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Proc Mixed - Right Options to get Right Output

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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'.
When used the proc mixed code without an estimate statement, we picked up the difference of estimates like: *mean, stderror, 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** = trtsort poolreg **sleepmb** week trtsort*week/ ddfm=kr solution'*

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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:

```
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:

Obs	Patient	visit window week	TRTSORT	TRTTXT	Pooled Region	Mean Sleep Interference Score Based T W	Weekly Mean Baseline Sleep Interference
1	10011001	0	101	XXXXX	PORTUGAL	3.86	3.86
2	10011001	1	101	XXXXX	PORTUGAL	3.43	3.86
3	10011001	2	101	XXXXX	PORTUGAL	3.00	3.86
4	10011001	3	101	XXXXX	PORTUGAL	2.86	3.86
5	10011001	4	101	XXXXX	PORTUGAL	3.14	3.86
6	10011001	5	101	XXXXX	PORTUGAL	3.57	3.86
7	10011001	6	101	XXXXX	PORTUGAL	3.29	3.86
8	10011001	7	101	XXXXX	PORTUGAL	3.29	3.86
9	10011001	8	101	XXXXX	PORTUGAL	3.14	3.86
10	10021001	0	101	XXXXX	PORTUGAL	3.00	3.00
11	10021001	1	101	XXXXX	PORTUGAL	2.25	3.00
12	10021001	2	101	XXXXX	PORTUGAL	2.50	3.00
13	10021001	3	101	XXXXX	PORTUGAL	1.71	3.00
14	10021001	4	101	XXXXX	PORTUGAL	2.00	3.00
15	10021001	5	101	XXXXX	PORTUGAL	1.71	3.00
16	10021001	6	101	XXXXX	PORTUGAL	1.17	3.00
17	10021001	7	101	XXXXX	PORTUGAL	1.29	3.00
18	10021001	8	101	XXXXX	PORTUGAL	1.71	3.00
19	10021002	0	102	PLACEBO	PORTUGAL	4.57	4.57
20	10021002	1	102	PLACEBO	PORTUGAL	6.83	4.57
21	10021002	2	102	PLACEBO	PORTUGAL	5.14	4.57
22	10021002	3	102	PLACEBO	PORTUGAL	3.57	4.57
23	10021002	4	102	PLACEBO	PORTUGAL	3.71	4.57
24	10021002	5	102	PLACEBO	PORTUGAL	2.86	4.57
25	10021002	6	102	PLACEBO	PORTUGAL	4.29	4.57
26	10021002	7	102	PLACEBO	PORTUGAL	3.29	4.57
27	10021002	8	102	PLACEBO	PORTUGAL	4.50	4.57
28	10021003	0	102	PLACEBO	PORTUGAL	4.29	4.29
29	10021003	1	102	PLACEBO	PORTUGAL	4.33	4.29
30	10021003	2	102	PLACEBO	PORTUGAL	2.71	4.29
31	10021003	3	102	PLACEBO	PORTUGAL	2.71	4.29
32	10021003	4	102	PLACEBO	PORTUGAL	4.14	4.29
33	10021003	5	102	PLACEBO	PORTUGAL	4.86	4.29
34	10021003	6	102	PLACEBO	PORTUGAL	6.00	4.29
35	10021003	7	102	PLACEBO	PORTUGAL	6.00	4.29
36	10021003	8	102	PLACEBO	PORTUGAL	6.00	4.29
37	10031002	0	102	PLACEBO	PORTUGAL	8.00	8.00
38	10031002	1	102	PLACEBO	PORTUGAL	7.50	8.00
39	10031002	2	102	PLACEBO	PORTUGAL	6.57	8.00
40	10031002	3	102	PLACEBO	PORTUGAL	5.86	8.00
41	10031002	4	102	PLACEBO	PORTUGAL	5.43	8.00
42	10031002	5	102	PLACEBO	PORTUGAL	5.50	8.00
43	10031002	6	102	PLACEBO	PORTUGAL	6.43	8.00
44	10031002	7	102	PLACEBO	PORTUGAL	5.43	8.00
45	10031002	8	102	PLACEBO	PORTUGAL	4.40	8.00
