 A3←ETTE2×ETTE3
 A12←(+/,A3×A3)-
2×+/,A3×(NB,1)ρDIAG(NB,NB) (0,NB)↓(⍉TE2)+.×ETTE7+.×TE2

A12←A12++/DIAG((NB,NB) (NB,0)↓(⍉TE2)+.×ETTE7+.×TE2)+.×(NB,NB) (0,NB
)↓(⍉TE2)+.×ETTE7+.×TE2
 →RMAXL2
MAXL2:
 A1←+/+/ETTE2×ETTE2
 A2←(ETTE2÷(NB,1) MEET2)×((-NB),1) MEET2
 A2←(+/,A2×A2)
 A12←ETTE2×ETTE3
 A12←+/,A12×A12
RMAXL2:
 A1←A1÷2×MPHI1*4
 A1←A1+((÷MPHI1*2)×(NB-2×RI1))÷2
 A2←A2÷2×MPHI2*4
 A2←A2+((÷MPHI2*2)×(NB-2×RI2))÷2
 A12←A12÷2×(MPHI1*2)×MPHI2*2
```

```
 A1←(DIAG⌹(2 2ρA1,A12,A12,A2))*0.5
 →(ML≠1)/PREM
 MLEF←MLEF,3 RND(((NT+RA),1)ρTS,ALF1),(((RA+NT),1)ρ(NT+RA) (DIAG
ETTE7)*0.5),((NT+RA),1)ρ(TS,ALF1)÷(NT+RA) (DIAG ETTE7)*0.5
 MPH←MPH,2
3ρMPHI1,(1 ,A1),(MPHI1÷(1 ,A1)),MPHI2,(¯1 A1),MPHI2÷¯1 A1
 ETA←L
 V←(¯4 ¯4 17 17 ETTE7)
 V←(+/DIAG
V)+2×(+/,((ιN)∘.=1+ιN)×V)+(+/,((ιN)∘.=2+ιN)×V)+(+/,((ιN)∘.=3+ιN)×V)
 MTREAT←MTREAT,[1]1
3ρ((+/4 1↓,ALF1)÷4),((V*0.5)÷4),(+/4 1↓,ALF1)÷V*0.5
 Y1←(ETA≤0)
 Y2←((ETA>0)∧ETA≤T1)
 Y3←((ETA>T1)∧ETA≤T2)
 Y4←((ETA>T2)∧ETA≤T3)
 Y5←(ETA>T3)
 E←(NB,RP)ρ(0×Y1)+(1×Y2)+(2×Y3)+(3×Y4)+4×Y5
 DL1 DL2 DL3 DL4 DL8←E∘=¨0 1 2 3 4
 DL5←(,1∘=(NB,1) 0 1↓RESPK)∘.×RPρι1

MPO←((1,RP)ρ+/[1]DL5×DL1),[1]((1,RP)ρ+/[1]DL5×DL2),[1]((1,RP)ρ+/[1]
DL5×DL3),[1]((1,RP)ρ+/[1]DL5×DL4),[1]((1,RP)ρ+/[1]DL5×DL8)
 DL5←(,2∘=(NB,1) 0 1↓RESPK)∘.×RPρι1

MPO←MPO,[1]((1,RP)ρ+/[1]DL5×DL1),[1]((1,RP)ρ+/[1]DL5×DL2),[1]((1,RP
)ρ+/[1]DL5×DL3),[1]((1,RP)ρ+/[1]DL5×DL4),[1]((1,RP)ρ+/[1]DL5×DL8)
 MPROP←MPROP,MPO
 MPRD←MPRD,(0 5↓RESPK)=(NB,RP)ρ(0×Y1)+(1×Y2)+(2×Y3)+(3×Y4)+4×Y5
 →(FNUM=4)/PRE
 FNUM←FNUM+1
 NT←12
 →AG
PRE:ML←2
 FNUM←1
 NT←12
 →AG
PREM:RLEF←RLEF,3
RND(((NT+RA),1)ρTS,ALF1),(((RA+NT),1)ρ(NT+RA) (DIAG
ETTE7)*0.5),((NT+RA),1)ρ(TS,ALF1)÷(NT+RA) (DIAG ETTE7)*0.5
 RPH←RPH,2
3ρMPHI1,(1 ,A1),(MPHI1÷(1 ,A1)),MPHI2,(¯1 A1),MPHI2÷¯1 A1
 ETA←L
⍝MVTREAT←MVTREAT,B0,B1
 V←(¯4 ¯4 17 17 ETTE7)
 V←(+/DIAG
V)+2×(+/,((ιN)∘.=1+ιN)×V)+(+/,((ιN)∘.=2+ιN)×V)+(+/,((ιN)∘.=3+ιN)×V)
TREAT←TREAT,[1]1
3ρ((+/4 1↓,ALF1)÷4),((V*0.5)÷4),(+/4 1↓,ALF1)÷V*0.5
 VTREAT←VTREAT,[1](¯4 ¯4 17 17 ETTE7),4 1ρ4 1↓ALF1
 Y1←(ETA≤0)
```

RESPVTK2 (continued)

