Log data analysis Assignment 1

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Task 3

Our first task is to generate a multivariate model and find the most parsimonious mean structure for it. Given that the data set is unbalanced we will use the gee and geepack libraries which allow us to conduct Generalized Estimating Equations. We will conduct these under the strict assumptions of Normality, however we will analyze the effects which different within subject covariate structures both with the help of Quasi-Information Criterium and the RMSE of the fitted Residuals. Holding the assumtion of Normality for the GEE models leads to functionally the same model as the Multivariate model described in the lecture. In this first step we will conduct some model searching in order to select the most parsimonious mean structure. We will start with a complete model as well as available interaction terms and slowly reduce it. We will compare all models against each other with the help of the QICu statistic (lower is better), the significance of the parameters as well as an ANOVA\MANOVA comparison. After we find the appropriate mean structure we will take care of selecting the appropriate covariance structure. The models run below are run under the assumption of independence between observations of the same individual.

```
mf <- formula(y ~ age+TIME+side+age:TIME+age:side+TIME:side)
gee1 <- geeglm(mf, data=df, id=id, corstr="independence")
QIC(gee1)[2]

## QICu
## 336295.1

mean(sqrt(resid(gee1)^2))

## [1] 6.540803

coef(summary(gee1))</pre>
```

```
Wald
##
                      Estimate
                                    Std.err
                                                            Pr(>|W|)
## (Intercept)
                  -4.735246112 0.923489548
                                             26.2918499 2.935247e-07
                   0.237289867 0.020042856 140.1648660 0.000000e+00
## age
## TIME
                  -0.047977954 0.139186881
                                              0.1188193 7.303186e-01
## sideright
                   0.258743907 0.630430628
                                              0.1684479 6.814949e-01
## age:TIME
                   0.004965421 0.003154596
                                              2.4775627 1.154811e-01
## age:sideright -0.005008229 0.012959024
                                              0.1493564 6.991512e-01
## TIME:sideright 0.011966651 0.034989705
                                              0.1169674 7.323472e-01
```

```
#mf2 <- formula(y ~ age+TIME+age:TIME+age:side+TIME:side)</pre>
#qee2 <- qeeqlm(mf2, data=df, id=id, corstr="independence")</pre>
#QIC(qee2)[2]
#mean(sqrt(resid(qee2)^2))
#coef(summary(gee2))
#mf3 <- formula(y ~ age+TIME+age:side+TIME:side)</pre>
#gee3 <- geeglm(mf3, data=df, id=id, corstr="independence")</pre>
#QIC(qee3)[2]
#mean(sqrt(resid(gee3)^2))
#coef(summary(gee3))
mf4 <- formula(y ~ age+TIME)</pre>
gee4 <- geeglm(mf4, data=df, id=id, corstr="independence")</pre>
QIC(gee4)[2]
##
     QICu
## 337008
mean(sqrt(resid(gee4)^2))
## [1] 6.556228
coef(summary(gee4))
##
                 Estimate
                              Std.err
                                            Wald
                                                     Pr(>|W|)
## (Intercept) -5.7536304 0.88071498 42.67889 6.450451e-11
                0.2577779 0.01857869 192.51343 0.000000e+00
## age
## TIME
                0.1985119 0.04500454 19.45630 1.029275e-05
mf5 <- formula(y ~ age)</pre>
gee5 <- geeglm(mf5, data=df, id=id, corstr="independence")</pre>
QIC(gee5)[2]
##
       QICu
## 341929.3
mean(sqrt(resid(gee5)^2))
## [1] 6.594221
coef(summary(gee5))
                                                      Pr(>|W|)
##
                 Estimate
                              Std.err
                                            Wald
## (Intercept) -4.2317764 0.85696267 24.38494 7.888314e-07
                0.2506885 0.01840205 185.58224 0.000000e+00
#mf6 <- formula(y ~ TIME)
#gee6 <- geeglm(mf6, data=df, id=id, corstr="independence")</pre>
#QIC(qee6)[2]
```

```
#mean(sqrt(resid(gee6)^2))
#coef(summary(qee6))
#anova(gee1, gee2)
#anova(gee1, gee3)
anova(gee1,gee4)
## Analysis of 'Wald statistic' Table
## Model 1 y ~ age + TIME + side + age:TIME + age:side + TIME:side
## Model 2 y ~ age + TIME
          X2 P(>|Chi|)
## Df
## 1 4 3.0084 0.5564
anova(gee1,gee5)
## Analysis of 'Wald statistic' Table
## Model 1 y ~ age + TIME + side + age:TIME + age:side + TIME:side
## Model 2 y ~ age
          X2 P(>|Chi|)
## Df
## 1 5 20.349 0.001074 **
## ---
## Signif. codes: 0 '*** 0.001 '** 0.01 '* 0.05 '.' 0.1 ' 1
#anova(gee1, gee6)
#anova(gee2, gee3)
#anova(gee2, gee4)
#anova(gee2, gee5)
#anova(qee2, qee6)
#anova(qee3, qee4)
#anova(gee3, gee5)
#anova(gee3, gee6)
anova(gee4,gee5)
## Analysis of 'Wald statistic' Table
## Model 1 y ~ age + TIME
## Model 2 y ~ age
## Df
          X2 P(>|Chi|)
## 1 1 19.456 1.029e-05 ***
## ---
## Signif. codes: 0 '*** 0.001 '** 0.01 '* 0.05 '.' 0.1 ' 1
#anova(gee4, gee6)
#anova(gee5, gee6)
```

