Multilevel model: repeated measurements

Contents

1. Introduction

Quite frequently, a subject may be measured at multiple time points. In such a case, the subject is treated as the level-2 unit with the repeated measures nested within each person at level-1. An example of this is the study of patients with prostate cancer. The patients were offered a new treatment aimed at reducing cancer activity in the prostate. However, not all patients opted in right away – some only entered the program later. Some patients also dropped out, so in that sense we are dealing with missing data.

The file **Psa.lsf** contains four variables:

- Patient: a patient identifier, used as the level-2 ID in our analysis
- Months: the time of measurement of the prostate specific antigen
- PSA: the pathogen specific antigen that is the outcome of interest here. PSA is an enzyme that is elevated in the presence of prostate cancer.
- Age: the age of the patient at the initial doctor visit

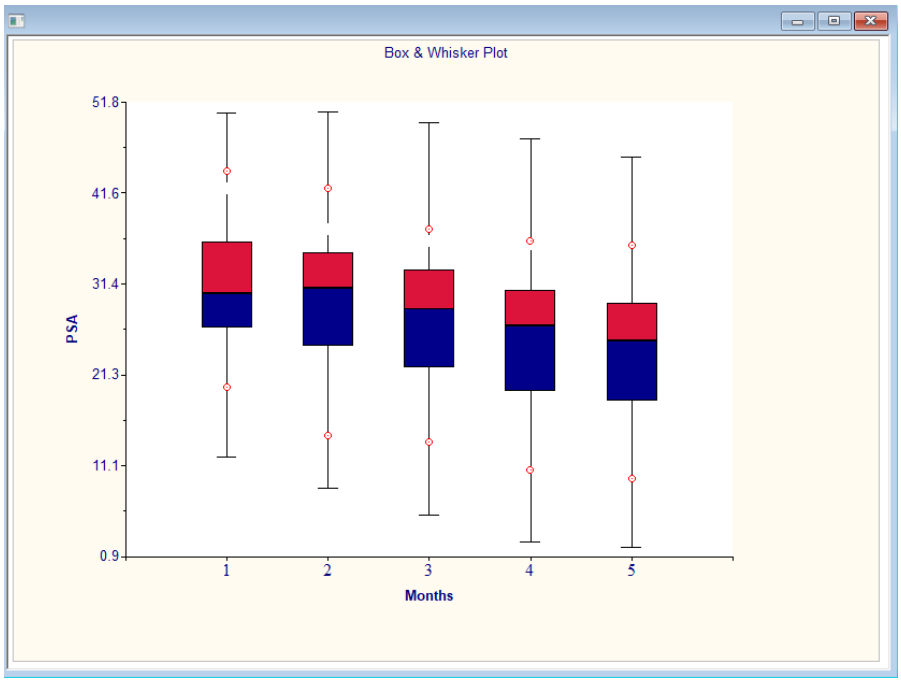
The first 20 lines of the data set are shown below. Data and syntax files can be found in the **MVABOOK\Chapter4** folder.

psa.LSF

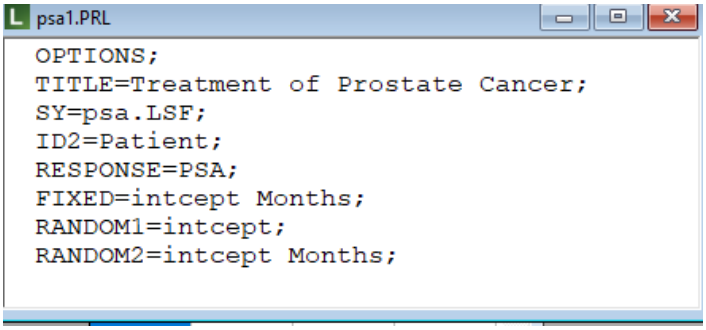
	Patient	Months	PSA	Age
1	1.00	0.00	30.40	69.00
2	1.00	3.00	28.00	69.00
3	1.00	6.00	26.90	69.00
4	1.00	9.00	25.20	69.00
5	1.00	12.00	19.60	69.00
6	2.00	0.00	27.80	58.00
7	2.00	3.00	26.70	58.00
8	2.00	6.00	20.50	58.00
9	2.00	9.00	18.70	58.00
10	2.00	12.00	18.80	58.00
11	3.00	0.00	26.60	53.00
12	3.00	3.00	21.80	53.00
13	3.00	6.00	17.80	53.00
14	3.00	9.00	17.90	53.00
15	3.00	12.00	14.50	53.00
16	4.00	0.00	24.80	61.00
17	4.00	3.00	24.50	61.00
18	4.00	6.00	20.20	61.00
19	4.00	9.00	19.80	61.00
20	4.00	12.00	18.80	61.00

2. Longitudinal analysis

As a first step, we look at the possible relationship between the PSA level and the time of measurement. A box-and-whisker plot of the PSA levels over the measurement occasions shows a steady decrease in PSA levels.



We allow both the intercept and time of measurement to vary randomly over the patients. The syntax file below specifies this model.