```
 Y2←((ETA>0)∧ETA≤T1)
 Y3←((ETA>T1)∧ETA≤T2)
 Y4←((ETA>T2)∧ETA≤T3)
 Y5←(ETA>T3)
 E←(NB,RP)ρ(0×Y1)+(1×Y2)+(2×Y3)+(3×Y4)+4×Y5
 DL1 DL2 DL3 DL4 DL8←E∘=¨0 1 2 3 4
 DL5←(,1∘=(NB,1) 0 1↓RESPK)∘.×RPρι1

RPO←((1,RP)ρ+/[1]DL5×DL1),[1]((1,RP)ρ+/[1]DL5×DL2),[1]((1,RP)ρ+/[1]
DL5×DL3),[1]((1,RP)ρ+/[1]DL5×DL4),[1]((1,RP)ρ+/[1]DL5×DL8)
 DL5←(,2∘=(NB,1) 0 1↓RESPK)∘.×RPρι1

RPO←RPO,[1]((1,RP)ρ+/[1]DL5×DL1),[1]((1,RP)ρ+/[1]DL5×DL2),[1]((1,RP
)ρ+/[1]DL5×DL3),[1]((1,RP)ρ+/[1]DL5×DL4),[1]((1,RP)ρ+/[1]DL5×DL8)
 RPROP←RPROP,RPO
 RPRD←RPRD,(0 5↓RESPK)=(NB,RP)ρ(0×Y1)+(1×Y2)+(2×Y3)+(3×Y4)+4×Y5
 →(FNUM=4)/LL2
 FNUM←FNUM+1
 NT←12
 →AG
 →LL2
LL1:COUNT←1
LL2:MLEF←MPH,[1]MLEF
 RLEF←RPH,[1]RLEF
```

RESPKAR1 fits AR(1) model to respiratory data.

```
RESPKAR1;T1;RP;Y2;Y3;Y4;Y5;Z;TET45;TET5;V11;V2;VAC;VIN;X1;Y1;RPO;SZ
;NB;NT;PHI1;RA;RB;DL5;DL8;E;ETA;FNUM;M;ML;MPO;A;B2;COUNT;DL1;DL2;DL
3;DL4;MPHI1;MPHI2;A12;A2;DL8;FC;I2;I3;I4;NO;PHI2;RI1;RI2;TE7;TS;X2;
X3;X4;X5;GI;A1;B0;B1;B11;B12;B13;C1;C11;C12;D;MPHI;N;NB;PHI;RA0;RA1
;RC;TR;TRJ;VI;VINR;VMPHI;TE21;TE32;TE43;TE54;TE65;A;B;CDF4;CDF5;CDF
6;CDF7;DL4;DL5;DL6;DL7;ETTE31;ETTE4;ETTE41;ETTE5;ETTE51;ETTE6;ETTE6
1;ETTE7;J;MEET4;MEET5;MEET6;MEET7;MET4;MET5;MET6;MET7;PDF4;PDF5;PDF
6;PDF7;PPDF4;PPDF5;PPDF6;PPDF7;T3;T4;T5;T6;TE4;TE5;TE6;TET211;TET23
;TET312;TET32;TET34;TET4;TET423;TET43;RET45;TET534;TET54;TET56;TET6
;TET645;TET65;TET7;G;E1;BLM;DL4;ETTE21;ETTE3;I;L;LSEF;MEET3;MET3;T2
;TE11;TET3;TE12;TE2;TE3;TET1;TET11;TET21;TET12;P0;PDF3;RI;RII;T;TET
2;V;V1;VBET;VCOM;VFIX;INF00;ALF1;ALF2;BET0;INF01;INF11;INF12;INF13;
INF21;INF22;INF23;IN;V0;DEL0;DEL;BLUP;E;NUP;DL1;DL2;DL3;CDF1;CDF2;P
PDF1;PPDF2;CDF3;PPDF3;PDF1;PDF2;EE;MET0;MEET0;MET1;MEET1;MET2;MEET2
;ETTE1;ETTE2;TE1;T
 COUNT←0
 ML←1
 NT←3
 E←0 5↓RESPK
 ⎕TRAP←11 'E' '→LL1'
 N←¯1 ρE
```

RESPKAR1 (continued)

