CME Article

Biostatistics 301. Repeated measurement analysis

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The simplest repeated measurement analysis is the pre-post type of study, where we have only two time-points. There are many situations where one collects information at baseline and then at regular intervals over time, say three monthly, and is interested to determine whether a treatment is effective over time.

Common techniques of analyses are[1-3]:

1. Mean response over time – Interest in overall treatment effect. No information on treatment effect changes over time.
2. Separate analyses at each time point – This is most common in medical journals. Repeated testing at each time point causes inflated type I error and results in interpretation problems. Treatment standard errors are less accurate as only observations at each time point used. Must be discouraged!
3. Analyses of response features – Area under the curve, minimum/maximum values, time to max values.

How should we analyse such data? Let us consider a dataset from SPSS (Table I) where the number of errors made by each subject as each repeats the same task over 4 trials were recorded.

Table I. Anxiety data set (Longitudinal form).

Subject	Anxiety	Trial 1	Trial 2	Trial 3	Trial 4
1	Low	18	14	12	6
2	Low	19	12	8	4
3	Low	14	10	6	2
4	Low	16	12	10	4
5	Low	12	8	6	2
6	Low	18	10	5	1
7	High	16	10	8	4
8	High	18	8	4	1
9	High	16	12	6	2
10	High	19	16	10	8
11	High	16	14	10	9
12	High	16	12	8	8

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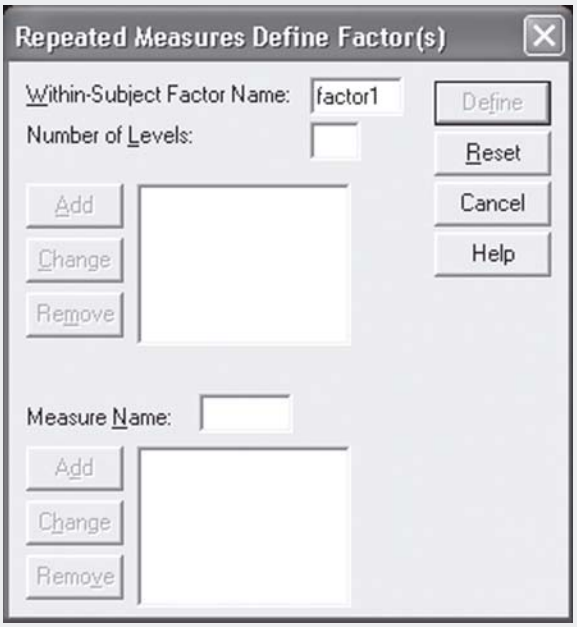
Three questions one would want to ask are:

1. Is there a difference in the number of errors made between the Low and High anxiety subjects? This is termed as the Between-Subject Factor – a factor that divides the sample of subjects into distinct subgroups.
2. Is there a reduction in the number of errors made over trials – a time trend? This is termed as the Within-Subject Factor - distinct measurements made on the same subject, for example, BP over time, thickness of the vertebrae of animals.
3. Is there a group time interaction? If there is a time trend, whether this trend exists for all groups or only for certain groups?

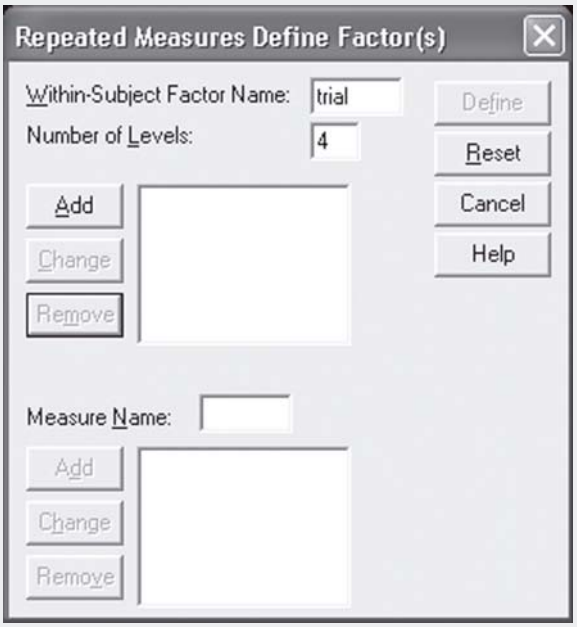
To perform a repeated measurement analysis in SPSS, go to ***Analyse, General Linear Model, Repeated Measures*** to get Template I.

Template I. Repeated measurement definition.



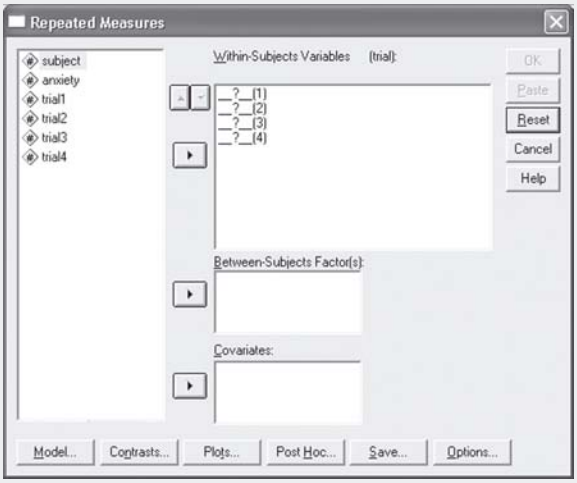
Change the Within-Subject Factor Name to "trial" (or any suitable term) and put "4" in the Number of Levels (number of repeated measurements) – see Template II.

Template II. Defining the number of levels.



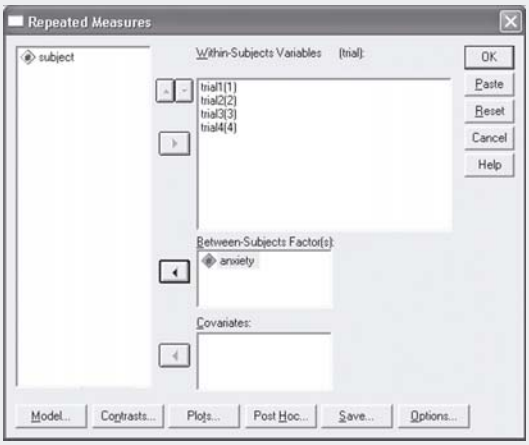
The Add button becomes visible, click on it and the Define button becomes visible too. Clicking on the Define button gives Template III.

Template III.



Bring the variables "trial1" to "trial4" over to Within-Subjects Variables panel and "anxiety" to the Between-Subjects Factor panel, see template IV.

Template IV.



The above steps set up the "basic" analyses for a repeated measurement analysis.

1. THE BETWEEN-SUBJECTS DIFFERENCE

Table IIa. Between-Subjects difference.

Tests of Between-Subjects effects

Measure: MEASURE_1
Transformed Variable: Average

Source	Type III sum of squares	df	Mean square	F	Sig.
Intercept	4800.000	1	4800.000	280.839	.000
Anxiety	10.083	1	10.083	.590	.460
Error	170.917	10	17.092		

Table IIa shows that there were no differences in the mean number of errors made over time between the Low and High anxiety groups (p=0.460).

Table IIb. Descriptive statistics by anxiety.

Anxiety

Measure: MEASURE_1

			95% Confidence interval	
Anxiety	Mean	Std. error	Lower bound	Upper bound
Low anxiety	9.542	.844	7.661	11.422
High anxiety	10.458	.844	8.578	12.339

Table IIc. Pairwise comparisons by anxiety.

