Subjects are measured at every level of a factor. For example, every subject gets all possible treatments. Previously, every subject received only one treatment. We’ll make this clear in the following.

Ex1. One-Factor Repeated Experiment
--------------------------------------
Have 2 factors: SUBJECT and DRUG.

Each subject is given all 4 treatments 1, 2, 3, 4 for pain relief. Then the subject’s pain tolerance is measured. Enough time is allowed to pass between treatments to prevent residual effects, and thus guarantee independence between measurements.

<table>
<thead>
<tr>
<th>Subject</th>
<th>Drug1</th>
<th>Drug2</th>
<th>Drug3</th>
<th>Drug4</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>5</td>
<td>9</td>
<td>6</td>
<td>11</td>
</tr>
<tr>
<td>2</td>
<td>7</td>
<td>12</td>
<td>8</td>
<td>9</td>
</tr>
<tr>
<td>3</td>
<td>11</td>
<td>12</td>
<td>10</td>
<td>14</td>
</tr>
<tr>
<td>4</td>
<td>3</td>
<td>8</td>
<td>5</td>
<td>8</td>
</tr>
</tbody>
</table>

DATA PAIN;
INPUT SUBJECT DRUG PAIN;
1 1 5
1 2 9
1 3 6
1 4 11
2 1 7
2 2 12
2 3 8
ETC.
Better way to read the data using a do loop.

```
OPTION PS=35 LS=70;

DATA PAIN;
  INPUT SUBJ @;
  DO DRUG=1 TO 4;
    INPUT PAIN @;
    OUTPUT;
  END;
DATALINES;
  1 5 9 6 11
  2 7 12 8 9
  3 11 12 10 14
  4 3 8 5 8
;

PROC PRINT DATA=PAIN;
RUN;
```

<table>
<thead>
<tr>
<th>Obs</th>
<th>SUBJ</th>
<th>DRUG</th>
<th>PAIN</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1</td>
<td>1</td>
<td>5</td>
</tr>
<tr>
<td>2</td>
<td>1</td>
<td>2</td>
<td>9</td>
</tr>
<tr>
<td>3</td>
<td>1</td>
<td>3</td>
<td>6</td>
</tr>
<tr>
<td>4</td>
<td>1</td>
<td>4</td>
<td>11</td>
</tr>
<tr>
<td>5</td>
<td>2</td>
<td>1</td>
<td>7</td>
</tr>
<tr>
<td>6</td>
<td>2</td>
<td>2</td>
<td>12</td>
</tr>
<tr>
<td>7</td>
<td>2</td>
<td>3</td>
<td>8</td>
</tr>
<tr>
<td>8</td>
<td>2</td>
<td>4</td>
<td>9</td>
</tr>
<tr>
<td>9</td>
<td>3</td>
<td>1</td>
<td>11</td>
</tr>
<tr>
<td>10</td>
<td>3</td>
<td>2</td>
<td>12</td>
</tr>
<tr>
<td>11</td>
<td>3</td>
<td>3</td>
<td>10</td>
</tr>
<tr>
<td>12</td>
<td>3</td>
<td>4</td>
<td>14</td>
</tr>
<tr>
<td>13</td>
<td>4</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>14</td>
<td>4</td>
<td>2</td>
<td>8</td>
</tr>
<tr>
<td>15</td>
<td>4</td>
<td>3</td>
<td>5</td>
</tr>
<tr>
<td>16</td>
<td>4</td>
<td>4</td>
<td>8</td>
</tr>
</tbody>
</table>

2
Now do 2-way ANOVA with 1 obs/cell (i.e. no interaction).

\[ y_{ij} = \mu + a_i + b_j + \epsilon_{ij} \]

PROC ANOVA DATA=PAIN;
CLASS SUBJ DRUG;
MODEL PAIN=SUBJ DRUG;
MEANS DRUG/SNK;
RUN;

The ANOVA Procedure

Class Level Information

Class           Levels  Values
SUBJ            4      1 2 3 4
DRUG            4      1 2 3 4

Number of Observations Read       16
Number of Observations Used        16

Dependent Variable: PAIN

\begin{tabular}{lrrrr}
  Source & DF & Sum of Squares & Mean Square & F Value
  \hline
  Model   & 6  & 120.5000000 & 20.0833333 & 13.64
  Error   & 9  & 13.2500000  & 1.4722222  &
  Corrected Total & 15 & 133.7500000 &            &
\end{tabular}

Source       Pr > F
Model         0.0005
Error         
Corrected Total

R-Square   Coeff Var  Root MSE   PAIN Mean
0.900935    14.06785  1.213352  8.625000

3
<table>
<thead>
<tr>
<th>Source</th>
<th>DF</th>
<th>Anova SS</th>
<th>Mean Square</th>
<th>F Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>SUBJ</td>
<td>3</td>
<td>70.25000000</td>
<td>23.41666667</td>
<td>15.91</td>
</tr>
<tr>
<td>DRUG</td>
<td>3</td>
<td>50.25000000</td>
<td>16.75000000</td>
<td>11.38</td>
</tr>
</tbody>
</table>

Therefore DRUG effects are not all zero: The 4 DRUGS not equally effective in treating pain.

