**Proc Mixed - Right Options to get Right Output**  
Shilpa Edupganti, Eliassen Group, CT  
Sheetal Nisal, Independent Consultant, CT

**ABSTRACT**

The Mixed Procedure fits a variety of mixed linear models to data that enables us to use these fitted models to make statistical inferences about the data. Once a model has been fit to the data, we can use it to make statistical inferences via both the fixed-effects and covariance parameters. Proc Mixed computes several different statistics suitable for generating hypothesis tests and confidence intervals and several other statistical parameters. The validity of these statistics depends upon the mean and variance-covariance model we select by the right ordering of the data and picking the right estimate difference, so it is important to choose the right model. We use Proc Mixed for statistical analyses very frequently and might have to do some trial and errors to check which model works best for us. There were few issues that we have overcome when running on large data and some of the trial output from Proc Mixed helped us to assess the model and compare it with others which gave us a lot of options to work on the mixed model changing the model itself with right treatment ordering and picking up the right treatment covariate interaction and other parameters. Based on multiple possibilities one option would be best for each of the possibility. So this presentation demonstrates different issues and its suitable method to pick the right parameter or model to deliver the desired output.

**INTRODUCTION**

In clinical trials, statistical analysis of clinical data often involves statistical model selection. To select the most desirable model for the statistical analysis is the ultimate goal of the investigator. In a typical situation of a large data and strict data analysis, model selection is often carried out by the automated procedures built into the software including frequently used forward, backward, and stepwise model selection procedures. However, these procedures have limited application when the model becomes more complicated to include repeated or longitudinal data, in which we not only need to deal with how to select the best mean structure but also the most optimal variance-covariance structure. The model flexibility enables the Mixed procedure to analyze a much wider range of linear models with more types of clinical data. This specific feature has made the Mixed procedure the desirable choice for statistical analysis of clinical data.

**MODEL AND OPTIONS**

Model selections often require trial and error methods to find out which model fits the best. This method of testing involves defining various options and providing the right type of variance-covariance structure. Then upon studying various outputs produced by the methods one can come up with a best model and right covariates. Below we present few scenarios and the best model and methods for each of them.

1. If one is interested in calculating the difference of estimates between two treatment groups in a particular order, then it would be better if we use an estimate statement with actual treatment groups. If not by default the treatment groups would be sorted by alphabetical order and one would just end up in calculating the difference of estimates in the wrong way around.

   *For Example*: For one of our study, we needed the difference of estimates between two treatment groups ‘XXXX’ and ‘PLACEBO’.

1
When used the proc mixed code without an estimate statement, we picked up the difference of estimates like: mean, stderr, 95%CI and P-value from the difference output dataset which would give us the difference of ‘PLACEBO vs XXXX’ but not the other way around as required. Hence upon using an estimate statement we can directly pick up the difference of estimates from estimates output data, which would be for ‘XXXX vs PLACEBO’.

2. If we want to calculate the difference of estimates b/w two treatment groups for ‘different parameters of a single variable’, then instead of using multiple estimate statements we can make a good practice to resolve this issue without using an estimate statement, and just picking up the values from the difference output data based on the covariate interaction effect.

*For Example:* In the same study, we needed the difference of estimates b/w two treatment groups for each week, where we had 8 weeks. So we need to calculate the difference of estimates for each week.

- Calculating estimates for each week separately would give us a different result because of the treatment*week interaction effect Or if we would have to go by the general procedure by using an estimate statement as mentioned above, then one would require eight estimate statements, which would be complicated.

- Instead, we could just sort the treatment groups by giving a sort order or by picking up the numeric sort variable ‘trtsort’ for treatment groups instead of character text of treatment groups, this would eliminate the problem of alphabetical sorting, and then picked up the records from the difference output dataset, matching the covariate interaction effect, i.e trtsort vs week for ‘trtsort = 101 and _trtsort = 102 and week = _week’. These records would represent solely the difference of estimates b/w ‘XXXX vs PLACEBO’ for each week.

- Similarly this approach can be followed for any covariate. Just a quick example if we have used this to calculate the difference of estimates for each country then simply the condition ‘country = _country’ would give the right estimates.

3. In the above mentioned scenario for estimates difference of ‘different parameters of a single variable’. If we are comparing analysis variable of an endpoint at baseline (dependent) against baseline variable of that endpoint at baseline (independent). In that case, it as good as comparing analysis variable at baseline by itself, which would give a warning: ‘Unable to make hessian positive definite’, which yields an infinite likelihood error and the output datasets are not created for the respective proc mixed code and the SAS® system stops.

