Statistics
Mixed-effects/multilevel models worksheet

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1 SPSS Exercises

1. Open the file `headaches_long.sav`. This is the same data as you analysed in the Repeated Measures worksheet. The data has been transposed (different observations are now in rows) to allow you to analyse it with a mixed effects model.

   (a) In repeated measures analysis, effects are usually defined as deviations from individual means. This corresponds to a participant specific intercept, which in a mixed effects model can be implemented as a random intercept for each subject. Let's try to estimate such a random intercept model. In the first menu of the "Mixed/Linear" option (called "Linear Mixed Model: Specify Subject and Repeated") use `id` as "Subject" variable. In this analysis, we will treat `Treatment` and `Time` as categorical predictors (SPSS calls these "factors"). When you specify the model, use `Treatment` and `Time` as fixed effects, and also include their interaction. Under random effects, don't add any variables, but do ask for an intercept and make sure you let it depend on `id`. For this exercise, use "Restricted Maximum Likelihood" as the estimation method. Compare the results to those obtained with a repeated measures analysis.

```
# read data
library(foreign)
dat <- as.data.frame(read.spss("headaches_long.sav"))
library(lme4)

## Loading required package:  Matrix
##
## Attaching package:  'lme4'
## The following object is masked from 'package:stats':
##
##     sigma

library(lmerTest)

##
## Attaching package:  'lmerTest'
## The following object is masked from 'package:lme4':
##
##     lmer
```

```
## The following object is masked from 'package:stats':
##
##     step
```

```
mod <- lmer(headaches ~ factor(Time)*factor(Treatment) +
            (1|id),data=dat)
# get the coefficients and tests
summary(mod)
```

```
## Linear mixed model fit by REML t-tests use Satterthwaite approximations
##   to degrees of freedom [lmerMod]
## Formula: headaches ~ factor(Time) * factor(Treatment) + (1 | id)
##    Data: dat
##
## REML criterion at convergence: 349.5
##
## Scaled residuals:
##     Min      1Q  Median      3Q     Max
## -3.2439 -0.5020 -0.0223  0.6731  2.0106
##
## Random effects:
##  Groups   Name        Variance Std.Dev.
##  id       (Intercept)  2.101   1.450
##  Residual             12.704   3.564
## Number of obs: 70, groups:  id, 14
##
## Fixed effects:
##                                           Estimate Std. Error      df
## (Intercept)                                 7.2857     1.4543 55.5300
## factor(Time)1                              -2.4286     1.9051 48.0000
## factor(Time)2                              -0.7143     1.9051 48.0000
## factor(Time)3                               1.1429     1.9051 48.0000
## factor(Time)4                               8.1429     1.9051 48.0000
## factor(Treatment)Cognitive                  1.5714     2.0567 55.5300
## factor(Time)1:factor(Treatment)Cognitive    4.4286     2.6943 48.0000
## factor(Time)2:factor(Treatment)Cognitive    4.4286     2.6943 48.0000
## factor(Time)3:factor(Treatment)Cognitive    1.4286     2.6943 48.0000
## factor(Time)4:factor(Treatment)Cognitive   -6.5714     2.6943 48.0000
##                                           t value Pr(>|t|)
## (Intercept)                                 5.010 5.88e-06 ***
## factor(Time)1                              -1.275   0.2085
## factor(Time)2                              -0.375   0.7094
## factor(Time)3                               0.600   0.5514
## factor(Time)4                               4.274 9.05e-05 ***
## factor(Treatment)Cognitive                  0.764   0.4481
```

```
## factor(Time)1:factor(Treatment)Cognitive   1.644   0.1068
## factor(Time)2:factor(Treatment)Cognitive   1.644   0.1068
## factor(Time)3:factor(Treatment)Cognitive   0.530   0.5984
## factor(Time)4:factor(Treatment)Cognitive  -2.439   0.0185 *
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Correlation of Fixed Effects:
##             (Intr) fc(T)1 fc(T)2 fc(T)3 fc(T)4 fc(T)C f(T)1: f(T)2: f(T)3
## factor(Tm)1 -0.655
## factor(Tm)2 -0.655  0.500
## factor(Tm)3 -0.655  0.500  0.500
## factor(Tm)4 -0.655  0.500  0.500  0.500
## fctr(Trtm)C -0.707  0.463  0.463  0.463  0.463
## fc(T)1:(T)C  0.463 -0.707 -0.354 -0.354 -0.354 -0.655
## fc(T)2:(T)C  0.463 -0.354 -0.707 -0.354 -0.354 -0.655  0.500
## fc(T)3:(T)C  0.463 -0.354 -0.354 -0.707 -0.354 -0.655  0.500  0.500
## fc(T)4:(T)C  0.463 -0.354 -0.354 -0.354 -0.707 -0.655  0.500  0.500  0.50
```

```
# get the omnibus tests
anova(mod)
```

```
## Analysis of Variance Table of type III  with  Satterthwaite
## approximation for degrees of freedom
##                                Sum Sq Mean Sq NumDF DenDF F.value
## factor(Time)                  231.514  57.879     4    48  4.5561
## factor(Treatment)              51.302  51.302     1    12  4.0384
## factor(Time):factor(Treatment) 285.914  71.479     4    48  5.6267
##                                   Pr(>F)
## factor(Time)                   0.0033608 **
## factor(Treatment)              0.0675114 .
## factor(Time):factor(Treatment) 0.0008508 ***
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

```
# get confidence intervals for random effects variances
confint(mod)
```

```
## Computing profile confidence intervals ...
```

```
##                                              2.5 %    97.5 %
## .sig01                                   0.0000000  2.667776
## .sigma                                   2.7716074  4.019800
## (Intercept)                              4.6068530  9.964576
## factor(Time)1                           -5.9457461  1.088603
## factor(Time)2                           -4.2314603  2.802889
```

```
## factor(Time)3                                -2.3743175  4.660032
## factor(Time)4                                 4.6256825 11.660032
## factor(Treatment)Cognitive                   -2.2170534  5.359911
## factor(Time)1:factor(Treatment)Cognitive  -0.5454646  9.402607
## factor(Time)2:factor(Treatment)Cognitive  -0.5454646  9.402607
## factor(Time)3:factor(Treatment)Cognitive  -3.5454646  6.402607
## factor(Time)4:factor(Treatment)Cognitive -11.5454646 -1.597393

## you can also test whether the variance of the random
## intercept is > 0:
mod0 <- lm(headaches ~ factor(Time)*factor(Treatment),data=dat)
modML <- refitML(mod)
anova(modML,mod0)

## Data: dat
## Models:
## mod0: headaches ~ factor(Time) * factor(Treatment)
## modML: headaches ~ factor(Time) * factor(Treatment) + (1 | id)
##       Df    AIC    BIC  logLik deviance  Chisq Chi Df Pr(>Chisq)
## mod0  11 398.51 423.24 -188.25   376.51
## modML 12 398.23 425.21 -187.12   374.23 2.2771      1     0.1313