Pairwise Comparisons

Measure: MEASURE_1

					95% Confidence interval for Difference[a]	
(I) Anxiety	(J) Anxiety	Mean difference (I-J)	Std. error	Sig.[a]	Lower bound	Upper bound
Low anxiety	High anxiety	-.917	1.193	.460	-3.576	1.742
High anxiety	Low anxiety	.917	1.193	.460	-1.742	3.576

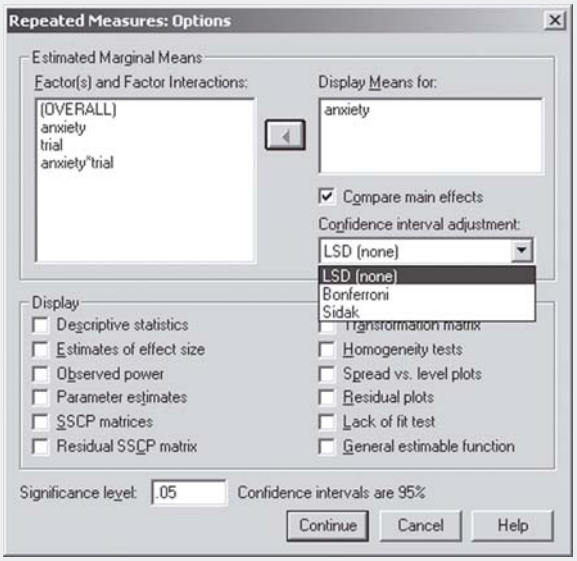
Based on estimated marginal means.

[a] Adjustment for multiple comparisons: Least Significant Difference (equivalent to no adjustments).

To obtain the descriptive statistics for each group (Table IIb) and the pairwise comparisons (Table IIc), click on Options in Template IV to obtain Template V.

To choose other methods to adjust the p values for multiple comparisons, in Template IV, click on the Post Hoc folder to get Template VI.

Template V. Options for Comparing Main effects.



Put "anxiety" in the Display Means panel- this will give Table IIb. To get Table IIc, tick the Compare main effects box and choose Bonferroni (using the most conservative technique to adjust the p value for multiple comparisons[4]). The LSD (none) does not adjust the p value for the multiple comparisons. For anxiety, the result is the same as the Between-Subject effect as there are only two groups. Table IId shows an example if there were three groups.

Template VI. Other Post Hoc options.

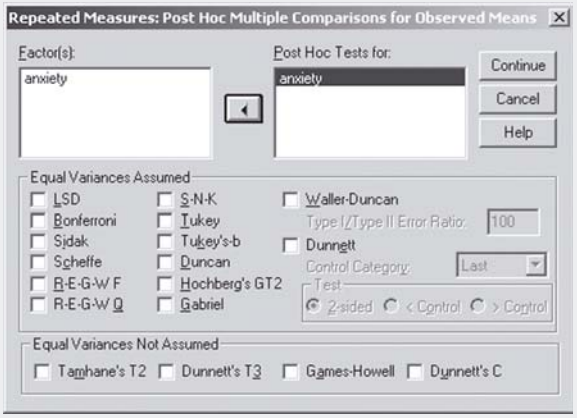


Fig. 1. Graphical plot for repeated measurement analysis

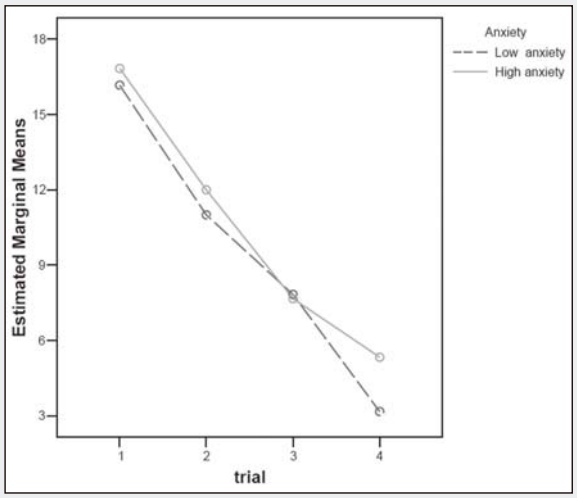


Table IId. Pairwise comparisons for more than two groups.

Pairwise comparisons

Measure: MEASURE_1

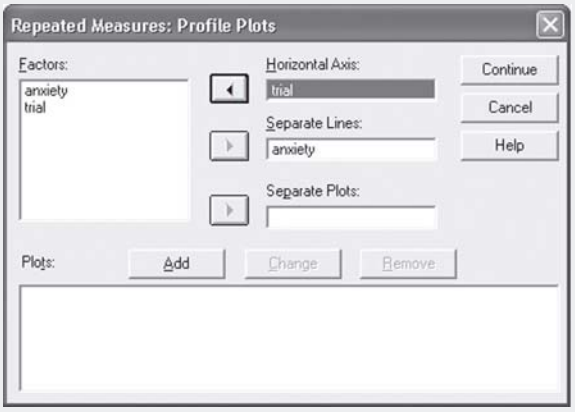
					95% Confidence interval for Difference[a]	
(I) Anxiety	(J) Anxiety	Mean difference (I-J)	Std. error	Sig.[a]	Lower bound	Upper bound
Low	Low					
	Mild	2.250	1.149	.246	-1.122	5.622
	High	-.937	1.149	1.000	-4.309	2.434
Mild	Low	-2.250	1.149	.246	-5.622	1.122
	Mild					
	High	-3.187	1.149	.065	-6.559	.184
High	Low	.937	1.149	1.000	-2.434	4.309
	Mild	3.187	1.149	.065	-.184	6.559
	High					

Based on estimated marginal means.

[a] Adjustment for multiple comparisons: Bonferroni.

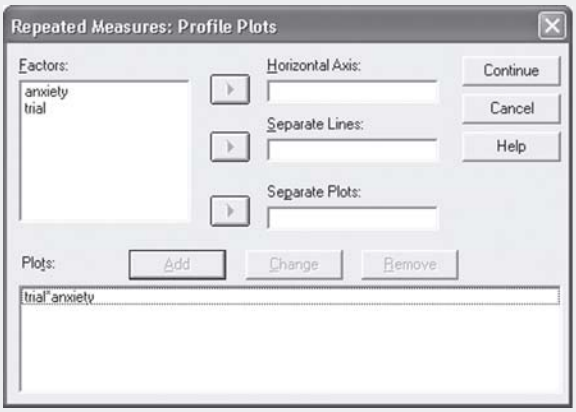
To get a helpful graphical plot (Fig. 1), click on the Plots folder in Template IV to get Template VII.

Template VII. Plot options.



Put "trial" in the Horizontal Axis and "anxiety" in the Separate Lines – the Add button becomes visible, click on it to get Template VIII.

Template VIII. Requesting for plots.



Click Continue and then click on OK in Template IV to run the analysis.

2. WITHIN SUBJECTS ANALYSIS

Table IIIa (obtained by ticking the Descriptive statistics box in Template V) shows the mean number of errors made over time by the anxiety groups.

Table IIIa. Descriptive statistics of trial by anxiety.

Descriptive statistics

	Anxiety	Mean	Std. deviation	N
Trial 1	Low anxiety	16.17	2.714	6
	High anxiety	16.83	1.329	6
	Total	16.50	2.067	12
Trial 2	Low anxiety	11.00	2.098	6
	High anxiety	12.00	2.828	6
	Total	11.50	2.431	12
Trial 3	Low anxiety	7.83	2.714	6
	High anxiety	7.67	2.338	6
	Total	7.75	2.417	12
Trial 4	Low anxiety	3.17	1.835	6
	High anxiety	5.33	3.445	6
	Total	4.25	2.864	12

Both anxiety groups do display a reduction in the number of errors over time, as observed from Fig. 1. Is this reduction trend significant for both groups or just for one group?