46	10031003	0	102	PLACEBO	PORTUGAL	3.57	3.57
47	10031003	1	102	PLACEBO	PORTUGAL	3.29	3.57
48	10031003	2	102	PLACEBO	PORTUGAL	3.57	3.57
49	10031003	3	102	PLACEBO	PORTUGAL	3.00	3.57
50	10031003	4	102	PLACEBO	PORTUGAL	2.00	3.57
51	10031003	5	102	PLACEBO	PORTUGAL	2.29	3.57
52	10031003	6	102	PLACEBO	PORTUGAL	2.57	3.57
53	10031003	7	102	PLACEBO	PORTUGAL	2.57	3.57
54	10031003	8	102	PLACEBO	PORTUGAL	2.20	3.57

55	10041001	0	102	PLACEBO	PORTUGAL	6.14	6.14
56	10041001	1	102	PLACEBO	PORTUGAL	6.29	6.14
57	10041001	2	102	PLACEBO	PORTUGAL	7.60	6.14
58	10041001	3	102	PLACEBO	PORTUGAL	5.00	6.14
59	10041001	4	102	PLACEBO	PORTUGAL	1.57	6.14
60	10041001	5	102	PLACEBO	PORTUGAL	1.00	6.14
61	10041001	6	102	PLACEBO	PORTUGAL	0.57	6.14
62	10041001	7	102	PLACEBO	PORTUGAL	0.57	6.14
63	10041001	8	102	PLACEBO	PORTUGAL	0.57	6.14
64	10041003	0	101	XXXXX	PORTUGAL	0.00	0.00
65	10041003	1	101	XXXXX	PORTUGAL	6.75	0.00
66	10041007	0	102	PLACEBO	PORTUGAL	0.00	0.00
67	10041007	1	102	PLACEBO	PORTUGAL	0.00	0.00
68	10041007	2	102	PLACEBO	PORTUGAL	0.00	0.00
69	10041007	3	102	PLACEBO	PORTUGAL	1.43	0.00
70	10041007	4	102	PLACEBO	PORTUGAL	0.00	0.00
71	10041007	5	102	PLACEBO	PORTUGAL	0.00	0.00
72	10041007	6	102	PLACEBO	PORTUGAL	0.14	0.00
73	10041007	7	102	PLACEBO	PORTUGAL	0.00	0.00
74	10041007	8	102	PLACEBO	PORTUGAL	0.00	0.00
75	10041009	0	101	XXXXX	PORTUGAL	2.14	2.14
76	10041009	1	101	XXXXX	PORTUGAL	1.71	2.14
77	10041009	2	101	XXXXX	PORTUGAL	2.57	2.14
78	10041009	3	101	XXXXX	PORTUGAL	2.14	2.14
79	10041009	4	101	XXXXX	PORTUGAL	0.71	2.14
80	10041009	5	101	XXXXX	PORTUGAL	0.71	2.14
81	10041009	6	101	XXXXX	PORTUGAL	0.71	2.14
82	10041009	7	101	XXXXX	PORTUGAL	1.00	2.14
83	10041009	8	101	XXXXX	PORTUGAL	0.71	2.14
84	10041010	0	101	XXXXX	PORTUGAL	4.43	4.43
85	10041010	1	101	XXXXX	PORTUGAL	4.29	4.43
86	10041010	2	101	XXXXX	PORTUGAL	3.71	4.43
87	10041010	3	101	XXXXX	PORTUGAL	4.71	4.43
88	10041010	4	101	XXXXX	PORTUGAL	4.57	4.43
89	10041010	5	101	XXXXX	PORTUGAL	4.14	4.43
90	10041010	6	101	XXXXX	PORTUGAL	1.00	4.43
91	10041010	7	101	XXXXX	PORTUGAL	1.00	4.43
92	10041010	8	101	XXXXX	PORTUGAL	1.14	4.43
93	10041011	0	101	XXXXX	PORTUGAL	3.29	3.29
94	10041011	1	101	XXXXX	PORTUGAL	2.00	3.29
95	10041011	2	101	XXXXX	PORTUGAL	3.00	3.29
96	10041011	3	101	XXXXX	PORTUGAL	3.14	3.29
97	10041011	4	101	XXXXX	PORTUGAL	3.00	3.29
98	10041011	5	101	XXXXX	PORTUGAL	2.57	3.29
99	10041011	6	101	XXXXX	PORTUGAL	1.71	3.29
100	10041011	7	101	XXXXX	PORTUGAL	2.00	3.29

For scenario 1, if we just have to calculate the difference of two estimates b/w 2 treatment groups by using the code below:

```
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 alpahetical order and hence we would end up getting difference b/w “Placebo vs XXXX” instead of “XXXX vs Placebo” just like below.