*For Example:* In the second mentioned scenario, we have taken the input data into proc mixed without week 0, i.e baseline. If not we would yield the hessian positive definite error for first iteration at week 0.

```
model sleepmw = TRTs sort poolreg sleepmb week TRTs sort*week/ ddfm=kr solution
```

Analysis variable at week 0 vs. baseline variable at week 0

Since both the values are equal we would not see any output data for the respective proc mixed code and hence yield the infinite likelihood error.
CODE and RESULTS

General Code:

```sas
proc mixed data=X;
  class var1 var2( classification variable)s;
  model var (Dependent) = trt var1 var2 etc... (independents); [Independents and dependents together are known as covariates]
  lsmeans trt / pdiff cl;
  estimate 'trt1 vs trt2' trt -1 1/ cl;
run;
```

For this presentation we have considered sample data of 12 subjects with 8 visit weeks and just for 1 region and all of the data and analysis is based on two treatment groups.

### Sample Data:

<table>
<thead>
<tr>
<th>Obs</th>
<th>Patient</th>
<th>week</th>
<th>TRTSORT</th>
<th>TRTTXT</th>
<th>Region</th>
<th>Pooled Interference</th>
<th>Mean Sleep Score Based Interference</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>10011001</td>
<td>0</td>
<td>101</td>
<td>XXXXX</td>
<td>PORTUGAL</td>
<td>3.86</td>
<td>3.86</td>
</tr>
<tr>
<td>2</td>
<td>10011001</td>
<td>1</td>
<td>101</td>
<td>XXXXX</td>
<td>PORTUGAL</td>
<td>3.43</td>
<td>3.86</td>
</tr>
<tr>
<td>3</td>
<td>10011001</td>
<td>2</td>
<td>101</td>
<td>XXXXX</td>
<td>PORTUGAL</td>
<td>3.00</td>
<td>3.86</td>
</tr>
<tr>
<td>4</td>
<td>10011001</td>
<td>3</td>
<td>101</td>
<td>XXXXX</td>
<td>PORTUGAL</td>
<td>2.86</td>
<td>3.86</td>
</tr>
<tr>
<td>5</td>
<td>10011001</td>
<td>4</td>
<td>101</td>
<td>XXXXX</td>
<td>PORTUGAL</td>
<td>3.14</td>
<td>3.86</td>
</tr>
<tr>
<td>6</td>
<td>10011001</td>
<td>5</td>
<td>101</td>
<td>XXXXX</td>
<td>PORTUGAL</td>
<td>3.57</td>
<td>3.86</td>
</tr>
<tr>
<td>7</td>
<td>10011001</td>
<td>6</td>
<td>101</td>
<td>XXXXX</td>
<td>PORTUGAL</td>
<td>3.29</td>
<td>3.86</td>
</tr>
<tr>
<td>8</td>
<td>10011001</td>
<td>7</td>
<td>101</td>
<td>XXXXX</td>
<td>PORTUGAL</td>
<td>3.29</td>
<td>3.86</td>
</tr>
<tr>
<td>9</td>
<td>10011001</td>
<td>8</td>
<td>101</td>
<td>XXXXX</td>
<td>PORTUGAL</td>
<td>3.14</td>
<td>3.86</td>
</tr>
<tr>
<td>10</td>
<td>10021001</td>
<td>0</td>
<td>101</td>
<td>XXXXX</td>
<td>PORTUGAL</td>
<td>3.00</td>
<td>3.00</td>
</tr>
<tr>
<td>11</td>
<td>10021001</td>
<td>1</td>
<td>101</td>
<td>XXXXX</td>
<td>PORTUGAL</td>
<td>2.25</td>
<td>3.00</td>
</tr>
<tr>
<td>12</td>
<td>10021001</td>
<td>2</td>
<td>101</td>
<td>XXXXX</td>
<td>PORTUGAL</td>
<td>2.50</td>
<td>3.00</td>
</tr>
<tr>
<td>13</td>
<td>10021001</td>
<td>3</td>
<td>101</td>
<td>XXXXX</td>
<td>PORTUGAL</td>
<td>1.71</td>
<td>3.00</td>
</tr>
<tr>
<td>14</td>
<td>10021001</td>
<td>4</td>
<td>101</td>
<td>XXXXX</td>
<td>PORTUGAL</td>
<td>2.00</td>
<td>3.00</td>
</tr>
<tr>
<td>15</td>
<td>10021001</td>
<td>5</td>
<td>101</td>
<td>XXXXX</td>
<td>PORTUGAL</td>
<td>1.71</td>
<td>3.00</td>
</tr>
<tr>
<td>16</td>