# or "by hand"
likratio <- -2*logLik(mod0) - -2*logLik(modML)
likratio

## 'log Lik.' 2.277086 (df=11)

# get the p-value
1-pchisq(as.numeric(likratio),df=1)

## [1] 0.1312983
```

Answer: Using "Restricted Maximum Likelihood" (REML) estimation, the tests of the time, treatment, and time × treatment effect are exactly the same as those for a repeated-measures ANOVA. This is because a mixed effects model with only random intercepts is structurally similar to a repeated-measures ANOVA, because the random intercepts are like individual means in a repeated-measures ANOVA.

If you use "Maximum likelihood" (ML) estimation, the results are comparable, but slightly different. While I advise to use ML estimation in general (because this is better for the model comparison approach, using likelihood-ratio tests), there is a (rather technical) discussion on which of these methods is better. For large samples, the results of both estimation techniques will be very similar. For small samples (such as for this data), REML can be more robust. I would not worry about the differences between ML and REML too much, but you should realise that they can lead to different results.

Mixed effect models are more general than a repeated-measures ANOVA. For instance, you can test whether there is evidence for significant variation in individual intercepts. For this test, you need to estimate the model with ML and also estimate a compact model (MODEL C) in which you fix the variance of the random intercepts to 0 (this is equivalent to not including random intercepts in the model). Model A with random intercepts gives a $-2 \log L = 374.230$, while a Model C without random intercepts gives $-2 \log L = 376.507$. The test then becomes

$$\chi^2 = 376.507 - 374.230 = 2.277$$

with $df = \text{PA} - \text{PC} = 12 - 11 = 1$. As $P(\chi^2_1 \geq 2.277) = .131$, the test is not significant, so the variance of the random intercepts is not significantly greater than 0.

(b) The previous analysis used `Time` as a categorical predictor. We can also assume just a linear effect of `Time`. To do so, treat the variable `Time` as a covariate (so that SPSS does not compute contrast codes for this variable). Estimate a model with fixed effects for `Treatment` and `Time`, as well as a fixed effect for the interaction between `Treatment` and `Time`. In contrast to repeated-measures ANOVA, we can allow the effect of `Time` to vary between individuals in a mixed-effects model. Include random slopes for `Time`, in addition to random intercepts. To allow the random intercepts and slopes to correlate, choose "unstructured" for the "covariance type" of the random effects. This is the most general type, which estimates each variance and covariance term separately. As we'll use the results of this analysis for model comparison, make sure you use "Maximum Likelihood" as the estimation method.

```
mod <- lmer(headaches~Time*Treatment +
            (1 + Time|id),data=dat,REML=FALSE)
anova(mod)

## Analysis of Variance Table of type III  with  Satterthwaite
## approximation for degrees of freedom
##                 Sum Sq Mean Sq NumDF  DenDF F.value   Pr(>F)
## Time           177.373 177.373     1 14.000 12.0877 0.003702 **
## Treatment      173.824 173.824     1 14.001 11.8459 0.003969 **
## Time:Treatment  83.191  83.191     1 14.000  5.6694 0.032009 *
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

Answer: The main effect of `Time` is significant. The main effect of `treatment` is also significant. Finally, there is a significant `Time` × `Treatment` interaction. To interpret these effects, you need to know something about how `Treatment` is coded, and which values `Time` takes. `Time` is numbered from 0 to 4. For "Factors" (categorical variables), SPSS uses dummy coding in mixed effects analysis, where the last level of each categorical variable is the reference group. Remember that the intercept is always the predicted value of the dependent variable when all

predictors have value 0. So here, the intercept represents the predicted number of headache-free days in the first week (`week` $= 0$) and the reference group, which is cognitive therapy. The slope for `Time` is the slope for the reference group, while the slope of the `Time` $\times$ `Treatment` interaction is the change in the slope of `Time` for the behavioural group. The estimated slope for `Time` is 0.371. If you look at the t-test for this slope, it is not significant. Strangely, the F-test for `Time` in the "Type III tests of fixed effects" table *is* significant. Confusingly, SPSS seems to use different coding scheme's for the Type III tests and those for the actual slopes. Here, the Type III test seems to test for an "average" effect of `Time` over both treatment groups, while the "parameter estimate" test is for the slope of `Time` in the reference group only (due to the dummy coding scheme used). So, we can conclude that there is (on average) an increase in the number of headache-free days, but this does not hold for the reference group (cognitive therapy). For the interaction, both tests agree. The slope for the `Time` $\times$ `Treatment` interaction is 1.614. So the slope of `Time` is larger (by 1.614) for the behavioral therapy group; in fact, the slope of `Time` is $b_{\texttt{Time}} = 0.371 + 1.614 = 1.985$ for this group.

(c) Allowing for covariation (correlation) between random effects is very general. But the additional covariance parameters estimated may not be necessary. In general, additional parameters will make the model fit a particular dataset better, but may reduce the generalization of the model to new datasets (a phenomenon usually called "overfitting"). To test whether the covariance is actually different from 0, you can check the Wald test for this parameter, but it is better to perform a likelihood-ratio test. To do this, re-estimate the model above, but now specify the covariance type for the random effects to be "diagonal" (this fixes all covariance terms to 0, but allows the variances of the random effects to differ). In the test, compare the "-2 log Likelihood" of this model to the value obtained for the previous model.

```
mod_diag <- lmer(headaches~Time*Treatment + (1|id) +
                 (0 + Time|id),data=dat,REML=FALSE)
summary(mod_diag)

## Linear mixed model fit by maximum likelihood t-tests use Satterthwaite
##   approximations to degrees of freedom [lmerMod]
## Formula: headaches ~ Time * Treatment + (1 | id) + (0 + Time | id)
##    Data: dat
##
##      AIC      BIC   logLik deviance df.resid
##    406.0    421.7   -196.0    392.0       63
##
## Scaled residuals:
##     Min      1Q  Median      3Q     Max
## -2.2221 -0.6185 -0.2347  0.7055  2.4740
##
## Random effects:
```

```
##  Groups   Name        Variance Std.Dev.
##  id       (Intercept)  0.3977  0.6306
##  id.1     Time         0.1631  0.4039
##  Residual             14.6237  3.8241
## Number of obs: 70, groups:  id, 14
##
## Fixed effects:
##                           Estimate Std. Error      df t value Pr(>|t|)
## (Intercept)                 4.5429     1.1447 33.6800   3.969 0.000358 ***
## Time                        1.9857     0.4819 33.6800   4.121 0.000232 ***
## TreatmentCognitive          5.5429     1.6188 33.6800   3.424 0.001639 **
## Time:TreatmentCognitive    -1.6143     0.6815 33.6800  -2.369 0.023728 *
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Correlation of Fixed Effects:
##             (Intr) Time   TrtmnC
## Time        -0.757
## TrtmntCgntv -0.707  0.536
## Tm:TrtmntCg  0.536 -0.707 -0.757
```

```
# likelihood-ratio test
anova(mod_diag,mod)
```

```
## Data: dat
## Models:
## object: headaches ~ Time * Treatment + (1 | id) + (0 + Time | id)
## ..1: headaches ~ Time * Treatment + (1 + Time | id)
##        Df    AIC    BIC  logLik deviance  Chisq Chi Df Pr(>Chisq)
## object  7 405.98 421.72 -195.99   391.98
## ..1     8 407.98 425.97 -195.99   391.98 0.0013      1     0.9716
```

Answer: The model with a diagonal covariance matrix for the random effects gives a -2 log Likelihood of $-2 \times \log L = 391.980$. Comparing this to the model with an unstructured covariance matrix gives a likelihood-ratio test of

$$\chi^2 = 391.980 - 391.978 = 0.002$$

with $P(\chi^2_1 \geq .002) = 0.964$. So there is no evidence that the intercepts and slopes covary.

