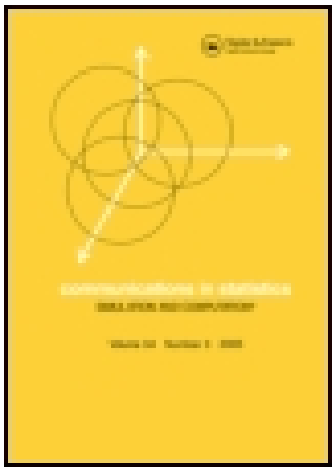

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Comparison of Methods for Analyzing Binary Repeated Measures Data: A Simulation Based Study

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(Comparison of Methods for Binary Repeated Measures)

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Abstract

In this study, some methods suggested for binary repeated measures, namely, Weighted Least Squares (WLS) , Generalized Estimating Equations (GEE) and Generalized Linear Mixed Models (GLMM) are compared with respect to power, type 1 error and properties of estimates. The results indicate that with adequate sample size, no missing data, the only covariate being time effect and a relatively limited number of time points, the WLS method performs well. The GEE approach performs well only for large sample sizes. The GLMM method is satisfactory with respect to type I error, but its estimates have poorer properties than the other methods.

Keywords: Binary Repeated Measures (BRM), Weighted Least Squares (WLS), Generalized Estimating Equation (GEE), Generalized Linear Mixed Models (GLMMs), Simulation Study, SAS

1. Introduction

Simply, Repeated Measures (RM**)** means, making multiple or repeated measurements on each experimental unit, elapsed over a given time period or under different experimental conditions (Diggle, Heagerty, Liang and Zeger, 2001). Methods for normally distributed RM are well developed. In practice, however binary RM (BRM) occurs commonly in biology, medicine, health sciences, psychology, and sociology and in many other practical fields. Though the development of methods for analyzing binary and categorical RMD has approached a new level recently, lack of understandability of these methods and the unavailability of easy to use reliable software has discouraged the use of various methods for scientists in these practical fields (Masaoud and Stryn, 2010 ; Szmaragd, Clark, Steele, 2013). Thus there arises the necessity of identifying adequate and equitable methodology and software for analyzing BRM. Estimation in correlated data models generally takes one of two forms, namely, subject-specific (random effect) approach and marginal (population averaged) approach. The random effects model is based on the usual normal errors mixed effects model where the parameter estimates are conditional on the subject or cluster. In the population averaged model the estimates are averaged over the clusters. Both the subject-specific and the population averaged models, can be fitted to data having subject-specific and cluster level covariates. The choice of which model to use should depend on what type of inferences the fitted model is intended to provide. The cluster-specific model is useful when the objective is to provide inferences for covariates that change within cluster, whereas the population-averaged methods are useful for making inferences about covariates that remain constant within a cluster (Hosmer, Lemeshow, Sturdivant, 2013 ; Diggle et al, 2001)

The literature consists of one extensive simulation study to assess statistical methods for binary repeated measures data (Masaoud and Stryn, 2010). In their study Masaoud and Stryn (2010) examine the performance of several marginal and random effects procedures. However, they examine and compare only the bias and efficiency of the estimates related to the various methods. Their simulation studies are small and balanced and within software R. The novelty of our study lies in the fact that in this paper the type I error of the tests, the power of the tests and numerous properties of the parameter estimates such as bias, efficiency, consistency and sufficiency together with results on convergence and speed of the methods are studied for small to large data sets. Correlated binary data are simulated according to Sebastian, Dominik and Friedrich (2011).

Nelder and Wedderburn (1972) proposed extensions of Generalized Linear Models to handle non-normal repeated measures data. This study is mainly focused on such distinctive methods, namely, Marginal or population averaged models and Random-effects or subject-specific models.

The main aim of this research is to find suitable analyzing methods for BRM. As this is an initial study it is carried out under the most basic conditions such as a small number of repeated measures, no missing data and only period as covariate. This paper will debate about some popular existing methods of analyzing BRM and induce changes in some of the existing propositions. In this paper the objectives are met by comparing and contrasting three methods of analyzing BRM, namely; the Weighted Least Squares (WLS) approach, the Generalizing Estimating Equations (GEE) approach and the Generalized Linear Mixed Models (GLMMs) approach using simulation studies within the statistical package SAS to identify the strengths and

weaknesses of each method. SAS was selected among other competing packages as it incorporates all three of the methods to be examined, it has easy to use procedures in modules, SAS/Base and SAS/Stat within which simulation programs can be developed and extensions and advances to the current research can easily be incorporated within SAS. In most of these competing packages the WLS, GEE and GLMM methods are incorporated similarly with little variation between the packages (Masaoud and Stryn, 2010). Thus, the results obtained here should be package independent. The methods are compared within SAS with respect to type 1 error and power, properties of estimates, ease of interpretation and speed of convergence of models. After the simulation study a real life data set available on the web has been analyzed by the methods mentioned above to illustrate these methods.

Weighted Least Squares (WLS) method was the first general method, which belonged to the marginal models family, for analyzing binary repeated measures data (Koch, Landis, Freeman and Lehnen ,1977). In SAS software PROC CATMOD procedure facilitates the WLS method. The WLS algorithms are available in other statistical software packages too (e.g. S-Plus/R and Stata) as well as in special-purpose, multi-level software (e.g., MLwiN and HLM). (Masaoud and Stryn, 2010)

Generalized Estimating Equation (GEE) method (Liang and Zeger, 1986) is one of the revolutionary population-averaged models for analyzing repeated binary responses. PROC GENMOD procedure in SAS accommodates the GEE method. The GEE procedure is available in most other statistical packages such as (e.g. S-Plus/R and Stata), with only slight differences in their implementation. (Masaoud and Stryn, 2010)

In Generalized Linear Mixed Models (GLMMs), random-effects models are used (Fitzmaurice and Molenberghs, 2008). In this model the intercept is allowed to vary across the individuals thus the model is often called random-intercept model. GLIMMIX procedure in SAS facilitates GLMMs method. For the data settings used here maximum likelihood method by numerical integration (quadrature) is known to be suitable and is available in many software packages such as Proc Glimmix in SAS and xtlogit and gllamm commands in Stata. (Hosmer, Lemeshow and Sturdivant, 2013)

Section 1 of the paper gives an introduction to the study, section 2 describes the design of the simulation study, Section 3 discusses the methodology involved in the study, section 4 gives the simulation results, section 5 applies the methods to a real life example and section 6 consists of a general discussion.