NOTE: Denominator df=9 comes from ERROR df in the first table.

Student-Newman-Keuls Test for PAIN

NOTE: This test controls the Type I experimentwise error rate under the complete null hypothesis but not under partial null hypotheses.

<table>
<thead>
<tr>
<th>Alpha</th>
<th>Error Degrees of Freedom</th>
<th>Error Mean Square</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0.05</td>
<td>9</td>
</tr>
<tr>
<td></td>
<td>1.472222</td>
<td></td>
</tr>
</tbody>
</table>

Number of Means | 2 | 3 | 4
Critical Range  | 1.9407923 | 2.3954582 | 2.6784122

Means with the same letter are not significantly different.
We see that DRUGS 4,2 and 3,1 are "same". Assuming a higher mean indicates greater pain, DRUGS 1,3 more effective in treating pain.

Now: Suppose the data were the results of assigning the 4 drugs at random to 16 subjects, then 1-Way ANOVA gives:

PROC ANOVA DATA=PAIN;
CLASS SUBJ DRUG;
MODEL PAIN=DRUG;
MEANS DRUG/SNK;
RUN;

The ANOVA Procedure

Class Level Information

<table>
<thead>
<tr>
<th>Class</th>
<th>Levels</th>
<th>Values</th>
</tr>
</thead>
<tbody>
<tr>
<td>SUBJ</td>
<td>4</td>
<td>1 2 3 4</td>
</tr>
<tr>
<td>DRUG</td>
<td>4</td>
<td>1 2 3 4</td>
</tr>
</tbody>
</table>

Number of Observations Read 16
Number of Observations Used 16

Dependent Variable: PAIN

<table>
<thead>
<tr>
<th>Source</th>
<th>DF</th>
<th>Sum of Squares</th>
<th>Mean Square</th>
<th>F Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Model</td>
<td>3</td>
<td>50.25000000</td>
<td>16.75000000</td>
<td>2.41</td>
</tr>
<tr>
<td>Error</td>
<td>12</td>
<td>83.50000000</td>
<td>6.95833333</td>
<td></td>
</tr>
<tr>
<td>Corrected Total</td>
<td>15</td>
<td>133.75000000</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Source        Pr > F
Model         0.1180
Error
Corrected Total
R-Square  Coeff Var  Root MSE  PAIN Mean
0.375701  30.58395  2.637865  8.625000

Source  DF  Anova SS  Mean Square  F Value
DRUG  3  50.25000000  16.75000000  2.41

Source  Pr > F
DRUG  0.1180

Student-Newman-Keuls Test for PAIN

NOTE: This test controls the Type I experimentwise error rate under the complete null hypothesis but not under partial null hypotheses.

Alpha  0.05
Error Degrees of Freedom  12
Error Mean Square  6.958333

Number of Means  2  3  4
Critical Range  4.0640501  4.9760399  5.5375686

Means with the same letter are not significantly different.

SNK Grouping  Mean  N  DRUG
A  10.500  4  4
A
A  10.250  4  2
A
A  7.250  4  3
A
A  6.500  4  1
We see: Before with only 4 subjects, the ERROR SS was only 13.25 with df=9, and the drugs effects were significant. But now with 16 subjects, the ERROR SS absorbed the SUBJ SS 70.25 and is equal to \(13.25 + 70.25 = 83.5\) with df=12, and the drug effects are not significant.

We see: Controlling for between-subject variability reduces the error SS, and allows us to identify small treatment differences with relatively fewer subjects.

