picture_book

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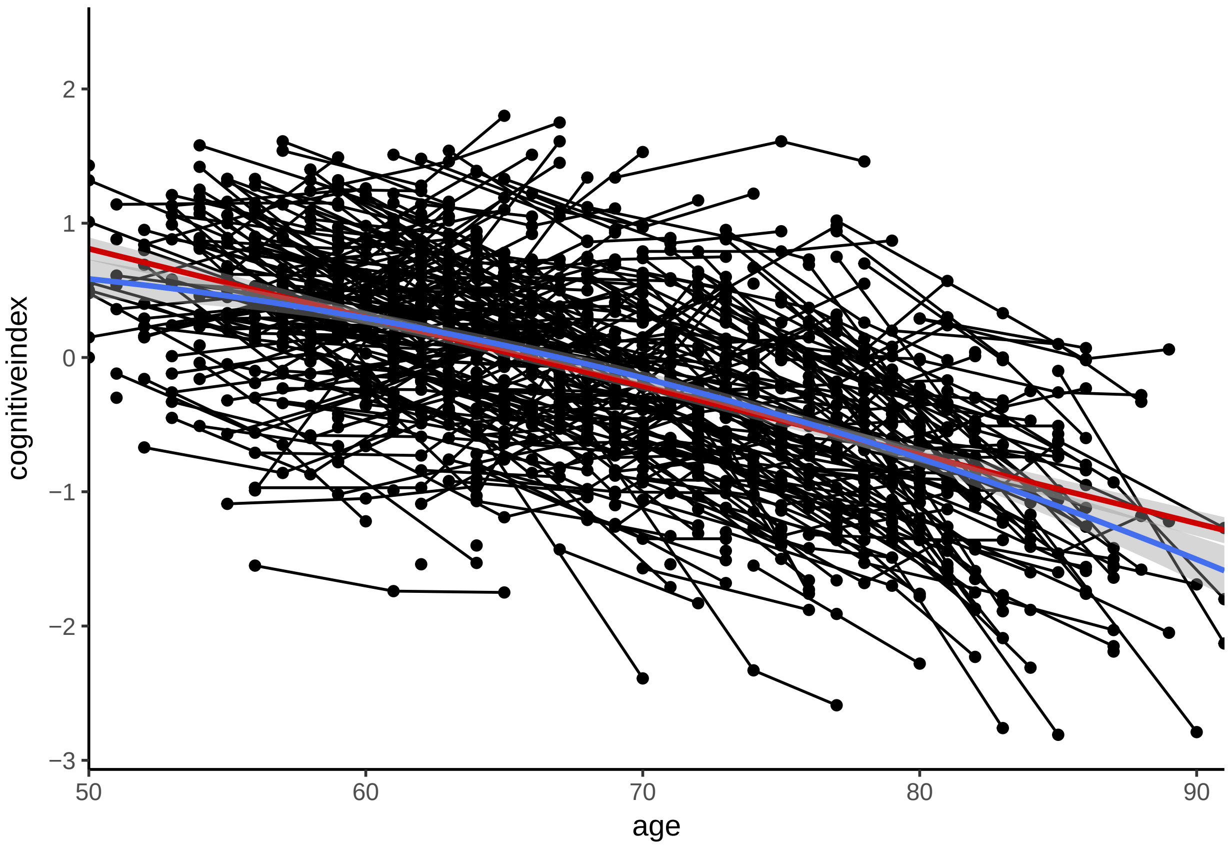
R Markdown

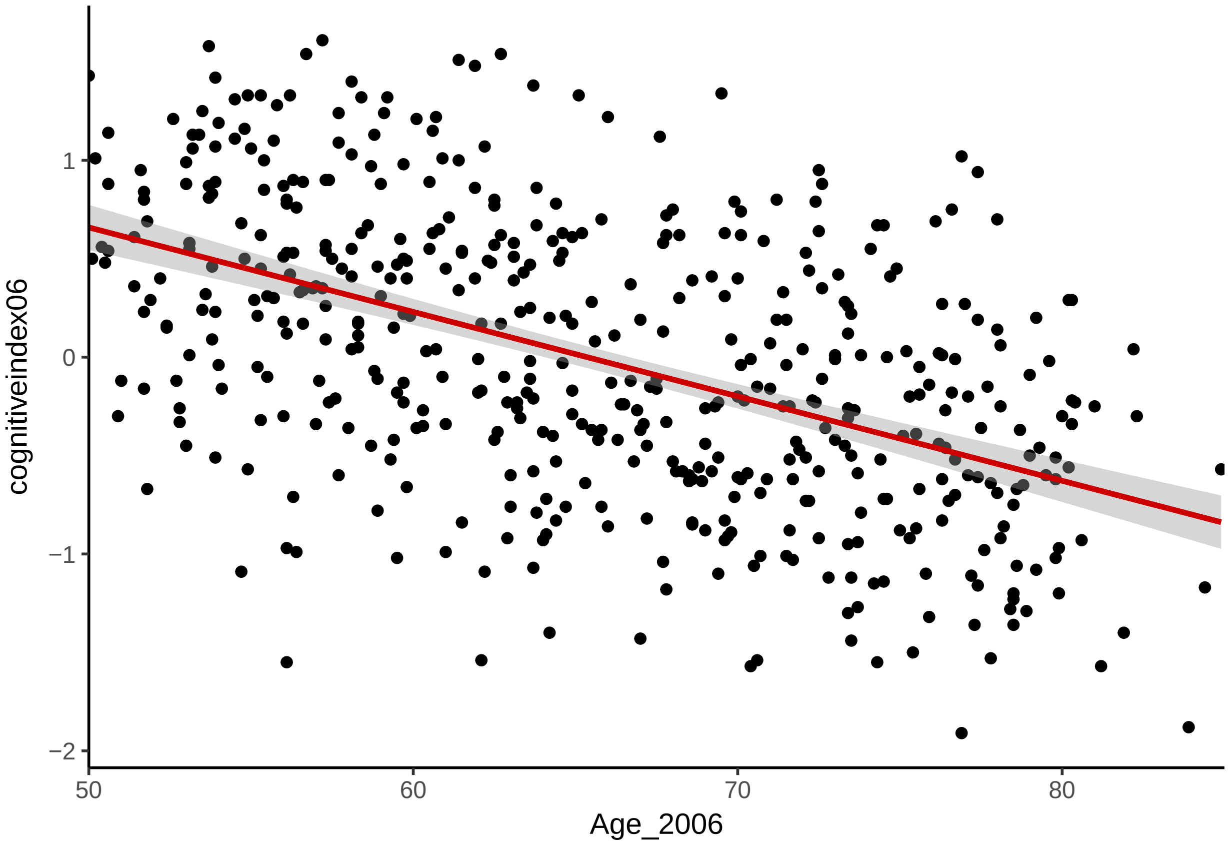
Firstly, let's examine the relationship between age and cognition. This graph is a terse description of the relationship between the two variables:



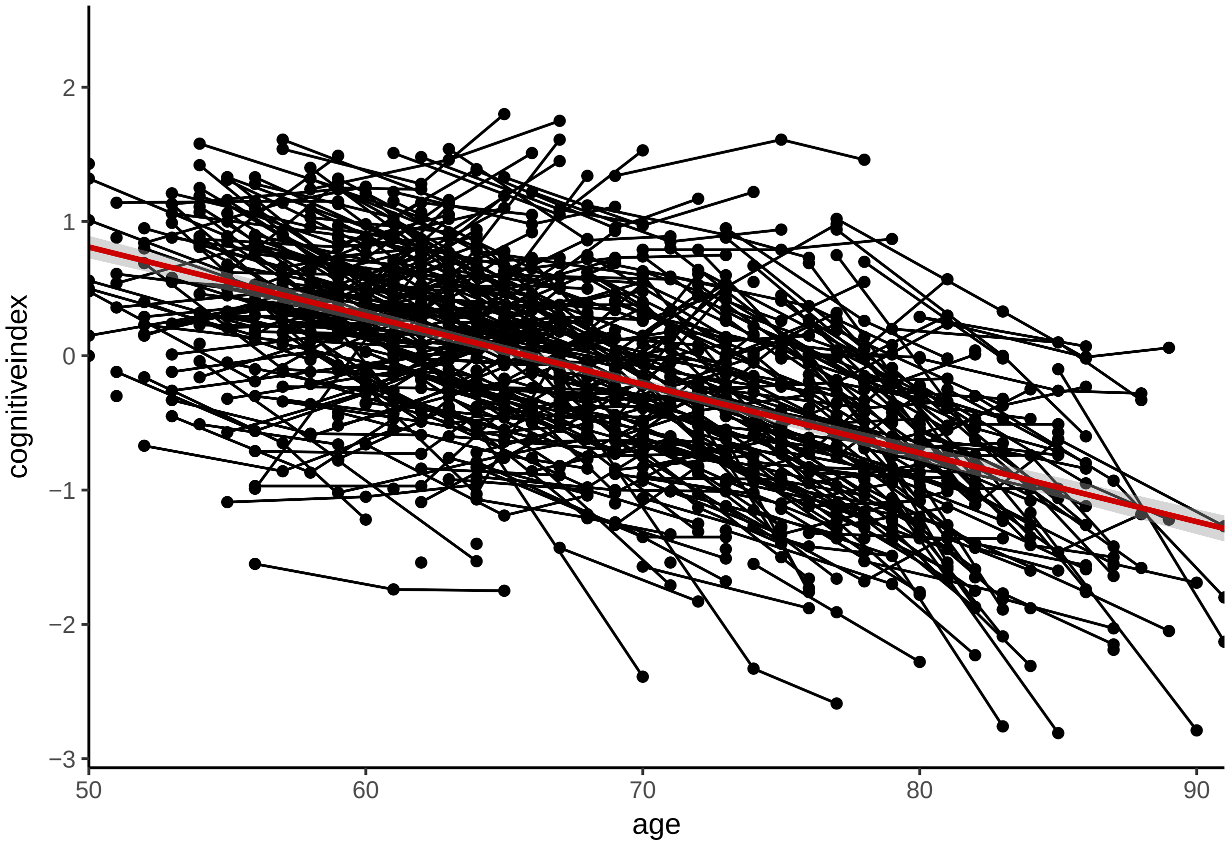
This contains all the information we can use in linear mixed effects regression (lmer). Let's break it down, step by step, so that each term in the model is interpretable.

First, the effects of age can be broken down into two variables: baseline age and time between follow-ups. First, the linear term for baseline age is simply expressing the cross-sectional correlation between age and cognition:

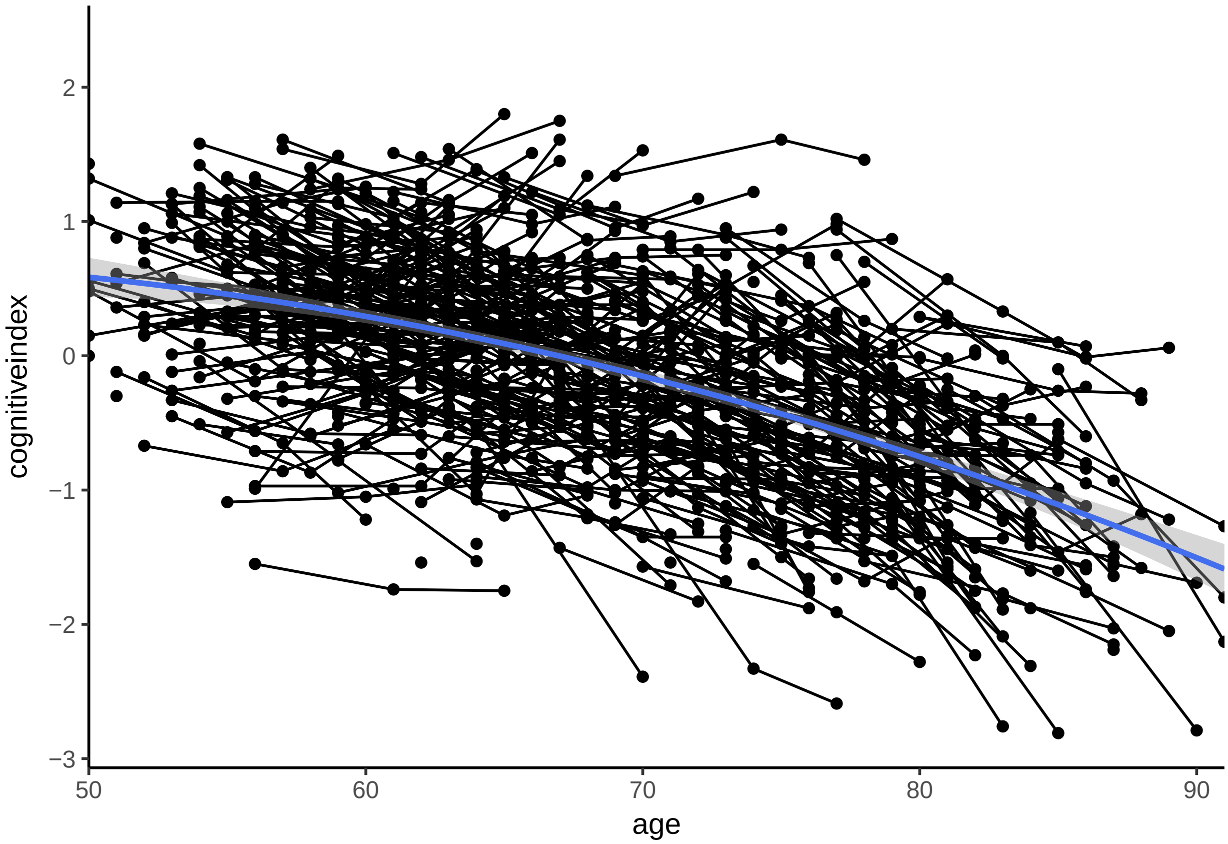
The quadratic is positive



The fixed effect of time between follow-ups expresses the linear trend between cognition and the passage of time:

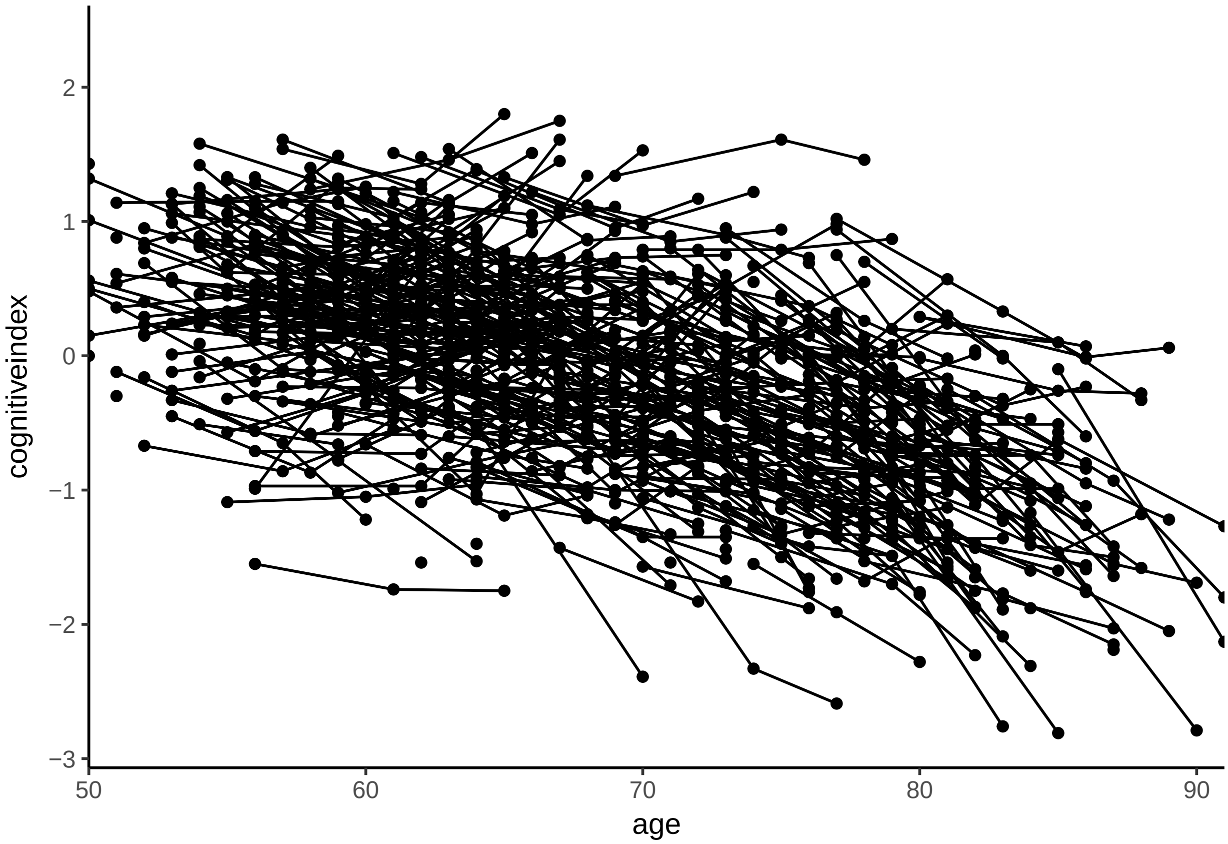


And the fixed effect of time squared between follow-ups expresses the quadratic trend between cognition and the passage of time:

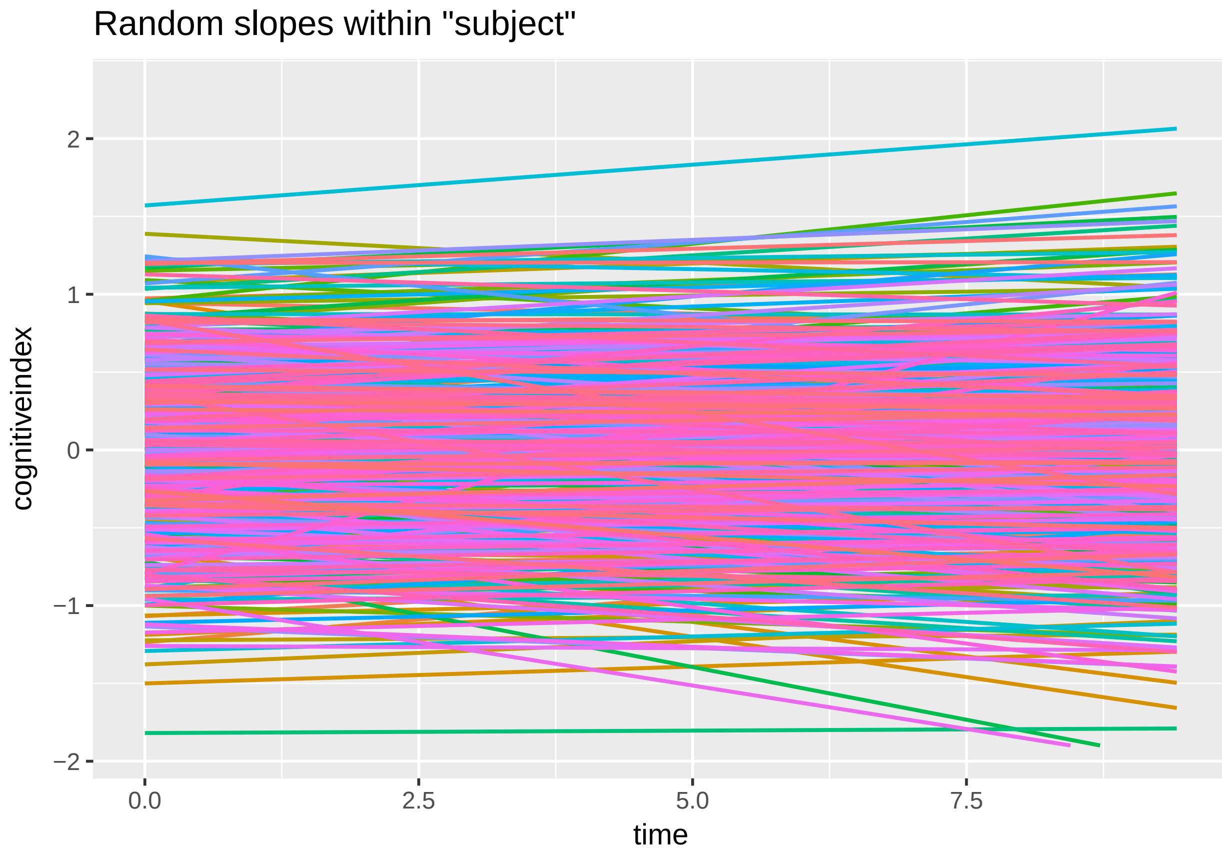


Then, two random effects are specified for intercept and slopes, grouped by subject. This expresses subject specific changes in cognition over time. The correlation between slope and intercept implies that we expect the rate of change for each subject to depend on their age (as evidenced by how cognition declines quadratically towards 80-90.

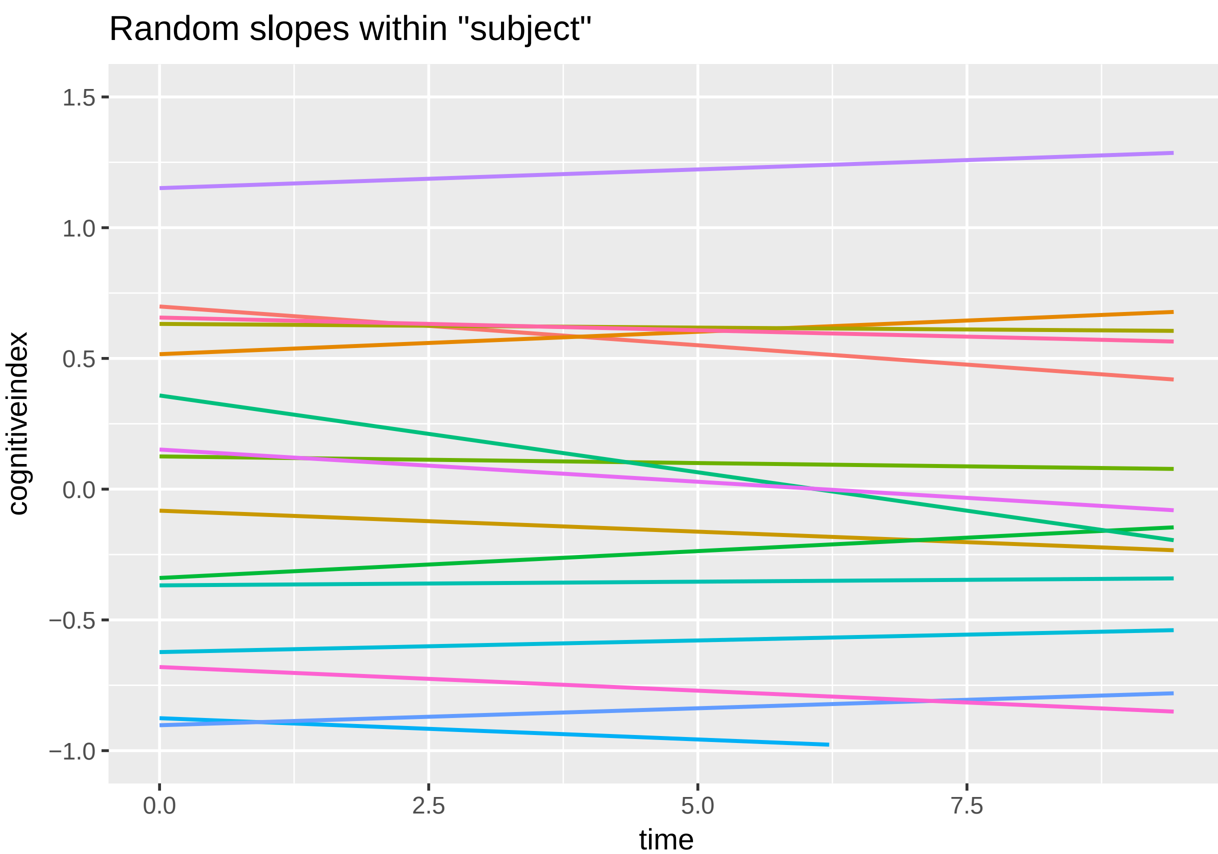
The random effect of each subject can be visualised as the total effect of each individual line segment:



To more easily see this relationship, we can examine individual line segments, plotted against each other with the same vertical axis (i.e., the baseline visit):



It is quite difficult to see individual trends, so we'll only plot a subset (n = 15):



These lines are fairly flat, suggesting that change in cognition for each individual subject is low between time points. This is reflected in the low variance of the slope term for time in the initial LMER, which only includes terms for age and time:

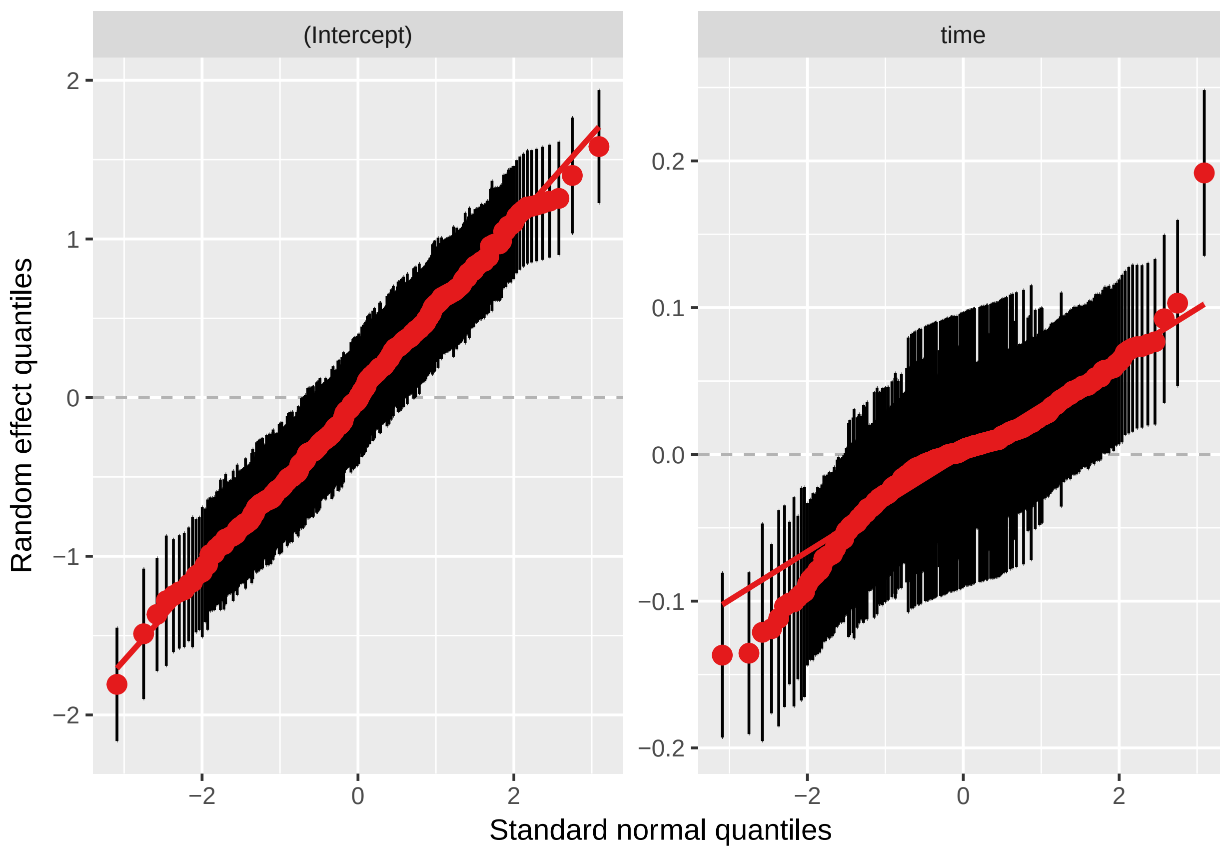
```
fit <- lmer(cognitiveindex ~ 1 + age06 + time + timesq + (1 + time|subject), data = dfLong)
summary(fit)
```

```
## Linear mixed model fit by REML t-tests use Satterthwaite approximations
##   to degrees of freedom [lmerMod]
## Formula: cognitiveindex ~ 1 + age06 + time + timesq + (1 + time | subject)
##    Data: dfLong
##
## REML criterion at convergence: 1637.3
##
## Scaled residuals:
##     Min      1Q  Median      3Q     Max
## -2.9920 -0.3744  0.0026  0.4026  2.5467
##
## Random effects:
##  Groups   Name        Variance Std.Dev. Corr
##  subject  (Intercept) 0.341072 0.58401
##           time        0.002342 0.04839  -0.18
##  Residual             0.050318 0.22432
## Number of obs: 1240, groups:  subject, 503
##
## Fixed effects:
##                 Estimate  Std. Error          df t value Pr(>|t|)
```

```
## (Intercept)  -0.0116614   0.0278943 493.9000000  -0.418    0.676
## age06        -0.4366309   0.0268378 504.5000000 -16.269   <2e-16 ***
## time         -0.1243878   0.0072728 472.1000000 -17.103   <2e-16 ***
## timesq        0.0092646   0.0008159 349.5000000  11.355   <2e-16 ***
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Correlation of Fixed Effects:
##        (Intr) age06  time
## age06   0.000
## time   -0.197  0.019
## timesq  0.093 -0.003 -0.908
```

The slope term is close to 0. This suggests that the timeframe for follow-ups is not sufficient to detect change on the individual level; indeed, the nonlinear relationship between age and cognitive change was only seen in the population range of 50-90. 10 years for a subject at 50 isn't likely going to show as much cognitive decline compared to, say, 10 years for a subject at 80. This likely reflects inclusion bias (e.g., younger participants were more likely to be enrolled because they have better functioning, as evidenced by how average age at enrollment was ~65; these may be more pronounced if average age was 75).

Indeed, there are some participants with a non-normal (compared to other subjects) random slope term, as evidenced by a qq-plot for all subjects:



Now, on to adding terms for WMH and HV. Since WMH progression has a significant quadratic change with time (van Leijsen et al., 2017), we must first examine interactions between WMH and either linear or quadratic terms. This is done at the population level (i.e., modelled as a fixed effect). We also include a random slope term for WMH to capture subject variability (which covers any higher polynomial that might govern an individual's developmental trajectory).