We find that the model y^- age+ TIME that is we use only the age at the start of the survey as well as the elapsed time since the survey began is the most parsimonious model. In essence the actual participant age is what is most important. We further find that the effect of the side variable, nor does any of its interaction terms, does not play a large role in predicting hearing loss. This is something we would intuitively expect, people are not prone on average to loosing hearing in one ear compared to the other. These conclusions hold for a much wider selection of models (we present here only sample of what we tested) or even when we filter the data under different conditions (Removing subjects with less than $n = \{2, 4, 5, 6\}$ observations,looking at only the right/left ear data base,treating each ear-subject pair as single subject, balancing the data, grouping the subjects in cohorts of $\{1, 5, 10, 15, 20\}$ years an creating dummy variables for them).

Now we will take a look at the covariance structure of the model. Certain structure are naturally excluded due to the nature of our data e.g. AR(n) or Toeplitz are not really meaningful when the time series points are not equally spaced. We will compare the same model mean structure i.e. y~ age+ TIME under different covariance structures and see which one produces the smallest Quasi Information Criterion (QIC) value. [Comment: the code for unstructured covariance will not run bellow as it takes some computing time and may be annoying on weaker machines]

```
mf <- formula(y ~ age+TIME)</pre>
gee_opt1 <- geeglm(mf, data=df, id=id, corstr="independence")</pre>
QIC(gee_opt1)
                                                                                 QICC
##
            QIC
                          QICu
                                  Quasi Lik
                                                      CIC
                                                                 params
    337035.2382 337007.9592 -168500.9796
                                                  16.6395
                                                                 3.0000
                                                                         337035.2825
mean(sqrt(resid(gee_opt1)^2))
## [1] 6.556228
gee_opt2 <- geeglm(mf, data=df, id=id, corstr="exchangeable")</pre>
QIC(gee opt2)
##
             QIC
                            QICu
                                     Quasi Lik
                                                           CTC
                                                                      params
    339239.30297
                   339221.28567 -169607.64284
##
                                                     12.00865
                                                                     3.00000
##
            QICC
    339239.37691
mean(sqrt(resid(gee_opt2)^2))
## [1] 6.636954
#gee_opt3 <- geeglm(mf, data=df, id=id, corstr="unstructured")
#QIC(gee_opt3)
```