(d) As the repeated measures ANOVA showed a significant quadratic effect of time, it may be a good idea to also allow for such an effect in the mixed effects model. The variable `TimeSq` was computed as `TimeSq` = `Time`^{2}, and corresponds to a quadratic effect of time. Re-estimate the model above, but now also include a fixed effect of `TimeSq`, a fixed interaction between `Treatment` and `TimeSq`, as well as random slopes for `TimeSq`. To reduce the number of parameters, specify the

covariance type to be "diagonal". Compare the results of this analysis to those obtained above. Is there evidence for a quadratic effect of time? Has the fit of the model increased?

```
mod_sq <- lmer(headaches ~ Time*Treatment + TimeSq*Treatment +
               (1|id) + (0+Time|id) + (0+TimeSq|id),data=dat,
               REML=FALSE)
summary(mod_sq)
```

```
## Linear mixed model fit by maximum likelihood t-tests use Satterthwaite
##   approximations to degrees of freedom [lmerMod]
## Formula: headaches ~ Time * Treatment + TimeSq * Treatment + (1 | id) +
##     (0 + Time | id) + (0 + TimeSq | id)
##    Data: dat
##
##      AIC      BIC   logLik deviance df.resid
##    392.0    414.4   -186.0    372.0       60
##
## Scaled residuals:
##      Min       1Q   Median       3Q      Max
## -2.41399 -0.58628 -0.08355  0.67265  2.14461
##
## Random effects:
##  Groups   Name        Variance Std.Dev.
##  id       (Intercept) 1.58163  1.2576
##  id.1     Time        0.00000  0.0000
##  id.2     TimeSq      0.03581  0.1892
##  Residual             9.07399  3.0123
## Number of obs: 70, groups:  id, 14
##
## Fixed effects:
##                            Estimate Std. Error      df t value Pr(>|t|)
## (Intercept)                  7.2571     1.1722 47.9600   6.191 1.28e-07 ***
## Time                        -3.4429     1.2693 41.1900  -2.712  0.00970 **
## TreatmentCognitive           1.5633     1.6578 47.9600   0.943  0.35041
## TimeSq                       1.3571     0.3126 49.4800   4.342 6.98e-05 ***
## Time:TreatmentCognitive      6.3449     1.7950 41.1900   3.535  0.00102 **
## TreatmentCognitive:TimeSq   -1.9898     0.4421 49.4800  -4.501 4.12e-05 ***
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Correlation of Fixed Effects:
##             (Intr) Time   TrtmnC TimeSq Tm:TrC
## Time        -0.672
## TrtmntCgntv -0.707  0.475
```

```
## TimeSq       0.505 -0.933 -0.357
## Tm:TrtmntCg  0.475 -0.707 -0.672  0.660
## TrtmntCg:TS -0.357  0.660  0.505 -0.707 -0.933
```

```
# likelihood-ratio test
anova(mod_diag,mod_sq)
```

```
## Data: dat
## Models:
## object: headaches ~ Time * Treatment + (1 | id) + (0 + Time | id)
## ..1: headaches ~ Time * Treatment + TimeSq * Treatment + (1 | id) +
## ..1:     (0 + Time | id) + (0 + TimeSq | id)
##        Df    AIC    BIC  logLik deviance  Chisq Chi Df Pr(>Chisq)
## object  7 405.98 421.72 -195.99   391.98
## ..1    10 391.96 414.45 -185.98   371.96 20.015      3  0.0001685 ***
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

```
## center Time and TimeSq and then re-estimate the model
dat$c_Time <- scale(dat$Time)
dat$c_TimeSq <- dat$c_Time^2
mod_csq <- lmer(headaches ~ c_Time*Treatment + c_TimeSq*Treatment +
               (1|id) + (0+c_Time|id) + (0+c_TimeSq|id),data=dat,
               REML=FALSE)
summary(mod_csq)
```

```
## Linear mixed model fit by maximum likelihood t-tests use Satterthwaite
##   approximations to degrees of freedom [lmerMod]
## Formula: headaches ~ c_Time * Treatment + c_TimeSq * Treatment + (1 |
##     id) + (0 + c_Time | id) + (0 + c_TimeSq | id)
##    Data: dat
##
##      AIC      BIC   logLik deviance df.resid
##    392.8    415.2   -186.4    372.8       60
##
## Scaled residuals:
##      Min       1Q   Median       3Q      Max
## -2.51872 -0.54671 -0.02357  0.53370  1.90894
##
## Random effects:
##  Groups   Name        Variance Std.Dev.
##  id       (Intercept) 1.5861   1.2594
##  id.1     c_Time      1.5303   1.2370
##  id.2     c_TimeSq    0.7537   0.8681
##  Residual             8.5457   2.9233
## Number of obs: 70, groups:  id, 14
```

```
##
## Fixed effects:
##                               Estimate Std. Error      df t value Pr(>|t|)
## (Intercept)                     5.8000     0.9053 23.7600   6.407 1.33e-06
## c_Time                          2.8285     0.6829 14.0000   4.142 0.000997
## TreatmentCognitive              6.2939     1.2803 23.7600   4.916 5.28e-05
## c_TimeSq                        2.7536     0.6831 23.7600   4.031 0.000495
## c_Time:TreatmentCognitive      -2.2994     0.9657 14.0000  -2.381 0.032009
## TreatmentCognitive:c_TimeSq    -4.0373     0.9661 23.7600  -4.179 0.000341
##
## (Intercept)                    ***
## c_Time                         ***
## TreatmentCognitive             ***
## c_TimeSq                       ***
## c_Time:TreatmentCognitive      *
## TreatmentCognitive:c_TimeSq    ***
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Correlation of Fixed Effects:
##             (Intr) c_Time TrtmnC c_TmSq c_T:TC
## c_Time       0.000
## TrtmntCgntv -0.707  0.000
## c_TimeSq    -0.572  0.000  0.405
## c_Tm:TrtmnC  0.000 -0.707  0.000  0.000
## TrtmntC:_TS  0.405  0.000 -0.572 -0.707  0.000

# likelihood-ratio test
anova(mod_diag,mod_csq)

## Data: dat
## Models:
## object: headaches ~ Time * Treatment + (1 | id) + (0 + Time | id)
## ..1: headaches ~ c_Time * Treatment + c_TimeSq * Treatment + (1 |
## ..1:     id) + (0 + c_Time | id) + (0 + c_TimeSq | id)
##        Df    AIC    BIC  logLik deviance  Chisq Chi Df Pr(>Chisq)
## object  7 405.98 421.72 -195.99   391.98
## ..1    10 392.76 415.25 -186.38   372.76 19.219      3  0.0002464 ***
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

Answer: Note that, at the start, SPSS gives a cryptic warning that the "final Hessian matrix is not positive definite". I won't try to explain what that means, but it indicates that the estimation of this model has not succeeded very well. That is because we are estimating a rather complex model with a limited dataset.

If you get a warning like this, you should probably reconsider whether you really want to estimate this model. I'll describe some of the results below, although this model is clearly too complex for this data. With R, there is no such estimation issue, by the way.