Now: use REPEATED option

Data must have the form: SUBJ PAIN1 PAIN2 PAIN3 PAIN4, where PAIN1-PAIN4 are the dependent obs from each drug.  Notice: The reference to the DRUG factor is through its levels.

```
DATA REPEAT1;
INPUT SUBJ PAIN1-PAIN4;
DATALINES;
  1 5 9 6 11
  2 7 12 8 9
  3 11 12 10 14
  4 3 8 5 8
;
PROC PRINT DATA=REPEAT1;
ID SUBJ;
RUN;
```

<table>
<thead>
<tr>
<th>SUBJ</th>
<th>PAIN1</th>
<th>PAIN2</th>
<th>PAIN3</th>
<th>PAIN4</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>5</td>
<td>9</td>
<td>6</td>
<td>11</td>
</tr>
<tr>
<td>2</td>
<td>7</td>
<td>12</td>
<td>8</td>
<td>9</td>
</tr>
<tr>
<td>3</td>
<td>11</td>
<td>12</td>
<td>10</td>
<td>14</td>
</tr>
<tr>
<td>4</td>
<td>3</td>
<td>8</td>
<td>5</td>
<td>8</td>
</tr>
</tbody>
</table>
PROC ANOVA DATA=REPEAT1;
MODEL PAIN1-PAIN4 = /NOUNI;  \(<--No\ univariate\ analysis\ for\ each\ pain\ variable.
REPEATED DRUG 4 (1 2 3 4);  \(<--DRUG\ has\ 4\ levels,\ labeled\ 1,2,3,4
RUN;

The SAS System

The ANOVA Procedure

   Number of Observations Read  4
   Number of Observations Used   4

Repeated Measures Analysis of Variance

Repeated Measures Level Information

<table>
<thead>
<tr>
<th>Dependent Variable</th>
<th>PAIN1</th>
<th>PAIN2</th>
<th>PAIN3</th>
<th>PAIN4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Level of DRUG</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
</tbody>
</table>

MANOVA Test Criteria and Exact F Statistics
for the Hypothesis of no DRUG Effect

\( H = \) Anova SSCP Matrix for DRUG
\( E = \) Error SSCP Matrix

S=1   M=0.5   N=-0.5

<table>
<thead>
<tr>
<th>Statistic</th>
<th>Value</th>
<th>F Value</th>
<th>Num DF</th>
<th>Den DF</th>
<th>Pr &gt; F</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wilks' Lambda</td>
<td>0.00909295</td>
<td>36.33</td>
<td>3</td>
<td>1</td>
<td>0.1212</td>
</tr>
<tr>
<td>Pillai’s Trace</td>
<td>0.99090705</td>
<td>36.33</td>
<td>3</td>
<td>1</td>
<td>0.1212</td>
</tr>
<tr>
<td>Hotelling-Lawley Trace</td>
<td>108.97530864</td>
<td>36.33</td>
<td>3</td>
<td>1</td>
<td>0.1212</td>
</tr>
<tr>
<td>Roy's Greatest Root</td>
<td>108.97530864</td>
<td>36.33</td>
<td>3</td>
<td>1</td>
<td>0.1212</td>
</tr>
</tbody>
</table>
The ANOVA Procedure
Repeated Measures Analysis of Variance
Univariate Tests of Hypotheses for Within Subject Effects

<table>
<thead>
<tr>
<th>Source</th>
<th>DF</th>
<th>Anova SS</th>
<th>Mean Square</th>
<th>F Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>DRUG</td>
<td>3</td>
<td>50.25000000</td>
<td>16.75000000</td>
<td>11.38</td>
</tr>
<tr>
<td>Error(DRUG)</td>
<td>9</td>
<td>13.25000000</td>
<td>1.47222222</td>
<td></td>
</tr>
</tbody>
</table>

Adj Pr > F

<table>
<thead>
<tr>
<th>Source</th>
<th>Pr &gt; F</th>
<th>G - G</th>
<th>H - F</th>
</tr>
</thead>
<tbody>
<tr>
<td>DRUG</td>
<td>0.0020</td>
<td>0.0123</td>
<td>0.0020</td>
</tr>
<tr>
<td>Error(DRUG)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Greenhouse-Geisser Epsilon 0.5998 <--GG-epsilon
Huynh-Feldt Epsilon 1.4433 <--HF-epsilon

Note:
The F test for DRUG is identical to the one from 2-Way ANOVA.

The adjusted p-valued G-G (Greenhouse-Geisser correction) and H-F (Huynh-Feldt correction) take into account correlation among the repeated measures and resort to the so called "sphericity assumption" where numerator and denominator degrees of freedom are multiplied by "epsilon", and the significance of the F ratio is evaluated with the new degrees of freedoms. Greenhouse-Geisser correction is more Conservative.