Differences of Least Squares Means

Effect	TRTTXT	_TRTTXT	Estimate	Standard Error	DF	t Value	Pr > |t|	Alpha	Lower	Upper
TRTTXT	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.

```
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;
```

Estimates

Label	Estimate	Standard Error	DF	t Value	Pr > |t|	Alpha	Lower	Upper
XXXX vs PLACEBO	-0.2616	0.3492	85	-0.75	0.4558	0.05	-0.9559	0.4326

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-covaraite 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  0 1 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 0 1 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 0 1 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 0 1 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 0 1 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 0 1 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/cl;  */
run;
```

Difference Dataset Output:

The Mixed Procedure

Differences of Least Squares Means

Effect	TRTSORT	visit window week	_TRTSORT	visit window week	Estimate	Standard Error	DF	t Value	Pr > |t|	Alpha	Lower	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	1.0520	5.63	1.05	0.3387	0.05	-1.5162	3.7154
TRTSORT*WEEK	101	1	101	4	1.0663	0.9746	3.67	1.09	0.3404	0.05	-1.7372	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	-1.5061	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
TRTSORT*WEEK	101	1	102	1	-0.01583	1.2197	9.92	-0.01	0.9899	0.05	-2.7362	2.7046
TRTSORT*WEEK	101	1	102	2	0.4239	1.0062	10.2	0.42	0.6824	0.05	-1.8131	2.6608
TRTSORT*WEEK	101	1	102	3	1.0953	0.9246	11.4	1.18	0.2602	0.05	-0.9306	3.1211
TRTSORT*WEEK	101	1	102	4	1.8810	0.9926	14.9	1.90	0.0777	0.05	-0.2359	3.9979
TRTSORT*WEEK	101	1	102	5	1.9405	1.0460	14	1.86	0.0847	0.05	-0.3026	4.1836
TRTSORT*WEEK	101	1	102	6	1.3572	1.1425	16.9	1.19	0.2513	0.05	-1.0549	3.7692
TRTSORT*WEEK	101	1	102	7	1.7143	1.1744	10.2	1.46	0.1744	0.05	-0.8943	4.3230
TRTSORT*WEEK	101	1	102	8	1.7453	1.1639	17.3	1.50	0.1518	0.05	-0.7075	4.1981
TRTSORT*WEEK	101	2	101	3	0.6921	0.6966	3.38	0.99	0.3862	0.05	-1.3906	2.7748
TRTSORT*WEEK	101	2	101	4	0.6588	1.0066	5.46	0.65	0.5394	0.05	-1.8649	3.1824
TRTSORT*WEEK	101	2	101	5	1.1115	1.2026	4.04	0.92	0.4072	0.05	-2.2156	4.4386
TRTSORT*WEEK	101	2	101	6	2.0018	1.3449	4.79	1.49	0.1993	0.05	-1.5008	5.5044
TRTSORT*WEEK	101	2	101	7	2.1738	1.4130	3.7	1.54	0.2045	0.05	-1.8801	6.2278
TRTSORT*WEEK	101	2	101	8	1.6740	1.3474	4.9	1.24	0.2702	0.05	-1.8100	5.1579
TRTSORT*WEEK	101	2	102	1	-0.4233	1.0303	10.6	-0.41	0.6894	0.05	-2.7021	1.8555
TRTSORT*WEEK	101	2	102	2	0.01636	0.7658	2.98	0.02	0.9843	0.05	-2.4293	2.4620