Again, there are differences between the "Type III" tests and the tests for the slopes. I'm going to focus on the latter here. These show a significant effect of `Time` and `TimeSq`. Remember that (because SPSS uses dummy coding for `Treatment`) these are the slopes for the reference group. So for the reference group, there is both a linear and quadratic effect of time. The `Time` × `Treatment` and `TimeSq` × `Treatment` effects are also significant, which indicates that the pattern of headache-free days is different between the conditions. It is easiest to see what this indicates in a graph. For the cognitive therapy group, the headache-free days rises initially, but then goes down again. For the behavioral therapy group, there is an initial dip, but the treatment then starts to have the desired effect.

We can compare the fit of this model to that without any effects of `TimeSq` (e.g., the model fitted in part c of this exercise), which gives a test result of

$$\chi^2 = 391.980 - 371.965 = 20.015$$

with df = PA − PC = 10 − 7 = 3 and an associated probability of $P(\chi^2_3 \geq 20.015) < .001$, so inclusion of `TimeSq` (as both a fixed and random effect) reduces the model error significantly. Of course, this omnibus test doesn't tell us where this effect lies. And for instance, just testing the variance of the random slopes of `TimeSq` shows that this is not significantly greater than 0, so inclusion of the fixed effects of `TimeSq` might be enough.

Part of the problem with the model estimated here is that there is a strong correlation between `Time` and `TimeSq`. If you first center time (and then recompute `TimeSq` also), there is no problem in the estimation of the model. One important thing to realise is that by centering Time, you change the location of the intercept. So the random slopes now represent variation between participants halfway during the therapies, rather than at the start of the therapies. See the SPSS output for the results of this analysis.

2. Open the dataset `Reisby.sav`. This is the data from the depression study discussed in the lecture. The dataset contains participants' scores on the Hamilton depression scale (`HamD`), the week in which the score was obtained (`Week` = 0,. . . , 5) and a contrast coded predictor for whether the depression was endogenous (`Endogenous` = 1) or exogenous (`Endogenous` = −1). Also included are the squared week (`WeekSq` = `Week`^{2}), as well as two predictors for the endogenous and (squared) week interactions (these are called `EndoWeek` and `EndoWeekSq` respectively). In this exercise, you will replicate the final analysis of this data discussed in the lecture.

   (a) Estimate the model:

$$\begin{aligned}\texttt{HamD}_{hi} =& \beta_{0i} + \beta_{1i}\texttt{Week}_{hi} + \beta_{2i}\texttt{WeekSq}_{hi} + \beta_3\texttt{Endogenous}_{hi} \\ &+ \beta_4\texttt{EndoWeek}_{hi} + \beta_5\texttt{EndoWeekSq}_{hi} + \epsilon_{hi}\end{aligned}$$

with, as Level 2 model:

$$\beta_{0i} = \beta_0 + \alpha_{0i}$$
$$\beta_{1i} = \beta_1 + \alpha_{1i}$$
$$\beta_{2i} = \beta_2 + \alpha_{2i}$$

Allow the random effects to co-vary/correlate, by choosing an "unstructured" covariance type. Plot the predicted curves for each individual. To get this plot, you will first need to save the "Predicted values" under the "Predicted Values and Residuals", You can then plot the predictions for each individual by using e.g. the option "Graphs/Legacy Dialogs/Line/Multiple" and then define the lines by subject `id`. If you wish, you can also ask for separate panels for each value of `Endogenous`.

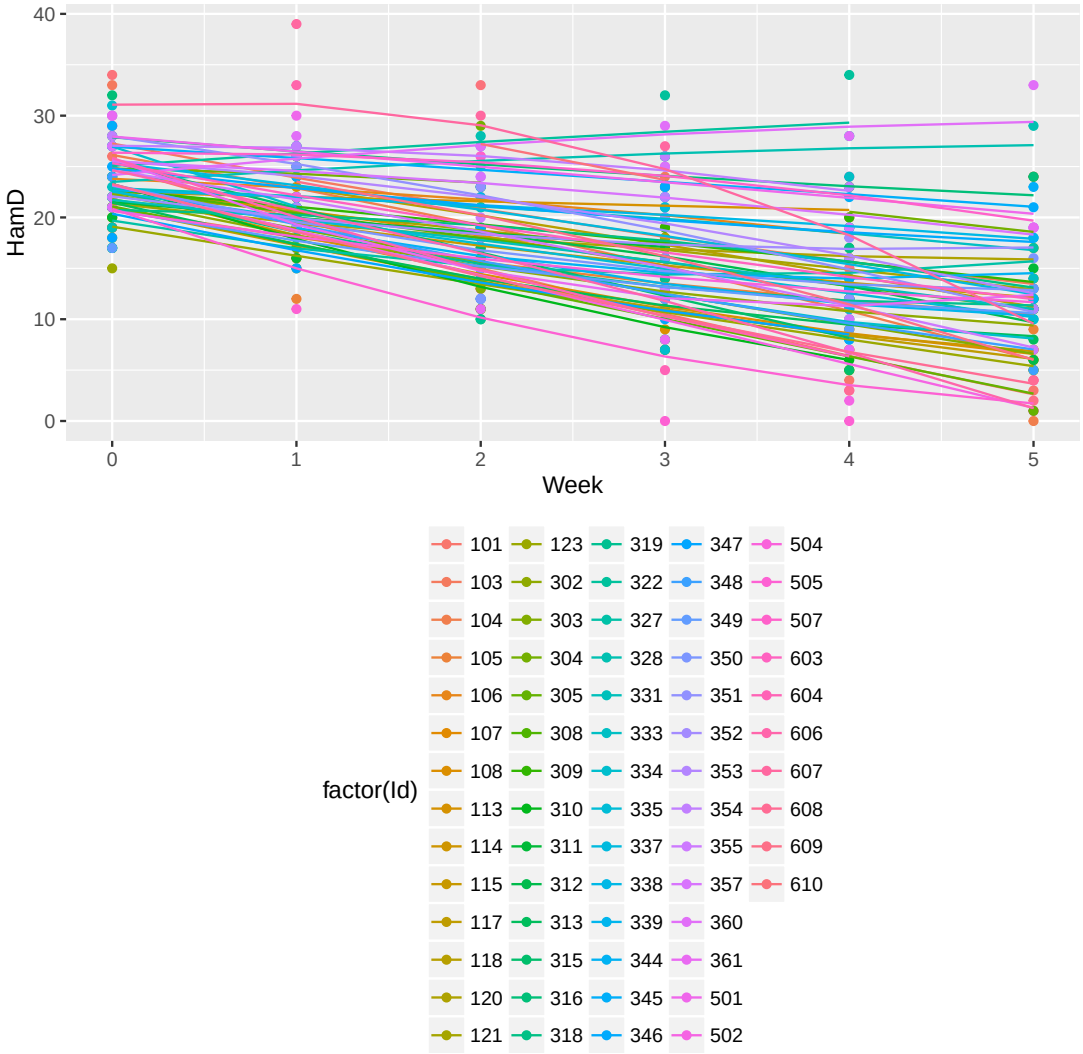
```
# read the data
dat <- as.data.frame(read.spss("Reisby.sav"))
# specify the model
mod <- lmer(HamD ~ Week + WeekSq + Endogenous +
            EndoWeek + EndoWeekSq +
            (1 + Week + WeekSq|Id),data=dat,REML=FALSE)
# summarize the results
summary(mod)
```

```
## Linear mixed model fit by maximum likelihood t-tests use Satterthwaite
##   approximations to degrees of freedom [lmerMod]
## Formula: HamD ~ Week + WeekSq + Endogenous + EndoWeek + EndoWeekSq + (1 +
##     Week + WeekSq | Id)
##    Data: dat
##
##      AIC      BIC   logLik deviance df.resid
##   2229.3   2280.4  -1101.7   2203.3      362
##
## Scaled residuals:
##     Min      1Q  Median      3Q     Max
## -2.6400 -0.5126  0.0290  0.4680  3.7799
##
## Random effects:
##  Groups   Name        Variance Std.Dev. Corr
##  Id       (Intercept)  9.8978  3.1461
##           Week         6.5697  2.5631   -0.15
##           WeekSq       0.1903  0.4362   -0.03 -0.82
##  Residual             10.5045  3.2411
## Number of obs: 375, groups:  Id, 66
##
## Fixed effects:
```

```
##              Estimate Std. Error       df t value Pr(>|t|)
## (Intercept) 23.68121    0.54678 63.68000  43.310  < 2e-16 ***
## Week        -2.68178    0.47999 63.00000  -5.587 5.27e-07 ***
## WeekSq       0.06098    0.08837 63.59000   0.690    0.493
## Endogenous   0.75646    0.54678 63.68000   1.383    0.171
## EndoWeek     0.35816    0.47999 63.00000   0.746    0.458
## EndoWeekSq  -0.07478    0.08837 63.59000  -0.846    0.401
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Correlation of Fixed Effects:
##             (Intr) Week   WeekSq Endgns EndoWk
## Week        -0.476
## WeekSq       0.322 -0.902
## Endogenous -0.093  0.034 -0.018
## EndoWeek    0.034 -0.095  0.082 -0.476
## EndoWeekSq -0.018  0.082 -0.089  0.322 -0.902
```