It appears that an independent covariance structure produces the lowest QIC value, nevertheless is behooves us to take a closer look at these two models. First lets consider the model with an exchangeable covariance structure.

```
mf <- formula(y ~ age+TIME)
gee_opt2_new<-gee(mf, data=df, id=id,family = gaussian, corstr = "exchangeable")</pre>
```

```
## Beginning Cgee S-function, @(#) geeformula.q 4.13 98/01/27
## running glm to get initial regression estimate
## (Intercept)
                       age
                                  TIME
## -5.7536304
                 0.2577779
                             0.1985119
summary(gee_opt2_new)$coefficients
                 Estimate Naive S.E.
##
                                       Naive z Robust S.E. Robust z
## (Intercept) -5.3392967 0.93172783 -5.730533
                                               0.80414355 -6.639731
                0.2496282 0.01682033 14.840865 0.01687625 14.791689
## TIME
                0.2851447 0.01897425 15.027977 0.02851307 10.000489
gee_opt2_new
##
##
   GEE: GENERALIZED LINEAR MODELS FOR DEPENDENT DATA
   gee S-function, version 4.13 modified 98/01/27 (1998)
##
##
## Model:
## Link:
                               Identity
  Variance to Mean Relation: Gaussian
  Correlation Structure:
                               Exchangeable
##
## Call:
## gee(formula = mf, id = id, data = df, family = gaussian, corstr = "exchangeable")
## Number of observations : 4419
##
## Maximum cluster size
                             29
##
##
## Coefficients:
## (Intercept)
                                  TIME
                       age
   -5.3392967
                 0.2496282
##
                             0.2851447
##
## Estimated Scale Parameter: 76.81489
## Number of Iterations: 3
##
## Working Correlation[1:4,1:4]
                       [,2]
##
             [,1]
                                 [,3]
## [1,] 1.0000000 0.6140421 0.6140421 0.6140421
## [2,] 0.6140421 1.0000000 0.6140421 0.6140421
## [3,] 0.6140421 0.6140421 1.0000000 0.6140421
## [4,] 0.6140421 0.6140421 0.6140421 1.0000000
##
##
## Returned Error Value:
## [1] 0
```

In the above output we notice that we get two standart errors: Naive and Robust. Normally we would want to use the Robust estimates because the variances of coefficient estimates tend to be too small when

responses within subjects are correlated (Bilder and Loughin, 2015), however in this case there is little difference between the Naive and Robust estimates. This further suggest that the independence assumption of the correlation structure seems realistic (Hothorn and Everitt, 2014). In the bottom we see a Working correlation output which shows an the upper 4×4 of the Variance-Covariance matrix used for this model (the size depends on the number of observations per individual with the largest beeing 29×29). Below we will report the best model we could find under the conditions of this task. It has the same parameter estimates as a least squares model with the same mean structure specification, however the robust errors in this model are more accurate, as some of the consitions of the least squares model are not fulfilled (e.g. Normaly distributed residuals)

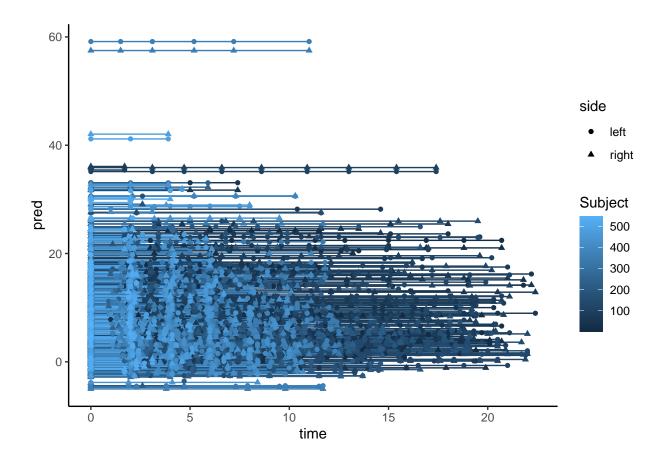
```
mf <- formula(y ~ age+TIME)</pre>
gee_opt1_new<-gee(mf, data=df, id=id,family = gaussian, corstr = "independence")</pre>
## Beginning Cgee S-function, @(#) geeformula.q 4.13 98/01/27
## running glm to get initial regression estimate
## (Intercept)
                                   TIME
                        age
   -5.7536304
                 0.2577779
                              0.1985119
summary(gee_opt1_new)$coefficients
##
                 Estimate Naive S.E.
                                          Naive z Robust S.E.
                                                                Robust z
## (Intercept) -5.7536304 0.458852942 -12.539160
                                                    0.88071498 -6.532909
## age
                0.2577779 0.007787969
                                        33.099505
                                                    0.01857869 13.874921
## TIME
                0.1985119 0.024714929
                                         8.032064
                                                    0.04500454 4.410930
gee_opt1_new
##
##
          GENERALIZED LINEAR MODELS FOR DEPENDENT DATA
##
    gee S-function, version 4.13 modified 98/01/27 (1998)
##
## Model:
##
   Link:
                                Identity
    Variance to Mean Relation: Gaussian
    Correlation Structure:
                                Independent
##
##
## Call:
## gee(formula = mf, id = id, data = df, family = gaussian, corstr = "independence")
##
## Number of observations :
                              4419
##
## Maximum cluster size
                              29
##
##
## Coefficients:
## (Intercept)
                                   TIME
                        age
##
    -5.7536304
                 0.2577779
                              0.1985119
##
## Estimated Scale Parameter: 76.31385
```

```
## Number of Iterations: 1
##
## Working Correlation[1:4,1:4]
##
        [,1] [,2] [,3] [,4]
## [1,]
  [2,]
                           0
##
           0
                 1
                      0
## [3,]
           0
                 0
                      1
                            0
## [4,]
           0
                 0
                      0
                            1
##
##
## Returned Error Value:
## [1] 0
```