```
 NB←1 ρE
 RP←N
 M←NB×N
 FNUM←1
 STDRESK
 RA←¯1 ρX1
 RB←¯1 ρZ
 MPH←2 0ρ0
 RPH←2 0ρ0
 TREAT←0 3ρ0
 VTREAT←(0,N+1)ρ0
 MTREAT←0 3ρ0
 MVTREAT←(0,N)ρ0
 VAC←(0,RA+1)ρ0
 MLEF←((RA+NT),0)ρ0
 RLEF←((RA+NT),0)ρ0
 MPRD←(NB,0)ρ0
 RPROP←10 0ρ0
 RPRD←(NB,0)ρ0
 MPROP←10 0ρ0
AG:E←0 5↓RESPK
 ⎕TRAP←11 'E' '→LL1'
 N←¯1 ρE
 NB←1 ρE
 RP←N
 M←NB×N
 RA←¯1 ρX1
 RB←¯1 ρZ
 MPHI←1
 RA0←0.9
 NO←1 ρZ
 E←(M,1)ρ,E
 RC←RB
 FC←RA
 I←0
 PHI←MPHI
 BET0←RBρ0
 ALF1←RAρ0
 T1←0.2
 T2←0.4
 T3←1
 T4←1.5
 T5←2
 T6←2.5
 TS←NT (1 ,T1),(1 ,T2),1 ,T3
 DL1 DL2 DL3 DL4 DL8←E∘=¨0 1 2 3 4
 T←⍉(((NT,NT)ρ1,NTρ0),(NT,RA+RB)ρ0),[1]((M,NT)ρ0),X1,Z
LOOP:L←(Z+.×((RB),1)ρBET0)+X1+.×(RA,1)ρALF1
 →(FNUM≠1)/E1
 PRHAZAD4
 →E4
```

RESPKAR1 (continued)

```
E1:→(FNUM≠2)/E2
 PRODDS
 →E4
E2:→(FNUM≠3)/E3
 PRHDS
 →E4
E3:PRXHDS
E4:→(NT≠1)/F1
 DERIV1
 →F3
F1:→(NT≠2)/F2
 DERIV31
 →F3
F2:DERIV43
F3:VINR←-RA0×(⍳RP)∘.=(1+⍳RP)
VINR←VINR+⍉VINR
 VINR←VINR+(RA0*2)×((RP,RP)⍴0)MATDIAG 0,((RP-2)⍴1),0
 VINR←((RP,RP)⍴1,RP⍴0)+VINR
 VINR←(M,RP)⍴,VINR÷1-RA0*2
 MEET2←((,MEET0)∘.×RP⍴⍳1)×(M,RP)⍴,(RP,RP)⍴1,RP⍴0
 MEET2←MEET2+VINR÷MPHI
 V0←⌹(RP,RP) MEET2
 J←RP
LP:V0←V0,[1]⌹(RP,RP) (J,0)↓MEET2
 →((M-RP)=J)/ED
 J←J+RP
 →LP
ED:MEET2←V0
 V0←0
 MEET3←X1×(,MEET0)∘.×RA⍴⍳1
 MEET3←ETTE1,MEET3
 DEL←T+.×TE1,[1]MET0

ETTE7←⍉(TET1,(⍉ETTE1)+.×X1),[1]((⍉X1)+.×ETTE1),(⍉X1)+.×((,MEET0)∘.×
RA⍴⍳1)×X1
 V0←((RP,RP) MEET2)+.×(RP,(RA+NT)) MEET3
 J←RP
LP1:V0←V0,[1]((RP,RP) (J,0)↓MEET2)+.×(RP,(RA+NT)) (J,0)↓MEET3
 →((M-RP)=J)/ED1
 J←J+RP
 →LP1
ED1:
 ETTE7←⌹ETTE7-(⍉MEET3)+.×V0
 V11←((RP,RP) VINR)+.×(RP,1)⍴RP BET0
 J←RP
LP31:V11←V11,[1]((RP,RP) (J,0)↓VINR)+.×((RP,1)⍴RP J↓BET0)
 →((M-RP)=J)/ED31
 J←J+RP
 →LP31
ED31:
 MET3←V11÷MPHI
```

RESPKAR1 (continued)