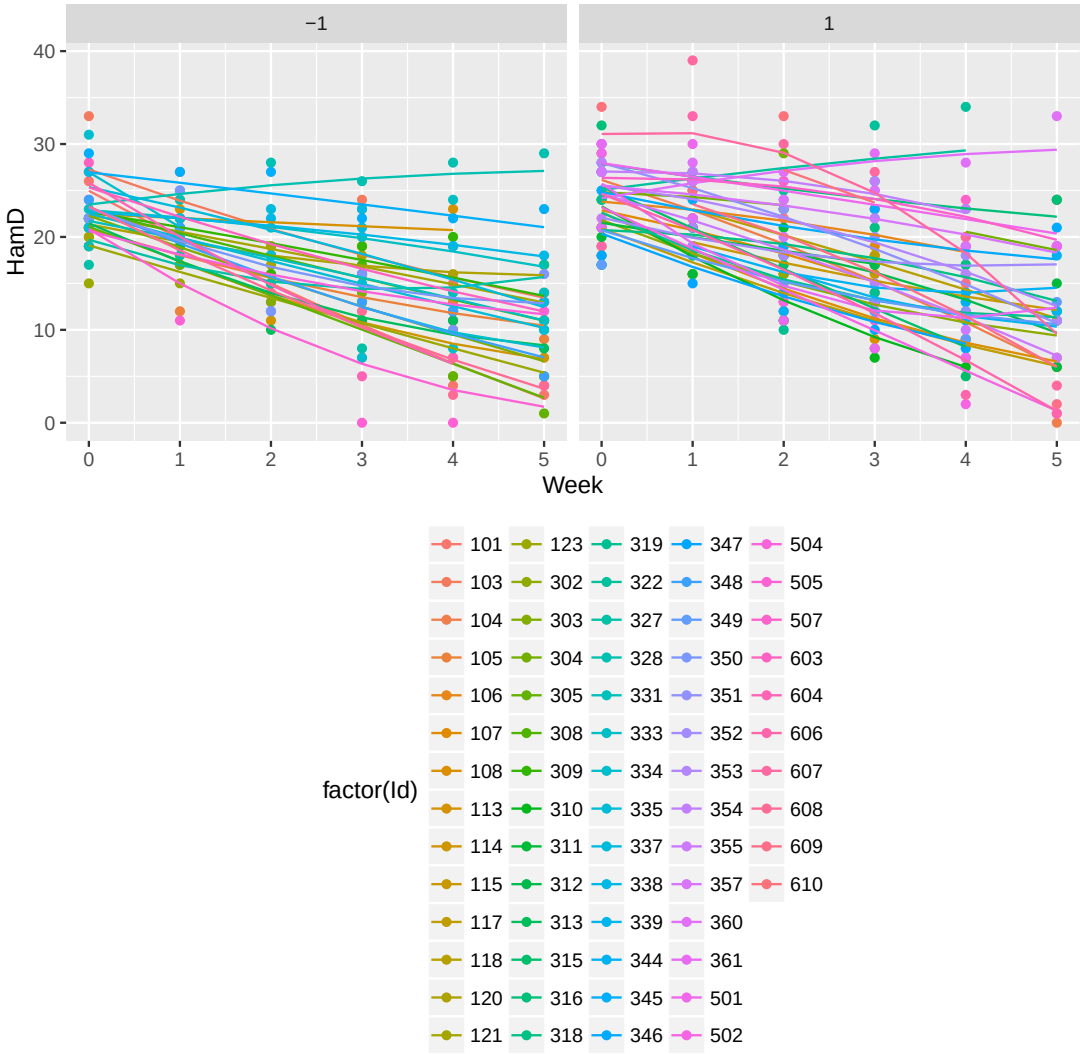
```
# plot the predictions
dat$pred[!is.na(dat$HamD)] <- predict(mod)
## load the ggplot2 package for pretty plots
library(ggplot2)
ggplot(dat,aes(y=HamD,x=Week,group=factor(Id),colour=factor(Id))) +
  geom_point() + geom_line(aes(y=pred,x=Week,group=factor(Id),colour=factor(
  theme(legend.position="bottom")
```

```
## Warning:  Removed 21 rows containing missing values (geom_point).
## Warning:  Removed 13 rows containing missing values (geom_path).
```




```
## you can also make separate plots for each level of endogeneous
ggplot(dat,aes(y=HamD,x=Week,group=factor(Id),colour=factor(Id))) +
  geom_point() + geom_line(aes(y=pred,x=Week,group=factor(Id),colour=factor(
  facet_wrap(~Endogenous) + theme(legend.position="bottom")

## Warning:  Removed 21 rows containing missing values (geom_point).
## Warning:  Removed 13 rows containing missing values (geom_path).
```



Answer: The analysis shows only a significant fixed effect for `Week`. The slope of `Week` is $b_{\texttt{Time}} = -2.682$, so on average, the Hamilton depression scale scores go down by 2.682 points every week.