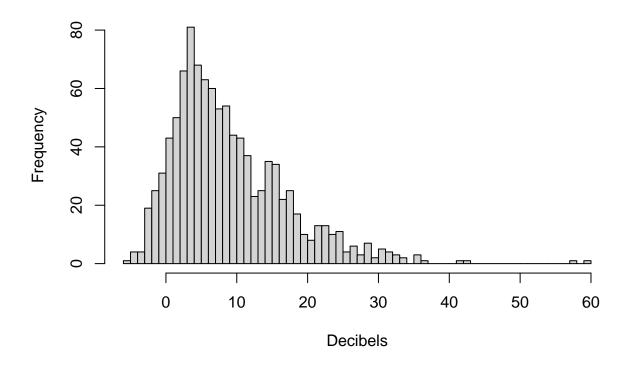
Task 4

In this task we will conduct an explicit two stage analysis of the data first computing the intecepts and then computing the slopes of the model. First let us take a look at the per subject/side intercept.

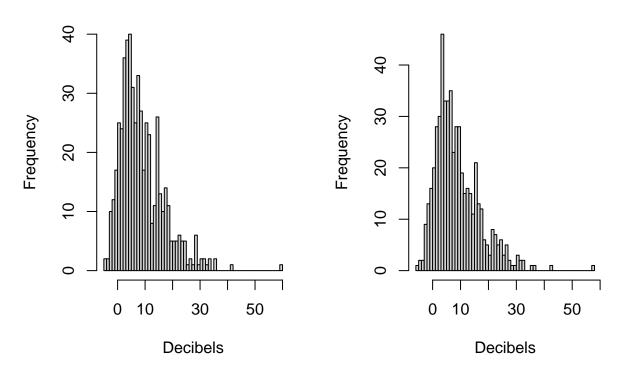
```
db_fixed = lme(y ~ 1,random=~1|id/age/side, data = df)
```



Distribution of all intercepts



Distribution of left eat intercept Distribution of right ear intercept



Further we can run a Komogorov-Smirnov test to see if the distribution of the left and right ear intercepts come from the same distribution

```
ks.test(left_intercepts,right_intercepts)

## Warning in ks.test(left_intercepts, right_intercepts): p-value will be
## approximate in the presence of ties

##

## Two-sample Kolmogorov-Smirnov test
##

## data: left_intercepts and right_intercepts
## D = 0.022838, p-value = 0.9991
## alternative hypothesis: two-sided
```