```
 MEET7←(⍉V0)+.×((-M),1) DEL
 MEET0←(⍉V0)+.×MET3
 2 RND,V←((((RA+NT)),1)ρTS,ALF1)+ETTE7+.×((((RA+NT)),1) DEL)+MEET0-
MEET7
 DEL0←MEET3+.×ETTE7+.×MEET7-((((RA+NT)),1) DEL)+MEET0
 MET0←V0
V0←((RP,RP) MEET2)+.×(RP,1) (((-M),1) DEL)+DEL0-MET3
 J←RP
LP2:V0←V0,[1]((RP,RP) (J,0)↓MEET2)+.×(RP,1) (J,0)↓(((-
M),1) DEL)+DEL0-MET3
 →(J=M-RP)/ED2
 J←J+RP
 →LP2
ED2:
 DEL0←((M,1)ρBET0)+V0
 BLUP←V,[1]DEL0
 BLM←((RB+(RA+NT)),1)ρTS,ALF1,BET0
 I←I+1
 DEL←0
 DEL0←0
 ALF1←RA NT↓,BLUP
 T1←1 ,BLUP
 T2←1 1↓,BLUP
 T3←1 2↓,BLUP
 T4←1 3↓,BLUP
 TS←NT ,BLUP
 BET0←(-RB) ,BLUP
 B0←((-RB),1) BLUP
 →(0.01>⌈/,|BLUP-BLM)/L1
 V←0
 →LOOP
L1:
 →(ML=1)/MAXL
 MEET7←((RP,(RA+NT)) MET0)+.×ETTE7+.×⍉(RP,(RA+NT)) MET0
 J←RP
FD:MEET7←MEET7,[1]((RP,(RA+NT)) (J,0)↓MET0)+.×ETTE7+.×⍉(RP,(RA+NT))
 (J,0)↓MET0
 →(J=M-RP)/EFD
 J←J+RP
 →FD
EFD:MEET2←MEET2+MEET7
MAXL:V1←((RP,RP) VINR)+.×(RP,RP) MEET2
 J←RP
LP4:V1←V1,[1]((RP,RP) (J,0)↓VINR)+.×(RP,RP) (J,0)↓MEET2
 →((M-RP)=J)/ED4
 J←J+RP
 →LP4
ED4:
 RI←(+/+/V1×(M,RP)ρ,(RP,RP)ρ1,RPρ0)
V11←((RP,RP) V1)+.×(RP,RP) MEET2
 J←RP
```

RESPKAR1 (continued)

```
LP44:V11←V11,[1]((RP,RP) (J,0)↓V1)+.×(RP,RP) (J,0)↓MEET2
 →((M-RP)=J)/ED44
 J←J+RP
 →LP44
ED44:
 V0←((RP,RP) VINR)+.×(RP,1) B0
 J←RP
LP5:V0←V0,[1]((RP,RP) (J,0)↓VINR)+.×(RP,1) (J,0)↓B0
 →((M-RP)=J)/ED5
 J←J+RP
 →LP5
ED5:
 MPHI←,(((⍉B0)+.×V0)+RI)÷RB
 →(0.001≥|MPHI-PHI)/L2
 PHI←MPHI
 →LOOP
L2:
 RC←RB
 FC←RA
 B11←((N,N)⍴0)MATDIAG 1,((RP-2)⍴2),1
 B12←-(⍳RP)∘.=(1+⍳RP)
 B12←B12+⍉B12
 V0←B11+.×(RP,RP) MEET2
 J←RP
LP71:V0←V0,[1]B11+.×(RP,RP) (J,0)↓MEET2
 →((M-RP)=J)/ED71
 J←J+RP
 →LP71
ED71:
 V←B12+.×(RP,RP) MEET2
 J←RP
LP7:V←V,[1]B12+.×(RP,RP) (J,0)↓MEET2
 →((M-RP)=J)/ED7
 J←J+RP
 →LP7
ED7:
 B11←B11∘.×(⍳NB)∘.=⍳NB
 B11←(M,M)⍴4 2 3 1⍉B11
 B12←B12∘.×(⍳NB)∘.=⍳NB
 B12←(M,M)⍴4 2 3 1⍉B12
 C11←((⍉B0)+.×B11+.×B0)++/+/V0×(M,RP)⍴,(RP,RP)⍴1,RP⍴0
 A1←2×(RP-1)×NB
B13←((⍉B0)+.×B12+.×B0)++/+/V×(M,RP)⍴,(RP,RP)⍴1,RP⍴0
 C1←C11÷MPHI
 B1←B13÷MPHI
 C1←2×C1-NB×RP-1
 D←B1
 RA1←RA0-
,((A1×RA0*3)+(B1×RA0*2)+(C1×RA0)+D)÷(3×A1×RA0*2)+(2×B1×RA0)+C1
 →(1≤|RA1)/LL1
 →(0.001>|RA1-RA0)/LL
```

RESPKAR1 (continued)