TRTSORT*WEEK	101	2	102	3	0.6878	0.6549	6.03	1.05	0.3338	0.05	-0.9125	2.2880
TRTSORT*WEEK	101	2	102	4	1.4735	0.7478	9.34	1.97	0.0791	0.05	-0.2088	3.1558
TRTSORT*WEEK	101	2	102	5	1.5330	0.8174	4.7	1.88	0.1233	0.05	-0.6091	3.6751
TRTSORT*WEEK	101	2	102	6	0.9497	0.9377	7.09	1.01	0.3445	0.05	-1.2621	3.1615
TRTSORT*WEEK	101	2	102	7	1.3068	0.9764	4.07	1.34	0.2507	0.05	-1.3862	3.9999
TRTSORT*WEEK	101	2	102	8	1.3378	0.9636	8.2	1.39	0.2016	0.05	-0.8752	3.5507
TRTSORT*WEEK	101	3	101	4	-0.03333	0.6621	5.34	-0.05	0.9617	0.05	-1.7030	1.6364
TRTSORT*WEEK	101	3	101	5	0.4194	0.7660	8.83	0.55	0.5976	0.05	-1.3185	2.1573
TRTSORT*WEEK	101	3	101	6	1.3097	1.0585	8.97	1.24	0.2474	0.05	-1.0861	3.7055
TRTSORT*WEEK	101	3	101	7	1.4817	1.0508	6.74	1.41	0.2030	0.05	-1.0230	3.9865
TRTSORT*WEEK	101	3	101	8	0.9819	1.0799	8.92	0.91	0.3872	0.05	-1.4644	3.4281
TRTSORT*WEEK	101	3	102	1	-1.1154	0.9384	11.7	-1.19	0.2581	0.05	-3.1655	0.9346
TRTSORT*WEEK	101	3	102	2	-0.6757	0.6368	5.89	-1.06	0.3302	0.05	-2.2408	0.8894
TRTSORT*WEEK	101	3	102	3	-0.00431	0.4979	3.54	-0.01	0.9936	0.05	-1.4610	1.4524
TRTSORT*WEEK	101	3	102	4	0.7814	0.6150	10.9	1.27	0.2303	0.05	-0.5737	2.1365

TRTSORT*WEEK	101	3	102	5	0.8409	0.6980	7.65	1.20	0.2643	0.05	-0.7818	2.4637
TRTSORT*WEEK	101	3	102	6	0.2576	0.8357	10	0.31	0.7642	0.05	-1.6039	2.1191
TRTSORT*WEEK	101	3	102	7	0.6147	0.8789	5.23	0.70	0.5142	0.05	-1.6154	2.8449
TRTSORT*WEEK	101	3	102	8	0.6457	0.8647	10.2	0.75	0.4721	0.05	-1.2769	2.5683
TRTSORT*WEEK	101	4	101	5	0.4527	0.3172	3.25	1.43	0.2421	0.05	-0.5145	1.4200
TRTSORT*WEEK	101	4	101	6	1.3430	0.6179	5.53	2.17	0.0766	0.05	-0.2009	2.8869
TRTSORT*WEEK	101	4	101	7	1.5151	0.7176	3.41	2.11	0.1143	0.05	-0.6216	3.6517
TRTSORT*WEEK	101	4	101	8	1.0152	0.6505	6.03	1.56	0.1694	0.05	-0.5746	2.6049
TRTSORT*WEEK	101	4	102	1	-1.0821	1.0368	15.6	-1.04	0.3125	0.05	-3.2846	1.1204
TRTSORT*WEEK	101	4	102	2	-0.6424	0.7745	9.57	-0.83	0.4271	0.05	-2.3787	1.0938
TRTSORT*WEEK	101	4	102	3	0.02902	0.6650	10.7	0.04	0.9660	0.05	-1.4396	1.4977
TRTSORT*WEEK	101	4	102	4	0.8147	0.7567	7.72	1.08	0.3141	0.05	-0.9413	2.5708
TRTSORT*WEEK	101	4	102	5	0.8743	0.8256	8.84	1.06	0.3177	0.05	-0.9987	2.7472
TRTSORT*WEEK	101	4	102	6	0.2909	0.9448	10.6	0.31	0.7641	0.05	-1.7982	2.3800
TRTSORT*WEEK	101	4	102	7	0.6481	0.9832	6.84	0.66	0.5314	0.05	-1.6880	2.9841
TRTSORT*WEEK	101	4	102	8	0.6790	0.9706	10.6	0.70	0.4993	0.05	-1.4678	2.8258
TRTSORT*WEEK	101	5	101	6	0.8903	0.4863	8.02	1.83	0.1044	0.05	-0.2305	2.0110
TRTSORT*WEEK	101	5	101	7	1.0623	0.5024	4.76	2.11	0.0909	0.05	-0.2486	2.3733
TRTSORT*WEEK	101	5	101	8	0.5624	0.5852	7.83	0.96	0.3652	0.05	-0.7921	1.9170
TRTSORT*WEEK	101	5	102	1	-1.5348	1.1043	14.8	-1.39	0.1852	0.05	-3.8920	0.8223