Repeated measurement analysis give us 2 "approaches" to analyse the Within-Subjects effect: **Univariate** and **Multivariate** (both approaches give the same result for the Between-Subject effect).

2.1 The **Univariate** approach needs the Within-Subjects variance-covariance to have a Type H structure (or circular in form – correlation between any two levels of Within-Subjects factor has the same constant value). This assumption is checked using the Mauchly's Sphericity test (Table IIIb).

Table IIIb. Sphericity test.

Mauchly's test of Sphericity[b]

Measure: MEASURE_1

					Epsilon[a]		
Within-Subjects Effect	Mauchly's W	Approx. Chi-Square	df	Sig.	Greenhouse-Geisser	Huynh-Feldt	Lower-bound
Trial	.283	11.011	5	.053	.544	.701	.333

Tests the null hypothesis that the error covariance matrix of the orthonormalised transformed dependent variables is proportional to an identity matrix.

[a] May be used to adjust the degrees of freedom for the averaged tests of significance. Corrected tests are displayed in the Tests of Within-Subjects Effects table.

[b] Design: Intercept + anxiety
Within Subjects Design: trial

Table IIIc. Univariate test of Within-Subjects effects.

Tests of Within-Subjects effects

Measure: MEASURE_1

Source		Type III sum of squares	df	Mean square	F	Sig.
Trial	Sphericity Assumed	991.500	3	330.500	128.627	.000
	Greenhouse-Geisser	991.500	1.632	607.468	128.627	.000
	Huynh-Feldt	991.500	2.102	471.773	128.627	.000
	Lower-bound	991.500	1.000	991.500	128.627	.000
Trial * anxiety	Sphericity Assumed	8.417	3	2.806	1.092	.368
	Greenhouse-Geisser	8.417	1.632	5.157	1.092	.346
	Huynh-Feldt	8.417	2.102	4.005	1.092	.357
	Lower-bound	8.417	1.000	8.417	1.092	.321
Error (trial)	Sphericity Assumed	77.083	30	2.569		
	Greenhouse-Geisser	77.083	16.322	4.723		
	Huynh-Feldt	77.083	21.016	3.668		
	Lower-bound	77.083	10.000	7.708		

We want the Sig to be >0.05 for the assumption of sphericity to be valid. If Sig <0.05, we can use the adjusted p values given by Greenhouse-Geisser, Huynh-Feldt or Lower-bound.

Table IIIc shows that there is a reduction of errors committed over trials ($p<0.001$ given by the Sig value of the Source = trial with sphericity assumed).

The Sig of source = trial*anxiety with sphericity assumed is 0.368 which means that there is no time*group interaction, i.e. both low and high anxiety groups had a reduction in the number of errors made over trials.

2.2 The **Multivariate** approach assumes that the correlation for each level of Within-Subjects factor is different and the vector of the dependent variables follows a multivariate normal distribution with the variance-covariance matrices being equal across the cells formed by the Between-subject effects. This homogeneity of the Between-Subjects variance-covariance is checked by using Box's M test (Table IIId); obtained by ticking the Homogeneity test box in Template V.

Table IIId. Box's M test.

Box's test of equality of Covariance Matrices[a]	
Box's M	21.146
F	1.161
df1	10
df2	478.088
Sig.	.315

Tests the null hypothesis that the observed covariance matrices of the dependent variables are equal across groups.

[a] Design: Intercept + anxiety
Within-Subjects design: trial

The p value for the Box's test is 0.315 (we want $p>0.05$), implying that the homogeneity assumption holds.

Table IIIe. Multivariate test of Within-Subjects effects.

Multivariate tests[b]

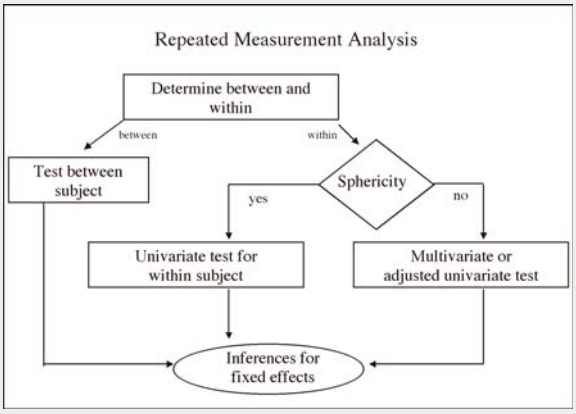
Effect		Value	F	Hypothesis df	Error df	Sig.
Trial	Pillai's Trace	.961	64.854[a]	3.000	8.000	.000
	Wilk's Lambda	.039	64.854[a]	3.000	8.000	.000
	Hotelling's Trace	24.320	64.854[a]	3.000	8.000	.000
	Roy's Largest Root	24.320	64.854[a]	3.000	8.000	.000
Trial * anxiety	Pillai's Trace	.479	2.451[a]	3.000	8.000	.138
	Wilk's Lambda	.521	2.451[a]	3.000	8.000	.138
	Hotelling's Trace	.919	2.451[a]	3.000	8.000	.138
	Roy's Largest Root	.919	2.451[a]	3.000	8.000	.138

[a] Exact statistic
[b] Design: Intercept + anxiety
Within-Subjects design: trial

Table IIIe shows the Within-Subjects analysis from the Multivariate procedure. Once again, there is a time trend effect ($p<0.001$) with no time*group interaction effects ($p=0.138$). Most of the time the results from Pillai's Trace, Wilks' Lambda, Hotelling's Trace and Roy's Largest Root should be the similar. In the event when the results are different, Wilks' Lambda should be chosen.

Now both assumptions for Univariate and Multivariate procedures were valid. Which procedure should we use? Figure II gives the flowchart for the decision. Check the Sphericity assumption first- if satisfied, use the results from the Univariate procedure. Otherwise, proceed with the adjusted Univariate or Multivariate tests.

Fig. 2 Flow chart for Repeated Measurement Analysis.



PAIRWISE COMPARISONS FOR WITHIN-SUBJECTS EFFECTS.

In Template V, put the variable "trial" in the Display Means panel with the Compare factor ticked using Bonferroni. Tables IVa and IVb will be obtained.

Table IVa. Descriptive statistics by trial.

Estimates

Measure: MEASURE_1

			95% Confidence interval	
Trial	Mean	Std. error	Lower bound	Upper bound
1	16.500	.617	15.125	17.875
2	11.500	.719	9.898	13.102
3	7.750	.731	6.121	9.379
4	4.250	.797	2.475	6.025

Table IVb shows all the pairwise comparisons between all time points which may not "make sense" for comparing trial 1 and trial 3. The interest here would be comparing adjacent timings as shown in Table IVc.

Table IVb Pairwise comparisons by trial.

Pairwise comparisons

Measure: MEASURE_1

					95% Confidence interval for difference[a]	
(I) Trial	(J) Trial	Mean difference (I-J)	Std. error	Sig.[a]	Lower bound	Upper bound
1	2	5.000*	.693	.000	3.455	6.545
	3	8.750*	.827	.000	6.906	10.594
	4	12.250*	.920	.000	10.201	14.299
2	1	-5.000*	.693	.000	-6.545	-3.455
	3	3.750*	.410	.000	2.837	4.663
	4	7.250*	.484	.000	6.171	8.329
3	1	-8.750*	.827	.000	-10.594	-6.906
	2	-3.750*	.410	.000	-4.663	-2.837
	4	3.500*	.394	.000	2.621	4.379
4	1	-12.250*	.920	.000	-14.299	-10.201
	2	-7.250*	.484	.000	-8.329	-6.171
	3	-3.500*	.394	.000	-4.379	-2.621

Based on estimated marginal means.

* The mean difference is significant at the .50 level.