With REPEATED statement, to get pairwise comparisons use: CONTRAST(n).
In our case
DRUG CONTRAST(1) gives comparisons of 1 vs 2,3,4
DRUG CONTRAST(2) gives comparisons of 2 vs 1,3,4
DRUG CONTRAST(3) gives comparisons of 1 vs 2,3,4
This is equivalent to multiple t-tests.
For example:

```
PROC ANOVA DATA=REPEAT1;
MODEL PAIN1-PAIN4 = /NOUNI;
REPEATED DRUG 4 CONTRAST(1)/NOM SUMMARY; <--No Multivariate stats.
RUN;
```

**The ANOVA Procedure**

```
Number of Observations Read 4
Number of Observations Used 4
```

**The ANOVA Procedure**

Repeated Measures Analysis of Variance

Repeated Measures Level Information

<table>
<thead>
<tr>
<th>Dependent Variable</th>
<th>PAIN1</th>
<th>PAIN2</th>
<th>PAIN3</th>
<th>PAIN4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Level of DRUG</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
</tbody>
</table>

**The ANOVA Procedure**

Repeated Measures Analysis of Variance

Univariate Tests of Hypotheses for Within Subject Effects

<table>
<thead>
<tr>
<th>Source</th>
<th>DF</th>
<th>Anova SS</th>
<th>Mean Square</th>
<th>F Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>DRUG</td>
<td>3</td>
<td>50.25000000</td>
<td>16.75000000</td>
<td>11.38</td>
</tr>
<tr>
<td>Error(DRUG)</td>
<td>9</td>
<td>13.25000000</td>
<td>1.47222222</td>
<td></td>
</tr>
</tbody>
</table>

```
Adj Pr > F
```

<table>
<thead>
<tr>
<th>Source</th>
<th>Pr &gt; F</th>
<th>G - G</th>
<th>H - F</th>
</tr>
</thead>
<tbody>
<tr>
<td>DRUG</td>
<td>0.0020</td>
<td>0.0123</td>
<td>0.0020</td>
</tr>
<tr>
<td>Error(DRUG)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Greenhouse-Geisser Epsilon 0.5998
Huynh-Feldt Epsilon 1.4433

10
The ANOVA Procedure
Repeated Measures Analysis of Variance
Analysis of Variance of Contrast Variables

DRUG_N represents the contrast between the nth level of DRUG and the 1st

Contrast Variable: DRUG_2

<table>
<thead>
<tr>
<th>Source</th>
<th>DF</th>
<th>Anova SS</th>
<th>Mean Square</th>
<th>F Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean</td>
<td>1</td>
<td>56.25000000</td>
<td>56.25000000</td>
<td>15.70</td>
</tr>
<tr>
<td>Error</td>
<td>3</td>
<td>10.75000000</td>
<td>3.58333333</td>
<td></td>
</tr>
</tbody>
</table>

Source Pr > F

Mean 0.0287<--1 and 2 not "same"
Error

NOTE: Apparently SAS is doing matched pair comparison with df=n-1=4-1=3 which makes sense if "wash-out" period is perceived too short.

Contrast Variable: DRUG_3

<table>
<thead>
<tr>
<th>Source</th>
<th>DF</th>
<th>Anova SS</th>
<th>Mean Square</th>
<th>F Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean</td>
<td>1</td>
<td>2.25000000</td>
<td>2.25000000</td>
<td>1.42</td>
</tr>
<tr>
<td>Error</td>
<td>3</td>
<td>4.75000000</td>
<td>1.58333333</td>
<td></td>
</tr>
</tbody>
</table>

Source Pr > F

Mean 0.3189<--1 and 3 are "same"
Error
The ANOVA Procedure
Repeated Measures Analysis of Variance
Analysis of Variance of Contrast Variables

DRUG_N represents the contrast between the nth level of DRUG and the 1st

Contrast Variable: DRUG_4

<table>
<thead>
<tr>
<th>Source</th>
<th>DF</th>
<th>Anova SS</th>
<th>Mean Square</th>
<th>F Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean</td>
<td>1</td>
<td>64.0000000000</td>
<td>64.0000000000</td>
<td>19.20</td>
</tr>
<tr>
<td>Error</td>
<td>3</td>
<td>10.0000000000</td>
<td>3.3333333333</td>
<td></td>
</tr>
</tbody>
</table>

Source Pr > F

Mean 0.0220 <-1 and 4 are not "same"
Error

Now PROC MIXED
-------------
The previous analysis assumes the interest focuses on the 4 subjects only. But if we think of the subjects as being a sample from a large population of subjects, then we deal with subject random effects. Many would say this is the best way to analyze our data. We can judge this by AIC, BIC!!!