Let's see which interaction (linear or quadratic) best describes the data:

```
fit1 <- lmer(cognitiveindex ~ 1 + age06 + time + timesq + (1 + time|subject) +
             lnwmh + lnwmh*time, data = dfLong)
fit2 <- lmer(cognitiveindex ~ 1 + age06 + time + timesq + (1 + time|subject) +
             lnwmh + lnwmh*timesq, data = dfLong)
summary(fit1)
```

```
## Linear mixed model fit by REML t-tests use Satterthwaite approximations
##   to degrees of freedom [lmerMod]
## Formula:
## cognitiveindex ~ 1 + age06 + time + timesq + (1 + time | subject) +
##     lnwmh + lnwmh * time
##    Data: dfLong
##
## REML criterion at convergence: 1457.8
##
## Scaled residuals:
##     Min      1Q  Median      3Q     Max
## -3.1949 -0.3615  0.0055  0.3915  2.3989
##
## Random effects:
##  Groups   Name        Variance Std.Dev. Corr
##  subject  (Intercept) 0.339546 0.58271
##           time        0.001733 0.04163  -0.24
##  Residual             0.046269 0.21510
## Number of obs: 1148, groups:  subject, 503
##
## Fixed effects:
##                 Estimate  Std. Error          df t value     Pr(>|t|)
## (Intercept)    0.0166011   0.0375730 611.0000000   0.442        0.659
## age06         -0.3958631   0.0302282 577.1000000 -13.096      < 2e-16 ***
## time          -0.1151543   0.0075418 412.3000000 -15.269      < 2e-16 ***
## timesq         0.0118443   0.0008763 365.8000000  13.517      < 2e-16 ***
## lnwmh         -0.0222502   0.0198662 757.0000000  -1.120        0.263
## time:lnwmh    -0.0122507   0.0021786 402.3000000  -5.623 0.0000000351 ***
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Correlation of Fixed Effects:
##            (Intr) age06  time   timesq lnwmh
## age06       0.314
## time       -0.162  0.034
## timesq      0.142  0.085 -0.804
## lnwmh      -0.676 -0.464  0.036 -0.123
## time:lnwmh  0.182  0.009 -0.229 -0.213 -0.268
```

```
summary(fit2)
```

```
## Linear mixed model fit by REML t-tests use Satterthwaite approximations
##   to degrees of freedom [lmerMod]
## Formula:
## cognitiveindex ~ 1 + age06 + time + timesq + (1 + time | subject) +
##     lnwmh + lnwmh * timesq
##    Data: dfLong
```

```
##
## REML criterion at convergence: 1460
##
## Scaled residuals:
##     Min      1Q  Median      3Q     Max
## -3.1902 -0.3614  0.0040  0.3729  2.4325
##
## Random effects:
##  Groups   Name        Variance Std.Dev. Corr
##  subject  (Intercept) 0.33945  0.58262
##           time        0.00178  0.04219  -0.24
##  Residual             0.04554  0.21339
## Number of obs: 1148, groups:  subject, 503
##
## Fixed effects:
##                Estimate Std. Error         df t value    Pr(>|t|)
## (Intercept)    0.024679   0.037277 620.300000   0.662       0.508
## age06         -0.393917   0.030211 577.300000 -13.039     < 2e-16 ***
## time          -0.131436   0.007389 410.900000 -17.788     < 2e-16 ***
## timesq         0.013899   0.001007 528.600000  13.807     < 2e-16 ***
## lnwmh         -0.028587   0.019547 800.800000  -1.462       0.144
## timesq:lnwmh  -0.001515   0.000262 444.500000  -5.781 0.000000014 ***
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Correlation of Fixed Effects:
##             (Intr) age06  time   timesq lnwmh
## age06        0.314
## time        -0.101  0.038
## timesq       0.083  0.074 -0.829
## lnwmh       -0.670 -0.469 -0.059 -0.047
## timsq:lnwmh  0.140  0.002  0.155 -0.535 -0.209
```

```r
anova(fit1, fit2)
```

```
## refitting model(s) with ML (instead of REML)
```

```
## Data: dfLong
## Models:
## object: cognitiveindex ~ 1 + age06 + time + timesq + (1 + time | subject) +
## object:     lnwmh + lnwmh * time
## ..1: cognitiveindex ~ 1 + age06 + time + timesq + (1 + time | subject) +
## ..1:     lnwmh + lnwmh * timesq
##        Df    AIC    BIC logLik deviance  Chisq Chi Df Pr(>Chisq)
## object 10 1428.2 1478.7 -704.1   1408.2
## ..1    10 1426.2 1476.7 -703.1   1406.2 2.0125      0  < 2.2e-16 ***
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

Interestingly, the quadratic interaction seems to better describe the data than the linear interaction, as well as the main effect of WMH.

Now to add HV to the models. We can test two models here easily: one is that HV and WMH are independent, while the other is that they interact. HV shall interact only with linear time (we have no reason to believe it's not linear at this stage in SVD):

```r
fit1 <- lmer(cognitiveindex ~ 1 + age06 + time + timesq + (1 + time|subject) +
             lnwmh + lnwmh*timesq + hv + hv*time, data = dfLong)
fit2 <- lmer(cognitiveindex ~ 1 + age06 + time + timesq + (1 + time|subject) +
             lnwmh + lnwmh*timesq + hv + hv*time + lnwmh*hv, data = dfLong)
summary(fit1)
```

```
## Linear mixed model fit by REML t-tests use Satterthwaite approximations
##   to degrees of freedom [lmerMod]
## Formula:
## cognitiveindex ~ 1 + age06 + time + timesq + (1 + time | subject) +
##     lnwmh + lnwmh * timesq + hv + hv * time
##    Data: dfLong
##
## REML criterion at convergence: 1396.3
##
## Scaled residuals:
##     Min      1Q  Median      3Q     Max
## -3.3636 -0.3836  0.0050  0.3988  2.3225
##
## Random effects:
##  Groups   Name        Variance Std.Dev. Corr
##  subject  (Intercept) 0.336288 0.57990
##           time        0.001291 0.03594  -0.20
##  Residual             0.043971 0.20969
## Number of obs: 1147, groups:  subject, 503
##
## Fixed effects:
##                  Estimate  Std. Error          df t value       Pr(>|t|)
## (Intercept)   -0.5579212   0.2158816 784.8000000  -2.584       0.009935
## age06         -0.3200175   0.0335723 629.3000000  -9.532        < 2e-16
## time          -0.2581968   0.0221128 501.0000000 -11.676        < 2e-16
## timesq         0.0130968   0.0009715 522.2000000  13.481        < 2e-16
## lnwmh         -0.0303407   0.0192797 820.8000000  -1.574       0.115940
## hv             0.0770521   0.0276711 794.6000000   2.785       0.005487
## timesq:lnwmh  -0.0009497   0.0002526 424.4000000  -3.760       0.000194
## time:hv        0.0177392   0.0027009 414.5000000   6.568 0.000000000153
##
## (Intercept)  **
## age06        ***
## time         ***
## timesq       ***
## lnwmh
## hv           **
## timesq:lnwmh ***
## time:hv      ***
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Correlation of Fixed Effects:
##             (Intr) age06  time   timesq lnwmh  hv     tmsq:l
## age06       -0.371
## time        -0.504  0.123
## timesq       0.054  0.042 -0.223
## lnwmh       -0.219 -0.374  0.086 -0.067
```

```
## hv          -0.985  0.425  0.501 -0.038  0.108
## timsq:lnwmh  0.097  0.002 -0.221 -0.505 -0.204 -0.075
## time:hv      0.461 -0.086 -0.943 -0.058 -0.104 -0.462  0.286
```