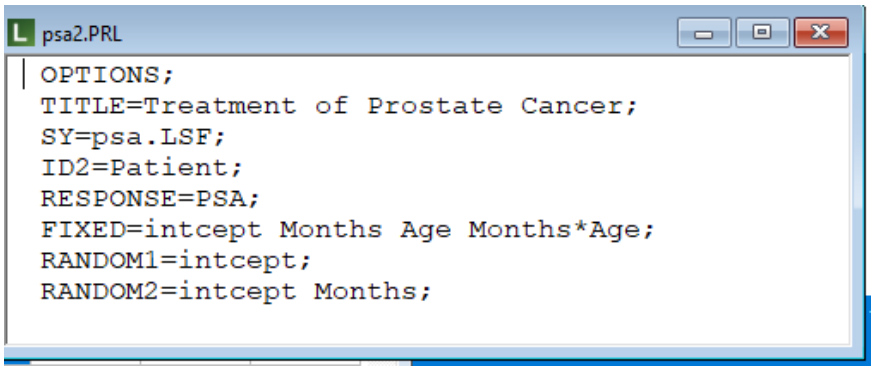
For this model, the following results were obtained:

```
                      +-----------------------+
                      | FIXED PART OF MODEL   |
                      +-----------------------+
-------------------------------------------------------------------------------
  COEFFICIENTS             BETA-HAT      STD.ERR.      Z-VALUE       PR > |Z|
-------------------------------------------------------------------------------
  intcept                  31.93378       0.57101      55.92473       0.00000
  Months                   -0.74214       0.01861     -39.86912       0.00000

                      +-----------------------+
                      |   -2 LOG-LIKELIHOOD   |
                      +-----------------------+

  DEVIANCE= -2*LOG(LIKELIHOOD) =    2008.60066876969
  NUMBER OF FREE PARAMETERS =               6

                      +-----------------------+
                      | RANDOM PART OF MODEL  |
                      +-----------------------+
-------------------------------------------------------------------------------
  LEVEL 2                        TAU-HAT      STD.ERR.     Z-VALUE   PR > |Z|
-------------------------------------------------------------------------------
  intcept /intcept              30.89912      4.61240      6.69914   0.00000
  Months  /intcept               0.30243      0.10758      2.81119   0.00494
  Months  /Months                0.00392      0.00539      0.72798   0.46663

-------------------------------------------------------------------------------
  LEVEL 1                        TAU-HAT      STD.ERR.     Z-VALUE   PR > |Z|
-------------------------------------------------------------------------------
  intcept /intcept               2.28753      0.20830     10.98199   0.00000
```

The average expected PSA level is expected to be 31.93378 at the beginning of the study period. For any unit increase in Month (i.e. 3 months), the PSA level is expected to drop by 0.75214 units. While there is evidence of random variation in intercept over the patients, there does not seem to be evidence of random variation in the measurement occasions.

3. Taking age into account

To see whether the age of the patient plays a role, we include Age as a predictor in the model. We also include an interaction term between the time of measurement and age in the model, leaving the random part of the model unchanged.



After convergence, the following estimates are obtained:

```
                      +-----------------------+
                      | FIXED PART OF MODEL   |
                      +-----------------------+
------------------------------------------------------------------------------
  COEFFICIENTS             BETA-HAT      STD.ERR.      Z-VALUE       PR > |Z|
------------------------------------------------------------------------------
  intcept                 15.89819       3.73784       4.25331       0.00002
  Months                  -0.60000       0.13558      -4.42535       0.00001
  Age                      0.28920       0.06676       4.33182       0.00001
  Months  *Age            -0.00255       0.00242      -1.05524       0.29131

                      +-----------------------+
                      |   -2 LOG-LIKELIHOOD   |
                      +-----------------------+

  DEVIANCE= -2*LOG(LIKELIHOOD) =    1988.75995647571
  NUMBER OF FREE PARAMETERS =               8

                      +-----------------------+
                      | RANDOM PART OF MODEL  |
                      +-----------------------+
------------------------------------------------------------------------------
  LEVEL 2                         TAU-HAT      STD.ERR.     Z-VALUE   PR > |Z|
------------------------------------------------------------------------------
  intcept /intcept               25.83839      3.89446      6.63465   0.00000
  Months  /intcept                0.34174      0.10006      3.41526   0.00064
  Months  /Months                 0.00407      0.00543      0.74940   0.45361

------------------------------------------------------------------------------
  LEVEL 1                         TAU-HAT      STD.ERR.     Z-VALUE   PR > |Z|
------------------------------------------------------------------------------
  intcept /intcept                2.27353      0.20692     10.98770   0.00000
```

The estimate effect of Age on the PSA level is 0.2892 per year, indicating an expected increase of 0.2892 per year of Age. The effect of Age on the rate at which PSA decreases, as denoted by the interaction term, is not significant. While the random variation in intercept over patients is significant, there is no evidence of random variation on the Months slope.

Patients' age range between 32 and 70. At the beginning of the study, the expected PSA levels for the youngest and oldest patient can be calculated as

$$\hat{y} = 15.89819 + 0.28920(32) = 25.14259$$
$$\hat{y} = 15.89819 + 0.28920(70) = 36.14219.$$

When similar values are calculated at each point of measurement, we can make the following scatterplot of the results. While the PSA levels of the oldest respondent are quite a bit higher than that of the youngest respondent, the effect of the treatment is a decrease in the PSA level over the study period, irrespective of age. This result is in line with the estimates obtained under the model and also follows the same downward trend observed in the raw data (see box-and-whisker plot).