[a] Adjustment for multiple comparisons: least significant difference (equivalent to no adjustments).

Table IVc. Pairwise comparison between adjacent trials.

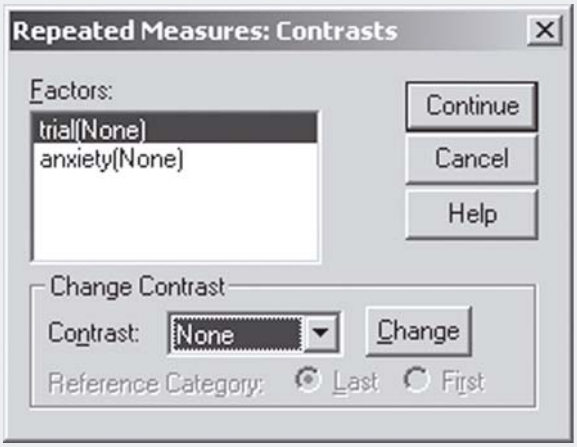
Tests of Within-Subjects effects

Measure: MEASURE_1

Source	Trial	Type III sum of squares	df	Mean square	F	Sig.
Trial	Level 1 vs. level 2	300.00	1	300.00	52.023	.000
	Level 2 vs. level 3	168.750	1	168.750	83.678	.000
	Level 3 vs. level 4	147.000	1	147.000	78.750	.000
Trial * anxiety	Level 1 vs. level 2	.333	1	.333	.058	.815
	Level 2 vs. level 3	4.083	1	4.083	2.025	.185
	Level 3 vs. level 4	16.333	1	16.333	8.750	.014
Error (trial)	Level 1 vs. level 2	57.667	10	5.767		
	Level 2 vs. level 3	20.167	10	2.017		
	Level 3 vs. level 4	18.667	10	1.867		

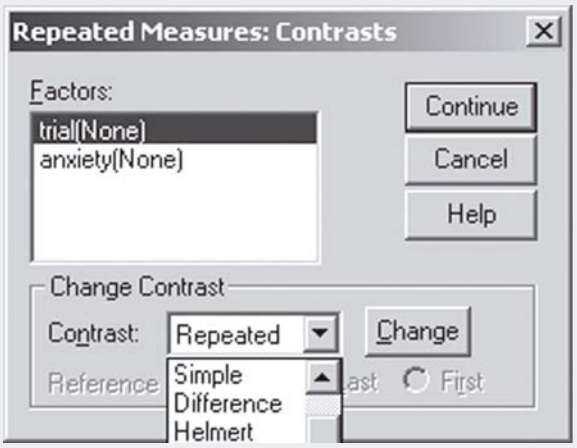
This table is obtained by clicking on the Contrast folder in Template IV to get Template IX.

Template IX. Contrast options.



The available options in the Contrast panel are: Deviation, Simple, Difference, Helmert, Repeated and Polynomial. Table IVc is obtained using the Repeated option (see Template X) and click Change. From Table IVc, we see that there is a reduction in the number of errors made between trials 1 and 2, trials 2 and 3 for both low and high anxiety groups but the significant reduction between trials 3 and 4 was only significant for the low anxiety group as shown by the interaction time*anxiety effect (level 3 vs level 4; p=0.014). This interpretation for the interaction has to be derived by looking at the slopes between trial 3 and trial 4 in Fig. 1.

Template X. Repeated Contrast.



Tables Va – Ve display the output for the other contrast options:

Table Va. Deviation Contrast.

Tests of Within-Subjects effects

Measure: MEASURE_1

Source	Trial	Type III sum of squares	df	Mean square	F	Sig.
Trial	Level 1 vs. mean	507.000	1	507.000	123.470	.000
	Level 2 vs. mean	27.000	1	27.000	37.349	.000
	Level 3 vs. mean	60.750	1	60.750	55.332	.000
Trial * anxiety	Level 1 vs. mean	.188	1	.188	.046	.835
	Level 2 vs. mean	.021	1	.021	.029	.869
	Level 3 vs. mean	3.521	1	3.521	3.207	.104
Error (trial)	Level 1 vs. mean	41.063	10	4.106		
	Level 2 vs. mean	7.229	10	.723		
	Level 3 vs. mean	10.979	10	1.098		

The comparison is with the overall mean of all trials. Observe that level 4 (by default) is not included in the analysis. To include level 4, we have to omit one of the levels 1 to 3. Say let us omit level 2, we have to specify in syntax Deviation (2) as shown:

```
GLM
  trial1 trial2 trial3 trial4 BY anxiety
  /WSFACTOR = trial 4 Deviation(2)
  /METHOD = SSTYPE(3)
  /EMMEANS = TABLES(anxiety) COMPARE ADJ(LSD)
  /CRITERIA = ALPHA(.05)
  /WSDESIGN = trial
  /DESIGN = anxiety
```

Table Vb. Simple Contrast.

Tests of Within-Subjects effects

Measure: MEASURE_1

Source	Trial	Type III sum of squares	df	Mean square	F	Sig.
Trial	Level 1 vs. level 4	1800.750	1	1800.750	177.414	.000
	Level 2 vs. level 4	630.750	1	630.750	223.935	.000
	Level 3 vs. level 4	147.000	1	147.000	78.750	.000
Trial * anxiety	Level 1 vs. level 4	6.750	1	6.750	.665	.434
	Level 2 vs. level 4	4.083	1	4.083	1.450	.256
	Level 3 vs. level 4	16.333	1	16.333	8.750	.014
Error (trial)	Level 1 vs. level 4	101.500	10	10.150		
	Level 2 vs. level 4	28.167	10	2.817		
	Level 3 vs. level 4	18.667	10	1.867		

The comparison is with the last level, which in this case is trial 4. To use level 2 as the reference, have to specify in syntax Simple(2).

Table Vc. Difference Contrast.

Tests of Within-Subjects effects

Measure: MEASURE_1

Source	Trial	Type III sum of squares	df	Mean square	F	Sig.
Trial	Level 2 vs. level 1	300.000	1	300.00	52.023	.000
	Level 3 vs. previous	468.750	1	468.750	127.551	.000
	Level 4 vs. previous	705.333	1	705.333	222.737	.000
Trial * anxiety	Level 2 vs. level 1	.333	1	.333	.058	.815
	Level 3 vs. previous	3.000	1	3.000	.816	.388
	Level 4 vs. previous	8.333	1	8.333	2.632	.136
Error (trial)	Level 2 vs. level 1	57.667	10	5.767		
	Level 3 vs. previous	36.750	10	3.675		
	Level 4 vs. previous	31.667	10	3.167		

Compare with the mean of previous levels, i.e.: level 3 vs previous (= mean of levels 1 and 2); level 4 vs previous (= mean of levels 1, 2 and 3)

Table Vd. Helmert Contrast (The reverse of Difference contrasts).

Tests of Within-Subjects effects

Measure: MEASURE_1

Source	Trial	Type III sum of squares	df	Mean square	F	Sig.
Trial	Level 1 vs. later	901.333	1	901.333	123.470	.000
	Level 2 vs. later	363.000	1	363.000	186.154	.000
	Level 3 vs. level 4	147.000	1	147.000	78.750	.000
Trial * anxiety	Level 1 vs. later	.333	1	.333	.046	.835
	Level 2 vs. later	.000	1	.000	.000	1.000
	Level 3 vs. level 4	16.333	1	16.333	8.750	.014
Error (trial)	Level 1 vs. later	73.000	10	7.300		
	Level 2 vs. later	19.500	10	1.950		
	Level 3 vs. level 4	18.667	10	1.867		

Compare with the mean of later levels, i.e: level 1 vs later (= mean of levels 2, 3 and 4); level 2 vs later (= mean of levels 3 and 4)

Table Ve. Polynomial Contrast.