<td>10021001</td>
<td>6</td>
<td>101</td>
<td>XXXXX</td>
<td>PORTUGAL</td>
<td>1.17</td>
<td>3.00</td>
</tr>
<tr>
<td>17</td>
<td>10021001</td>
<td>7</td>
<td>101</td>
<td>XXXXX</td>
<td>PORTUGAL</td>
<td>1.29</td>
<td>3.00</td>
</tr>
<tr>
<td>18</td>
<td>10021001</td>
<td>8</td>
<td>101</td>
<td>XXXXX</td>
<td>PORTUGAL</td>
<td>1.71</td>
<td>3.00</td>
</tr>
<tr>
<td>19</td>
<td>10021002</td>
<td>0</td>
<td>102</td>
<td>PLACEBO</td>
<td>PORTUGAL</td>
<td>4.57</td>
<td>4.57</td>
</tr>
<tr>
<td>20</td>
<td>10021002</td>
<td>1</td>
<td>102</td>
<td>PLACEBO</td>
<td>PORTUGAL</td>
<td>6.83</td>
<td>4.57</td>
</tr>
<tr>
<td>21</td>
<td>10021002</td>
<td>2</td>
<td>102</td>
<td>PLACEBO</td>
<td>PORTUGAL</td>
<td>5.14</td>
<td>4.57</td>
</tr>
<tr>
<td>22</td>
<td>10021002</td>
<td>3</td>
<td>102</td>
<td>PLACEBO</td>
<td>PORTUGAL</td>
<td>3.57</td>
<td>4.57</td>
</tr>
<tr>
<td>23</td>
<td>10021002</td>
<td>4</td>
<td>102</td>
<td>PLACEBO</td>
<td>PORTUGAL</td>
<td>3.71</td>
<td>4.57</td>
</tr>
<tr>
<td>24</td>
<td>10021002</td>
<td>5</td>
<td>102</td>
<td>PLACEBO</td>
<td>PORTUGAL</td>
<td>2.86</td>
<td>4.57</td>
</tr>
<tr>
<td>25</td>
<td>10021002</td>
<td>6</td>
<td>102</td>
<td>PLACEBO</td>
<td>PORTUGAL</td>
<td>4.29</td>
<td>4.57</td>
</tr>
<tr>
<td>26</td>
<td>10021002</td>
<td>7</td>
<td>102</td>
<td>PLACEBO</td>
<td>PORTUGAL</td>
<td>3.29</td>
<td>4.57</td>
</tr>
<tr>
<td>27</td>
<td>10021002</td>
<td>8</td>
<td>102</td>
<td>PLACEBO</td>
<td>PORTUGAL</td>
<td>4.50</td>
<td>4.57</td>
</tr>
<tr>
<td>28</td>
<td>10021003</td>
<td>0</td>
<td>102</td>
<td>PLACEBO</td>
<td>PORTUGAL</td>
<td>4.29</td>
<td>4.29</td>
</tr>
<tr>
<td>29</td>
<td>10021003</td>
<td>1</td>
<td>102</td>
<td>PLACEBO</td>
<td>PORTUGAL</td>
<td>4.33</td>
<td>4.29</td>
</tr>
<tr>
<td>Trial</td>
<td>ID</td>
<td>Visit</td>
<td>Treatment</td>
<td>Country</td>
<td>Placebo</td>
<td>Placebo</td>
<td>2</td>
</tr>
<tr>
<td>--------</td>
<td>----------</td>
<td>-------</td>
<td>-----------</td>
<td>---------</td>
<td>---------</td>
<td>-------------</td>
<td>----------</td>
</tr>
<tr>
<td>30</td>
<td>10021003</td>
<td>2</td>
<td>PLACEBO</td>
<td>PORTUGAL</td>
<td>2.71</td>
<td>4.29</td>
<td></td>
</tr>
<tr>
<td>31</td>
<td>10021003</td>
<td>3</td>
<td>PLACEBO</td>
<td>PORTUGAL</td>
<td>2.71</td>
<td>4.29</td>
<td></td>
</tr>
<tr>
<td>32</td>
<td>10021003</td>
<td>4</td>
<td>PLACEBO</td>
<td>PORTUGAL</td>
<td>4.14</td>
<td>4.29</td>
<td></td>
</tr>
<tr>
<td>33</td>
<td>10021003</td>
<td>5</td>
<td>PLACEBO</td>
<td>PORTUGAL</td>
<td>4.86</td>
<td>4.29</td>
<td></td>
</tr>
<tr>
<td>34</td>
<td>10021003</td>
<td>6</td>
<td>PLACEBO</td>
<td>PORTUGAL</td>
<td>6.00</td>
<td>4.29</td>
<td></td>
</tr>
<tr>
<td>35</td>
<td>10021003</td>
<td>7</td>
<td>PLACEBO</td>
<td>PORTUGAL</td>
<td>6.00</td>
<td>4.29</td>
<td></td>
</tr>
<tr>
<td>36</td>
<td>10021003</td>
<td>8</td>
<td>PLACEBO</td>
<td>PORTUGAL</td>
<td>6.00</td>
<td>4.29</td>
<td></td>
</tr>
<tr>
<td>37</td>
<td>10031002</td>
<td>0</td>
<td>PLACEBO</td>
<td>PORTUGAL</td>
<td>8.00</td>
<td>8.00</td>
<td></td>
</tr>
<tr>
<td>38</td>
<td>10031002</td>
<td>1</td>
<td>PLACEBO</td>
