

Chapter 33

Generalized Linear Mixed Models for Outcome Prediction from Mixed Data (20 Patients)

General Purpose

To assess whether generalized linear mixed models can be used to train clinical samples with both fixed and random effects about individual future patients

Specific Scientific Question

In a parallel-group study of two treatments, each patient was measured weekly for 5 weeks. As repeated measures in one patient are more similar than unrepeated ones, a random interaction effect between week and patient was assumed.

Example

In a parallel-group study of two cholesterol reducing compounds, patients were measured weekly for 5 weeks. As repeated measures in one patient are more similar than unrepeated ones, we assumed that a random interaction variable between week and patient would appropriately adjust this effect.

| Patient_id | week | hdl-cholesterol (mmol/l) | treatment (0 or 1) |
|------------|------|--------------------------|--------------------|
| 1 | 1 | 1,66 | 0 |
| 1 | 2 | 1,62 | 0 |
| 1 | 3 | 1,57 | 0 |
| 1 | 4 | 1,52 | 0 |
| 1 | 5 | 1,50 | 0 |
| 2 | 1 | 1,69 | 0 |

(continued)

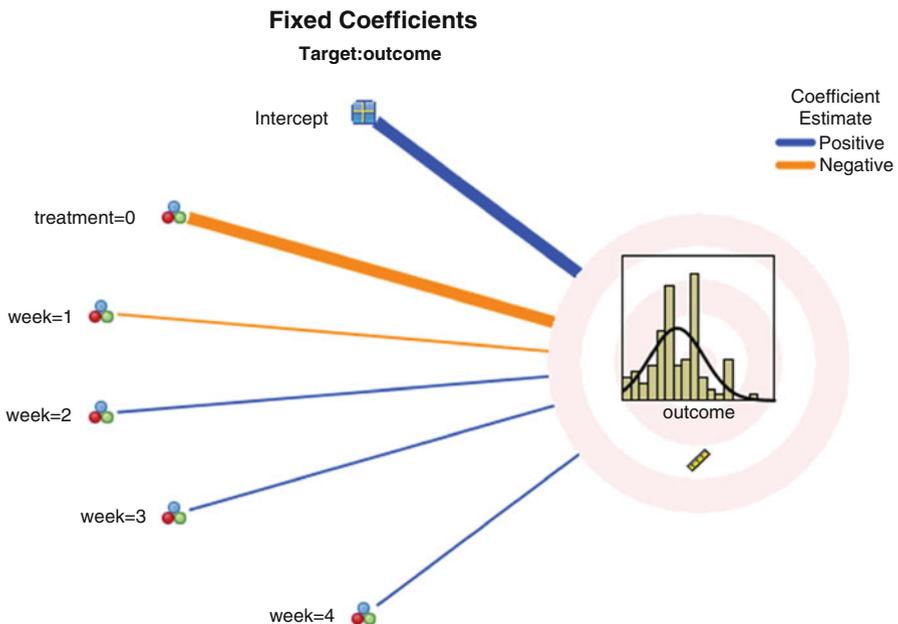
This chapter was previously published in “Machine learning in medicine-cookbook 2” as Chap. 9, 2014.

| Patient_id | week | hdl-cholesterol (mmol/l) | treatment (0 or 1) |
|------------|------|--------------------------|--------------------|
| 2 | 2 | 1,71 | 0 |
| 2 | 3 | 1,60 | 0 |
| 2 | 4 | 1,55 | 0 |
| 2 | 5 | 1,56 | 0 |

Only the first 2 patients of the data file is shown. The entire file entitled “fixedandrandomeffects” is in extras.springer.com. We will try and develop a mixed model (mixed means a model with both fixed and random predictors) for testing the data. Also, SPSS will be requested to produce a ZIP (compressed file that can be unzipped) file from the intervention study, which could then be used for making predictions about cholesterol values in future patients treated similarly. We will start by opening the intervention study’s data file.