2. Simulation Study Design

2.1 Description

The main aspiration of this study is to compare three available analyzing methods for BRM. To accomplish this objective, a simulation study was conducted using SAS. In the simulation study, data were simulated under both null and alternative hypotheses in a way that responses are correlated (an extension of Sebastian, Dominik, Friedrich, 2011 method). This extension of Sebastian et al.'s algorithm is explained as follows.

Consider our case of simulating 3 correlated binary variables, each taking the values 0 or 1. Let these 3 variables be denoted by Y_1, X_1 and X_2 respectively. Let the distribution of variable Y_1 be

given by $P_{Y1} = Pr(Y_1=0)$. Then the expectation and variance of Y_1 is given by $E(Y_1) = P_{Y1}$ and $Var(Y_1) = P_{Y1}(1- P_{Y1})$ respectively. Similarly the distributions, expectation and variance of X_1 and X_2 can be defined.

Consider the binary variable X_1 which is correlated to Y_1. Then the joint distribution of Y_1 and X_1 is denoted by $P_{Y1X1} = Pr(Y_1=0, X_1=0)$. This can be fully determined by the marginal and conditional distributions P_{Y1} and $P(X_1=0| Y_1=0)=P_{X1|Y1}$ using the theorem of conditional probabilities given by $P_{X1|Y1} = \frac{P_{Y1X1}}{P_{Y1}}$. The rest of the probabilities can be derived using Bayes theorem. This method can be generalized to determine the trivariate distribution of $P_{Y1X1X2.}$

Sebastian et al. (2011) show that the correlation between the two binary variables Y_1 and X_1 is given by $r_{Y1X1} = \frac{P_{Y1X1} - P_{Y1}P_{X1}}{\sqrt{P_{Y1}(1-P_{Y1})P_{X1}(1-P_{x1})}}$

2.2 Simulation under the null hypothesis

The null hypothesis corresponds to no period effect. This implies that $P_{Y1} = P_{X1} = P_{X2}$. This condition of the null hypothesis can only be satisfied by $P_{Y1} = 0.5$.

The steps are given as follows.

1. Take $P_{Y1} = 0.5$.

2. To incorporate high positive correlation between the values of the 1st and 2nd periods , that is between Y_1 and X_1 the conditional probability is selected as $P_{X1| Y1} = 0.7$. From the theorem of conditional probabilities P_{Y1X1} can be found to be 0.35. By defining the entire range of

conditional probabilities (as shown in the SAS programs) and by using Bayes theorem it can be shown that P_{X1}=0.5. From the formula for correlation r_{Y1X1} can be derived as 0.4.

3. To incorporate high correlation between Y_1 , X_1 and X_2, the conditional probability $P_{X2|\,Y1X1}$ was taken to be 0.7. From the theorem of conditional probabilities P_{Y1X1X2} can be found to be 0.245. From Bayes theorem it can be shown that P_{X2}=0.5 and from the formula for correlation it can be shown that r_{Y1X2} =0.22 and r_{X1X2} =0.34.

2.2 Simulation under the alternative hypothesis

The alternative hypothesis corresponds to the presence of a period effect. This implies that not all of $P_{Y1,}$ $P_{X1,}$ P_{X2} are equal.

The steps are given as follows.

1. Take P_{Y1} = 0.25. This value should be different to 0.5.

2. To incorporate high positive correlation between the values of the 1st and 2nd periods , that is between Y_1 and X_1 the conditional probability is selected as $P_{X1|\,Y1}$ = 0.7. From the theorem of conditional probabilities P_{Y1X1} can be found to be 0.175. Then from Bayes theorem it can be shown that P_{X1}=0.4. From the formula for correlation r_{Y1X1} can be derived as 0.35.

3. To incorporate high correlation between Y_1 , X_1 and X_2, the conditional probability $P_{X2|\,Y1X1}$ was taken to be 0.7. From the theorem of conditional probabilities P_{Y1X1X2} can be found to be 0.1225. By defining the entire range of conditional probabilities (as shown in the SAS programs)

and by using Bayes theorem it can be shown that P_{X2}=0.445. The formula for correlation can be used to show that r_{Y1X2} =0.19 and r_{X1X2} =0.33.

2.3 Simulation in SAS

Data were simulated under five different sample sizes, namely 20, 50, 100, 250 and 500. For each case data were simulated 1000 times. In SAS, PROC CATMOD facilitates the WLS approach, PROC GENMOD facilitates the GEE method and both of these procedures are available in SAS version 9.0 or later. PROC GLIMMIX facilitates GLMMs method and this procedure is only available in the versions of SAS 9.2 or later.

From the results obtained, averaged estimated probabilities of being in each period, the proportion of rejections of H_0 when H_0 is true (type 1 error) and when H_1 is true (power), number of non-convergent results and average variance of the period estimates were obtained. The change in percentage of estimated variance over true variance was calculated from the output. The significance level used in the study is 5%=0.05. The three methods were compared with respect to the above mentioned results.

3. Methodology

3.1 Methods of Analysis considered

Davis (2002) gives a good account of all three methods considered and also gives some historical remarks.

3.1.1. Weighted Least Squares (WLS) Method

The WLS method was the first approach developed to analyze categorical repeated measures. This approach was initially established by Grizzle et al. (1969) and further developed by Koch et al. (1977) and Stanish and Koch (1984). The WLS method does not make any assumptions regarding the time structure of the repeated measurements and can therefore be considered as nonparametric because it is only based on the multinomial sampling model for count data. WLS method allows to fit logistic regression models to repeated binary data under some restrictions. They are ; study should be balanced with no presence of missing data and all covariates must be categorical. Asymptotically WLS method is equivalent to the maximum likelihood estimation procedure. Because the RMD corresponds to correlated data this data cannot be analyzed using usual methods for logistic regression. Therefore weighted least squares is used. This allows the observations to be correlated. In the WLS approach the data is structured in a two way contingency table where the rows correspond to the sub-populations formed by the cross-classification of the factors and the columns represent the response variable. Agresti (1990) provides a detailed explanation of the application of the WLS approach to categorical RMD.

Johnston and Stokes (1996) discusses advances in categorical data analysis in SAS. They explain that in PROC CATMOD for repeated measures, noniterative generalized least squares is applied to response functions that are of interest using an observed covariance matrix as the weights. It presumes adequate sample sizes for assuming that the response functions have an approximate multivariate normal distribution which lets hypothesis tests concerning linear combinations of response functions be carried out.