(b) Use a likelihood-ratio test to determine whether you need random slopes for `WeekSq`. In this test, you need to compare the model above to a similar model with as (Level 2) model:

$$\begin{aligned}\beta_{0i} &= \beta_0 + \alpha_{0i}\\ \beta_{1i} &= \beta_1 + \alpha_{1i}\\ \beta_{2i} &= \beta_2\end{aligned}$$

```
# re-estimate the mixed-effects model without random slopes for TimeSq
modC <- lmer(HamD ~ Week + WeekSq + Endogenous +
             EndoWeek + EndoWeekSq + (1 + Week|Id),
             data=dat,REML=FALSE)
```

```
# likelihood-ratio test
anova(modC,mod)

## Data: dat
## Models:
## object: HamD ~ Week + WeekSq + Endogenous + EndoWeek + EndoWeekSq + (1 +
## object:     Week | Id)
## ..1: HamD ~ Week + WeekSq + Endogenous + EndoWeek + EndoWeekSq + (1 +
## ..1:     Week + WeekSq | Id)
##        Df    AIC    BIC  logLik deviance  Chisq Chi Df Pr(>Chisq)
## object 10 2233.5 2272.8 -1106.8   2213.5
## ..1    13 2229.3 2280.3 -1101.7   2203.3 10.212      3    0.01685 *
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

Answer: This model gives a -2 log Likelihood of $-2\log L(C) = 2213.513$. For the previous model, the value was $-2\log L(A) = 2203.301$. The likelihood-ratio test is thus

$$\chi^2 = 2213.513 - 2203.301 = 10.212$$

with $\text{PA} - \text{PC} = 13 - 10 = 3$ and $P(\chi^2_3 \geq 10.212) = .016$, so there is clear evidence that there is individual variation in the slope of `TimeSq`, as well as that this slope may covary with the random slopes of `Time` and the random intercepts.

3. Open the dataset `TVSFSP.sav`. This is the data from the smoking prevention study discussed in the lecture. As for the previous exercise, you will replicate the results from the lecture (and try something new).

   (a) Estimate a multilevel model for `PostTHKS`, with fixed effects for `PreTHKS`, `CC`, `TV`, and `CCTV`, and random intercepts for classes (within schools), and schools.

```
dat <- as.data.frame(read.spss("TVSFP.sav"))
head(dat)

##   SchoolID ClassID PostTHKS PreTHKS CC TV CCTV
## 1      193  193101        2       1 -1 -1   -1
## 2      193  193101        2       3 -1 -1   -1
## 3      193  193101        3       0 -1 -1   -1
## 4      193  193101        2       3 -1 -1   -1
## 5      193  193101        1       1 -1 -1   -1
## 6      193  193101        2       2 -1 -1   -1

mod <- lmer(PostTHKS ~ PreTHKS + CC + TV +
            CCTV + (1|SchoolID/ClassID),data=dat,
            REML=FALSE)
summary(mod)
```

```
## Linear mixed model fit by maximum likelihood t-tests use Satterthwaite
##   approximations to degrees of freedom [lmerMod]
## Formula: PostTHKS ~ PreTHKS + CC + TV + CCTV + (1 | SchoolID/ClassID)
##    Data: dat
##
##      AIC      BIC   logLik deviance df.resid
##   5373.4   5416.4  -2678.7   5357.4     1592
##
## Scaled residuals:
##     Min      1Q  Median      3Q     Max
## -2.5282 -0.7012 -0.0205  0.6840  3.1632
##
## Random effects:
##  Groups           Name        Variance Std.Dev.
##  ClassID:SchoolID (Intercept) 0.06358  0.2522
##  SchoolID         (Intercept) 0.02575  0.1605
##  Residual                     1.60201  1.2657
## Number of obs: 1600, groups:  ClassID:SchoolID, 135; SchoolID, 28
##
## Fixed effects:
##               Estimate Std. Error         df t value Pr(>|t|)
## (Intercept)    1.94544    0.08984   54.10000  21.654  < 2e-16 ***
## PreTHKS        0.30720    0.02584 1593.10000  11.888  < 2e-16 ***
## CC             0.31960    0.07361   23.20000   4.342 0.000236 ***
## TV             0.08905    0.07182   22.80000   1.240 0.227602
## CCTV          -0.16021    0.10275   23.70000  -1.559 0.132201
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Correlation of Fixed Effects:
##         (Intr) PrTHKS CC     TV
## PreTHKS -0.590
## CC      -0.409  0.017
## TV      -0.415  0.010  0.499
## CCTV     0.568  0.003 -0.716 -0.699

# confidence intervals for random effects
confint(mod)

## Computing profile confidence intervals ...

##                    2.5 %     97.5 %
## .sig01       0.13219028 0.36324393
## .sig02       0.00000000 0.28911272
## .sigma       1.22127459 1.31286562
```

```
## (Intercept)  1.76761539 2.12677391
## PreTHKS       0.25610271 0.35832730
## CC            0.17012725 0.47095747
## TV           -0.05641447 0.23800545
## CCTV         -0.37580118 0.04625083
```

Answer: This model shows a significant fixed effect of `CC`. The slope of `CC` is positive, so the classroom curriculum increased students' knowledge of tobacco and health. The Wald test shows significant variability between classes within schools, although there does not seem to be evidence for variation between schools. But as I said before, these tests are not overly reliable.

(b) Although the model above makes intuitive sense (as classes are nested within schools), it may be the case schools do not differ much in their average values for `PostTHKS`. Try an alternative model, in which you disregard the school-level, and use only random effects for `classID`. Use a likelihood-ratio test to compare this model to the previous one.

```
mod_class <- lmer(PostTHKS ~ PreTHKS + CC + TV +
                  CCTV + (1|ClassID),data=dat,REML=FALSE)
summary(mod_class)

## Linear mixed model fit by maximum likelihood t-tests use Satterthwaite
##   approximations to degrees of freedom [lmerMod]
## Formula: PostTHKS ~ PreTHKS + CC + TV + CCTV + (1 | ClassID)
##    Data: dat
##
##      AIC      BIC   logLik deviance df.resid
##   5374.0   5411.6  -2680.0   5360.0     1593
##
## Scaled residuals:
##     Min      1Q  Median      3Q     Max
## -2.6175 -0.7111 -0.0200  0.6819  3.2257
##
## Random effects:
##  Groups   Name        Variance Std.Dev.
##  ClassID  (Intercept) 0.08697  0.2949
##  Residual             1.60301  1.2661
## Number of obs: 1600, groups:  ClassID, 135
##
## Fixed effects:
##               Estimate Std. Error         df t value Pr(>|t|)
## (Intercept)    1.93661    0.07923  320.90000  24.443  < 2e-16 ***
## PreTHKS        0.31157    0.02580 1599.60000  12.076  < 2e-16 ***
## CC             0.31649    0.05931  110.80000   5.336  5.1e-07 ***
## TV             0.07983    0.05835  106.60000   1.368    0.174
```

```
## CCTV          -0.13734    0.08390  109.80000  -1.637    0.104
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Correlation of Fixed Effects:
##         (Intr) PrTHKS CC     TV
## PreTHKS -0.668
## CC      -0.376  0.028
## TV      -0.376  0.019  0.486
## CCTV     0.527 -0.005 -0.707 -0.695
```

```
# likelihood ratio test comparing the models
anova(mod_class,mod)
```

```
## Data: dat
## Models:
## object: PostTHKS ~ PreTHKS + CC + TV + CCTV + (1 | ClassID)
## ..1: PostTHKS ~ PreTHKS + CC + TV + CCTV + (1 | SchoolID/ClassID)
##        Df    AIC    BIC  logLik deviance  Chisq Chi Df Pr(>Chisq)
## object  7 5374.0 5411.6 -2680.0   5360.0
## ..1     8 5373.4 5416.4 -2678.7   5357.4 2.6055      1     0.1065
```

Answer: In terms of the fixed effects, this model is very similar to the previous one. But we can now test whether the variation between schools is significant or not. Using a likelihood-ratio test gives

$$\chi^2 = 5359.964 - 5357.359 = 2.605$$

with $\text{PA} - \text{PC} = 8 - 7 = 1$ and $P(\chi^2_1 \geq 2.605) = 0.107$. There is thus no evidence for significant variation between schools. However, as I indicated in the lecture, the p-values for the likelihood-ratio tests for *variances* are roughly twice the size they should be, so there could be marginally significant evidence for variation between schools. In any case, the variation seems much less important than variation between classrooms.

(c) As another alternative model, you could assume that there is little difference between classes within a school, although there might be substantial variance between schools. Estimate an alternative model, in which you disregard the class-level, and use only random effects for `schoolID`. Use a likelihood-ratio test to compare this model to the model in the first part of this exercise.