<td>PORTUGAL</td>
<td>7.50</td>
<td>8.00</td>
<td></td>
</tr>
<tr>
<td>39</td>
<td>10031002</td>
<td>2</td>
<td>PLACEBO</td>
<td>PORTUGAL</td>
<td>6.57</td>
<td>8.00</td>
<td></td>
</tr>
<tr>
<td>40</td>
<td>10031002</td>
<td>3</td>
<td>PLACEBO</td>
<td>PORTUGAL</td>
<td>5.86</td>
<td>8.00</td>
<td></td>
</tr>
<tr>
<td>41</td>
<td>10031002</td>
<td>4</td>
<td>PLACEBO</td>
<td>PORTUGAL</td>
<td>5.43</td>
<td>8.00</td>
<td></td>
</tr>
<tr>
<td>42</td>
<td>10031002</td>
<td>5</td>
<td>PLACEBO</td>
<td>PORTUGAL</td>
<td>5.50</td>
<td>8.00</td>
<td></td>
</tr>
<tr>
<td>43</td>
<td>10031002</td>
<td>6</td>
<td>PLACEBO</td>
<td>PORTUGAL</td>
<td>6.43</td>
<td>8.00</td>
<td></td>
</tr>
<tr>
<td>44</td>
<td>10031002</td>
<td>7</td>
<td>PLACEBO</td>
<td>PORTUGAL</td>
<td>5.43</td>
<td>8.00</td>
<td></td>
</tr>
<tr>
<td>45</td>
<td>10031002</td>
<td>8</td>
<td>PLACEBO</td>
<td>PORTUGAL</td>
<td>4.40</td>
<td>8.00</td>
<td></td>
</tr>
<tr>
<td>46</td>
<td>10031003</td>
<td>0</td>
<td>PLACEBO</td>
<td>PORTUGAL</td>
<td>3.57</td>
<td>3.57</td>
<td></td>
</tr>
<tr>
<td>47</td>
<td>10031003</td>
<td>1</td>
<td>PLACEBO</td>
<td>PORTUGAL</td>
<td>3.29</td>
<td>3.57</td>
<td></td>
</tr>
<tr>
<td>48</td>
<td>10031003</td>
<td>2</td>
<td>PLACEBO</td>
<td>PORTUGAL</td>
<td>3.57</td>
<td>3.57</td>
<td></td>
</tr>
<tr>
<td>49</td>
<td>10031003</td>
<td>3</td>
<td>PLACEBO</td>
<td>PORTUGAL</td>
<td>3.00</td>
<td>3.57</td>
<td></td>
</tr>
<tr>
<td>50</td>
<td>10031003</td>
<td>4</td>
<td>PLACEBO</td>
<td>PORTUGAL</td>
<td>2.00</td>
<td>3.57</td>
<td></td>
</tr>
<tr>
<td>51</td>
<td>10031003</td>
<td>5</td>
<td>PLACEBO</td>
<td>PORTUGAL</td>
<td>2.29</td>
<td>3.57</td>
<td></td>
</tr>
<tr>
<td>52</td>
<td>10031003</td>
<td>6</td>
<td>PLACEBO</td>
<td>PORTUGAL</td>
<td>2.57</td>
<td>3.57</td>
<td></td>
</tr>
<tr>
<td>53</td>
<td>10031003</td>
<td>7</td>
<td>PLACEBO</td>
<td>PORTUGAL</td>
<td>2.57</td>
<td>3.57</td>
<td></td>
</tr>
<tr>
<td>54</td>
<td>10031003</td>
<td>8</td>
<td>PLACEBO</td>
<td>PORTUGAL</td>
<td>2.20</td>
<td>3.57</td>
<td></td>
</tr>
<tr>
<td>55</td>
<td>10041001</td>
<td>0</td>
<td>PLACEBO</td>
<td>PORTUGAL</td>
<td>6.14</td>
<td>6.14</td>
<td></td>
</tr>
<tr>
<td>56</td>
<td>10041001</td>
<td>1</td>
<td>PLACEBO</td>
<td>PORTUGAL</td>
<td>6.29</td>
<td>6.14</td>
<td></td>
</tr>
<tr>
<td>57</td>
<td>10041001</td>
<td>2</td>
<td>PLACEBO</td>
<td>PORTUGAL</td>
<td>7.60</td>
<td>6.14</td>
<td></td>
</tr>
<tr>
<td>58</td>
<td>10041001</td>
<td>3</td>
<td>PLACEBO</td>
<td>PORTUGAL</td>
<td>5.00</td>
<td>6.14</td>
<td></td>
</tr>
<tr>
<td>59</td>
<td>10041001</td>
<td>4</td>
<td>PLACEBO</td>
<td>PORTUGAL</td>
<td>1.57</td>
<td>6.14</td>
<td></td>
</tr>
<tr>
<td>60</td>
<td>10041001</td>
<td>5</td>
<td>PLACEBO</td>
<td>PORTUGAL</td>
<td>1.00</td>
<td>6.14</td>
<td></td>
</tr>
<tr>
<td>61</td>
<td>10041001</td>
<td>6</td>
<td>PLACEBO</td>
<td>PORTUGAL</td>
<td>0.57</td>
<td>6.14</td>
<td></td>
</tr>
<tr>
<td>62</td>
<td>10041001</td>
<td>7</td>
<td>PLACEBO</td>
<td>PORTUGAL</td>
<td>0.57</td>
<td>6.14</td>
<td></td>
</tr>
<tr>
<td>63</td>
<td>10041001</td>
<td>8</td>
<td>PLACEBO</td>