DATA PAIN;
INPUT SUBJ @;
DO DRUG=1 TO 4;
INPUT PAIN @;
OUTPUT;
END;
DATALINES;
1 5 9 6 11
2 7 12 8 9
3 11 12 10 14
4 3 8 5 8
;
PROC MIXED DATA=PAIN;
CLASS SUBJ DRUG;
MODEL PAIN=DRUG;
RANDOM SUBJ; <- Random component. Random effects.
RUN;
QUIT;

The SAS System

The Mixed Procedure

Model Information

Data Set WORK.PAIN
Dependent Variable PAIN
Covariance Structure Variance Components
Estimation Method REML <----- The default method.
Residual Variance Method Profile
Fixed Effects SE Method Model-Based
Degrees of Freedom Method Containment

Class Level Information

<table>
<thead>
<tr>
<th>Class</th>
<th>Levels</th>
<th>Values</th>
</tr>
</thead>
<tbody>
<tr>
<td>SUBJ</td>
<td>4</td>
<td>1 2 3 4</td>
</tr>
<tr>
<td>DRUG</td>
<td>4</td>
<td>1 2 3 4</td>
</tr>
</tbody>
</table>

Dimensions

Covariance Parameters 2
Columns in X 5
Columns in Z 4
Subjects 1
Max Obs Per Subject 16
Number of Observations

Number of Observations Read 16
Number of Observations Used 16
Number of Observations Not Used 0

The Mixed Procedure

Iteration History

<table>
<thead>
<tr>
<th>Iteration</th>
<th>Evaluations</th>
<th>-2 Res Log Like</th>
<th>Criterion</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>1</td>
<td>62.87898203</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>1</td>
<td>52.54100308</td>
<td>0.00000000</td>
</tr>
</tbody>
</table>

Convergence criteria met.

Covariance Parameter Estimates

<table>
<thead>
<tr>
<th>Cov Parm</th>
<th>Estimate</th>
</tr>
</thead>
<tbody>
<tr>
<td>SUBJ</td>
<td>5.4861   &lt;--Subject variance.</td>
</tr>
<tr>
<td>Residual</td>
<td>1.4722   &lt;--Resid variance.</td>
</tr>
</tbody>
</table>

Fit Statistics

-2 Res Log Likelihood 52.5
AIC (smaller is better) 56.5
AICC (smaller is better) 57.9
BIC (smaller is better) 55.3
Type 3 Tests of Fixed Effects

<table>
<thead>
<tr>
<th>Effect</th>
<th>Num DF</th>
<th>Den DF</th>
<th>F Value</th>
<th>Pr &gt; F</th>
</tr>
</thead>
<tbody>
<tr>
<td>DRUG</td>
<td>3</td>
<td>9</td>
<td>11.38</td>
<td>0.0020</td>
</tr>
</tbody>
</table>

If we use fixed effects as in two-way ANOVA as before we get better AIC and BIC(!) as we see next.

PROC MIXED DATA=PAIN;
   CLASS SUBJ DRUG;
   MODEL PAIN=SUBJ DRUG; <--No RANDOM component!!!
RUN;
QUIT;

The Mixed Procedure

Model Information

Data Set WORK.PAIN
Dependent Variable PAIN
Covariance Structure Diagonal
Estimation Method REML <------@@@@ @
Residual Variance Method Profile
Fixed Effects SE Method Model-Based
Degrees of Freedom Method Residual

Class Level Information

<table>
<thead>
<tr>
<th>Class</th>
<th>Levels</th>
<th>Values</th>
</tr>
</thead>
<tbody>
<tr>
<td>SUBJ</td>
<td>4</td>
<td>1 2 3 4</td>
</tr>
<tr>
<td>DRUG</td>
<td>4</td>
<td>1 2 3 4</td>
</tr>
</tbody>
</table>
Dimensions

Covariance Parameters  1
Columns in X  9
Columns in Z  0
Subjects  1
Max Obs Per Subject  16

Covariance Parameter
Estimates

Cov Parm  Estimate
Residual  1.4722

Fit Statistics

-2 Res Log Likelihood  37.3
AIC (smaller is better)  39.3 <--Smaller
AICC (smaller is better)  39.9
BIC (smaller is better)  39.5 <--Smaller

Type 3 Tests of Fixed Effects

<table>
<thead>
<tr>
<th>Effect</th>
<th>Num DF</th>
<th>Den DF</th>
<th>F Value</th>
<th>Pr &gt; F</th>
</tr>
</thead>
<tbody>
<tr>
<td>SUBJ</td>
<td>3</td>
<td>9</td>
<td>15.91</td>
<td>0.0006</td>
</tr>
<tr>
<td>DRUG</td>
<td>3</td>
<td>9</td>
<td>11.38</td>
<td>0.0020</td>
</tr>
</tbody>
</table>

NOTE: This ANOVA is identical to 2-Way above.
Now compare with NON-RESTRICTED ML:

Recall the mixed effects model from above:

\[ y_{ij} = \mu + a_i + \beta_j + \epsilon_{ij}, \quad i,j=1,2,3,4 \]

OPTION PS=35 LS=70;