```
mod_school <- lmer(PostTHKS ~ PreTHKS + CC + TV +
                     CCTV + (1|SchoolID),data=dat,REML=FALSE)
summary(mod_school)
```

```
## Linear mixed model fit by maximum likelihood t-tests use Satterthwaite
##   approximations to degrees of freedom [lmerMod]
```

```
## Formula: PostTHKS ~ PreTHKS + CC + TV + CCTV + (1 | SchoolID)
##    Data: dat
##
##      AIC      BIC   logLik deviance df.resid
##   5380.0   5417.7  -2683.0   5366.0     1593
##
## Scaled residuals:
##      Min       1Q   Median       3Q      Max
## -2.70340 -0.73337 -0.01266  0.71269  3.06566
##
## Random effects:
##  Groups   Name        Variance Std.Dev.
##  SchoolID (Intercept) 0.03717  0.1928
##  Residual             1.65225  1.2854
## Number of obs: 1600, groups:  SchoolID, 28
##
## Fixed effects:
##               Estimate Std. Error         df t value Pr(>|t|)
## (Intercept)    1.94164    0.08873   62.40000  21.883  < 2e-16 ***
## PreTHKS        0.31029    0.02592 1594.90000  11.970  < 2e-16 ***
## CC             0.33005    0.07201   26.60000   4.583 9.63e-05 ***
## TV             0.10120    0.07006   24.90000   1.444   0.1611
## CCTV          -0.18482    0.10054   26.00000  -1.838   0.0775 .
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Correlation of Fixed Effects:
##         (Intr) PrTHKS CC     TV
## PreTHKS -0.602
## CC      -0.398  0.011
## TV      -0.407  0.008  0.496
## CCTV     0.556  0.010 -0.716 -0.697
```

```
# likelihood ratio test comparing the models
anova(mod_school,mod)
```

```
## Data: dat
## Models:
## object: PostTHKS ~ PreTHKS + CC + TV + CCTV + (1 | SchoolID)
## ..1: PostTHKS ~ PreTHKS + CC + TV + CCTV + (1 | SchoolID/ClassID)
##        Df    AIC    BIC  logLik deviance  Chisq Chi Df Pr(>Chisq)
## object  7 5380.0 5417.7 -2683.0   5366.0
## ..1     8 5373.4 5416.4 -2678.7   5357.4 8.6547      1   0.003262 **
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

Answer: In terms of the fixed effects, the results of this model are again very similar to the other ones, although there is now a trend for a `CC` × `TV` interaction. Using a likelihood-ratio test to compare this model to the one in part a of this exercise gives

$$\chi^2 = 5366.013 - 5357.359 = 8.654$$

with PA − PC = 8 − 7 = 1 and $P(\chi^2_1 \geq 8.654) = 0.003$ so there is clear evidence for variation between classrooms. Concluding, we might say that teachers seem to have a strong effect on the effectiveness of the programme (as we've included the `PreTHKS` as a covariate, intercepts effectively reflect differences between `PostTHKS` and `PreTHKS`). But there does not seem to be overwhelming evidence that schools differ in the effectiveness of the programme.

4. Open the dataset `ReisbyCov.sav`. This is again data from the study discussed in the lecture, but here you will fit a more complicated model, in which you also take patients' weekly imipramine levels into account. Because imipramine biotransforms into the active metabolite desmethylimipramine (or desipramine), the researchers also measured patients' desipramine plasma levels. Imipramine and desipramine levels were only measured after the first (placebo) week, so for this analysis, we will only use the data from the treatment weeks. The objective of this analysis is to investigate the relation between changes in Hamilton depression scores and imipramine and desipramine levels. Imipramine and desipramine levels vary from week to week. Inclusion of such time-varying covariates is not possible in repeated measures ANOVA, but is quite easy in a mixed-effects model.

   In the dataset, you will find `HamDchange`, which is, for each participant, the change in Hamilton depression score from the baseline measure (at week 0), i.e.

$$\texttt{HamDchange}_{hi} = \texttt{HamD}_{hi} - \texttt{HamD}_{0i}$$

   for $h = 2, \ldots, 5$ (week 2 to week 5). We analyse these difference scores, rather than the actual values on the Hamilton depression scale, because we are interested whether imipramine and desipramine levels *decrease* depression. Note that the variable `Week` in this dataset has been rescaled to start at 0 (to make the intercept more interpretable).

   Because there were large individual differences in the levels of these two variables, both imipramine and desipramine measurements were first log-transformed. This helps to ensure that the estimated regression coefficients are not unduly influenced by extreme values on these covariates. The variables were then centered, so that the intercept reflects predictions for average levels of (log) imipramine and (log) desipramine. You can find the corresponding variables in the dataset as `logImi` and `logDmi`.

   (a) Estimate the model

$$\begin{aligned}\texttt{HamDchange}_{hi} =& \beta_{0i} + \beta_{1i}\texttt{Week} + \beta_2\texttt{Endogenous} + \beta_3\texttt{EndoWeek} \\ &+ \beta_4 \times \texttt{logImi}_{hi} + \beta_5 \times \texttt{logDmi} + \epsilon_{hi}\end{aligned}$$