<td>PORTUGAL</td>
<td>0.57</td>
<td>6.14</td>
<td></td>
</tr>
<tr>
<td>64</td>
<td>10041003</td>
<td>0</td>
<td>XXXXX</td>
<td>PORTUGAL</td>
<td>0.00</td>
<td>0.00</td>
<td></td>
</tr>
<tr>
<td>65</td>
<td>10041003</td>
<td>1</td>
<td>XXXXX</td>
<td>PORTUGAL</td>
<td>6.75</td>
<td>0.00</td>
<td></td>
</tr>
<tr>
<td>66</td>
<td>10041007</td>
<td>0</td>
<td>PLACEBO</td>
<td>PORTUGAL</td>
<td>0.00</td>
<td>0.00</td>
<td></td>
</tr>
<tr>
<td>67</td>
<td>10041007</td>
<td>1</td>
<td>PLACEBO</td>
<td>PORTUGAL</td>
<td>0.00</td>
<td>0.00</td>
<td></td>
</tr>
<tr>
<td>68</td>
<td>10041007</td>
<td>2</td>
<td>PLACEBO</td>
<td>PORTUGAL</td>
<td>0.00</td>
<td>0.00</td>
<td></td>
</tr>
<tr>
<td>69</td>
<td>10041007</td>
<td>3</td>
<td>PLACEBO</td>
<td>PORTUGAL</td>
<td>1.43</td>
<td>0.00</td>
<td></td>
</tr>
<tr>
<td>70</td>
<td>10041007</td>
<td>4</td>
<td>PLACEBO</td>
<td>PORTUGAL</td>
<td>0.00</td>
<td>0.00</td>
<td></td>
</tr>
<tr>
<td>71</td>
<td>10041007</td>
<td>5</td>
<td>PLACEBO</td>
<td>PORTUGAL</td>
<td>0.00</td>
<td>0.00</td>
<td></td>
</tr>
<tr>
<td>72</td>
<td>10041007</td>
<td>6</td>
<td>PLACEBO</td>
<td>PORTUGAL</td>
<td>0.14</td>
<td>0.00</td>
<td></td>
</tr>
<tr>
<td>73</td>
<td>10041007</td>
<td>7</td>
<td>PLACEBO</td>
<td>PORTUGAL</td>
<td>0.00</td>
<td>0.00</td>
<td></td>
</tr>
<tr>
<td>74</td>
<td>10041007</td>
<td>8</td>
<td>PLACEBO</td>
<td>PORTUGAL</td>
<td>0.00</td>
<td>0.00</td>
<td></td>
</tr>
<tr>
<td>75</td>
<td>10041009</td>
<td>0</td>
<td>XXXXX</td>
<td>PORTUGAL</td>
<td>2.14</td>
<td>2.14</td>
<td></td>
</tr>
<tr>
<td>76</td>
<td>10041009</td>
<td>1</td>
<td>XXXXX</td>
<td>PORTUGAL</td>
<td>1.71</td>
<td>2.14</td>
<td></td>
</tr>
<tr>
<td>77</td>
<td>10041009</td>
<td>2</td>
<td>XXXXX</td>
<td>PORTUGAL</td>
<td>2.57</td>
<td>2.14</td>
<td></td>
</tr>
<tr>
<td>78</td>
<td>10041009</td>
<td>3</td>
<td>XXXXX</td>
<td>PORTUGAL</td>
<td>2.14</td>
<td>2.14</td>
<td></td>
</tr>
<tr>
<td>79</td>
<td>10041009</td>
<td>4</td>
<td>XXXXX</td>
<td>PORTUGAL</td>
<td>0.71</td>
<td>2.14</td>
<td></td>
</tr>
<tr>
<td>80</td>
<td>10041009</td>
<td>5</td>
<td>XXXXX</td>
<td>PORTUGAL</td>
<td>0.71</td>
<td>2.14</td>
<td></td>
</tr>
<tr>
<td>81</td>
<td>10041009</td>
<td>6</td>
<td>XXXXX</td>
<td>PORTUGAL</td>
<td>0.71</td>
<td>2.14</td>
<td></td>
</tr>
<tr>
<td>82</td>
<td>10041009</td>
<td>7</td>
<td>XXXXX</td>
<td>PORTUGAL</td>
<td>1.00</td>
<td>2.14</td>
<td></td>
</tr>
<tr>
<td>83</td>
<td>10041009</td>
<td>8</td>
<td>XXXXX</td>
<td>PORTUGAL</td>
<td>0.71</td>
<td>2.14</td>
<td></td>
</tr>
<tr>
<td>84</td>
<td>10041010</td>
<td>0</td>
<td>XXXXX</td>
<td>PORTUGAL</td>
<td>4.43</td>
<td>4.43</td>
<td></td>
</tr>
<tr>
<td>85</td>
<td>10041010</td>
<td>1</td>
<td>XXXXX</td>
<td>PORTUGAL</td>
<td>4.29</td>
<td>4.43</td>
<td></td>
</tr>
</tbody>
</table>
For scenario 1, if we just have to calculate the difference of two estimates b/w 2 treatment groups by using the code below:

```plaintext
Ods output diffs = diff;
proc mixed data=x noclprint = 8;
   class trttxt poolreg;
   model sleepmw = trttxt poolreg sleepmb/ ddfm=kr solution;
   lsmeans trttxt / cl pdiff ;
run;
```