Next we will run a series of linear models for each model, as we will see

Warning in Ops.factor(id/age, side): '/' not meaningful for factors

```
df1<-cbind(df,fitted(db_fixed))
colnames(df1)[8]<-"fitted_val"

res.list1 <- lmList(I(y-fitted_val) ~0+age+ TIME|id/age/side, data=df1)

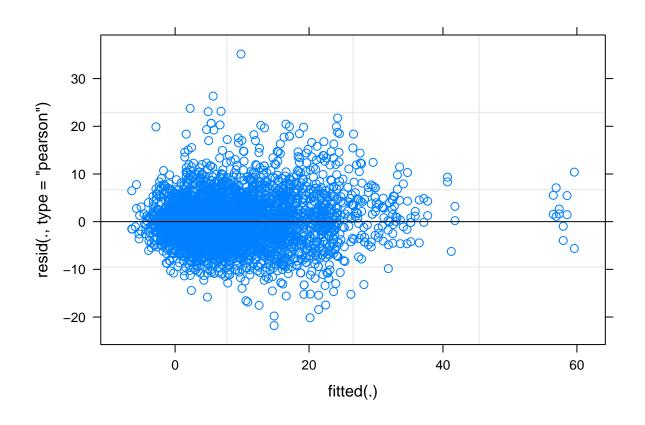
## Warning in Ops.factor(id, age): '/' not meaningful for factors</pre>
```

notes on how slopes are more dispersed at lower ages, how age effects when taken out of the entire datase (age is fixed for an id), still need to plot correlation between slopes and intercepts

Task 5

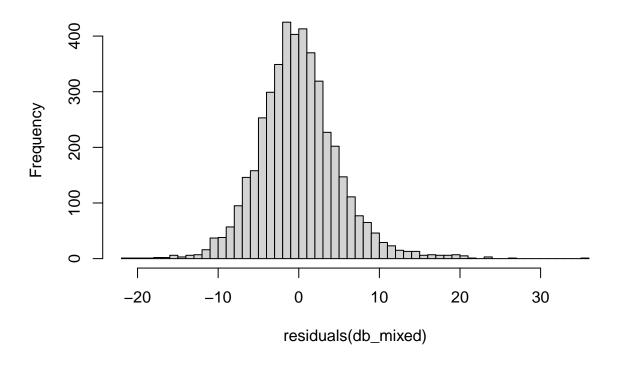
```
db_mixed = lmer(y ~ age+TIME+ (1 | id), data = df)
summary(db_mixed)
## Linear mixed model fit by REML ['lmerMod']
## Formula: y ~ age + TIME + (1 | id)
##
     Data: df
## REML criterion at convergence: 28674.7
## Scaled residuals:
      Min 1Q Median
                            3Q
                                     Max
## -4.1008 -0.5748 -0.0442 0.5048 6.6171
##
## Random effects:
                       Variance Std.Dev.
## Groups Name
## id
                              6.971
            (Intercept) 48.60
## Residual
                       28.23
                                5.313
## Number of obs: 4419, groups: id, 546
## Fixed effects:
              Estimate Std. Error t value
## (Intercept) -5.32864 0.94126 -5.661
## age
              0.24942 0.01700 14.675
```

plot(db_mixed)

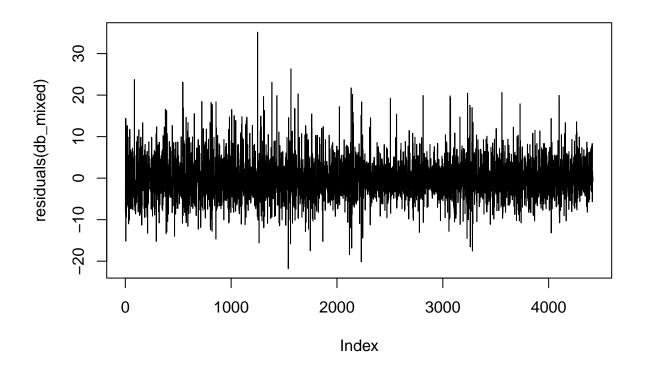


hist(residuals(db_mixed), breaks = 50)

Histogram of residuals(db_mixed)



plot(residuals(db_mixed), type = "1")