Carter et al. (2009) have developed the theory behind the weighted least squares estimation for the case of one covariate and two correlated binary responses measured at two time points. We extend this development to our case of no covariates and three correlated binary responses measured at three time points. The next paragraphs under section 3.1.1. explains this extension briefly.

Our scenario can be exemplified by a 2x2x2 contingency table in which the three dimensions are the paired binomial responses. The multinomial probability vector associated with this contingency table is given by

$$\pi = \left[\pi_{000,} \pi_{001,} \pi_{010,} \pi_{011,} \pi_{100,} \pi_{101,} \pi_{110,} \pi_{111} \right]$$

Let the variance covariance matrix of π be denoted by V(π). Let the frequency distribution and cell probabilities for three paired binomial responses measured at 3 time points be denoted by n_{ijk} and π_{ijk} respectively, where i, j and k are the values of the three binary responses at time points 1,2 and 3 respectively. Note that I, j, k = {0,1}. Since the interest of the study is in the 7 marginal outcome probabilities, the response functions of interest are

$$f(\pi) = [f_1, f_2, f_3, f_4, f_5, f_6, f_7]' = [\log(\frac{\pi_{000}}{\pi_{111}}), \log\left(\frac{\pi_{001}}{\pi_{111}}\right), \log(\frac{\pi_{010}}{\pi_{111}},) \ldots\ldots\ldots\ldots, \log(\frac{\pi_{110}}{\pi_{111}})]'$$

The estimated cell probabilities are given by $P_{ijk} = \widehat{\pi_{ijk}} = \frac{n_{ijk}}{n_{\ldots}}$. This yields the estimated probabilities $P' = [\frac{n_{000}}{n_{\ldots}}, \frac{n_{001}}{n_{\ldots}}, \ldots\ldots\ldots \frac{n_{111}}{n_{\ldots}}]$. An estimated variance covariance matrix of f(P) can be obtained by the delta method as S=H*V(P)*H' where V(P) is the sample estimate of V(π)

and H is given by $H=\frac{\partial f}{\partial \pi} \mid \pi = P$. Then the model will be of the form $f(\pi)=X\beta$ where β corresponds to the unknown parameters and X is the design matrix. The WLS estimates of β are then given by $\hat{\beta} = (X'S^{-1}X)^{-1}X'S^{-1}f(P)$ and the estimated variance covariance matrix is $Cov(\hat{\beta}) = (X'S^{-1}X)^{-1}$.

The test used to identify the study size and power in Proc Catmod is the Wald chi-square test given in the Analysis of Variance table for the weighted least squares analysis.

3.1.2 Generalized Estimating Equations (GEE) Method

GEE approach is based on quasi- likelihood estimation and widely used in marginal models (Liang and Zeger, 1986). The GEE method does not require full specification of the multivariate distribution of the repeated responses, and requires only specification of the first two moments of the outcome vectors. Thus the GEE method is semi-parametric as the estimating equations are derived, without the joint distribution of a subjects' observations. Instead, only the likelihood of marginal distributions and a working correlation matrix of the repeated measurements on each subject is specified. The correlation structure is treated as a nuisance. Correlated data can be modeled with the same link function and same linear predictor set up (systematic component) as the independence case. The variance functions of the random component are described by the same functions as in the independence case, however the covariance structure of the correlated responses should also be modeled (Liang and Zeger 1986). The GEE approach assumes independence across observations to estimate consistently the variance of the regression

coefficients. Zeger (1988), Zeger et al (1988) and Liang et al (1992) give more information on the GEE methodology.

To develop the model for our situation where there are no covariates and 3 repeated measurements the following notation is defined. Suppose Y_{ij} denotes whether subject i experienced an event in period j where j=1,2,3. Then let $E(Y_{ij}) = Pr[Y_{ij}=0] = P_{ij}$. When a logistic link function is used the model can be expressed as logit $(P_{ij})=X_{ij}\beta$ where β is a vector of unknown coefficients and $X=\{X_{ij}\}$ is the design matrix. The covariance structure of the correlated measurements must be modeled in RMD analysis. Liang and Zeger (1986) explain how this can be done and how a working correlation structure can be selected. With small time series and large numbers of subjects (≥ 50) the standard recommendations (Hardin and Hilbe, 2013) is to use unstructured correlations for GEE. Alternatively, autoregressive structures are recommended for repeated measures data. The solutions, $\widehat{\beta}$ and var-cov($\widehat{\beta}$) can be obtained iteratively as described in Zeger and Liang(1986). The test used to identify the study size and power in Proc Genmod is the Wald normal test given in the Analysis of GEE Parameter Estimates table.

3.1.3 Generalized Linear Mixed Models

Random effects or subject specific models for RMD in generalized linear models require numerical methods for evaluation of the likelihood. Parameters are estimated by maximizing an approximation to the likelihood integrated over the random effects. Different integral approximations are available, but in this study adaptive Gaussian quadrature is used.

Generalized linear mixed models for repeated measures are further discussed in Davidian and Giltinan (1995); Vonesh and Chinchilli (1996); McCulloch and Searle (2000) and Diggle, Heargerty, Liang & Zeger, 2001.

For the case considered by us consider the same notation as for GEE. Then the random intercept model is specified as logit (P_{ij}) = $X_{ij}\beta$ + u_i where β is a vector of unknown coefficients and X =$\{X_{ij}\}$ is the design matrix. Here it is assumed that the repeated observations between experimental units are independent of one another. Finally, the model requires an assumption about the distribution of the u_i across the population. Typically, a parametric model such as the Gaussian with mean zero and unknown variance, σ_u^2 where this variance represents the degree of heterogeneity across the experimental units, which is unobservable. That is $u_i \sim N(0, \sigma_u^2)$.

Generalized Linear Mixed Models (GLMMs) have their foundation in simple random-effects models for binary data. Fitzmaurice and Molenberghs (2008), Ashford and Sowden (1970), Pierce and Sands (1975) and Korn and Whittmore (1979), laid foundation for the concepts of the GLMMs. In GLMMs the basis of inferences for fixed-effects parameters is marginal likelihood and complemented with empirical-Bayes estimation of the random effects. A general approach for fitting GLMMs is maximum likelihood estimation by numerical integration (quadrature).

The test used to identify the study size and power in Proc Glimmix is the Type III test of fixed effects.

