CMPE 235: User Evaluation of Technology

Repeated Measures

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Repeated Measures

Hypothetical Cholesterol Study

<table>
<thead>
<tr>
<th>Group</th>
<th>Initial</th>
<th>2 mo.</th>
<th>4 mo.</th>
<th>6 mo.</th>
<th>8 mo.</th>
<th>10 mo.</th>
<th>12 mo.</th>
</tr>
</thead>
<tbody>
<tr>
<td>DRUG</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Placebo</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

Questions of Interest:
1) Is there a change in the cholesterol levels of subjects over time, i.e. is there a TIME EFFECT? (within-subjects effect)
2) Is there a TREATMENT EFFECT? (between-subjects effect)
3) Is the effect of TIME the same for both TREATMENTS? (within-subjects effect)

THIS IS OF PRIMARY INTEREST!

Profile Plots Illustrating the Questions of Interest

TIME EFFECT ONLY

Cholesterol Levels for both groups decreased over TIME however the decrease appears to be the same for both treatment groups, i.e. there is NO TREATMENT effect nor a TIME*TREATMENT interaction.

TIME and TREATMENT EFFECT

Cholesterol Levels for both groups decreased over TIME and the trend over time was the same for both groups, however the decrease for those receiving the drug was larger, i.e. there is a TREATMENT EFFECT.

TIME*TREATMENT INTERACTION

Here the effect of time is NOT the same for both groups. Thus we say that there is TIME and TREATMENT interaction.
Example: Homeopathy vs. placebo in treating pain after surgery

Mean pain assessments by visual analogue scales (VAS)


Example: Two treatment groups with four measurements taken over equally spaced time intervals (e.g., A = treatment B = placebo)

<table>
<thead>
<tr>
<th>id</th>
<th>group</th>
<th>time1</th>
<th>time2</th>
<th>time3</th>
<th>time4</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>A</td>
<td>31</td>
<td>29</td>
<td>15</td>
<td>26</td>
</tr>
<tr>
<td>2</td>
<td>A</td>
<td>24</td>
<td>28</td>
<td>20</td>
<td>32</td>
</tr>
<tr>
<td>3</td>
<td>A</td>
<td>14</td>
<td>20</td>
<td>28</td>
<td>30</td>
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<tr>
<td>4</td>
<td>B</td>
<td>38</td>
<td>34</td>
<td>30</td>
<td>34</td>
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<tr>
<td>5</td>
<td>B</td>
<td>25</td>
<td>29</td>
<td>25</td>
<td>29</td>
</tr>
<tr>
<td>6</td>
<td>B</td>
<td>30</td>
<td>28</td>
<td>16</td>
<td>34</td>
</tr>
</tbody>
</table>

Hypothetical data from Twisk; chapter 3, page 40, table 3.7

Profile plots by group

Mean profile plots by group

Questions of Interest

1. Overall, are there significant differences between TIME points?
   From plots it looks like some differences over time, in particular times 3 and 4 look different.

2. Do the two groups differ at any time points, i.e. is there a TREATMENT effect?
   From plots it looks like the groups differ at baseline and there are some difference everywhere else.

3. Do the two groups differ in their responses over time, i.e. is there a TIME*TREATMENT interaction?
   Their response profiles looks similar over time, though A and B are closer by the end.

Two Main Methods of Analyses

► Option 1: Use repeated-measures ANOVA using the “Univariate” approach (restrictive assumptions)
► Option 2: "Multivariate" ANOVA approach, i.e. MANOVA (less restrictive assumptions)

Assumptions

1. Both repeated-measures ANOVA and MANOVA assume that time intervals are equally spaced.
2. Both methods assume response is normally distributed, but both approaches are robust against violations of normality.
3. Repeated-measures ANOVA sphericity, or compound symmetry (see next slide)
4. Both approaches require complete data for all subjects, i.e. no missing data for any subject.
Sphericity/Compound Symmetry

Repeated Measures ANOVA required **compound symmetry** which is:
(a) The variances of the response variable must be the same at each time point
(b) The correlation between repeated measurements are equal, regardless of the time interval between measurements.

Tested using Mauchly’s Sphericity Test.
- Violation of sphericity assumption leads to inflated F statistics and hence inflated type I error.

Correcting violation of sphericity:
- Adjust the degrees of freedom using a correction factor called E (lies between 1/k-1 to 1, where k is the # levels in the within subject factor).
- E.g., Greenhouse-Geisser, Huynh-Feldt, Lower Bound.

(a) Variances at each time point
Does variance look equal across time points?
Looks like most variability is at Time1 and least at Time 4.

![Graph showing variance across time points]

Looks like the condition for compound symmetry is not met
Time 1 and Time 2 are highly positively correlated, but Time 1 and Time 3 are negatively correlated!

Hypothetical Example in SPSS

Subject ID, group and a numeric group (A = 1, B = 2) identifier are entered. The repeated measurements over time are entered in separate columns.

Select Analyze > General Linear Model > Repeated Measures… You are first expected to enter a name for the within-subject factor (usually Time) and the number of levels it has (4 in this case) then click Add.

Hypothetical Example in SPSS

Set up Mean Profile Plots by clicking here.

Mean Profile Plots in SPSS

![Graph showing mean profile plots]
Hypothetical Example in SPSS

**Hypothetical Example in SPSS (MANOVA Results and Sphericity Test)**

<table>
<thead>
<tr>
<th>Source</th>
<th>Type II Sum of Squares</th>
<th>df</th>
<th>Mean Square</th>
<th>Sig.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Between Cases</td>
<td>175.042</td>
<td>1</td>
<td>175.042</td>
<td>.141</td>
</tr>
<tr>
<td>Error</td>
<td>27.542</td>
<td>4</td>
<td>6.887</td>
<td></td>
</tr>
</tbody>
</table>

Mauchly’s Sphericity Test is not significant (p = .324).

Hypothetical Example in SPSS

There is not a significant treatment effect (p = .141). This test result is the same regardless of approach used for the within-subject effects.

Other Ways to Test for Changes Over Time

- **Deviation** – each mean vs. mean of the rest
- **Simple** – each mean vs. baseline
- **Difference** – each mean vs. mean of previous
- **Helmert** – each mean vs. mean of following time periods
- **Repeated** – each mean vs. previous mean
- **Polynomial** – linear, quadratic, and cubic time trends

Other Ways to Test for Changes Over Time (SPSS)

Select desired contrast and then click Change button to make the change.

Other Ways to Test for Changes Over Time (SPSS ~ Deviation Contrast)

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<thead>
<tr>
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<th>df</th>
<th>Mean Square</th>
<th>Sig.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time</td>
<td>2.542</td>
<td>1</td>
<td>2.542</td>
<td>.141</td>
</tr>
<tr>
<td>Group Time</td>
<td>1.395</td>
<td>1</td>
<td>1.395</td>
<td>.245</td>
</tr>
<tr>
<td>Error</td>
<td>27.542</td>
<td>4</td>
<td>6.887</td>
<td></td>
</tr>
</tbody>
</table>

The mean at time 2 ($\mu_2$) is not significantly mean of the rest (p = .414). The nature of the difference between mean at time 2 and the mean of the rest does not depend on treatment received (p = .970), i.e. no interaction.
Replacing Missing Values

► Often times in measuring subjects over the course of time they drop out of the study for whatever reason.

► A standard/simple approach is to fill missing values with the last observed value. This is called "Last Observation Carried Forward (LOCF)".

► Many more complicated schemes exist
  ▪ Replace with means
  ▪ Moving average of the 1/2/3... previous and after