with as (Level 2) model

$$\beta_{0i} = \beta_0 + \alpha_{0i}$$
$$\beta_{1i} = \beta_1 + \alpha_{1i}$$

Are imipramine and desipramine levels related to reductions in depression?

```
dat <- as.data.frame(read.spss("ReisbyCov.sav"))
head(dat)
```

```
##    id HamDchange Week Endogenous EndoWeek  logImi  logDmi
## 1 101         -8    0         -1        0 4.04305 4.20469
## 2 101        -19    1         -1       -1 3.93183 4.81218
## 3 101        -22    2         -1       -2 4.33073 4.96284
## 4 101        -23    3         -1       -3 4.36945 4.96284
## 5 103        -18    0         -1        0 2.77259 5.23644
## 6 103         -9    1         -1       -1 3.46574 5.20949
```

```
mod <- lmer(HamDchange ~ Week + Endogenous + EndoWeek +
            logImi + logDmi + (1+Week|id),data=dat,REML=FALSE)
summary(mod)
```

```
## Linear mixed model fit by maximum likelihood t-tests use Satterthwaite
##   approximations to degrees of freedom [lmerMod]
## Formula: HamDchange ~ Week + Endogenous + EndoWeek + logImi + logDmi +
##     (1 + Week | id)
##    Data: dat
##
##      AIC      BIC   logLik deviance df.resid
##   1517.7   1552.9   -748.8   1497.7      240
##
## Scaled residuals:
##      Min       1Q   Median       3Q      Max
## -2.49834 -0.47124 -0.01299  0.51656  2.56670
##
## Random effects:
##  Groups   Name        Variance Std.Dev. Corr
##  id       (Intercept) 20.050   4.478
##           Week         2.768   1.664    0.12
##  Residual             10.526   3.244
## Number of obs: 250, groups:  id, 66
##
## Fixed effects:
##             Estimate Std. Error       df t value Pr(>|t|)
## (Intercept)   1.6551     3.7246 131.6000   0.444  0.65750
```

```
## Week         -1.9496     0.2862  64.8800  -6.813 3.73e-09 ***
## Endogenous    0.7078     0.6559  63.9400   1.079  0.28458
## EndoWeek     -0.1177     0.2822  61.9400  -0.417  0.67796
## logImi        0.5923     0.8172 120.1200   0.725  0.46996
## logDmi       -1.9830     0.6003 126.8100  -3.303  0.00124 **
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Correlation of Fixed Effects:
##             (Intr) Week   Endgns EndoWk logImi
## Week         0.110
## Endogenous   0.033  0.040
## EndoWeek     0.008 -0.106 -0.212
## logImi      -0.682 -0.041 -0.033  0.033
## logDmi      -0.510 -0.151 -0.037 -0.042 -0.258
```

```
# confidence intervals for random effects
confint(mod)
```

```
## Computing profile confidence intervals ...
```

```
##                  2.5 %     97.5 %
## .sig01       3.4510159  5.7066532
## .sig02      -0.2765003  0.6442735
## .sig03       1.0773214  2.2669518
## .sigma       2.8665906  3.7109461
## (Intercept) -5.9480389  9.1685809
## Week        -2.5172302 -1.3758714
## Endogenous  -0.5954913  2.0152795
## EndoWeek    -0.6786627  0.4450015
## logImi      -1.0230019  2.2339944
## logDmi      -3.2001015 -0.7655761
```

Answer: There is a significant fixed effect for `Week`, as well as for `logDmi`. Both slopes are negative, so that increases in `Week` and `logDMI` result in decreases in the dependent variable, which is here a difference in Hamilton depression score from a baseline measure (at week 0). So depression decreases more over time and with higher levels of desipramine. Interestingly, there is no effect of imipramine. From this analysis, you can conclude that the imipramine reduces depression only once biotransformed into desipramine. Both the random intercepts and slopes for `Week` have a variance which is significantly greater than 0 (see e.g. the Wald tests). From the Wald test there is no indication that the intercepts and slopes co-vary, but you should really test this with a likelihood-ratio test...

(b) Investigate whether the effect of imipramine and desipramine is moderated by the type of depression (endogenous or exogenous). Create two predictors for

the interaction between `Endogenous` and `logImi` and `logDmi` respectively (I have called them `EndoLogImi` and `EndoLogDmi`). Include these as additional covariates (with fixed slopes) in the model above. Compare the results to those obtained in the previous analysis. What do you conclude about the effect of imipramine and desipramine on the change in depression?

```
dat$EndoLogImi <- dat$Endogenous*dat$logImi
dat$EndoLogDmi <- dat$Endogenous*dat$logDmi
mod_inter <- lmer(HamDchange ~ Week + Endogenous + EndoWeek +
                  logImi + logDmi + EndoLogImi + EndoLogDmi +
                  (1+Week|id),data=dat,REML=FALSE)
summary(mod_inter)
```

```
## Linear mixed model fit by maximum likelihood t-tests use Satterthwaite
##   approximations to degrees of freedom [lmerMod]
## Formula: HamDchange ~ Week + Endogenous + EndoWeek + logImi + logDmi +
##     EndoLogImi + EndoLogDmi + (1 + Week | id)
##    Data: dat
##
##      AIC      BIC   logLik deviance df.resid
##   1514.9   1557.2   -745.5   1490.9      238
##
## Scaled residuals:
##     Min      1Q  Median      3Q     Max
## -2.5617 -0.4652 -0.0086  0.4718  2.6044
##
## Random effects:
##  Groups   Name        Variance Std.Dev. Corr
##  id       (Intercept) 18.111   4.256
##           Week         2.732   1.653    0.16
##  Residual             10.409   3.226
## Number of obs: 250, groups:  id, 66
##
## Fixed effects:
##             Estimate Std. Error       df t value Pr(>|t|)
## (Intercept)   1.6865     3.8376 136.0000   0.439 0.661024
## Week         -1.9755     0.2847  65.0700  -6.939 2.21e-09 ***
## Endogenous    4.8135     3.8376 136.0000   1.254 0.211880
## EndoWeek     -0.1217     0.2847  65.0700  -0.428 0.670395
## logImi        0.7592     0.8005 119.8300   0.948 0.344812
## logDmi       -2.1285     0.6294 133.7900  -3.382 0.000944 ***
## EndoLogImi   -2.0007     0.8005 119.8300  -2.499 0.013796 *
## EndoLogDmi    0.8417     0.6294 133.7900   1.337 0.183367
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

```
##
## Correlation of Fixed Effects:
##             (Intr) Week   Endgns EndoWk logImi logDmi EndLgI
## Week         0.120
## Endogenous -0.290 -0.051
## EndoWeek   -0.051 -0.112  0.120
## logImi     -0.667 -0.048  0.104  0.045
## logDmi     -0.567 -0.152  0.282  0.026 -0.214
## EndoLogImi  0.104  0.045 -0.667 -0.048 -0.109 -0.026
## EndoLogDmi  0.282  0.026 -0.567 -0.152 -0.026 -0.358 -0.214
```

```
confint(mod_inter)
```

```
## Computing profile confidence intervals ...
```

```
##                   2.5 %     97.5 %
## .sig01        3.2467359  5.4493840
## .sig02       -0.2465262  0.7002536
## .sig03        1.0708289  2.2524401
## .sigma        2.8517339  3.6888916
## (Intercept) -6.0290917  9.3350599
## Week        -2.5404306 -1.4057740
## Endogenous  -2.8214022 12.3911548
## EndoWeek    -0.6871459  0.4460167
## logImi      -0.8226681  2.3578176
## logDmi      -3.3874526 -0.8644922
## EndoLogImi  -3.5801598 -0.4163953
## EndoLogDmi  -0.4042337  2.0977959
```

Answer: In addition to the results found previously, this analysis shows a significant interaction between endogeneity and (log) imipramine. While there is no average effect of `logImi`, there is evidence that its effect depends on the type of depression. The estimate of the slope for this interaction is negative. For people with endogenous depression, we would add this value to the slope of `logImi`, which gives $.756 - 1.990 = -1.234$. Thus, for people with endogenous depression, (log) imipramine has a negative effect on the difference scores (i.e., it decreases depression relative to the baseline score). For people with exogenous depression, the slopes becomes $.756 + 1.990 = 2.746$, so that (log) imipramine has a positive effect, making the difference scores smaller or even positive. As such, it seems to be the case that imipramine (by itself) only reduces endogeneous depression, but not exogenous depression. Both types of depression are reduced by desipramine.