```
 PHI←MPHI
 RA0←RA1
 →LOOP
LL:
 B12←((N,N)ρ0)MATDIAG 1,((RP-2)ρ2),1
 B12←2×RA1×B12÷(1-RA1*2)*2
 B11←(1+RA1*2)×-(ιRP)∘.=(1+ιRP)
 B11←B11+⍉B11
 B11←B11÷(1-RA1*2)*2
 VIN←⌹(RP,RP) VINR
 J←RP
LP91:VIN←VIN,[1]⌹(RP,RP) (J,0)↓VINR
 →(J=M-RP)/ED91
 J←J+RP
 →LP91
ED91:
 V2←((RP,RP) V1)+.×(RP,RP) V1
 J←RP
LP9:V2←V2,[1]((RP,RP) (J,0)↓V1)+.×(RP,RP) (J,0)↓V1
 →(J=M-RP)/ED9
 J←J+RP
 →LP9
ED9:
 A1←((+/+/V2×(M,RP)ρ,(RP,RP)ρ1,RPρ0)÷2×MPHI*4)
 A1←A1+((÷MPHI*2)×(M-2×RI÷MPHI))÷2
 V←(B11+B12)+.×((RP,RP) VIN)+.×B11+B12
 J←RP
LP10:V←V,[1](B11+B12)+.×((RP,RP) (J,0)↓VIN)+.×B11+B12
 →(J=M-RP)/ED10
 J←J+RP
 →LP10
ED10:
 B2←(B11+B12)+.×((RP,RP) MEET2)+.×(B11+B12)+.×(RP,RP) MEET2
 J←RP
LP21:B2←B2,[1](B11+B12)+.×((RP,RP) (J,0)↓MEET2)+.×(B11+B12)+.×(RP,R
P) (J,0)↓MEET2
 →(J=M-RP)/ED21
 J←J+RP
 →LP21
ED21:B2←(+/+/B2×(M,RP)ρ,(RP,RP)ρ1,RPρ0)÷MPHI*2
 V0←((RP,RP) V)+.×((RP,RP) VIN)
 J←RP
LP22:V0←V0,[1]((RP,RP) (J,0)↓V)+.×((RP,RP) (J,0)↓VIN)
 →(J=M-RP)/ED22
 J←J+RP
 →LP22
ED22:V0←+/+/V0×(M,RP)ρ,(RP,RP)ρ1,RPρ0
 B1←((RP,RP) V)+.×((RP,RP) MEET2)
 J←RP
LP13:B1←B1,[1]((RP,RP) (J,0)↓V)+.×((RP,RP) (J,0)↓MEET2)
 →(J=M-RP)/ED13
```