DATA PAIN;
  INPUT SUBJ @;
  DO DRUG=1 TO 4;
    INPUT PAIN @;
    OUTPUT;
  END;
DATALINES;
1 5 9 6 11
2 7 12 8 9
3 11 12 10 14
4 3 8 5 8
;

PROC MIXED DATA=PAIN METHOD=ML; <--Default is REML.
CLASS SUBJ DRUG;
MODEL PAIN=DRUG;
RANDOM SUBJ;
RUN;
QUIT;

The SAS System
The Mixed Procedure

Model Information

Data Set WORK.PAIN
Dependent Variable PAIN
Covariance Structure Variance Components
Estimation Method ML (Before it was REML)
Residual Variance Method Profile
Fixed Effects SE Method Model-Based
Degrees of Freedom Method Containment

Class Level Information

<table>
<thead>
<tr>
<th>Class</th>
<th>Levels</th>
<th>Values</th>
</tr>
</thead>
<tbody>
<tr>
<td>SUBJ</td>
<td>4</td>
<td>1 2 3 4</td>
</tr>
<tr>
<td>DRUG</td>
<td>4</td>
<td>1 2 3 4</td>
</tr>
</tbody>
</table>

Dimensions

- Covariance Parameters: 2
- Columns in X: 5
- Columns in Z: 4
- Subjects: 1
- Max Obs Per Subject: 16

The Mixed Procedure

Number of Observations

- Number of Observations Read: 16
- Number of Observations Used: 16
- Number of Observations Not Used: 0

Iteration History

<table>
<thead>
<tr>
<th>Iteration</th>
<th>Evaluations</th>
<th>-2 Log Like</th>
<th>Criterion</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>1</td>
<td>71.84215962</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>1</td>
<td>58.05818768</td>
<td>0.00000000</td>
</tr>
</tbody>
</table>

Convergence criteria met.

Covariance Parameter Estimates
Cov Parm Estimate

SUBJ 4.1146 (With REML get 5.4861)
Residual 1.1042 (With REML get 1.4722)

Fit Statistics

-2 Log Likelihood 58.1 (With REML get 52.5)
AIC (smaller is better) 70.1 (With REML get 56.5)
AICC (smaller is better) 79.4
BIC (smaller is better) 66.4

Type 3 Tests of Fixed Effects

<table>
<thead>
<tr>
<th>Effect</th>
<th>Num DF</th>
<th>Den DF</th>
<th>F Value</th>
<th>Pr &gt; F</th>
</tr>
</thead>
<tbody>
<tr>
<td>DRUG</td>
<td>3</td>
<td>9</td>
<td>15.17</td>
<td>0.0007 (With REML get 0.002)</td>
</tr>
</tbody>
</table>

Ex2. Two-Factor Repeated Experiment:
Repeated measure on one factor.

Subjects are randomly assigned to control or treatment group. Then each subject is measured before (PRE) and after (POST) treatment. The treatment for the control group is a placebo or no treatment at all.

<table>
<thead>
<tr>
<th>GROUP</th>
<th>SUBJ</th>
<th>PRE</th>
<th>POST</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1</td>
<td>80</td>
<td>83</td>
</tr>
<tr>
<td>Control</td>
<td>2</td>
<td>85</td>
<td>86</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>83</td>
<td>88</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>82</td>
<td>94</td>
</tr>
<tr>
<td>Treatment</td>
<td>5</td>
<td>87</td>
<td>93</td>
</tr>
</tbody>
</table>

NOTE: Subject nested within group!
Method I: Two-Sample t-test applied to the difference scores of POST-PRE to compare the difference means of the two groups. NOTE: Data assumed normal with equal variance.

For Control: D1=3, D2=1, D3=5
For Treatment: D1=12, D2=6, D3=14

H_0: mu_C = mu_T, H_1: mu_C not equal mu_T

DATA PREPOST;
  INPUT SUBJ GROUP $ PRE POST;
  DIFF = POST-PRE;
DATALINES;
  1 C 80 83
  2 C 85 86
  3 C 83 88
  4 T 82 94
  5 T 87 93
  6 T 84 98
;

PROC TTEST DATA=PREPOST;
  CLASS GROUP;
  VAR DIFF;
RUN;

The SAS System

The TTEST Procedure

Statistics

20
### Variable GROUP N Mean Mean Mean Std Dev

<table>
<thead>
<tr>
<th>DIFF</th>
<th>C</th>
<th>3</th>
<th>-1.968</th>
<th>3</th>
<th>7.9683</th>
<th>1.0413</th>
</tr>
</thead>
<tbody>
<tr>
<td>DIFF</td>
<td>T</td>
<td>3</td>
<td>0.3244</td>
<td>3</td>
<td>10.667</td>
<td>21.009</td>
</tr>
<tr>
<td>DIFF</td>
<td>Diff (1-2)</td>
<td></td>
<td>-15.07</td>
<td>-7.667</td>
<td>-0.263</td>
<td>1.9568</td>
</tr>
</tbody>
</table>