TRTSORT*WEEK	101	5	102	2	-1.0951	0.8628	5.05	-1.27	0.2597	0.05	-3.3067	1.1164
TRTSORT*WEEK	101	5	102	3	-0.4237	0.7661	7.98	-0.55	0.5953	0.05	-2.1910	1.3436
TRTSORT*WEEK	101	5	102	4	0.3620	0.8469	8.86	0.43	0.6793	0.05	-1.5585	2.2825
TRTSORT*WEEK	101	5	102	5	0.4215	0.9090	5.57	0.46	0.6604	0.05	-1.8448	2.6879
TRTSORT*WEEK	101	5	102	6	-0.1618	1.0185	7.78	-0.16	0.8778	0.05	-2.5220	2.1984
TRTSORT*WEEK	101	5	102	7	0.1953	1.0542	4.96	0.19	0.8603	0.05	-2.5215	2.9122
TRTSORT*WEEK	101	5	102	8	0.2263	1.0424	8.44	0.22	0.8333	0.05	-2.1557	2.6083
TRTSORT*WEEK	101	6	101	7	0.1721	0.2795	4.06	0.62	0.5710	0.05	-0.5996	0.9437
TRTSORT*WEEK	101	6	101	8	-0.3278	0.3532	8.56	-0.93	0.3788	0.05	-1.1331	0.4775
TRTSORT*WEEK	101	6	102	1	-2.4251	1.2369	17.2	-1.96	0.0663	0.05	-5.0323	0.1821
TRTSORT*WEEK	101	6	102	2	-1.9854	1.0271	7.55	-1.93	0.0914	0.05	-4.3785	0.4076
TRTSORT*WEEK	101	6	102	3	-1.3140	0.9472	9.87	-1.39	0.1959	0.05	-3.4284	0.8004
TRTSORT*WEEK	101	6	102	4	-0.5283	1.0137	10.4	-0.52	0.6132	0.05	-2.7760	1.7194
TRTSORT*WEEK	101	6	102	5	-0.4688	1.0661	7.9	-0.44	0.6719	0.05	-2.9327	1.9952
TRTSORT*WEEK	101	6	102	6	-1.0521	1.1609	7.68	-0.91	0.3923	0.05	-3.7486	1.6444
TRTSORT*WEEK	101	6	102	7	-0.6949	1.1924	5.85	-0.58	0.5818	0.05	-3.6311	2.2412
TRTSORT*WEEK	101	6	102	8	-0.6640	1.1819	8.35	-0.56	0.5890	0.05	-3.3697	2.0417
TRTSORT*WEEK	101	7	101	8	-0.4999	0.3866	2.9	-1.29	0.2893	0.05	-1.7543	0.7546
TRTSORT*WEEK	101	7	102	1	-2.5972	1.2592	11	-2.06	0.0636	0.05	-5.3693	0.1750
TRTSORT*WEEK	101	7	102	2	-2.1575	1.0539	4.51	-2.05	0.1021	0.05	-4.9570	0.6421
TRTSORT*WEEK	101	7	102	3	-1.4860	0.9762	5.79	-1.52	0.1805	0.05	-3.8957	0.9236
TRTSORT*WEEK	101	7	102	4	-0.7003	1.0409	7.09	-0.67	0.5224	0.05	-3.1555	1.7548
TRTSORT*WEEK	101	7	102	5	-0.6408	1.0920	5.14	-0.59	0.5822	0.05	-3.4255	2.1439
TRTSORT*WEEK	101	7	102	6	-1.2241	1.1847	5.81	-1.03	0.3426	0.05	-4.1462	1.6980
TRTSORT*WEEK	101	7	102	7	-0.8670	1.2156	4.08	-0.71	0.5144	0.05	-4.2172	2.4832
TRTSORT*WEEK	101	7	102	8	-0.8360	1.2053	6.23	-0.69	0.5129	0.05	-3.7592	2.0871
TRTSORT*WEEK	101	8	102	1	-2.0973	1.2697	17.4	-1.65	0.1165	0.05	-4.7713	0.5767
TRTSORT*WEEK	101	8	102	2	-1.6576	1.0664	8.59	-1.55	0.1561	0.05	-4.0877	0.7725
TRTSORT*WEEK	101	8	102	3	-0.9862	0.9897	9.91	-1.00	0.3428	0.05	-3.1941	1.2218
TRTSORT*WEEK	101	8	102	4	-0.2004	1.0535	10.3	-0.19	0.8528	0.05	-2.5384	2.1375
TRTSORT*WEEK	101	8	102	5	-0.1409	1.1040	8.51	-0.13	0.9014	0.05	-2.6603	2.3785
TRTSORT*WEEK	101	8	102	6	-0.7243	1.1958	8.36	-0.61	0.5608	0.05	-3.4611	2.0126
TRTSORT*WEEK	101	8	102	7	-0.3671	1.2264	6.3	-0.30	0.7743	0.05	-3.3332	2.5990
TRTSORT*WEEK	101	8	102	8	-0.3362	1.2162	7.98	-0.28	0.7893	0.05	-3.1419	2.4696