3.2 Some Desirable Properties of Estimators

The properties of unbiasedness, consistency, efficiency and sufficiency of estimators are well explained in Mood, Graybill and Boes (2010). With regard to binary repeated measures McCullagh (1983) has examined the consistency of estimators given by the GEE method. Davis (2002) discusses the cautions concerning the use of GEE and explain the factors affecting the bias and efficiency of estimators for finite samples for GEE. Chaganty and Joe (2004) discuss the efficiency of GEE estimators for binary responses. Bartolucci (2008) discusses bias and consistency of the conditional logistic estimator for repeated binary outcomes. In their paper, Butler and Louis (1997) talk about the property of consistency in Maximum Likelihood Estimators with respect to general random effects models for binary responses. Fitzmaurice, Laird and Ware (2012) discuss the sufficiency of subject-specific model estimators for binary repeated measures.

There is a lot of discussion about the properties of the GEE and GLMM model estimators in the literature. However, there is little exploration about the properties of the WLS estimators and there is no comparison between the properties of the estimators given by the three methods of analysis available in SAS. Thus an important part of this study is to determine these properties for all three methods and compare properties between the methods.

Bias, consistency and efficiency of the estimators can directly be determined (Mood, Graybill and Boes (2010)). However sufficiency of estimators is harder to determine. In this study an empirical method based on the percentage change in the variance of the sample variance of the estimators from the population variance of the estimators is used for this purpose. Mantravadi and Veeravelli (2001) explain this approach in more detail. The formula used for this empirical

method of determining sufficiency is $\frac{(\text{True variance} - \text{estimated variance})}{\text{True variance}} * 100$. The true variance is determined by $P_i(1-P_i)$ / n where P_i is the probability of success in period i and n is the sample size.

4. Simulation Results

This section will present important results given by the simulation study and comment on these results. The following data summaries will highlight the results obtained from the simulation study of the three methods WLS, GEE and GLMM within procedures in SAS, namely, CATMOD, GENMOD and GLIMMIX respectively. For each method, five different sample sizes of 20, 50, 100 250 and 500 were used. Each combination was simulated 1000 times under the null and alternative hypotheses. The procedure simulated correlated binary data for each observation to imitate the repeated binary structure in the data (Sebastian, Dominik, Friedrich, 2011). The data has been simulated in such a way so as the correlation structure is close to an autoregressive structure which is usually expected in repeated measures data. Three repeated binary observations were simulated for three periods for each observation. All data sets are fully balanced, include three time points and their analysis uses time as the only predictor of interest. Thus, these are one sample settings. Speed of computation, Convergence, Type 1 error and Power of each procedure was determined and compared for each combination while the

properties of the estimates of each method, namely, unbiasedness, efficiency, consistency and sufficiency for each combination was determined and compared.

4.1 Initiation

4.1.1 Hypothesis of interest

The null and alternative hypotheses can be specified as follows.

H_0: All the time (period) effects are equal

H_1: At least one time (period) effect is significantly different from the others

4.1.2 Initial probabilities

As observed in the simulation study design section (section 2), three different initial probabilities are obtained for the three different responses under H_0 and H_1 and this is same for all three methods, and data were simulated. Table 1 gives the initial probabilities under H_0 and H_1. Here P_i corresponds to the success probability at the i^{th} period.

Table 1 should come here.

4.2 Results for WLS method given by SAS PROC CATMOD

The results for the WLS method in CATMOD procedure are given in table 2. Table 2 has two sections. The first section assumes the null hypothesis, the second section assumes an alternative hypothesis where each period effect is different from one another. Each section of the table gives the number of non-convergent results, the proportion of rejections of H_0 , true probability used for simulation (P_i 's), averaged estimated probability for each period averaged over a 1000

simulations, bias, averaged estimated variance, percentage difference between estimated and true variance for each period for the WLS method facilitated by PROC CATMOD procedure. These results were obtained for each combination of hypothesis and sample size.

Table 2 should come here

The 95% probability interval for an error rate of 5%=0.05 for 1000 samples is [0.036, 0.064]. For the WLS method where the sample size is 20, the proportion of rejections of H_0 when H_0 is true is outside this probability interval indicating inflated type I error. Thus, for WLS method in PROC CATMOD, Type 1 error is inflated for small sample sizes and for larger sample sizes of 50 and over the proportion of rejections of H_0 when H_0 is true is within the required probability interval. For a sample of size 20 there are 2 trials which do not converge. For all other sample sizes all 1000 trials converge. These non-convergent results occur due to zero counts in the contingency tables.

When considering the proportion of rejections of H_0 when H_1 is true (power), the power increases when sample size increases as expected. The power reaches a maximum of one for samples of size 250 and 500. For small samples of size 20 there are 5 non-convergent results while for all other sample sizes this problem does not occur.

From table 2, it is clear that the average of the estimated probability values, for WLS method in PROC CATMOD, is close to the true probability values, under both null and alternative hypotheses, for all sample sizes examined. This property conveys the unbiasedsness of estimates

given by the WLS method for PROC CATMOD procedure, for every sample size under both hypotheses. When looking at the average variance, under both null and alternative hypotheses, this value is decreasing significantly when the sample size increases. Since the average variance of the estimated values, can be considered as a measure of variability, decrement in average variance with sample size, implies consistency of parameter estimates of the WLS method given by PROC CATMOD procedure. Sufficiency is another property to be looked at. For that percentage difference between the estimated and true variance of period effect components estimates is needed. The final column of Table 2 gives the percentage values of the difference between estimated and true variance of period effect components estimates for the WLS method in PROC CATMOD procedure. According to table 2, the percentage of difference between the true and estimated variance estimates are between -6.67% and 4.17% for all the sample sizes for all hypotheses. That is, the sample explains the population well for period effects. As a statistic is sufficient for a family of probability distributions, if the sample from which it is calculated gives no additional information than does that statistic (Mood, Graybill and Boes, 2010) this implies that the period effect estimates are sufficient for the WLS method given by PROC CATMOD procedure (Mantravadi and Veeravelli, 2001; Nadarajah and Sooriyarachchi, 2009). The properties of efficiency and speed will be looked at when comparing the three methods within SAS. These results imply that, except for very small sample sizes (20) the GLS procedure of PROC CATMOD performs very well.