### Statistics

<table>
<thead>
<tr>
<th>Variable</th>
<th>GROUP</th>
<th>Std Dev</th>
<th>Std Dev</th>
<th>Std Err</th>
<th>Minimum</th>
<th>Maximum</th>
</tr>
</thead>
<tbody>
<tr>
<td>DIFF</td>
<td>C</td>
<td>2</td>
<td>12.569</td>
<td>1.1547</td>
<td>1</td>
<td>5</td>
</tr>
<tr>
<td>DIFF</td>
<td>T</td>
<td>4.1633</td>
<td>26.165</td>
<td>2.4037</td>
<td>6</td>
<td>14</td>
</tr>
<tr>
<td>DIFF</td>
<td>Diff (1-2)</td>
<td>3.266</td>
<td>9.385</td>
<td>2.6667</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### T-Tests

<table>
<thead>
<tr>
<th>Variable</th>
<th>Method</th>
<th>Variances</th>
<th>DF</th>
<th>t Value</th>
<th>Pr &gt;</th>
<th>t</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>DIFF</td>
<td>Pooled</td>
<td>Equal</td>
<td>4</td>
<td>-2.88</td>
<td>0.0452</td>
<td>&lt;--</td>
<td></td>
</tr>
<tr>
<td>DIFF</td>
<td>Satterthwaite</td>
<td>Unequal</td>
<td>2.88</td>
<td>-2.88</td>
<td>0.0671</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Equality of Variances

<table>
<thead>
<tr>
<th>Variable</th>
<th>Method</th>
<th>Num DF</th>
<th>Den DF</th>
<th>F Value</th>
<th>Pr &gt; F</th>
</tr>
</thead>
<tbody>
<tr>
<td>DIFF</td>
<td>Folded F</td>
<td>2</td>
<td>2</td>
<td>4.33</td>
<td>0.3750</td>
</tr>
</tbody>
</table>

Check:

---------
Bar(Diff_C) - Bar(Diff_T) = 3-10.667 = -7.667
StdError(Bar(Diff_C) - Bar(Diff_T)) = 2.6667 with 4 df

> -7.667/2.6667

[1] -2.875089 approx -2.88 OK.
Thus, at alpha=0.05, the treatment mean difference is significantly different from the control mean difference.

Method II: Two-way ANOVA with factors GROUP and TIME, with TIME as a repeated measure.

DATA PREPOST;
INPUT SUBJ GROUP $ PRE POST;
DIFF = POST-PRE;
DATALNES;
1 C 80 83
2 C 85 86
3 C 83 88
4 T 82 94
5 T 87 93
6 T 84 98;

PROC ANOVA DATA=PREPOST;
CLASS GROUP;
MODEL PRE POST = GROUP/NOUNI;
REPEATD TIME 2 (0 1);
MEANS GROUP;
RUN;

The ANOVA Procedure

Class Level Information

<table>
<thead>
<tr>
<th>Class</th>
<th>Levels</th>
<th>Values</th>
</tr>
</thead>
<tbody>
<tr>
<td>GROUP</td>
<td>2</td>
<td>C T</td>
</tr>
</tbody>
</table>

Number of Observations Read     6
Number of Observations Used     6
Repeated Measures Analysis of Variance

Repeated Measures Level Information

Dependent Variable       PRE   POST
Level of TIME        0      1

MANOVA Test Criteria and Exact F Statistics
for the Hypothesis of no TIME Effect
H = Anova SSCP Matrix for TIME
E = Error SSCP Matrix

<table>
<thead>
<tr>
<th>Statistic</th>
<th>Value</th>
<th>F Value</th>
<th>Num DF</th>
<th>Den DF</th>
<th>Pr &gt; F</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wilks' Lambda</td>
<td>0.13216314</td>
<td>26.27</td>
<td>1</td>
<td>4</td>
<td>0.0069</td>
</tr>
<tr>
<td>Pillai’s Trace</td>
<td>0.86783686</td>
<td>26.27</td>
<td>1</td>
<td>4</td>
<td>0.0069</td>
</tr>
<tr>
<td>Hotelling-Lawley Trace</td>
<td>6.56640625</td>
<td>26.27</td>
<td>1</td>
<td>4</td>
<td>0.0069</td>
</tr>
<tr>
<td>Roy's Greatest Root</td>
<td>6.56640625</td>
<td>26.27</td>
<td>1</td>
<td>4</td>
<td>0.0069</td>
</tr>
</tbody>
</table>

