AN APPROACH TO THE ANALYSIS OF PROFILE DATA: DATA SET 1

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Our analysis of these data consisted of the following steps:

1. Examination of a graph of these data (see graphs of the data). The graphs we constructed included mean profiles, and graphs for each treatment were overlayed. It was noted that individual 1 (and maybe 7) had conspicuously low weights and that there was some evidence of a supplementation effect, particularly several weeks after therapy began.

2. Analysis of variance was calculated with time as a split factor. This analysis included a sub-model for the time x treatment interaction (relevant only after week 4) and linear contrasts for the time effect plus a partitioning of the treatment effect into contrasts for control versus supplementation and the difference between low and high of supplementation (see Table 1).
   Although the analysis of variance provides a convenient summary of a possible mean model for these data, it does not provide a valid basis for significance testing since the covariance structure assumed for the complete analysis is unlikely to be appropriate due to time-dependence.
   However this analysis does facilitate residual analysis which may indicate aberrant 'subjects' or observations, possible variance heterogeneity and/or the need for a scale change. It also provides appropriate residuals for the calculation of the semi-variogram, a diagnostic tool which may provide insight into the nature of the covariance structure.
   Examination of the 'subject' residuals highlighted subject 1 - standardized residual of 2. In absence of additional evidence subject 1 was not excluded from subsequent analysis.

Table 1
Analysis of variance of weight

Source of variation	d.f.	s.s	m.s
Between 'subjects'			
Supplementation	1	17940	17940
Between VitE_levels	1	608	608
Residual	12	105434	8786
Within 'subjects'			
time	5	142554	28511
Suppl. time (after week 4)	3	7090	2363
Linear contrast	1	5125	5125
Deviations from linear	2	1965	983
VitE_levels.time (after week 4)	3	1124	375
VitE_levels.linear contrast	1	750	750
Deviations	2	374	187
Residual	64	34101	5833
Total	89	308853	

The residual plot (Figure 1) shows a suitably random pattern indicating that the assumption of constant variance is reasonable.

3. The covariance structure was examined by graphing the semi-variogram (Figure 2) and calculating the order of ante-dependence (Kenward, [1]). Ante-dependence is defined as
'a set of variates observed at successive times is said to have ante-dependence structure of order r if each i^{th} variable ($i > r$) given the preceding r, is independent of all further preceeding variates'.
The ante-dependence order for these data was 2.

Figure 1: Plot of residuals versus fitted values.

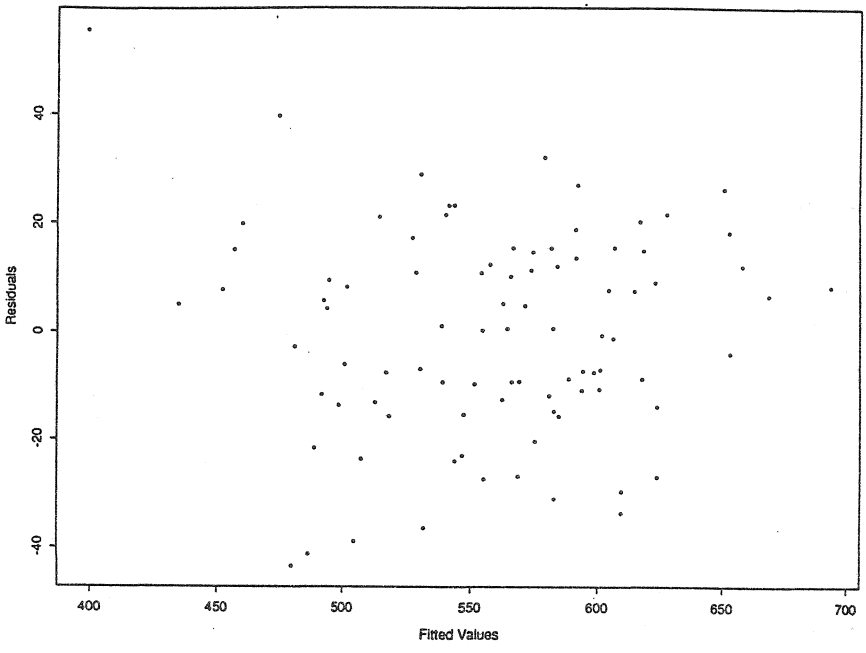
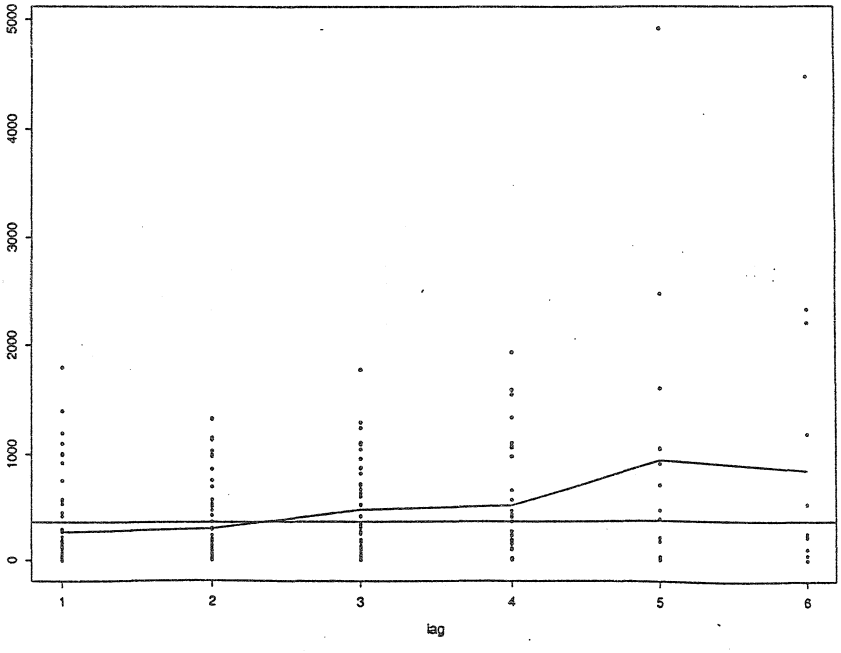