```
 J←J+RP
 →LP13
ED13:B1←(+/+/B1×(M,RP)ρ,(RP,RP)ρ1,RPρ0)×2÷MPHI
 B1←(V0+B2-B1)÷2
 V←(B11+B12)+.×((RP,RP) VIN)
 J←RP
LP14:V←V,[1](B11+B12)+.×((RP,RP) (J,0)↓VIN)
 →(J=M-RP)/ED14
 J←J+RP
 →LP14
ED14:B2←(+/+/V×(M,RP)ρ,(RP,RP)ρ1,RPρ0)÷MPHI
 V←(B11+B12)+.×((RP,RP) MEET2)+.×((RP,RP) VINR)+.×(RP,RP) MEET2
 J←RP
LP15:V←V,[1](B11+B12)+.×((RP,RP) (J,0)↓MEET2)+.×((RP,RP) (J,0)↓VINR
)+.×(RP,RP) (J,0)↓MEET2
 →(J=M-RP)/ED15
 J←J+RP
 →LP15
ED15:B2←B2+(+/+/V×(M,RP)ρ,(RP,RP)ρ1,RPρ0)÷MPHI*3
 V←(B11+B12)+.×((RP,RP) MEET2)
 J←RP
LP16:V←V,[1](B11+B12)+.×((RP,RP) (J,0)↓MEET2)
 →(J=M-RP)/ED16
 J←J+RP
 →LP16
ED16:B2←(((2×+/+/V×(M,RP)ρ,(RP,RP)ρ1,RPρ0)÷MPHI*2)-B2)÷2
 A1←(DIAG⌹2 2ρA1,B2,B2,B1)*0.5
→(ML≠1)/PREM
 MLEF←MLEF,3 RND(((NT+RA),1)ρTS,ALF1),(((RA+NT),1)ρ(NT+RA) (DIAG
ETTE7)*0.5),((NT+RA),1)ρ(TS,ALF1)÷(NT+RA) (DIAG ETTE7)*0.5
 MPH←MPH,2 3ρMPHI,(1 ,A1),(MPHI÷(1 ,A1)),RA1,(¯1 A1),RA1÷¯1 A1
 ETA←L
 V←(¯4 ¯4 8 8 ETTE7)
 V←(+/DIAG
V)+2×(+/,((⍳N)∘.=1+⍳N)×V)+(+/,((⍳N)∘.=2+⍳N)×V)+(+/,((⍳N)∘.=3+⍳N)×V)
 MTREAT←MTREAT,[1]1
3ρ((+/4 1↓,ALF1)÷4),((V*0.5)÷4),(+/4 1↓,ALF1)÷V*0.5
 Y1←(ETA≤0)
 Y2←((ETA>0)∧ETA≤T1)
 Y3←((ETA>T1)∧ETA≤T2)
 Y4←((ETA>T2)∧ETA≤T3)
 Y5←(ETA>T3)
 E←(NB,RP)ρ(0×Y1)+(1×Y2)+(2×Y3)+(3×Y4)+4×Y5
 DL1 DL2 DL3 DL4 DL8←E∘=¨0 1 2 3 4
 DL5←(,1∘=(NB,1) 0 1↓RESPK)∘.×RPρ⍳1

MPO←((1,RP)ρ+/[1]DL5×DL1),[1]((1,RP)ρ+/[1]DL5×DL2),[1]((1,RP)ρ+/[1]
DL5×DL3),[1]((1,RP)ρ+/[1]DL5×DL4),[1]((1,RP)ρ+/[1]DL5×DL8)
 DL5←(,2∘=(NB,1) 0 1↓RESPK)∘.×RPρ⍳1
MPO←MPO,[1]((1,RP)ρ+/[1]DL5×DL1),[1]((1,RP)ρ+/[1]DL5×DL2),[1]((1,RP
)ρ+/[1]DL5×DL3),[1]((1,RP)ρ+/[1]DL5×DL4),[1]((1,RP)ρ+/[1]DL5×DL8)
```

RESPKAR1 (continued)

```
 MPROP←MPROP,MPO
 MPRD←MPRD,(0 5↓RESPK)=(NB,RP)ρ(0×Y1)+(1×Y2)+(2×Y3)+(3×Y4)+4×Y5
 →(FNUM=4)/PRE
 FNUM←FNUM+1
 NT←3
 →AG
PRE:ML←2
 FNUM←1
 NT←3
 →AG
PREM:RLEF←RLEF,3
RND(((NT+RA),1)ρTS,ALF1),(((RA+NT),1)ρ(NT+RA) (DIAG
ETTE7)*0.5),((NT+RA),1)ρ(TS,ALF1)÷(NT+RA) (DIAG ETTE7)*0.5
RPH←RPH,2 3ρMPHI,(1 ,A1),(MPHI÷(1 ,A1)),RA1,(¯1 A1),RA1÷¯1 A1
 ETA←L
 V←(¯4 ¯4 8 8 ETTE7)
 V←(+/DIAG
V)+2×(+/,((ιN)∘.=1+ιN)×V)+(+/,((ιN)∘.=2+ιN)×V)+(+/,((ιN)∘.=3+ιN)×V)
 TREAT←TREAT,[1]1
3ρ((+/4 1↓,ALF1)÷4),((V*0.5)÷4),(+/4 1↓,ALF1)÷V*0.5
 VTREAT←VTREAT,[1](¯4 ¯4 8 8 ETTE7),4 1ρ4 1↓,ALF1
 Y1←(ETA≤0)
 Y2←((ETA>0)∧ETA≤T1)
 Y3←((ETA>T1)∧ETA≤T2)
 Y4←((ETA>T2)∧ETA≤T3)
 Y5←(ETA>T3)
 E←(NB,RP)ρ(0×Y1)+(1×Y2)+(2×Y3)+(3×Y4)+4×Y5
 DL1 DL2 DL3 DL4 DL8←E∘=¨0 1 2 3 4
 DL5←(,1∘=(NB,1) 0 1↓RESPK)∘.×RPρι1