```r
summary(fit2)
```

```
## Linear mixed model fit by REML t-tests use Satterthwaite approximations
##   to degrees of freedom [lmerMod]
## Formula:
## cognitiveindex ~ 1 + age06 + time + timesq + (1 + time | subject) +
##     lnwmh + lnwmh * timesq + hv + hv * time + lnwmh * hv
##    Data: dfLong
##
## REML criterion at convergence: 1395.6
##
## Scaled residuals:
##     Min      1Q  Median      3Q     Max
## -3.3900 -0.3794  0.0029  0.4036  2.2757
##
## Random effects:
##  Groups   Name        Variance Std.Dev. Corr
##  subject  (Intercept) 0.335746 0.57944
##           time        0.001281 0.03579  -0.21
##  Residual             0.043787 0.20925
## Number of obs: 1147, groups:  subject, 503
##
## Fixed effects:
##                   Estimate   Std. Error           df t value   Pr(>|t|)
## (Intercept)    -0.1292065    0.2674581  905.6000000  -0.483    0.62915
## age06          -0.3142944    0.0335771  630.3000000  -9.360    < 2e-16 ***
## time           -0.2312357    0.0241638  650.9000000  -9.570    < 2e-16 ***
## timesq          0.0125187    0.0009919  546.3000000  12.621    < 2e-16 ***
## lnwmh          -0.3446942    0.1180872 1024.2000000  -2.919    0.00359 **
## hv              0.0243706    0.0337815  906.5000000   0.721    0.47084
## timesq:lnwmh   -0.0007398    0.0002634  498.2000000  -2.809    0.00517 **
## time:hv         0.0144297    0.0029525  545.6000000   4.887 0.00000135 ***
## lnwmh:hv        0.0408428    0.0151276 1044.6000000   2.700    0.00705 **
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Correlation of Fixed Effects:
##             (Intr) age06  time   timesq lnwmh  hv     tmsq:l tim:hv
## age06       -0.255
## time        -0.133  0.142
## timesq      -0.086  0.026 -0.287
## lnwmh       -0.612 -0.133 -0.390  0.203
## hv          -0.990  0.304  0.142  0.094  0.582
## timsq:lnwmh  0.251  0.023 -0.072 -0.534 -0.324 -0.230
## time:hv      0.100 -0.108 -0.953  0.038  0.388 -0.112  0.129
## lnwmh:hv     0.591  0.073  0.408 -0.217 -0.987 -0.575  0.296 -0.409
```

```r
anova(fit1, fit2)
```

```
## refitting model(s) with ML (instead of REML)
```

```
## Data: dfLong
```

```
## Models:
## object: cognitiveindex ~ 1 + age06 + time + timesq + (1 + time | subject) +
## object:     lnwmh + lnwmh * timesq + hv + hv * time
## ..1: cognitiveindex ~ 1 + age06 + time + timesq + (1 + time | subject) +
## ..1:     lnwmh + lnwmh * timesq + hv + hv * time + lnwmh * hv
##        Df    AIC    BIC  logLik deviance  Chisq Chi Df Pr(>Chisq)
## object 12 1350.5 1411.0 -663.25   1326.5
## ..1    13 1345.2 1410.8 -659.60   1319.2 7.2996      1   0.006897 **
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

Interesting eh? It makes sense that WMH and HV become non-significant when adding respective interaction terms with time (as we expect both WMH progression and HV atrophy to be "symptoms" of age-related cognitive decline). Interestingly it seems like the interaction with WMH renders HV non-significant. Perhaps Wallerian degeneration driven by WMH does this.