4.3.Results from the GEE method incorporated in PROC GENMOD of SAS

With small time series and large number of subjects the standard recommendation (Hardin and Hilbe, 2013) is to use unstructured correlations for GEE. Therefore, except for sample size 20 for all other cases an unstructured correlation matrix is used. For size 20 an autoregressive structure which is alternatively recommended for repeated measures when using GEE is utilized. The results for the GEE method as given by SAS PROC GENMOD using the recommended correlation structures are given in Table 3. This gives the similar results as Table 2 but for the GEE method.

Table 3 Should come here

Table 3 depicts that there are no non-convergence issues in the GEE method of PROC GENMOD procedure under both H_0 and H_1. The Type 1 error for the GEE method as output from PROC GENMOD lies between the 95% probability interval for 1000 simulations [0.036, 0.064] only for very large sample sizes of 250 and 500. For smaller sample sizes the Type I error is inflated. In the case of H_1 the power of the GEE method given by PROC GENMOD is very similar to the WLS method given by PROC CATMOD for corresponding sample size.

In the GEE method of PROC GENMOD also, average predicted probability values are close to the true values under both null and alternative hypotheses for all sample sizes. This property conveys the unbiasedsness of estimates given by the GEE method of PROC GENMOD for every sample size under both hypotheses.

When looking at the average variance, under both null and alternative hypotheses, this value is decreasing significantly when the sample size increases. Since the average variance of the estimated values, can be considered as a measure of variability, decrement in the average

variance with sample size, implies consistency of parameter estimates given by the GEE method of PROC GENMOD. When examining the property of sufficiency of the GEE method, the percentage difference between estimated and true variance of period effect are quite small for the cases of H_0 and H_1. Therefore, overall it can be concluded that the estimated period effects given by GEE of PROC GENMOD are sufficient (Mantravadi and Veeravelli, 2001; Nadarajah and Sooriyarachchi, 2009). It can be seen that the GEE method with an unstructured correlation matrix for all other sample sizes except 20 and AR(1) procedure for size 20 in PROC GENMOD performs well only for very large sample sizes greater than or equal to 250.

4.4 Results from the GLMMôs obtained from PROC GLIMMIX procedure in SAS

The results of the GLIMMIX procedure with Quadrature estimation are given in Table 4. This gives the similar results as Table 2 but for GLMMôs in GLIMMIX procedure.

Table 4 should come here.

From table 4, illustrating the results for GLMM method (using Quadrature) given by the GLIMMIX procedure, both positive and negative comments can be made. One of the important points that have to be highlighted is that similar to the WLS method in PROC CATMOD the Type I error is outside the 95% probability interval only for sample size 20 but in this case the estimated type I error is conventional. In all other cases the Type I error is within the stipulated 95% probability interval. There are no non-convergence issues in the GLMM method of GLIMMIX procedure under both the null and alternative hypotheses.

It can be seen from the results of the GLMM method of GLIMMIX procedure that its power is less than that of both WLS method of PROC CATMOD and GEE method of PROC GENMOD for all sample sizes.

The GLMMs method in PROC GLIMMIX also has predictor probability values which are close to the true probability values under both null and alternative hypotheses for all sample sizes. However, in period 1 the estimates are more biased than those given by the other two methods but in the other 2 periods the bias decreases. This property conveys the approximate unbiasedsness of estimates given by GLMM, Quadrature method of estimation for PROC GLIMMIX for every sample size under both hypotheses.

When looking at the average variance, under both null and alternative hypotheses, this value is decreasing significantly when the sample size increases. Since the average variance of the estimated values, can be considered as a measure of variability, decrement in average variance with sample size, implies consistency of parameter estimates given by the GLMM method. When examining the property of sufficiency, given by GLMM method, the percentage difference between estimated and true variance of period effect are generally large under both H_0 and H_1 for all sample sizes. Therefore, it can be concluded that the estimated period effects given by GLMM method of PROC GLIMMIX are not sufficient (Mantravadi and Veeravelli, 2001; Nadarajah and Sooriyarachchi, 2009)

4.5 Efficiency and Speed of the three procedures.

When comparing the average variance of the estimated probabilities it can be clearly seen that these are minimum for the WLS estimates given by PROC CATMOD followed closely by the

GEE estimates given by PROC GENMOD and this is largest for the quadrature estimates of the GLMM method under PROC GLIMMIX. As the average variance (for each P_i , each sample size and each hypothesis) denotes variability it can be mentioned that the WLS estimates in PROC CATMOD are the least variable that is the most efficient, followed closely by the GEE estimates in PROC GENMOD while the quadrature estimates of GLMMôs in PROC GLIMMIX are the most variable that is least efficient.

When the speed of computation is considered the WLS method in PROC CATMOD is fastest, followed by the GEE method in PROC GENMOD and the slowest is GLMM method in PROC GLIMMIX.

4.6 Comparison of the three methods.

Table 5 compares the three methods WLS of PROC CATMOD, GEE under PROC GEMMOD and GLMM of PROC GLIMMIX under H_0 and H_1 .

Table 5 should come here

Table 5 indicates that with respect to all the properties considered, it can be concluded that with adequately large samples of size 50 or more, no missing data, the only covariate being time (period) effect and relatively limited number of repeated measures (time points), the WLS method performs better than the GEE method and GLMMs approach. The GEE approach performs well for very large samples of sizes greater than or equal to 250 and the GLMM's approach generally is satisfactory for samples of size greater than 20. However the properties of the estimates given by the GLMM procedure are inferior to the properties of the estimates given

by the WLS procedure. All three procedures perform poorly for sample size 20. Developing methodology for very small sample sizes in a repeated measures context with binary responses is a challenging new problem which can be studied further.

5. An Example based on Real Data

5.1 Details of the dataset

This data set has been obtained from Bansback, et al., 2007. Originally there were patients from two different locations for this study, 319 patients from Canada and 151 patients from the United Kingdom. Since location could become a nuisance factor, the authors had selected a random sample of 141 patients from Canada. Patients were diagnosed for the presence of Rheumatology arthritis (present/absent) in three different time periods. Table 6 gives the response patterns in the data set.

Table 6 should come here.

The null hypothesis to be tested is

H_0: Marginal probability of patients having Rheumatology arthritis is same for all time points

Against the alternative hypothesis

H_1: Marginal probability of patients having Rheumatology arthritis is not same for all time points

The correlation between the data points were found to be 0.4002, 0.3158 and 0.4466 between time points (1,2), (1,3) and (2,3) respectively. Thus, it can be seen clearly that this correlation structure is very close to the correlation structure we are simulating from.