Tests of Within-Subjects effects

Measure: MEASURE_1

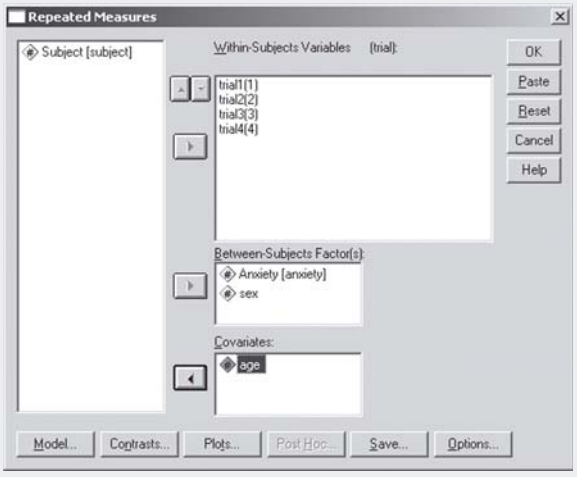
Source	Trial	Type III sum of squares	df	Mean square	F	Sig.
Trial	Linear	984.150	1	984.150	190.051	.000
	Quadratic	6.750	1	6.750	4.154	.069
	Cubic	.600	1	.600	.663	.434
Trial * anxiety	Linear	1.667	1	1.667	.322	.583
	Quadratic	3.000	1	3.000	1.846	.204
	Cubic	3.750	1	3.750	4.144	.069
Error (trial)	Linear	51.783	10	5.178		
	Quadratic	16.250	10	1.625		
	Cubic	9.050	10	.905		

The polynomial contrast looks at the "pattern" of the data rather than comparing mean differences. Since there are 4 trials, the order of the pattern is up to cubic (number of repeated measurements – 1). Linear ($p<0.001$) shows that there is a straight line trend and from the above table, both Low and High anxiety groups display this trend as the interaction (trial*anxiety) is not significant ($p=0.583$). There is no Quadratic (V shape) and no Cubic (Z shape) pattern – seen from Fig. 1.

ADJUSTING FOR COVARIATES

To adjust for covariates, for example age and sex, in a repeated measurement analysis, put "sex" in the Between-Subjects panel and "age" in the Covariates panel. Any variable that is categorical has to be in the Between-Subjects panel and all continuous variables have to be in the Covariates panel.

Template XI. Adjusting for covariates



Tables VIa and VIb display the Between-Subjects and Within-Subjects effects, respectively.

Table VIa. Between-Subjects effect with covariates.

Tests of Within-Subjects effects

Measure: MEASURE_1
Transformed variable: average

Source	Type III sum of squares	df	Mean square	F	Sig.
Intercept	105.062	1	105.062	7.583	.028
Age	30.083	1	30.083	2.171	.184
Anxiety	50.320	1	50.320	3.632	.098
Sex	61.023	1	61.023	4.405	.074
Anxiety * sex	10.642	1	10.642	.768	.410
Error	96.979	7	13.854		

Table VIb. Within-Subjects effects with covariates (Univariate procedure).

Tests of Within-Subjects effects

Measure: MEASURE_1

Source		Type III sum of squares	df	Mean square	F	Sig.
Trial	Sphericity Assumed	11.048	3	3.683	2.038	.139
	Greenhouse-Geisser	11.048	1.591	6.943	2.038	.180
	Huynh-Feldt	11.048	3.000	3.683	2.038	.139
	Lower-bound	11.048	1.000	11.048	2.038	.196
Trial * age	Sphericity Assumed	28.250	3	9.417	5.213	.008
	Greenhouse-Geisser	28.250	1.591	17.753	5.213	.031
	Huynh-Feldt	28.250	3.000	9.417	5.213	.008
	Lower-bound	28.250	1.000	28.250	5.213	.056
Trial * anxiety	Sphericity Assumed	28.294	3	9.431	5.221	.008
	Greenhouse-Geisser	28.294	1.591	17.780	5.221	.031
	Huynh-Feldt	28.294	3.000	9.431	5.221	.008
	Lower-bound	28.294	1.000	28.294	5.221	.056
Trial * sex	Sphericity Assumed	23.844	3	7.948	4.400	.015
	Greenhouse-Geisser	23.844	1.591	14.984	4.400	.046
	Huynh-Feldt	23.844	3.000	7.948	4.400	.015
	Lower-bound	23.844	1.000	23.844	4.400	.074
Trial * anxiety * sex	Sphericity Assumed	16.225	3	5.408	2.994	.054
	Greenhouse-Geisser	16.225	1.591	10.196	2.994	.099
	Huynh-Feldt	16.225	3.000	5.408	2.994	.054
	Lower-bound	16.225	1.000	16.225	2.994	.127
Error (trial)	Sphericity Assumed	37.938	21	1.807		
	Greenhouse-Geisser	37.938	11.139	3.406		
	Huynh-Feldt	37.938	21.000	1.807		
	Lower-bound	37.938	7.000	5.420		

The results obtained in Tables VIa and VIb were from a full-factorial model; the default is that all n-way interaction terms will be produced for all the categorical variables- see Table VIc (with race included).

We can custom the model by clicking on the Model folder in Template IV to get Template XII.

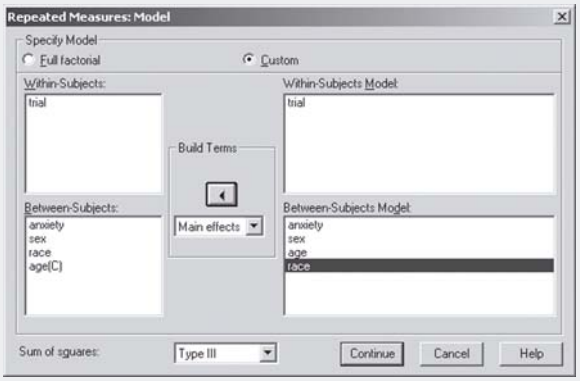
Table VIc. Full Factorial model (Between-Subjects effects).

Tests of Within-Subjects effects

Measure: MEASURE_1
Transformed variable: average

Source	Type III sum of squares	df	Mean square	F	Sig.
Intercept	72.155	1	72.155	3.883	.143
Age	21.125	1	21.125	1.137	.365
Anxiety	37.038	1	37.038	1.993	.253
Sex	46.107	1	46.107	2.481	.213
Race	24.038	1	24.038	1.294	.338
Anxiety * sex	8.393	1	8.393	.452	.550
Anxiety * race	3.846	1	3.846	.207	.680
Sex * race	5.538	1	5.538	.298	.623
Anxiety * sex * race	16.962	1	16.962	.913	.410
Error	55.750	3	18.583		

Template XII . Customing the Model with covariates.



Click on the Custom button. Put "trial" in the Within-Subjects Model panel. For the Between-Subjects Model panel, if we do not want the interaction terms between anxiety, race and sex, choose Main effects and put all available variables in that panel. Tables VId and VIe display the Between-Subjects and Within-Subjects effects, respectively.

Table VId. Between-Subjects effects: Custom model.

Tests of Within-Subjects effects

Measure: MEASURE_1
Transformed variable: average

Source	Type III sum of squares	df	Mean square	F	Sig.
Intercept	228.653	1	228.653	16.194	.005
Anxiety	56.744	1	56.744	4.019	.085
Sex	67.902	1	67.902	4.809	.064
Age	31.735	1	31.735	2.248	.178
Race	8.783	1	8.783	.622	.456
Error	98.838	7	14.120		

Table VIe. Within-Subjects effects: Custom model.