Let's try it with mice!:

```r
library(mice)
dfTemp <- mice(dfLong)
```

```
##
##  iter imp variable
##   1   1  age  time  times  timesqrt  tbv  gmv  wmv  wmh  depression06  mmse  lac_pres  mb_pres  hv
##   1   2  age  time  times  timesqrt  tbv  gmv  wmv  wmh  depression06  mmse  lac_pres  mb_pres  hv
##   1   3  age  time  times  timesqrt  tbv  gmv  wmv  wmh  depression06  mmse  lac_pres  mb_pres  hv
##   1   4  age  time  times  timesqrt  tbv  gmv  wmv  wmh  depression06  mmse  lac_pres  mb_pres  hv
##   1   5  age  time  times  timesqrt  tbv  gmv  wmv  wmh  depression06  mmse  lac_pres  mb_pres  hv
##   2   1  age  time  times  timesqrt  tbv  gmv  wmv  wmh  depression06  mmse  lac_pres  mb_pres  hv
##   2   2  age  time  times  timesqrt  tbv  gmv  wmv  wmh  depression06  mmse  lac_pres  mb_pres  hv
##   2   3  age  time  times  timesqrt  tbv  gmv  wmv  wmh  depression06  mmse  lac_pres  mb_pres  hv
##   2   4  age  time  times  timesqrt  tbv  gmv  wmv  wmh  depression06  mmse  lac_pres  mb_pres  hv
##   2   5  age  time  times  timesqrt  tbv  gmv  wmv  wmh  depression06  mmse  lac_pres  mb_pres  hv
##   3   1  age  time  times  timesqrt  tbv  gmv  wmv  wmh  depression06  mmse  lac_pres  mb_pres  hv
##   3   2  age  time  times  timesqrt  tbv  gmv  wmv  wmh  depression06  mmse  lac_pres  mb_pres  hv
##   3   3  age  time  times  timesqrt  tbv  gmv  wmv  wmh  depression06  mmse  lac_pres  mb_pres  hv
##   3   4  age  time  times  timesqrt  tbv  gmv  wmv  wmh  depression06  mmse  lac_pres  mb_pres  hv
##   3   5  age  time  times  timesqrt  tbv  gmv  wmv  wmh  depression06  mmse  lac_pres  mb_pres  hv
##   4   1  age  time  times  timesqrt  tbv  gmv  wmv  wmh  depression06  mmse  lac_pres  mb_pres  hv
##   4   2  age  time  times  timesqrt  tbv  gmv  wmv  wmh  depression06  mmse  lac_pres  mb_pres  hv
##   4   3  age  time  times  timesqrt  tbv  gmv  wmv  wmh  depression06  mmse  lac_pres  mb_pres  hv
##   4   4  age  time  times  timesqrt  tbv  gmv  wmv  wmh  depression06  mmse  lac_pres  mb_pres  hv
##   4   5  age  time  times  timesqrt  tbv  gmv  wmv  wmh  depression06  mmse  lac_pres  mb_pres  hv
##   5   1  age  time  times  timesqrt  tbv  gmv  wmv  wmh  depression06  mmse  lac_pres  mb_pres  hv
##   5   2  age  time  times  timesqrt  tbv  gmv  wmv  wmh  depression06  mmse  lac_pres  mb_pres  hv
##   5   3  age  time  times  timesqrt  tbv  gmv  wmv  wmh  depression06  mmse  lac_pres  mb_pres  hv
##   5   4  age  time  times  timesqrt  tbv  gmv  wmv  wmh  depression06  mmse  lac_pres  mb_pres  hv
##   5   5  age  time  times  timesqrt  tbv  gmv  wmv  wmh  depression06  mmse  lac_pres  mb_pres  hv
```

```r
fit1 <- with(dfTemp, lmer(cognitiveindex ~ 1 + age06 + time + timesq + (1 + time|subject) +
             lnwmh + lnwmh*timesq + hv + hv*time))
fit2 <- with(dfTemp, lmer(cognitiveindex ~ 1 + age06 + time + timesq + (1 + time|subject) +
             lnwmh + lnwmh*timesq + hv + hv*time + lnwmh*hv))
fit3 <- with(dfTemp, lmer(cognitiveindex ~ 1 + age06 + poly(time, 2) + (1 + time|subject) +
             lnwmh + lnwmh*timesq + hv + hv*time))
```

```
## Warning: Some predictor variables are on very different scales: consider
## rescaling

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## rescaling

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## rescaling

## Warning: Some predictor variables are on very different scales: consider
## rescaling

## Warning: Some predictor variables are on very different scales: consider
## rescaling
```

```r
summary(pool(fit1))
```

```
##                      est           se          t         df
## (Intercept)   0.234366296 0.2020257628   1.160081  191.11361
## age06        -0.405142563 0.0317406729 -12.764145 1083.24027
## time         -0.256884582 0.0245924719 -10.445659  370.03941
## timesq        0.013789970 0.0010942688  12.601995  293.31066
## lnwmh        -0.020974930 0.0208743421  -1.004819   98.49473
## hv           -0.028904074 0.0252510611  -1.144668  250.02380
## timesq:lnwmh -0.001498715 0.0002842447  -5.272624  124.01723
## time:hv       0.016293487 0.0030024751   5.426685  441.25447
##                      Pr(>|t|)        lo 95         hi 95 nmis        fmi
## (Intercept)  0.24746291118239 -0.164120332  0.6328529235   NA 0.14008654
## age06        0.00000000000000 -0.467422726 -0.3428623994   NA 0.02139345
## time         0.00000000000000 -0.305243108 -0.2085260557  262 0.09012952
## timesq       0.00000000000000  0.011636356  0.0159435837  262 0.10623454
## lnwmh        0.31744633307831 -0.062396782  0.0204469217  360 0.20724620
## hv           0.25344143968882 -0.078635975  0.0208278275  358 0.11815117
## timesq:lnwmh 0.00000057790958 -0.002061315 -0.0009361162   NA 0.18147694
## time:hv      0.00000009487947  0.010392558  0.0221944153   NA 0.07872883
##                  lambda
## (Intercept)  0.13113440
## age06        0.01958830
## time         0.08522508
## timesq       0.10016092
## lnwmh        0.19131060
## hv           0.11112515
## timesq:lnwmh 0.16838237
## time:hv      0.07456258
```

```r
summary(pool(fit2))
```

```
##                      est           se           t         df
## (Intercept)   0.343210235 0.2891636878   1.1869064   36.65465
## age06        -0.403621814 0.0316770268 -12.7417834 1149.93139
## time         -0.251130394 0.0261785455  -9.5929850  270.56582
## timesq        0.013697881 0.0010954872  12.5039168  350.94002
## lnwmh        -0.096009917 0.1252034935  -0.7668310   27.55331
## hv           -0.042206132 0.0359586381  -1.1737411   38.57487
## timesq:lnwmh -0.001464935 0.0002863744  -5.1154517  146.61235
```

```
## time:hv       0.015558529 0.0032344928   4.8101913  258.27200
## lnwmh:hv      0.009640842 0.0159157072   0.6057439   26.86786
##                   Pr(>|t|)        lo 95         hi 95 nmis        fmi
## (Intercept)  0.2429001945187 -0.242877438  0.9292979079   NA 0.35714754
## age06        0.0000000000000 -0.465773062 -0.3414705663   NA 0.01537647
## time         0.0000000000000 -0.302669942 -0.1995908461  262 0.11214988
## timesq       0.0000000000000  0.011543335  0.0158524271  262 0.09367111
## lnwmh        0.4497029451848 -0.352665093  0.1606452587  360 0.41511422
## hv           0.2476948756847 -0.114964981  0.0305527158  358 0.34754831
## timesq:lnwmh 0.0000009648422 -0.002030890 -0.0008989794   NA 0.16445157
## time:hv      0.0000025653143  0.009189193  0.0219278656   NA 0.11565333
## lnwmh:hv     0.5497682565895 -0.023023009  0.0423046924   NA 0.42059232
##                  lambda
## (Intercept)  0.32300289
## age06        0.01366547
## time         0.10561113
## timesq       0.08852064
## lnwmh        0.37414624
## hv           0.31457529
## timesq:lnwmh 0.15313072
## time:hv      0.10883156
## lnwmh:hv     0.37900982
```

```r
summary(pool(fit3))
```

```
##                         est           se          t         df
## (Intercept)     -0.482675918 0.1815950066  -2.657980   38.92699
## age06           -0.405142566 0.0317406725 -12.764146 1083.24001
## poly(time, 2)1 -19.635210542 3.4051023598  -5.766408  313.99842
## poly(time, 2)2   4.590840275 0.3640766833  12.609542  297.13779
## lnwmh           -0.020974931 0.0208743423  -1.004819   98.49472
## hv              -0.028904073 0.0252510619  -1.144668  250.02370
## lnwmh:timesq    -0.001498715 0.0002842447  -5.272623  124.01723
## hv:time          0.016293487 0.0030024751   5.426685  441.25452
##                        Pr(>|t|)        lo 95          hi 95 nmis
## (Intercept)    0.01134530473951  -0.850008518  -0.1153433177   NA
## age06          0.00000000000000  -0.467422728  -0.3428624028   NA
## poly(time, 2)1 0.00000001937530 -26.334911983 -12.9355091016   NA
## poly(time, 2)2 0.00000000000000   3.874344720   5.3073358307   NA
## lnwmh          0.31744632832202  -0.062396783   0.0204469218  360
## hv             0.25344146199824  -0.078635976   0.0208278296  358
## lnwmh:timesq   0.00000057791001  -0.002061315  -0.0009361162   NA
## hv:time        0.00000009487958   0.010392558   0.0221944153   NA
##                       fmi     lambda
## (Intercept)    0.34586957 0.31310323
## age06          0.02139347 0.01958832
## poly(time, 2)1 0.10136980 0.09566418
## poly(time, 2)2 0.10529954 0.09929761
## lnwmh          0.20724621 0.19131062
## hv             0.11815120 0.11112518
## lnwmh:timesq   0.18147694 0.16838237
## hv:time        0.07872882 0.07456258
```