5.2 Results for PROC CATMOD procedure

The response functions for time points 1,2 and 3 for the CATMOD procedure were found to be 0.77551, 0.63265 and 0.70068 respectively. It is clear that response functions for the three different time points are different. Table 7 gives the weighted least squares estimates.

Table 7 should come here

Table 7 indicates that the marginal response for time 1 is significantly different from the marginal response values for time 3 and the marginal response for time 2 is also significantly different from marginal response values for time 3.

5.3 Results for PROC GENMOD procedure

As the size of the data set is over 100 and can be considered as large the correlation structure was considered to be unstructured. Table 8 gives the Analysis of GEE parameter estimates.

Table 8 should come here.

The model considered here is,

$logit\left(P\left(Y_t=1\right)\right)=\alpha+\beta_t$ Where t=1, 2,3

According to table 8 the marginal proportion of patients having Rheumatology arthritis for time 1 and time 2, are not significantly different (as the p-values are greater than 0.05) from the marginal proportion of time 3.

The working correlation matrix obtained under the GENMOD procedure for GEE method.

$$R_{(Unstruc)}=\begin{pmatrix}1.000 & 0.4759 & 0.3293\\ 0.4759 & 1.000 & 0.4635\\ 0.3293 & 0.4635 & 1.000\end{pmatrix}$$

Unstructured ñworkingò correlation illustrates that the responses per an individual are considerably correlated.

4.4 Results for PROC GLIMMIX procedure

Table 9 gives the Analysis of GLIMMIX parameter estimates

Table 9 should come here

Table 9 gives the results of analysis of GLIMMIX parameter estimates gives the same results as obtained on the dataset as for GEE method. Since the P-values >0.05, marginal proportion of

patients having Rheumatology arthritis at time 1 and time 2, is not significantly different from marginal proportions of patients having Rheumatology arthritis at time 3.

5.5 Comparison of the three methods

Table 10 gives the Estimated marginal probabilities and S.Es for the three methods

Table 10 should come here.

As shown in table 10 all three methods give similar parameter estimates. PROC CATMOD procedure for WLS and PROC GENMOD for GEE method provide estimates for marginal proportions with less variability. However the GLIMMIX procedure for GLMMs method has high variability for the estimated marginal proportions values.

6. Discussion

6.1 Important Conclusions and Recommendations

WLS method has outstanding performances when the sample size is adequately large with a relatively small number of time points, with no missing values and with no covariates except periods. However, there are some techniques available in PROC CATMOD procedure in SAS for WLS method to deal with missing cases.

The GEE method only works well in analyzing binary RMD when the sample size is large. This is because with sufficient number of experimental units still consistent estimates can be obtained even if the ñworkingò correlation matrix is specified incorrectly (Liang and Zeger, 1986)

The GLMMs method with quadrature estimation produces satisfactory results with respect to type I error in the analysis of binary RMD. However the properties of its estimates are inferior when compared to the properties of the estimates of the WLS method.

Thus, under the conditions tested for reasonably large samples of size 50 or over WLS method given by PROC CATMOD can be recommended. For very large samples of size 250 or over GEE method incorporated in PROC GENMOD too can be recommended. The GLMM's method given by PROC GLIMMIX is satisfactory with respect to type I error, but the properties of its estimates are poor.

In SAS software PROC CATMOD facilitates the WLS method, PROC GENMOD facilitates the GEE method and PROC GLIMMIX facilitates the GLMMs method. In order to accomplish the ultimate objective of the study a simulation study was carried out using SAS. Here it should be noted that though this entire study has been conducted with SAS it could just as well have used either R or Stata too. Masaoud and Stryn (2010) explain that the computational procedures used within the three statistical packages are quite similar so these results could be generalized to any platform thus results should be package independent.

6.2 Further Work

This study is only focused on analysis of balanced binary RMD, but this study can be extended to areas such as; analysis of RMD when the response variable is categorical (nominal and

ordinal), analysis of RMD for data with multiple response variables, analysis of RMD including missing values and analysis of RMD when time variant and time invariant covariates are present.

References

1.Ashford, J.R. and Sowden, R. R. (1970) Multivariate probit analysis. *Biometrics* 26 :535-46

2.Bansback, N., Marra, C., Tsuchiya, A., Anis, A., Guh, D., Hammond, T., & Brazier, J. (2007). Using the health assessment questionnaire to estimate preference-based single indices in patients with Rheumatoid arthritis. *Arthritis Care & Research*, *57*(6), 963-971.

3.Brown, H. and Prescott, R. (2006) Applied Mixed Models in Medicine, Wiley

4.Davis, C.S. (2002) Statistical Methods for the analysis of repeated measurements. Springer, Mathematics.

5. Diggle, P., Heagerty, P., Liang, K. Y., & Zeger, S. (2001). *Analysis of longitudinal data* (No. 25). Oxford University Press.

6. Fitzmaurice, G. and Molenberghs, G. (2008). Advances in Longitudinal Data Analysis: A Historical Perspective . Chapter 1 *Longitudinal data analysis*. CRC Press.

7 Fitzmaurice, G., Davidian, M., Verbeke, G., & Molenberghs, G. (Eds.). (2008).*Longitudinal data analysis*. CRC Press.

8.Grizzle, J. E., Starmer, C.F. and Koch, G.G. (1969) Analysis of Categorical data by linear models. *Biometrics,* 25 489-504

9.Hardin, J.W. and Hilbe J.M. (2013) Generalized Estimating Equations. Second Edition. CRC Press.

10. Hosmer, D.W. Lemeshow, S.(2000) Applied Logistic Regression, Second Edition. Wiley.

11.Johnston, G., and Stokes, M. (1996). Repeated measures analysis with discrete data using the SAS system. *SAS Institute Inc., Cary, NC*.

12.Koch and Reinfurt (1971) The analysis of categorical data from mixed model. *Biometrics,* 27, 157-173

13. Koch, G. G., Landis, J. R., Freeman, J. Land Lehnen, R. G. (1977). A general methodology for the analysis of experiments with repeated measurement of categorical data, Biometrics, 33, 133ï 158

14. Liang, K. Y., and Zeger, S. L. (1986). Longitudinal data analysis using generalized linear models. *Biometrika*, *73*(1), 13-22.

15. Mantravadi, A. Veeravalli, V.V. (2001) On Chip-Matched filtering and discrete sufficient statistics for asynchronous band-limited CDMA systems. *IEEE Transactions on Communications* 49(8) : 1457-1467

16. Masaoud, E., and Stryhn, H. (2010). A simulation study to assess statistical methods for binary repeated measures data. *Preventive veterinary medicine,93*(2), 81-97.