RPO←((1,RP)ρ+/[1]DL5×DL1),[1]((1,RP)ρ+/[1]DL5×DL2),[1]((1,RP)ρ+/[1]
DL5×DL3),[1]((1,RP)ρ+/[1]DL5×DL4),[1]((1,RP)ρ+/[1]DL5×DL8)
 DL5←(,2∘=(NB,1) 0 1↓RESPK)∘.×RPρι1

RPO←RPO,[1]((1,RP)ρ+/[1]DL5×DL1),[1]((1,RP)ρ+/[1]DL5×DL2),[1]((1,RP
)ρ+/[1]DL5×DL3),[1]((1,RP)ρ+/[1]DL5×DL4),[1]((1,RP)ρ+/[1]DL5×DL8)
 RPROP←RPROP,RPO
 RPRD←RPRD,(0 5↓RESPK)=(NB,RP)ρ(0×Y1)+(1×Y2)+(2×Y3)+(3×Y4)+4×Y5
 →(FNUM=4)/LL2
 FNUM←FNUM+1
 NT←3
 →AG
 →LL2
LL1:COUNT←1
LL2:MLEF←MPH,[1]MLEF
 RLEF←RPH,[1]RLEF
```

DERMVT

```
MET0←DL1×-PDF1÷CDF1
MEET0←DL1×(-(PDF1÷CDF1)*2)+PPDF1÷CDF1

MET1←DL2×(PDF1-PDF2)÷CDF2-CDF1
MEET1←DL2×(-((PDF1-PDF2)÷(CDF2-CDF1))*2)+(PPDF2-PPDF1)÷CDF2-CDF1
ETTE1←DL2×-((PDF2÷CDF2-CDF1)×((PDF1-PDF2)÷(CDF2-
CDF1)))+PPDF2÷CDF2-CDF1
TE1←DL2×PDF2÷CDF2-CDF1
TET1←DL2×(-(PDF2÷CDF2-CDF1)*2)+PPDF2÷CDF2-CDF1
MET2←DL3×(PDF2-PDF3)÷CDF3-CDF2
MEET2←DL3×(-((PDF2-PDF3)÷(CDF3-CDF2))*2)+(PPDF3-PPDF2)÷CDF3-CDF2
ETTE21←DL3×((PDF2÷CDF3-CDF2)×((PDF2-PDF3)÷(CDF3-
CDF2)))+PPDF2÷CDF3-CDF2
ETTE2←DL3×-((PDF3÷CDF3-CDF2)×((PDF2-PDF3)÷(CDF3-
CDF2)))+PPDF3÷CDF3-CDF2
TE2←DL3×PDF3÷CDF3-CDF2
TE21←DL3×PDF2÷CDF3-CDF2
TET12←DL3×(PDF3×PDF2)÷(CDF3-CDF2)*2
TET2←DL3×(-(PDF3÷CDF3-CDF2)*2)+PPDF3÷CDF3-CDF2
TET211←DL3×-((PDF2÷CDF3-CDF2)*2)+PPDF2÷CDF3-CDF2
TET21←DL3×(PDF3×PDF2)÷(CDF3-CDF2)*2
MET3←DL4×(PDF3-PDF4)÷CDF4-CDF3
MEET3←DL4×(-((PDF3-PDF4)÷(CDF4-CDF3))*2)+(PPDF4-PPDF3)÷CDF4-CDF3
ETTE31←DL4×((PDF3÷CDF4-CDF3)×((PDF3-PDF4)÷(CDF4-
CDF3)))+PPDF3÷CDF4-CDF3
ETTE3←DL4×-((PDF4÷CDF4-CDF3)×((PDF3-PDF4)÷(CDF4-
CDF3)))+PPDF4÷CDF4-CDF3
TE3←DL4×PDF4÷CDF4-CDF3
TE32←DL4×PDF3÷CDF4-CDF3
TET23←DL4×(PDF3×PDF4)÷(CDF4-CDF3)*2
TET3←DL4×(-(PDF4÷CDF4-CDF3)*2)+PPDF4÷CDF4-CDF3
TET312←DL4×-((PDF3÷CDF4-CDF3)*2)+PPDF3÷CDF4-CDF3
TET32←DL4×(PDF4×PDF3)÷(CDF4-CDF3)*2