Tests of Within-Subjects effects

Measure: MEASURE_1

Source		Type III sum of squares	df	Mean square	F	Sig.
Trial	Sphericity Assumed	.920	3	.307	.145	.932
	Greenhouse-Geisser	.920	1.452	.634	.145	.801
	Huynh-Feldt	.920	2.781	.331	.145	.921
	Lower-bound	.920	1.000	.920	.145	.715
Trial * anxiety	Sphericity Assumed	12.165	3	4.055	1.912	.159
	Greenhouse-Geisser	12.165	1.452	8.376	1.912	.199
	Huynh-Feldt	12.165	2.781	4.374	1.912	.164
	Lower-bound	12.165	1.000	12.165	1.912	.209
Trial * sex	Sphericity Assumed	6.768	3	2.256	1.064	.385
	Greenhouse-Geisser	6.768	1.452	4.660	1.064	.357
	Huynh-Feldt	6.768	2.781	2.434	1.064	.383
	Lower-bound	6.768	1.000	6.768	1.064	.337
Trial * age	Sphericity Assumed	13.025	3	4.342	2.048	.138
	Greenhouse-Geisser	13.025	1.452	8.968	2.048	.183
	Huynh-Feldt	13.025	2.781	4.684	2.048	.144
	Lower-bound	13.025	1.000	13.025	2.048	.196
Trial * race	Sphericity Assumed	9.635	3	3.212	1.515	.240
	Greenhouse-Geisser	9.635	1.452	6.634	1.515	.259
	Huynh-Feldt	9.635	2.781	3.465	1.515	.243
	Lower-bound	9.635	1.000	9.635	1.515	.258
Error (trial)	Sphericity Assumed	44.527	21	2.120		
	Greenhouse-Geisser	44.527	10.166	4.380		
	Huynh-Feldt	44.527	19.466	2.287		
	Lower-bound	44.527	7.000	6.361		

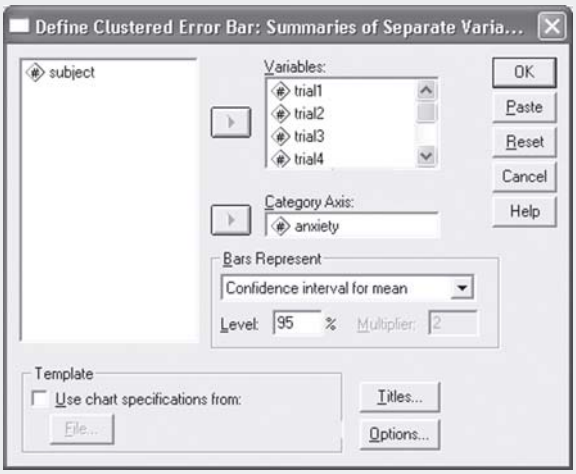
ERROR BARS PLOT

Usually, we would want to present the variation on the graphical plots, that is, to include the 95% CI in Fig. 1. With the given data structure as shown in Table I and in SPSS, we use Graphs, Error Bar to get Template XIII.

Template XIII. Error bar definition.

Choose the Clustered option and tick on Summaries of separate variables, click Define to get Template XIV.

Template XIV. Setting up the Error bar plot.



Put "trial1" to "trial4" in the variables panel and "anxiety" in the category axis panel, click OK to get Fig. 3.

Fig. 3 Error bar plot by anxiety then by trial.

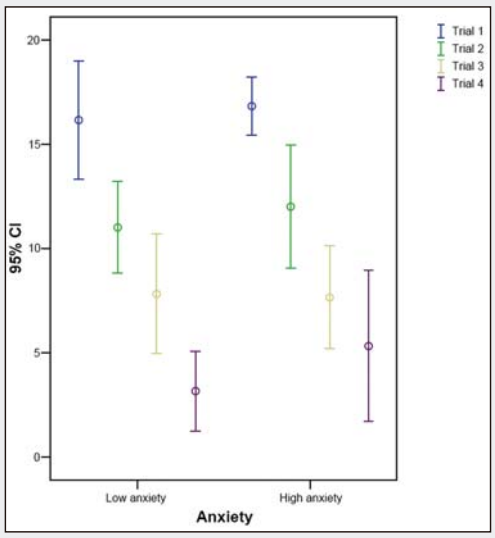
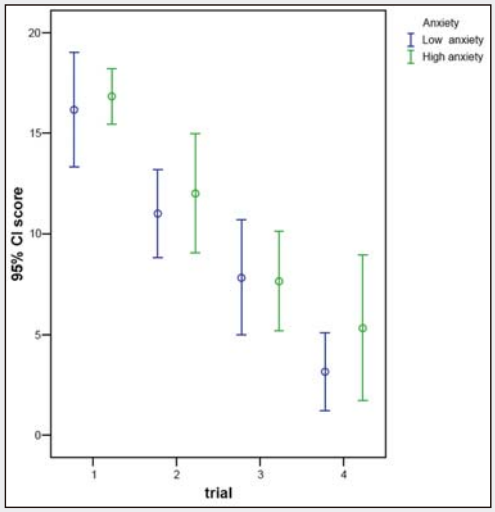


Fig. 3 shows the error bars for each trial by anxiety group – not a very useful presentation. Fig. 4 shows a more appropriate presentation.

Fig. 4 Error bar by trial then by anxiety.



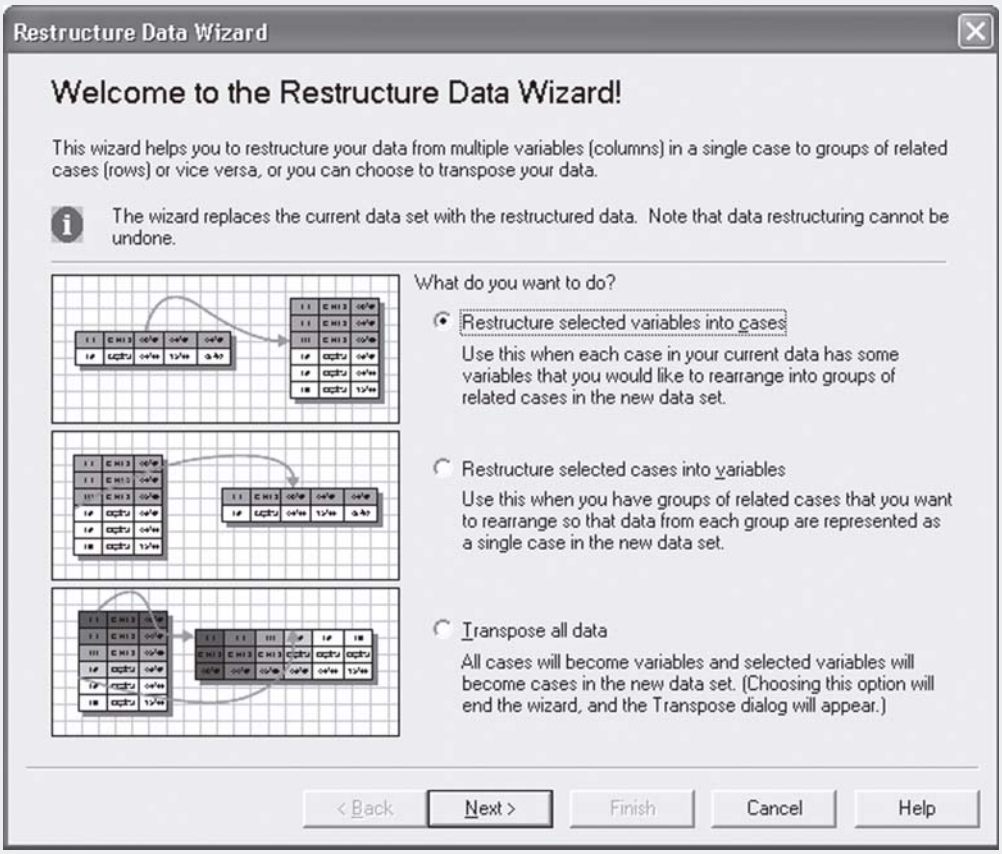
To get Fig. 4, we have to organise the data structure in a "relational form" as shown in Table VII.