Command:

click Transform...click Random Number Generators...click Set Starting Point...click Fixed Value (2000000)...click OK...click Analyze...Mixed Linear...Generalized Mixed Linear Models...click Data Structure...click left mouse and drag patient_id to Subjects part of the canvas...click left mouse and drag week to Repeated Measures part of the canvas...click Fields and Effects...click Target...check that the variable outcome is already in the Target window...check that Linear model is marked...click Fixed Effects...drag treatment and week to Effect builder...click Random Effects...click Add Block...click Add a custom term...move week*treatment (* is symbol multiplication and interaction) to the Custom term window...click Add term...click OK...click Model Options...click Save Fields...mark Predicted Values...click Export model... type exportfixedandrandom...click Browse...in the appropriate folder enter in File name: mixed...click Run.



| Source | F | df1 | df2 | Sig. |
|-----------------|--------|-----|-----|------|
| Corrected model | 5,027 | 5 | 94 | ,000 |
| Treatment | 23,722 | 1 | 94 | ,000 |
| Week | 0,353 | 4 | 94 | ,041 |

Probability distribution:Normal
 Link function:Identity

In the output sheet a graph is observed with the mean and standard errors of the outcome value displayed with the best fit Gaussian curve. The F-value of 23.722 indicates that one treatment is very significantly better than the other with $p < 0.0001$. The thickness of the lines are a measure for level of significance, and so the significance of the 5 week is very thin and thus very weak. Week 5 is not shown. It is redundant, because it means absence of the other 4 weeks. If you click at the left bottom of the graph panel, a table comes up providing similar information in written form. The effect of the interaction variable is not shown, but implied in the analysis.

If we return to the data file page, we will observe that the software has produced a predicted value for each actually measured cholesterol value. The predicted and actual values are very much the same.

We will now use the ZIP file to make predictions about cholesterol values in future patients treated similarly.

| week | treatment | patient_id |
|------|-----------|------------|
| 1 | 0 | 21 |
| 2 | 0 | 21 |
| 3 | 0 | 21 |
| 4 | 0 | 21 |
| 5 | 0 | 21 |
| 1 | 1 | 22 |
| 2 | 1 | 22 |
| 3 | 1 | 22 |
| 4 | 1 | 22 |
| 5 | 1 | 22 |

Command:

click Utilities....click Scoring Wizard....click Browse....click Select...Folder: enter the mixed ZIP file entitled "exportfixedandrandom"....click Select....in Scoring Wizard click Next....click Finish.

In the data file now the predicted cholesterol values are given.

| week | treatment | patient_id | predicted cholesterol |
|------|-----------|------------|-----------------------|
| 1 | 0 | 21 | 1,88 |
| 2 | 0 | 21 | 1,96 |
| 3 | 0 | 21 | 1,94 |

(continued)

| week | treatment | patient_id | predicted cholesterol |
|------|-----------|------------|-----------------------|
| 4 | 0 | 21 | 1,91 |
| 5 | 0 | 21 | 1,89 |
| 1 | 1 | 22 | 2,12 |
| 2 | 1 | 22 | 2,20 |
| 3 | 1 | 22 | 2,18 |
| 4 | 1 | 22 | 2,15 |
| 5 | 1 | 22 | 2,13 |

Conclusion

The module Generalized mixed linear models provides the possibility to handle both fixed and random effects, and is, therefore appropriate to adjust data with repeated measures and presumably a strong correlation between the repeated measures. Also individual future patients treated similarly can be assessed for predicted cholesterol values using a ZIP file.

Note

More background theoretical and mathematical information of models with both fixed and random variables is given in:

1. Machine learning in medicine part one, Chap. 6, Mixed linear models, pp 65–76, 2013,
2. Statistics applied to clinical studies 5th edition, Chap. 56, Advanced analysis of variance, random effects and mixed effects models, pp 607–618, 2012,
3. SPSS for starters part one, Chap. 7, Mixed models, pp 25–29, 2010, and,
4. Machine learning in medicine part three, Chap. 9, Random effects, pp 81–94, 2013.

All of these references are from the same authors and have been edited by Springer Heidelberg Germany.