then by default as mentioned above the difference output would give by alphabetical order and hence we would end up getting difference b/w “Placebo vs XXXX” instead of “XXXX vs Placebo” just like below.

| Effect | TRTXXT  _TRTXXT | Estimate | Error | DF  | t Value | Pr > |t| | Alpha | Lower | Upper |
|--------|----------------|----------|-------|-----|---------|------|---|------|-------|-------|
| TRTXXT PLACEBO XXXXX | 0.2616 | 0.3492 | 85  | 0.75 | 0.4558 | 0.05 | -0.4326 | 0.9559 |

To avoid this we could either use the numeric variable for trttxt i.e TRTSort or best option would be to use a single estimate statement as below and can pick the difference from estimates dataset instead of diffs dataset.

```plaintext
Ods output estimates = est;
proc mixed data=x noclprint = 8;
   class trttxt poolreg;
   model sleepmw = trttxt poolreg sleepmb/ ddfm=kr solution;
   lsmeans trttxt / cl pdiff ;
estimate 'XXXX vs PLACEBO' trttxt -1 1/ cl;
run;
```
For Scenario 2, if we have to calculate the treatment interaction for each week, then we might end up using 8 estimate statements since we have 8 weeks. But instead we can avoid the estimate statement and pick the variate-covariate estimates from the difference dataset itself. For this we could use just the numeric variable of trttxt ‘trtsort’ so that it could be ordered in the right way and makes it easy for us to pick up the right estimates.