TRTSORT*WEEK	102	1	102	2	0.4397	0.6008	2.91	0.73	0.5187	0.05	-1.5055	2.3849
TRTSORT*WEEK	102	1	102	3	1.1111	1.0327	5.48	1.08	0.3270	0.05	-1.4748	3.6970
TRTSORT*WEEK	102	1	102	4	1.8968	0.9212	3.35	2.06	0.1220	0.05	-0.8677	4.6614
TRTSORT*WEEK	102	1	102	5	1.9563	1.1703	3.54	1.67	0.1791	0.05	-1.4669	5.3796
TRTSORT*WEEK	102	1	102	6	1.3730	1.2162	3	1.13	0.3410	0.05	-2.4970	5.2430
TRTSORT*WEEK	102	1	102	7	1.7302	1.4019	3.41	1.23	0.2954	0.05	-2.4424	5.9027
TRTSORT*WEEK	102	1	102	8	1.7611	1.2237	2.95	1.44	0.2472	0.05	-2.1709	5.6931
TRTSORT*WEEK	102	2	102	3	0.6714	0.6435	2.97	1.04	0.3740	0.05	-1.3864	2.7293
TRTSORT*WEEK	102	2	102	4	1.4571	0.8554	4.64	1.70	0.1537	0.05	-0.7940	3.7083
TRTSORT*WEEK	102	2	102	5	1.5167	1.0463	3.34	1.45	0.2341	0.05	-1.6287	4.6620
TRTSORT*WEEK	102	2	102	6	0.9333	1.1524	4	0.81	0.4634	0.05	-2.2656	4.1323
TRTSORT*WEEK	102	2	102	7	1.2905	1.2436	3.07	1.04	0.3741	0.05	-2.6151	5.1960
TRTSORT*WEEK	102	2	102	8	1.3214	1.1482	4.09	1.15	0.3125	0.05	-1.8378	4.4806
TRTSORT*WEEK	102	3	102	4	0.7857	0.5632	4.53	1.39	0.2276	0.05	-0.7090	2.2804
TRTSORT*WEEK	102	3	102	5	0.8452	0.6393	8.74	1.32	0.2197	0.05	-0.6074	2.2979
TRTSORT*WEEK	102	3	102	6	0.2619	0.8829	8.95	0.30	0.7735	0.05	-1.7371	2.2609

TRTSORT*WEEK	102	3	102	7	0.6190	0.8847	6.01	0.70	0.5103	0.05	-1.5447	2.7828
TRTSORT*WEEK	102	3	102	8	0.6500	0.8963	8.84	0.73	0.4871	0.05	-1.3831	2.6831
TRTSORT*WEEK	102	4	102	5	0.05952	0.2951	2.89	0.20	0.8535	0.05	-0.8997	1.0188
TRTSORT*WEEK	102	4	102	6	-0.5238	0.5250	4.71	-1.00	0.3668	0.05	-1.8985	0.8509
TRTSORT*WEEK	102	4	102	7	-0.1667	0.6418	2.87	-0.26	0.8126	0.05	-2.2608	1.9274
TRTSORT*WEEK	102	4	102	8	-0.1357	0.5433	5.18	-0.25	0.8124	0.05	-1.5178	1.2463
TRTSORT*WEEK	102	5	102	6	-0.5833	0.4066	7.61	-1.43	0.1912	0.05	-1.5293	0.3627
TRTSORT*WEEK	102	5	102	7	-0.2262	0.4306	3.97	-0.53	0.6273	0.05	-1.4248	0.9724
TRTSORT*WEEK	102	5	102	8	-0.1952	0.4806	7.26	-0.41	0.6963	0.05	-1.3235	0.9330
TRTSORT*WEEK	102	6	102	7	0.3571	0.2679	3.79	1.33	0.2570	0.05	-0.4031	1.1174
TRTSORT*WEEK	102	6	102	8	0.3881	0.2818	8.23	1.38	0.2047	0.05	-0.2585	1.0347
TRTSORT*WEEK	102	7	102	8	0.03095	0.3408	2.43	0.09	0.9346	0.05	-1.2126	1.2745

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.

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

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

Class	Levels	Values
PT	12	not printed
TRTSORT	2	101 102
POOLREG	1	PORTUGAL
WEEK	9	not printed

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, straight-forward, 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

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