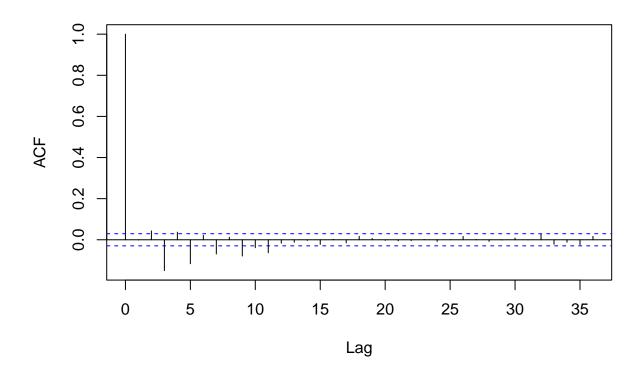


shapiro.test(residuals(db_mixed))

```
##
## Shapiro-Wilk normality test
##
## data: residuals(db_mixed)
## W = 0.97432, p-value < 2.2e-16</pre>
```

acf(residuals(db_mixed))

Series residuals(db_mixed)



confint(db_mixed)

Computing profile confidence intervals ...

```
## 2.5 % 97.5 %
## .sig01 6.5201576 7.4364912
## .sigma 5.1967604 5.4332566
## (Intercept) -7.1728196 -3.4834673
## age 0.2161043 0.2827228
## TIME 0.2494176 0.3221347
```

ranef(db_mixed)\$id %>% head(5)

```
## (Intercept)
## 1 6.014858
## 2 -4.935227
## 3 -7.522855
## 4 -6.913778
## 5 -2.064345
```

coef(db_mixed)\$id %>% head(5)

(Intercept) age TIME

```
## 1 0.6862164 0.2494233 0.2858142

## 2 -10.2638683 0.2494233 0.2858142

## 3 -12.8514967 0.2494233 0.2858142

## 4 -12.2424199 0.2494233 0.2858142

## 5 -7.3929867 0.2494233 0.2858142
```

REsim(db_mixed)