/**All in red are commented out **/
ods output diffs = diff;
proc mixed data=x noclprint = 8;
class pt trtsort poolreg week;
model sleepmw = trtsort poolreg sleepmb week trtsort*week/ ddfm=kr solution;
repeated week / subject = pt type = un;
lsmeans trtsort*week / cl pdiff;
/* Redundancy…..
  Estimate 'xxxx vs placebo at week1' trttxt -1 1 week*trttxt -1 0 0 0 0 0 0 0 1 0 0 0 0 0 0 0/cl;
  Estimate 'xxxx vs placebo at week2' trttxt -1 1 week*trttxt 0 -1 0 0 0 0 0 0 1 0 0 0 0 0 0 0/cl;
  Estimate 'xxxx vs placebo at week3' trttxt -1 1 week*trttxt 0 0 -1 0 0 0 0 0 0 1 0 0 0 0 0 0 0/cl;
  Estimate 'xxxx vs placebo at week4' trttxt -1 1 week*trttxt 0 0 0 -1 0 0 0 0 0 0 1 0 0 0 0 0 0 0/cl;
  Estimate 'xxxx vs placebo at week5' trttxt -1 1 week*trttxt 0 0 0 0 -1 0 0 0 0 0 0 1 0 0 0 0 0 0 0/cl;
  Estimate 'xxxx vs placebo at week6' trttxt -1 1 week*trttxt 0 0 0 0 0 -1 0 0 0 0 0 0 1 0 0 0 0 0 0 0/cl;
  Estimate 'xxxx vs placebo at week7' trttxt -1 1 week*trttxt 0 0 0 0 0 0 -1 0 0 0 0 0 0 1 0 0 0 0 0 0 0/cl;
  Estimate 'xxxx vs placebo at week8' trttxt -1 1 week*trttxt 0 0 0 0 0 0 0 -1 0 0 0 0 0 0 0 1 0 0 0 0 0 0 0/cl; */
run;}
### The Mixed Procedure

#### Differences of Least Squares Means

| Effect  | TRTSORT*WEEK | visit window | _TRTSORT_ week | _TRTSORT_ week | Estimate | Standard Error | t Value | Pr > |t| | Alpha Lower | Alpha Upper |
|---------|--------------|--------------|----------------|----------------|----------|----------------|---------|-------|---------|-------------|-------------|
| TRTSORT*WEEK 101 1 101 2 | 0.4075 | 0.6459 | 3.27 | 0.63 | 0.5695 | 0.05 | -1.5550 | 2.3700 |
| TRTSORT*WEEK 101 1 101 3 | 1.0996 | 0.1050 | 5.63 | 1.05 | 0.3337 | 0.05 | -1.562 | 3.7154 |
| TRTSORT*WEEK 101 1 101 4 | 1.0663 | 0.9746 | 3.67 | 1.09 | 0.3404 | 0.05 | -1.7327 | 3.8698 |
| TRTSORT*WEEK 101 1 101 5 | 1.5190 | 1.2288 | 3.83 | 1.24 | 0.2868 | 0.05 | -1.9538 | 4.9918 |
| TRTSORT*WEEK 101 1 101 6 | 2.4093 | 1.3107 | 3.38 | 1.84 | 0.1528 | 0.05 | -1.506 | 6.3247 |
| TRTSORT*WEEK 101 1 101 7 | 2.5813 | 1.4797 | 3.72 | 1.74 | 0.1613 | 0.05 | -1.6509 | 6.8135 |
| TRTSORT*WEEK 101 1 101 8 | 2.0814 | 1.3300 | 3.36 | 1.57 | 0.2058 | 0.05 | -1.9032 | 6.0661 |
From the above output the highlighted ones are the actual estimates b/w XXXX vs Placebo at each week. This can be subsetted by taking “week = _week” from diff dataset created.
Final Estimates picked up from diff dataset as mentioned above.