17. Mood, A. M., Graybill, F. A., and Boes, D. C. (2010). Introduction to the theory of statistics (9^{th} ed). New Delhi: McGraw Hill

18. Nadarajah, K. and Sooriyarachchi, M.R. (2009) óA monte-carlo Simulation study of the properties of Residual Maximum Likelihood (REML) estimators for the linear Gaussian mixed modelô *Sri Lankan Journal of Applied Statistics*. Volume 10 pages 119-136

19.Nelder, J.A. and R. W.M. Wedderburn (1972) Generalized Linear Models. *Journal of the Royal Statistical Society Series A* 138(3), 370-384

20.Pierce, D.A. and Sands, B.R. (1975). Extra Bernoulli variation in Binary data. Technical Report 46, Department of Statistics, University of Oregon

21. Rasbash, J., Steel, F., Browne, W., and Prosser, B. (2006). MLwiN user's manual. *Bristol, UK: Centre for Multilevel Modelling*.

22 Sebastian, K., Dominik, T., Friedrich, L. (2011). Generating correlated ordinal random values. Technical Report number 94. Department of Statistics, University of Munich.

23.Stanish, W.M. and Koch, G.G. (1984). The use of CATMOD for repeated measurement analysis of categorical data. Proceedings of the 9th Annual SAS users group International conference, Cary, NC SAS Institute Inc, 761-770

24. Stiratelli, R., Laird, N. and Ware, J.H. (1984). Random effects models for serial observations with Binary response. *Biometrics,* 40(4), 961-971

25. Szmaragd, C., Clarke, P. and Steele, F. (2013) Subject specific and population average models for binary longitudinal data: a tutorial *Longitudinal and Life Course Studies*, 42 (2). 147-165.

26. Ware, J.H., Lipsitz, S. and Speizer, F.E. (1988) Issues in the analysis of repeated categorical outcomes. *Statistics in Medicine* 7(1-2) 95-107.

Table 1 - Probabilities (P_i) associated with the responses

Hypothesis	P_i	Probability
H_0	P_1	0.500
	P_2	0.500
	P_3	0.500
H_1	P_1	0.250
	P_2	0.400
	P_3	0.445

Table 2 - Results obtained from the WLS method in PROC CATMOD

Hypothesis	Sample size	Number of non-convergent trials	Proportion of trials out of 1000 rejecting H_0	True probability (P_i)		Averaged estimated P_i's	Bias	Average Variance	Change in % Variance
H_0	**20**	2	0.090	P_1	0.5	0.495	-0.005	0.012	-4.00
				P_2	0.5	0.497	-0.003	0.012	
				P_3	0.5	0.502	0.002	0.012	
	50	0	0.060	P_1	0.5	0.501	0.001	0.0049	-2.00
				P_2	0.5	0.498	-0.002	0.0049	
				P_3	0.5	0.502	0.002	0.0049	
	100	0	0.057	P_1	0.5	0.502	0.002	0.0025	0.00
				P_2	0.5	0.502	0.002	0.0025	
				P_3	0.5	0.500	0.000	0.0025	
	250	0	0.050	P_1	0.5	0.499	-0.001	0.001	0.00
				P_2	0.5	0.500	0.000	0.001	
				P_3	0.5	0.501	0.001	0.001	
	500	0	0.049	P_1	0.5	0.500	0.000	0.0005	0.00
				P_2	0.5	0.500	0.000	0.0005	
				P_3	0.5	0.500	0.000	0.0005	
H_1	**20**	5	0.343	P_1	0.25	0.246	-0.004	0.009	-4.00
				P_2	0.40	0.396	-0.004	0.0112	-5.83
				P_3	0.445	0.443	-0.002	0.0117	-4.88
	50	0	0.641	P_1	0.25	0.250	0.000	0.0036	-4.00
				P_2	0.40	0.399	-0.001	0.0047	-2.08
				P_3	0.445	0.443	-0.002	0.0048	-2.82
	100	0	0.911	P_1	0.25	0.249	-0.001	0.0019	1.33
				P_2	0.40	0.402	-0.002	0.0024	0.00
				P_3	0.445	0.447	0.002	0.0024	-2.82
	250	0	1.000	P_1	0.25	0.250	0.000	0.0007	-6.67
				P_2	0.40	0.400	0.000	0.001	0.00
				P_3	0.445	0.446	0.001	0.001	4.17

	500	0	1.000	P_1	0.25	0.251	0.001	0.00038	1.33
				P_2	0.40	0.400	0.000	0.00048	0.00
				P_3	0.445	0.445	0.000	0.00049	-0.80

Table 3 - Results obtained from the GEE method in PROC GENMOD

Hypothesis	Sample size	Number of non-convergent trials	Proportion of trials out of 1000 rejecting H_0	True probabilities (P_i)		Averaged estimated P_i's	Bias	Average Variance	Change in % Variance
H_0	**20**	0	0.142	P_1	0.5	0.502	0.002	0.012	-4.00
				P_2	0.5	0.494	-0.006	0.012	
				P_3	0.5	0.496	-0.004	0.012	
	50	0	0.097	P_1	0.5	0.504	0.004	0.0049	-2.00
				P_2	0.5	0.501	0.001	0.0049	
				P_3	0.5	0.502	0.002	0.0049	
	100	0	0.084	P_1	0.5	0.500	0.000	0.0025	0.00
				P_2	0.5	0.500	0.000	0.0025	
				P_3	0.5	0.501	0.001	0.0025	
	250	0	0.057	P_1	0.5	0.500	0.000	0.001	0.00
				P_2	0.5	0.499	-0.001	0.00093	-7.00
				P_3	0.5	0.501	0.001	0.001	0.00
	500	0	0.051	P_1	0.5	0.500	0.000	0.0005	0.00
				P_2	0.5	0.500	0.000	0.0005	
				P_3	0.5	0.501	0.001	0.0005	
H_1	**20**	0	0.235	P_1	0.25	0.247	-0.003	0.009	-4.00
				P_2	0.40	0.399	-0.001	0.012	0.00
				P_3	0.445	0.454	-0.009	0.012	-2.82
	50	0	0.690	P_1	0.25	0.249	-0.001	0.0037	-1.32
				P_2	0.40	0.402	0.002	0.0047	-2.08
				P_3	0.445	0.449	0.004	0.0049	-0.80
	100	0	0.906	P_1	0.25	0.250	0.000	0.0019	1.33
				P_2	0.40	0.400	0.000	0.0024	0.00
				P_3	0.445	0.444	-0.001	0.0024	-2.80
	250	0	1.000	P_1	0.25	0.251	0.001	0.0007	-6.67
				P_2	0.40	0.402	0.002	0.001	4.17
				P_3	0.445	0.447	0.002	0.001	1.23
	500	0	1.000	P_1	0.25	0.250	0.000	0.00037	-1.33
				P_2	0.40	0.401	0.001	0.0005	4.17
				P_3	0.445	0.445	0.000	0.0005	1.22