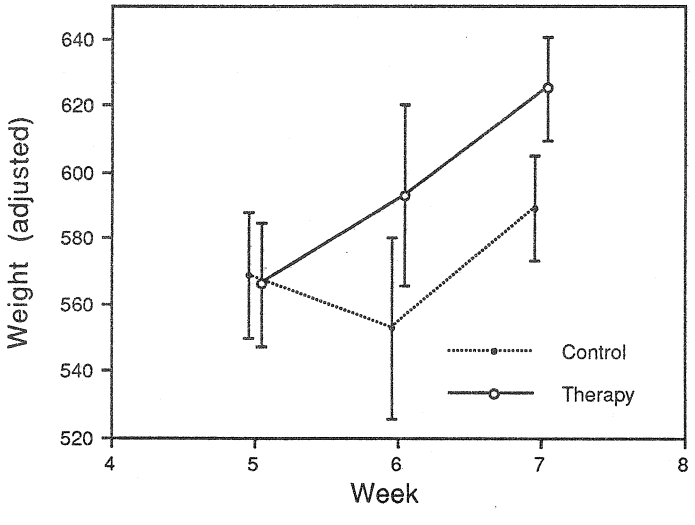
Figure 2: Plot of the empirical semi-variogram



4. KENWARD [1] provides an overall test of the treatment effects based on a specified order of ante-dependence. For order 2 this test yielded test statistics of 11.14 and 3.22 for the supplementation effect and between levels of supplementation, respectively. These statistics are approximately χ^2 on 4 degrees of freedom. Thus the null hypothesis of no supplementation effect on weight is untenable ($p = 0.025$) and there is insufficient evidence to suggest a level of supplementation effect.

5. To further understand the supplementation effect, individual times were analysed individually using analysis of covariance adjusting for the two previous times. This provides information on the times at which the treatment effect occurred. As there was no measurement at week 3, a single covariate - week 4 - was used for the analysis of the weight at week 5.
   As can be seen in Figure 2, the evidence for supplement effect on weight is convincing at week 7.

Figure 3: Summary of the covariance analyses: mean weights adjusted for preceding weights, with 95% confidence intervals.



SUMMARY

The method due to KENWARD [1] has the advantage that no assumption on the form of the time response is necessary. It provides an overall test which can be decomposed into a series of covariance analyses that provide insight into the nature of the effect, if present.

The preferred method of analysis is the formulation and fitting of a statistical model of the form proposed by VERBYLA and CULLIS [2]. However the method used here requires few assumptions and uses familiar methodology and hence rates high on comprehensibility.

DISCUSSION

At the Workshop, a question was raised by Brian Cullis about the efficiency of the overall significance test of Kenward's. It was suggested that this approach may be over-parameterized.

REFERENCES

[1] KENWARD, M.G. (1987), A method for comparing profiles of repeated measurements. *Applied Statistics*, **36**, pp. 296-308, 1987.

[2] VERBYLA, A.P. and CULLIS, B.R. (1991), A general approach for the analysis of repeated measures experiments. Ibid.

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