##		groupFctr	groupID	term	mean	median	sd
##	1	id	1	(Intercept)	5.921031836	5.860712755	1.366516
##	2	id	2	(Intercept)	-4.996040683	-5.008911261	1.171684
##	3	id	3	(Intercept)	-7.886633460	-8.107774999	3.470295
##	4	id	4	(Intercept)	-6.951297557	-6.990019795	1.258812
##	5	id	5	(Intercept)	-2.330901047	-2.519356490	3.328282
##	6	id	6	(Intercept)	-7.669912809	-7.674402670	1.270620
##	7	id	7	(Intercept)	-12.568907244	-12.597502079	
##	8	id	8	(Intercept)	-7.988868957	-7.986361721	
##	9	id	9	(Intercept)	-5.962095737	-5.862016672	
	10	id	10	(Intercept)	-10.194796774	-10.185347007	
##	11	id	11	(Intercept)	-8.076079789	-8.095644518	
##	12	id	12	(Intercept)	1.130938492	1.145627117	
##	13	id	13	(Intercept)	-13.869218793	-13.920167181	
##	14	id	14	(Intercept)	-2.270955241	-2.365255062	
##	15	id	15	(Intercept)	9.998212350	10.032754051	
##	16	id	16	(Intercept)	-8.077019399	-8.056256011	
##	17	id	17	(Intercept)	-0.426320949	-0.251604272	
##	18	id	18	(Intercept)	7.060957873	7.049878069	
	19	id	19	(Intercept)	-5.311856133	-5.316481348	
	20	id	20	(Intercept)	-7.295888801	-7.322648399	
	21	id	21	(Intercept)	7.654549763	7.714388080	
	22	id	22	(Intercept)	-5.693999242	-5.633268348	
	23	id	23	(Intercept)	-4.363659179	-4.413557929	
	24	id	24	(Intercept)	0.179264919	0.158678902	
##		id	25	(Intercept)	-2.543036133	-2.875650215	
	26	id	26	(Intercept)	1.272896422	1.247734077	
##		id	27	(Intercept)	-4.078896500	-4.239929885	
	28 29	id id	28 29	(Intercept)	-4.754164793 8.201360378	-4.883406100 8.218657627	
	30	id	30	(Intercept)	-9.688396042	-9.652876500	
##	31	id	31	<pre>(Intercept) (Intercept)</pre>	-4.016531384	-3.914637372	
##	32	id	32	(Intercept)	-1.950965563	-2.042390213	
##	33	id	33	(Intercept)	4.749398396	4.780090243	
##	34	id	34	(Intercept)	3.911287553	3.962017533	
##	35	id	35	(Intercept)	-6.960832533	-6.965553464	
##		id		(Intercept)	-2.794882470	-2.972946048	
##		id		(Intercept)		-4.888972199	
##		id		(Intercept)		-13.859064182	
##		id	39	(Intercept)	-3.100395813	-3.113127587	
##		id	40	(Intercept)	2.292037026	2.443413414	
##		id		(Intercept)	0.587407715	0.626166655	
##		id		(Intercept)	-5.677681187	-5.721519768	
##		id		(Intercept)	-0.888290029	-0.926354957	
##		id		(Intercept)	0.766801784	0.776980063	
##		id		(Intercept)	2.262405261	2.280819734	
	-		0				=

```
## 46
               id
                        46 (Intercept)
                                                         2.749485870 1.579428
                                          2.749059836
## 47
               id
                           (Intercept)
                                                        -1.120363282 1.933561
                                         -1.092701973
##
  48
               id
                           (Intercept)
                                          6.841771968
                                                         6.861385704 1.496735
##
  49
               id
                        49
                           (Intercept)
                                         18.014091058
                                                        17.821336652 2.260245
##
  50
               id
                       50
                           (Intercept)
                                        -13.956288683
                                                        -14.245124173 3.356692
## 51
               id
                           (Intercept)
                                         -8.613237439
                                                         -8.717669500 2.027129
## 52
               id
                           (Intercept)
                                          4.466121448
                                                         4.317082639 2.093094
                       53
## 53
               id
                           (Intercept)
                                          2.376137677
                                                         2.334387933 1.235526
##
  54
               id
                       54
                           (Intercept)
                                         -7.789257496
                                                        -7.617959305 2.417250
## 55
               id
                           (Intercept)
                                         -5.092380733
                                                        -5.214133434 1.904805
##
  56
               id
                           (Intercept)
                                         -3.194241915
                                                         -3.105287581 1.270109
## 57
               id
                           (Intercept)
                                         17.512552152
                                                        17.426748236 1.348248
##
   58
                        58
                           (Intercept)
               id
                                          1.578650598
                                                         1.459842211 1.779038
## 59
               id
                           (Intercept)
                                         -0.940649453
                                                        -0.917934172 1.252281
## 60
               id
                           (Intercept)
                                          7.459574669
                                                         7.453529214 1.480080
##
  61
               id
                           (Intercept)
                                                         1.852824359 1.214324
                                          1.814089812
##
  62
               id
                           (Intercept)
                                                        10.175820077 3.197804
                                         10.162366778
##
   63
               id
                           (Intercept)
                                                        -0.871354993 1.061295
                                         -0.909703391
               id
##
  64
                           (Intercept)
                                                        -3.479677838 1.423370
                                         -3.386310855
##
   65
               id
                        65
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                                          5.744472583
                                                         5.677732192 1.649669
## 418
               id
                      418
                           (Intercept)
                                        -10.232386159
                                                       -10.267892679 1.607549
## 419
               id
                      419
                           (Intercept)
                                                        16.244564775 2.060931
                                         16.436759335
## 420
               id
                      420
                           (Intercept)
                                                        -2.493110408 1.622590
                                         -2.460400042
## 421
               id
                           (Intercept)
                                          0.005057436
                                                        -0.101600366 1.993608
## 422
               id
                      422 (Intercept)
                                         -0.358459569
                                                        -0.469065899 2.029103
## 423
               id
                      423 (Intercept)
                                         -1.755325314
                                                        -1.861417283 1.653017
```