Table 4 - Results obtained from the Quadrature estimation in GLMM method of PROC GLIMMIX

Hypothesis	Sample size	Number of non-convergent trials	Proportion of trials out of 1000 rejecting H_0	True probabilities (P_i)		Averaged estimated P_i's	Bias	Average Variance	Change in % Variance
H_0	20	0	0.007	1	0.5	0.50472	0.004724	0.026824	-114
				2	0.5	0.50065	0.000649	0.027362	-195
				3	0.5	0.50160	0.001602	0.027023	-196
	50	0	0.036	1	0.5	0.50001	0.000005	0.011009	-195
				2	0.5	0.50342	0.003423	0.011097	-199
				3	0.5	0.49852	-0.001484	0.010997	-197
	100	0	0.044	1	0.5	0.49763	-0.002365	0.005434	-197
				2	0.5	0.50015	0.000150	0.005425	-199
				3	0.5	0.50119	0.001189	0.005433	-199
	250	0	0.056	1	0.5	0.49985	-0.000150	0.002166	-199
				2	0.5	0.49878	-0.001224	0.002168	-199
				3	0.5	0.49969	-0.000310	0.002167	-199
	500	0	0.05	1	0.5	0.50062	0.000621	0.001081	-200
				2	0.5	0.50000	0.000005	0.001081	-200
				3	0.5	0.50025	0.000246	0.001080	-200
H_1	20	0	0.051	1	0.25	0.23398	-0.0160239	0.012983	-125
				2	0.4	0.39077	-0.0092291	0.024040	-158
				3	0.45	0.45087	0.0008719	0.027384	-177
	50	0	0.537	1	0.25	0.22798	-0.022023	0.004885	-117
				2	0.4	0.39761	-0.0023857	0.009516	-164
				3	0.45	0.44637	-0.0036278	0.010285	-178
	100	0	0.882	1	0.25	0.22799	-0.0220061	0.002451	-120

				2	0.4	0.39432	-0.0056803	0.004766	-163
				3	0.45	0.44235	-0.0076493	0.005157	-178
	250	0	1	1	0.25	0.22739	-0.0226129	0.000983	-120
				2	0.4	0.39318	-0.0068221	0.001900	-163
				3	0.45	0.44545	-0.0045515	0.002058	-180
	500	0	1	1	0.25	0.22618	-0.0238179	0.000489	-120
				2	0.4	0.39316	-0.0068409	0.000945	-164
				3	0.45	0.44652	-0.0034779	0.001024	-180

Table 5 - Comparison of the 3 methods of estimation in SAS

Property	Under H_0		
	WLS(CATMOD)	GEE(GENMOD)	Quadrature(GLIMMIX)
Type I error : Small samples : Large samples	Does not hold for size 20 Holds for size $\geq$ 20	Does not hold for size <250 Holds for size $\geq$ 250	Does not hold for size 20 Holds for size $\geq$ 20
Unbiased	Yes	Yes	Yes
Efficiency (in order)	1	1	3
Consistent	Yes	Yes	Yes
Sufficient	Yes	Yes	No
Speed (in order)	1	2	3

Property	Under overall H_1		
	WLS(CATMOD)	GEE(GENMOD)	Quadrature(GLIMMIX)
Power (in descending order)	1	1	3
Convergence :Small samples (20) : Large samples	Few problems No problems	No problems No problems	No problems No problems
Unbiased	Yes	Yes	Bigger bias than other 2 methods for period 1 but bias decreases with periods 2 and 3
Efficiency (in order)	1	1	3

Consistent	Yes	Yes	Yes
Sufficient	Yes	Yes	No
Speed (in order)	1	2	3

Table 6 - Response patterns in the example data sets.

Response (1-Present 0-Absent)				
	Time 1	Time 2	Time 3	No of patients
1	1	1	1	17
2	1	1	0	9
3	1	0	1	2
4	1	0	0	5
5	0	1	1	14
6	0	1	0	14
7	0	0	1	11
8	0	0	0	75
Total				147

Table 7 -Analysis of WLS estimates

Effect	Estimate	S.E	Chi sq	P>Chi sq
Intercept	0.7029	0.0292	1060.88	<0.0001
Time 1	0.0726	0.0232	6.12	**0.0134**
Time 2	-0.0703	0.0223	4.98	**0.0257**

Time 3 is the base

Table 8 - Analysis of GEE parameter estimates

Parameter	Estimate	S.E	95% CL		Z	Pr> |Z|
Intercept	0.8505	0.1801	0.4975	1.2035	4.72	<0.0001
Time 1	0.3892	0.2200	-0.0420	0.8203	1.77	**0.0769**
Time 2	-0.3069	0.1831	-0.6658	0.0520	-1.68	**0.0937**

Time 3 is the base.

Table 9 - Analysis of GLIMMIX parameter estimates using quadrature estimation

Effect	Estimate	S.E	t-value	P > t	LCL	UCL
Intercept	1.5416	0.3483	4.43	<0.0001	0.8533	2.2300
Time 1	0.6730	0.3564	1.89	**0.0600**	-0.0285	1.3744
Time 2	-0.5476	0.3354	-1.63	**0.1037**	-1.2077	0.1126

Solutions for Fixed Effects

Table 10 - Estimated marginal probabilities and S.Es for the three methods

Procedure	P_i	Estimated marginal proportions	Standard errors
PROC CATMOD	P_1	0.77551	0.0344135
	P_2	0.63265	0.0397618
	P_3	0.70068	0.0377717
PROC GENMOD	P_1	0.7755102	0.0344137
	P_2	0.6326531	0.0397618
	P_3	0.7006803	0.0377717
PROC GLIMMIX	P_1	0.7966814	0.2269085
	P_2	0.6390608	0.2926679
	P_3	0.7149935	0.2699947