<table>
<thead>
<tr>
<th>Obs</th>
<th>TRTSORT</th>
<th>WEEK</th>
<th>_TRTSORT</th>
<th>_WEEK</th>
<th>ESTIMATE</th>
<th>PROBT</th>
<th>LOWER</th>
<th>UPPER</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>101</td>
<td>1</td>
<td>102</td>
<td>1</td>
<td>-0.01583</td>
<td>0.9899</td>
<td>-2.7362</td>
<td>2.7046</td>
</tr>
<tr>
<td>2</td>
<td>101</td>
<td>2</td>
<td>102</td>
<td>2</td>
<td>0.01636</td>
<td>0.9843</td>
<td>-2.4293</td>
<td>2.4620</td>
</tr>
<tr>
<td>3</td>
<td>101</td>
<td>3</td>
<td>102</td>
<td>3</td>
<td>-0.00431</td>
<td>0.9936</td>
<td>-1.4610</td>
<td>1.4524</td>
</tr>
<tr>
<td>4</td>
<td>101</td>
<td>4</td>
<td>102</td>
<td>4</td>
<td>0.8147</td>
<td>0.3141</td>
<td>-0.9413</td>
<td>2.5708</td>
</tr>
<tr>
<td>5</td>
<td>101</td>
<td>5</td>
<td>102</td>
<td>5</td>
<td>0.4215</td>
<td>0.6604</td>
<td>-1.8448</td>
<td>2.6879</td>
</tr>
<tr>
<td>6</td>
<td>101</td>
<td>6</td>
<td>102</td>
<td>6</td>
<td>-1.0521</td>
<td>0.3923</td>
<td>-3.7486</td>
<td>1.6444</td>
</tr>
<tr>
<td>7</td>
<td>101</td>
<td>7</td>
<td>102</td>
<td>7</td>
<td>-0.8670</td>
<td>0.5144</td>
<td>-4.2172</td>
<td>2.4832</td>
</tr>
<tr>
<td>8</td>
<td>101</td>
<td>8</td>
<td>102</td>
<td>8</td>
<td>-0.3362</td>
<td>0.7893</td>
<td>-3.1419</td>
<td>2.4696</td>
</tr>
</tbody>
</table>

For Scenario 3, if we consider the entire sample data mentioned above for scenario 2 then the model would not converge and would give the output as below.

The Mixed Procedure

Model Information

Data Set WORK.X
Dependent Variable SLEEPMW
Covariance Structure Unstructured
Subject Effect PT
Estimation Method REML
Residual Variance Method None
Fixed Effects SE Method Prasad-Rao-Jeske- Kackar-Harville
Degrees of Freedom Method Kenward-Roger

Class Level Information

<table>
<thead>
<tr>
<th>Class</th>
<th>Levels</th>
<th>Values</th>
</tr>
</thead>
<tbody>
<tr>
<td>PT</td>
<td>12</td>
<td>not printed</td>
</tr>
<tr>
<td>TRTSORT</td>
<td>2</td>
<td>101 102</td>
</tr>
<tr>
<td>POOLREG</td>
<td>1</td>
<td>PORTUGAL</td>
</tr>
<tr>
<td>WEEK</td>
<td>9</td>
<td>not printed</td>
</tr>
</tbody>
</table>

WARNING: Unable to make hessian positive definite.

Depending upon the data, sometimes it would give a warning as “Unable to Converge”. As explained before in case 3 in Model and Options section, when the analysis variable at baseline is compared with baseline variable it would not converge the data and hence would not produce the output. In order to avoid this variants-covariate mis-interaction we would subset the data going into case 2 to eliminate Baseline visit ‘Week 0’ and keep all the other visits to get proper converged output.
CONCLUSION

The Mixed procedure is discussed and SAS® codes are presented to implement the mixed-effects model selections. The program is simple, straightforward, efficient and easy to implement. Using the same strategy, similar cases demonstrated above can also be used for other model testing and selection procedures. With the help of above mentioned options and methods, user can easily overcome any further issues related to similar cases and will have more experience to handle any other cases by taking this as a base and by doing similar trial and error process.

CONTACT INFORMATION

Your queries and comments are valued and encouraged. Contact the authors at:
   Name: Shilpa Edupganti
   E-mail: shilpaedupganti@gmail.com

   Name: Sheetal Nisal
   E-mail: sheetalnisal@gmail.com

TRADEMARKS

SAS® and all other SAS Institute Inc. product or service names are registered trademarks or trademarks of SAS Institute Inc. in the USA and other countries. ® Indicates USA registration.

Other brand and product names are registered trademarks or trademarks of their respective companies.