Table VII. Relational form of data structure.

Subject	Anxiety	Trial	Score
1	Low	1	18
1	Low	2	14
1	Low	3	12
1	Low	4	6
2	Low	1	19
2	Low	2	12
2	Low	3	8
2	Low	4	4
Etc			

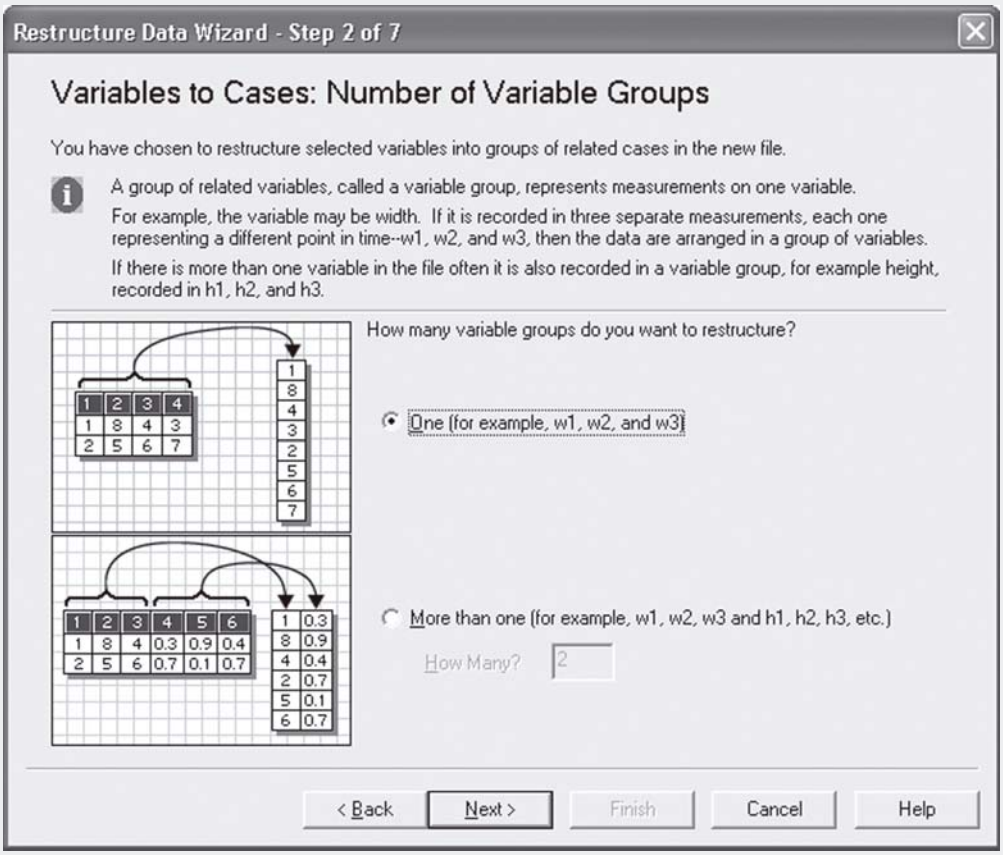
To convert the longitudinal dataset (Table I) to the relational form (Table VII), in SPSS, go to ***Data, Restructure*** to get Template XV.

Template XV. Data Restructuring.



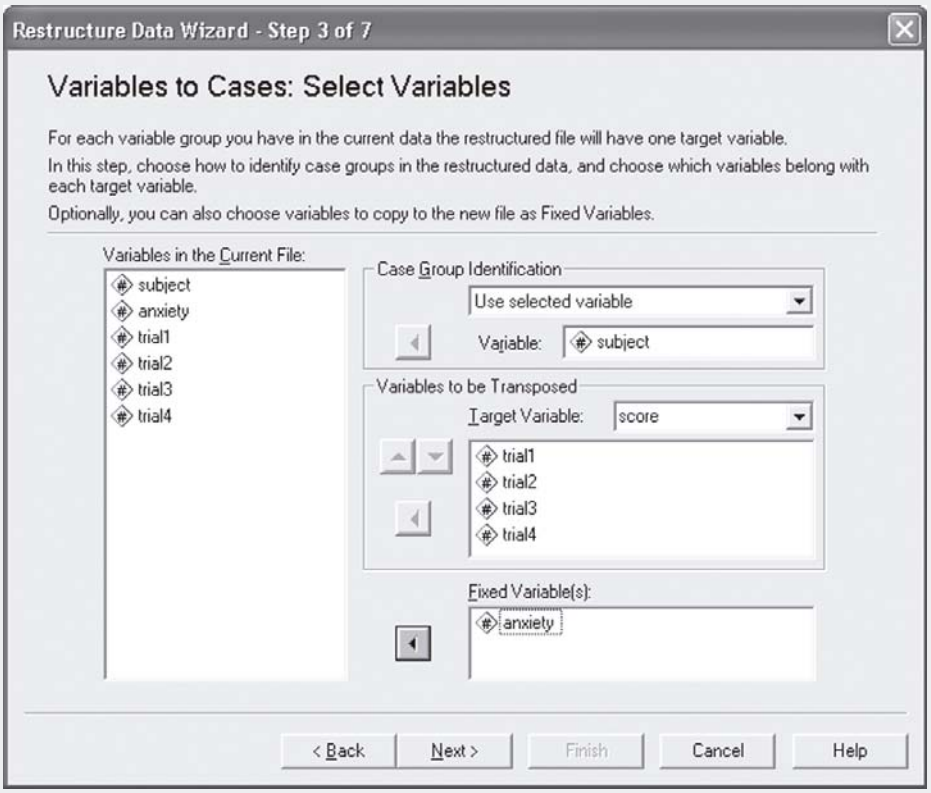
We want to restructure the variables into cases- click Next for Template XVI.

Template XVI. Defining the number of variables.



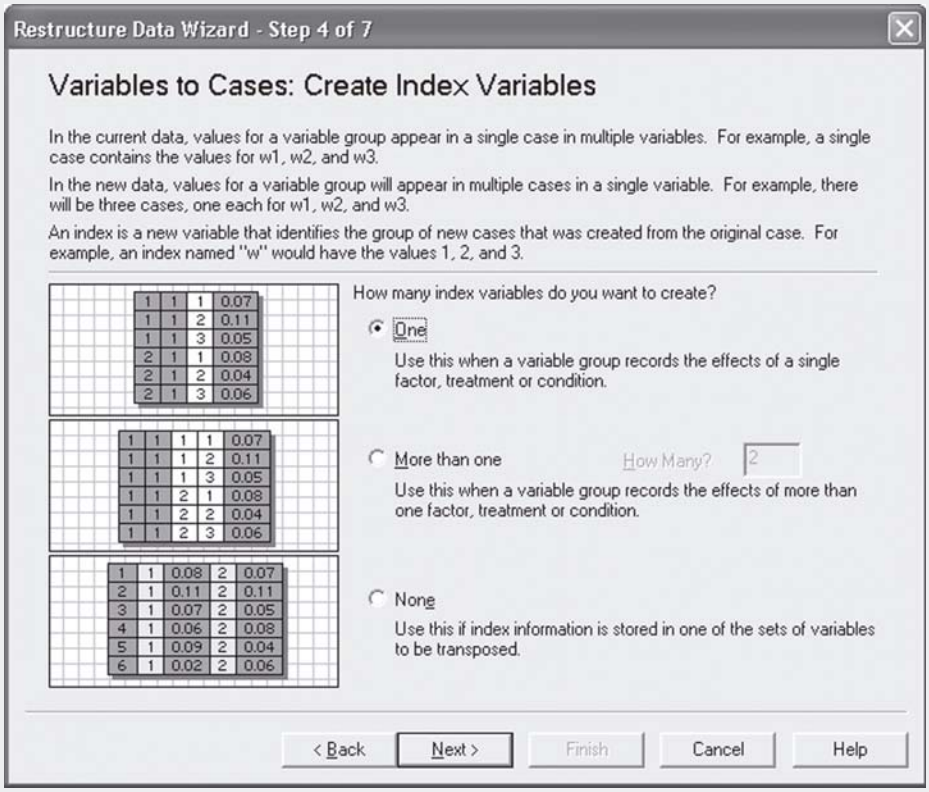
We have only 1 variable group (Trial) to restructure, click on Next for Template XVII

Template XVII. Defining the variables to be transposed.