The ANOVA Procedure
Repeated Measures Analysis of Variance

MANOVA Test Criteria and Exact F Statistics
for the Hypothesis of no TIME*GROUP Effect
H = Anova SSCP Matrix for TIME*GROUP
E = Error SSCP Matrix

<table>
<thead>
<tr>
<th>Statistic</th>
<th>Value</th>
<th>F Value</th>
<th>Num DF</th>
<th>Den DF</th>
<th>Pr &gt; F</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wilks' Lambda</td>
<td>0.32611465</td>
<td>8.27</td>
<td>1</td>
<td>4</td>
<td>0.0452</td>
</tr>
<tr>
<td>Pillai’s Trace</td>
<td>0.67388535</td>
<td>8.27</td>
<td>1</td>
<td>4</td>
<td>0.0452</td>
</tr>
</tbody>
</table>
The ANOVA Procedure
Repeated Measures Analysis of Variance
Tests of Hypotheses for Between Subjects Effects

<table>
<thead>
<tr>
<th>Source</th>
<th>DF</th>
<th>Anova SS</th>
<th>Mean Square</th>
<th>F Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>GROUP</td>
<td>1</td>
<td>90.75000000</td>
<td>90.75000000</td>
<td>11.84</td>
</tr>
<tr>
<td>Error</td>
<td>4</td>
<td>30.66666667</td>
<td>7.66666667</td>
<td></td>
</tr>
</tbody>
</table>

Source Pr > F
GROUP 0.0263 <---Groups are different.
Error

The ANOVA Procedure
Repeated Measures Analysis of Variance
Univariate Tests of Hypotheses for Within Subject Effects

<table>
<thead>
<tr>
<th>Source</th>
<th>DF</th>
<th>Anova SS</th>
<th>Mean Square</th>
<th>F Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>TIME</td>
<td>1</td>
<td>140.0833333</td>
<td>140.0833333</td>
<td>26.27</td>
</tr>
<tr>
<td>TIME*GROUP</td>
<td>1</td>
<td>44.0833333</td>
<td>44.0833333</td>
<td>8.27</td>
</tr>
<tr>
<td>Error(TIME)</td>
<td>4</td>
<td>21.3333333</td>
<td>5.3333333</td>
<td></td>
</tr>
</tbody>
</table>

Source Pr > F
TIME 0.0069
TIME*GROUP 0.0452<--Interaction significant
Error(TIME)

The ANOVA Procedure

Level of ------------PRE------------- ------------POST-------------
GROUP   N  Mean  Std Dev   Mean  Std Dev
C       3  82.6666667  2.51661148  85.6666667  2.51661148
Interesting to compare with simple TWO-WAY ANOVA with GROUP at 2 levels and TIME at 2 levels as factors, and 3 obs/cell.

DATA PREPOST;
INPUT GROUP $ TIME $ Y @@;
DATALINES;
C PRE 80 C POST 83
C PRE 85 C POST 86
C PRE 83 C POST 88
T PRE 82 T POST 94
T PRE 87 T POST 93
T PRE 84 T POST 98
;
PROC ANOVA DATA=PREPOST;
CLASS GROUP TIME;
MODEL Y = GROUP TIME GROUP*TIME;
RUN;

The ANOVA Procedure

Class Level Information

Class   Levels   Values
GROUP   2         C T
TIME    2         POST PRE

Number of Observations Read   12
Number of Observations Used   12

Dependent Variable: Y

<table>
<thead>
<tr>
<th>Source</th>
<th>DF</th>
<th>Sum of Squares</th>
<th>Mean Square</th>
<th>F Value</th>
</tr>
</thead>
</table>

25
<table>
<thead>
<tr>
<th>Source</th>
<th>DF</th>
<th>Anova SS</th>
<th>Mean Square</th>
<th>F Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>GROUP</td>
<td>1</td>
<td>90.7500000</td>
<td>90.7500000</td>
<td>13.96</td>
</tr>
<tr>
<td>TIME</td>
<td>1</td>
<td>140.0833333</td>
<td>140.0833333</td>
<td>21.55</td>
</tr>
</tbody>
</table>

Source Pr > F

GROUP 0.0057 <--Sig
TIME 0.0017 <--Sig

Dependent Variable: Y

<table>
<thead>
<tr>
<th>Source</th>
<th>DF</th>
<th>Anova SS</th>
<th>Mean Square</th>
<th>F Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>GROUP*TIME</td>
<td>(2-1)(2-1)=1</td>
<td>44.0833333</td>
<td>44.0833333</td>
<td>6.78</td>
</tr>
</tbody>
</table>