⍝ MET4←DL5×(PDF4-PDF5)÷CDF5-CDF4
⍝ MEET4←DL5×(-((PDF4-PDF5)÷(CDF5-CDF4))*2)+(PPDF5-PPDF4)÷CDF5-CDF4
⍝ ETTE41←DL5×((PDF4÷CDF5-CDF4)×((PDF4-PDF5)÷(CDF5-
CDF4)))+PPDF4÷CDF5-CDF4
⍝ ETTE4←DL5×-((PDF5÷CDF5-CDF4)×((PDF4-PDF5)÷(CDF5-
CDF4)))+PPDF5÷CDF5-CDF4
⍝ TE4←DL5×PDF5÷CDF5-CDF4
⍝ TE43←DL5×PDF4÷CDF5-CDF4
⍝ TET34←DL5×(PDF4×PDF5)÷(CDF5-CDF4)*2
⍝ TET4←DL5×(-(PDF5÷CDF5-CDF4)*2)+PPDF5÷CDF5-CDF4
⍝ TET423←DL5×-((PDF4÷CDF5-CDF4)*2)+PPDF4÷CDF5-CDF4
⍝ TET43←DL5×(PDF5×PDF4)÷(CDF5-CDF4)*2
MET7←DL8×PDF4÷1-CDF4
MEET7←DL8×-((PDF4÷1-CDF4)*2)+PPDF4÷1-CDF4
ETTE7←DL8×((PDF4÷1-CDF4)*2)+PPDF4÷1-CDF4
TET7←DL8×-((PDF4÷1-CDF4)*2)+PPDF4÷1-CDF4
TE7←DL8×PDF4÷1-CDF4
TE6←(RP,RP)⍴0
ETTE1←-(ETTE1+ETTE21),(ETTE2+ETTE31),ETTE3+ETTE7
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 J←0
 ETTE2←TE6 MATDIAG RP J↓,(M,1) ETTE1
 J←RP
E1:ETTE2←ETTE2,[1]TE6 MATDIAG RP J↓,(M,1) ETTE1
 →(J=M-RP)/EE1
 J←J+RP
 →E1
EE1:J←0
 ETTE3←TE6 MATDIAG RP J↓,(M,1) 0 1↓ETTE1
 J←RP
E2:ETTE3←ETTE3,[1]TE6 MATDIAG RP J↓,(M,1) 0 1↓ETTE1
 →(J=M-RP)/EE2
 J←J+RP
 →E2
EE2:J←0
 TE4←TE6 MATDIAG RP J↓,0 2↓ETTE1
 J←RP
E3:TE4←TE4,[1]TE6 MATDIAG RP J↓,0 2↓ETTE1
 →(J=M-RP)/EE3
 J←J+RP
 →E3
EE3:ETTE1←ETTE2,ETTE3,TE4
 J←0
 TE1←(RP,1)ρ(+/[1](NB,RP)ρTE1)-+/[1](NB,RP)ρTE21
 TE2←(RP,1)ρ(+/[1](NB,RP)ρTE2)-+/[1](NB,RP)ρTE32
 TE3←(RP,1)ρ(+/[1](NB,RP)ρTE3)-+/[1](NB,RP)ρTE7
 MET0←MET0+MET1+MET2+MET3+MET7
 MEET0←-MEET0+MEET1+MEET2+MEET3+MEET7
 TET1←-(TE6 MATDIAG+/[1](NB,RP)ρTET1+TET211),(TE6
MATDIAG+/[1](NB,RP)ρTET12),TE6
 TET2←-(TE6 MATDIAG+/[1](NB,RP)ρTET21),(TE6
MATDIAG+/[1](NB,RP)ρTET2+TET312),TE6 MATDIAG+/[1](NB,RP)ρTET23
 TET3←-TE6,(TE6 MATDIAG+/[1](NB,RP)ρTET32),TE6
MATDIAG+/[1](NB,RP)ρTET3+TET7
 TET1←TET1,[1]TET2,[1]TET3
 TE1←TE1,[1]TE2,[1]TE3
```