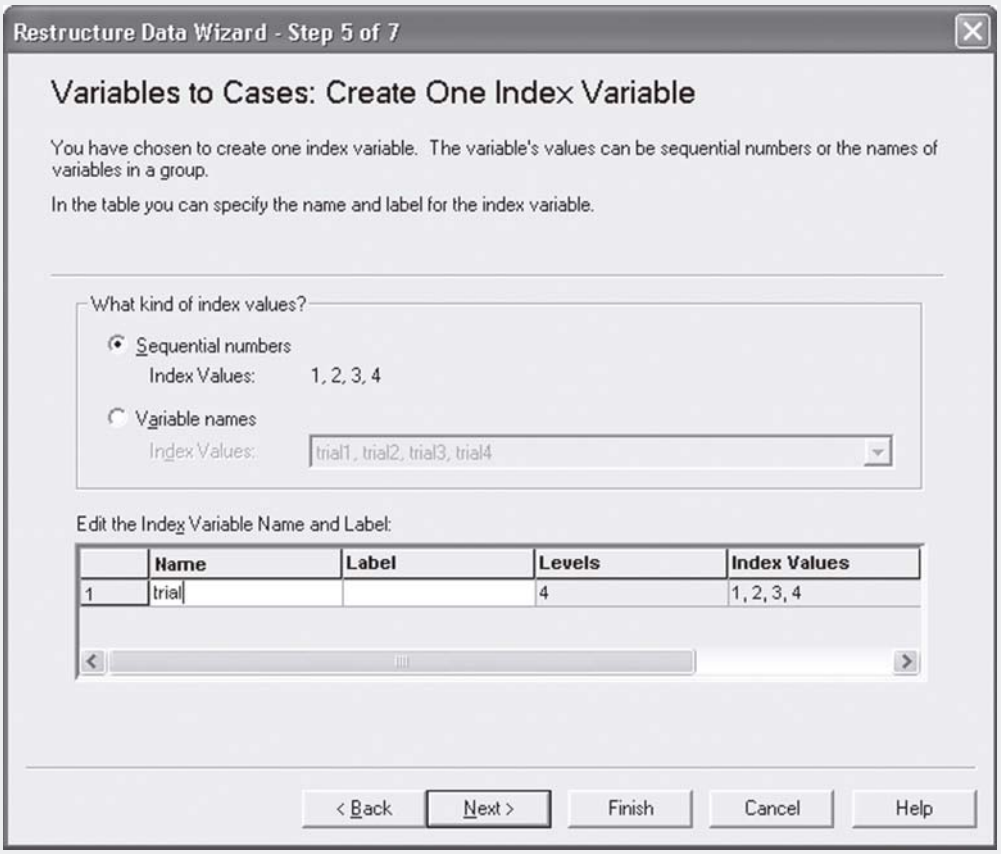
For Case Group Identification, choose the Use selected variable option and put "subject" into the Variable panel. Type in "score" (or any appropriate name) for Target Variable and put "trial1" to "trial4" into the Variables to be Transposed panel. Put "anxiety" in the Fixed Variable panel. Click Next (Template XVIII).

Template XVIII. Defining the number of index variables.



One index variable will do as we have only 1 score (trial), click Next (Template XVIX)

Template XVIX. Naming the index variable.



Key in "trial" for the Name panel and click Finish. Data will be restructured- save new datafile.

The above results for the repeated measurement analysis were generated using the **GLM (General Linear Model)** technique which has the disadvantage of "losing subjects" whenever there is a missing value in any of the time points. Table VIII shows that subjects 2 and 3 will be "lost to analysis".

Table VIII. Data with missing values.

Subject	Time 1	Time 2	Time 3
1	xxxx	xxxx	xxxx
2	xxxx	missing	xxxx
3	xxxx	xxxx	missing

Another constraint with the GLM method is the availability to model the variance-covariance structure (only have Univariate and Multivariate) and what happens when both assumptions are not valid? Our next article, "Biostatistics 301a. Repeated measurement analysis (mixed models)", will discuss how to handle missing data points and to model other variance-covariance structures.

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1. Matthews JNS, Altman DG, Campbell MJ, Royston P. Analysis of serial measurements in medical research. Br Med J 1990; 300:230-5.
2. Frison L, Pocock SJ. Repeated measures in clinical trials: analysis using mean summary statistics and its implications for design. Statistics Med 1992; 11:1685-704.
3. Matthews JNS. A refinement to the analysis of serial data using summary measures. Statistics Med 1993; 12:27-37.
4. Chan YH. Biostatistics 102. Quantitative data – parametric and non-parametric tests. Singapore Med J 2003; 44:391-6.

SINGAPORE MEDICAL COUNCIL CATEGORY 3B CME PROGRAMME

Multiple Choice Questions (Code SMJ 200408A)

	True	False
Question 1. To apply the results from the Univariate procedure of repeated measurement analysis:		
(a) Both Sphericity and Box's M assumptions must be satisfied.	❑	❑
(b) Only Sphericity will do.	❑	❑
(c) Only Box's M will do.	❑	❑
(d) Either one will do.	❑	❑
Question 2. Given that both the Sphericity and Box's M assumptions were not satisfied, we can use the results from:		
(a) Multivariate procedure.	❑	❑
(b) Univariate procedure.	❑	❑
(c) Adjusted Univariate procedure.	❑	❑
(d) None of the above.	❑	❑
Question 3. The GLM technique has the following disadvantages:		
(a) Subjects lost due to incomplete repeated measurements data.	❑	❑
(b) Cannot handle adjustment for covariates.	❑	❑
(c) Do not allow the capability for user to define own model.	❑	❑
(d) Limited choices of variance-covariance structures.	❑	❑
Question 4. The following statements are true:		
(a) The polynomial contrast is used to compare the pattern trends between Groups.	❑	❑
(b) The Pillai's Trace is the statistics to use in the Multivariate Within-Subjects effect.	❑	❑
(c) The Plot option allows us to create error bar plots.	❑	❑
(d) The Univariate procedure gives better results than the Multivariate procedure.	❑	❑
Question 5. Repeated measurement analysis can be applied for the following designs:		
(a) Subjects randomised to one of three antihypertensive drugs to assess the BP change from baseline.	❑	❑
(b) The distance shot-putted by each subject with 3 different fixed weights.	❑	❑
(c) The visual field loss in both eyes of each subject over 6 monthly assessments.	❑	❑
(d) Measurements of itch intensity on both hands and legs of each subject.	❑	❑

Doctor's particulars:

Name in full: _____

MCR number: _____ Specialty: _____

Email address: _____

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3. Passing mark is 60%. No mark will be deducted for incorrect answers.
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