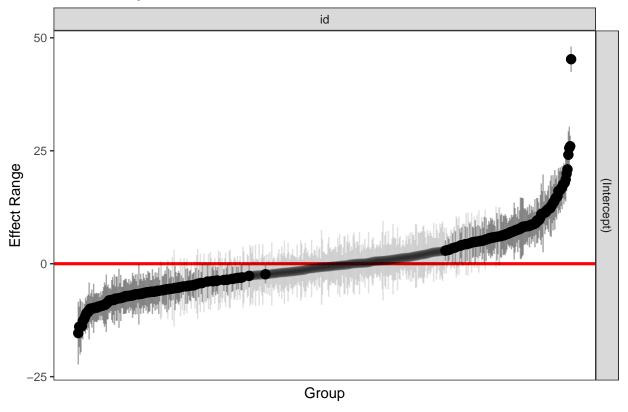
```
## 424
               id
                      424 (Intercept)
                                         -6.475915873
                                                        -6.332140894 1.918599
## 425
                                         -4.163474025
               id
                      425
                          (Intercept)
                                                        -4.168676339 2.538336
## 426
               id
                           (Intercept)
                                          0.140615011
                                                         0.169447103 1.567757
## 427
                      427
                           (Intercept)
               id
                                         -9.319504145
                                                        -9.385383462 1.458863
## 428
               id
                      428
                           (Intercept)
                                         -6.487325057
                                                        -6.359822266 2.397389
## 429
               id
                      429
                           (Intercept)
                                         -5.165254481
                                                        -5.156201942 1.710129
## 430
               id
                      430
                           (Intercept)
                                          1.139702230
                                                         1.120063693 1.531350
## 431
               id
                      431
                           (Intercept)
                                         -0.820331994
                                                        -0.963467000 2.238967
## 432
               id
                      432
                           (Intercept)
                                         -5.639885508
                                                        -5.681393206 2.018920
## 433
               id
                      433
                           (Intercept)
                                         -5.514490559
                                                        -5.661165692 2.696039
## 434
               id
                           (Intercept)
                                          1.818559094
                                                         1.893566465 2.182422
## 435
               id
                      435
                           (Intercept)
                                          2.848935944
                                                         2.710949497 3.592699
##
  436
                      436
                           (Intercept)
                                                         0.347648055 2.140574
               id
                                          0.157344825
                           (Intercept)
                                          6.136992099
##
  437
               id
                                                         6.163925884 2.162904
## 438
               id
                      438
                           (Intercept)
                                       -10.944524918
                                                       -11.029297895 1.881426
## 439
               id
                      439
                           (Intercept)
                                                        11.712891959 1.600097
                                         11.480766607
## 440
               id
                      440
                           (Intercept)
                                                        -0.025752040 1.598309
                                         -0.082624948
## 441
               id
                           (Intercept)
                                                        17.905224732 2.060020
                                         17.877719316
## 442
               id
                           (Intercept)
                                         -1.207129953
                                                        -1.024414423 1.791605
## 443
               id
                           (Intercept)
                                         -9.248602077
                                                        -9.399185003 1.952915
##
  444
               id
                      444
                           (Intercept)
                                          5.479911152
                                                         5.565605790 2.031576
## 445
                           (Intercept)
               id
                      445
                                          6.960201884
                                                         7.033108887 1.742904
## 446
               id
                      446
                           (Intercept)
                                         -6.131457787
                                                        -6.021269235 3.304092
                           (Intercept)
## 447
               id
                      447
                                          5.070468954
                                                         5.156946274 3.027578
                                                        -4.576496484 2.610992
## 448
               id
                      448
                           (Intercept)
                                         -4.616908243
## 449
               id
                      449
                           (Intercept)
                                         14.359921050
                                                        14.413741629 2.156788
## 450
                      450
               id
                           (Intercept)
                                         -0.409120687
                                                        -0.463372764 2.332007
##
  451
               id
                      451
                           (Intercept)
                                          8.237484059
                                                         8.119849597 2.267675
## 452
               id
                           (Intercept)
                                         -4.917205263
                                                        -4.916742016 1.888782
## 453
                      453
                           (Intercept)
                                                        -3.841647183 3.135939
               id
                                         -3.795523890
## 454
               id
                      454
                           (Intercept)
                                          2.627689494
                                                         2.619085402 1.882503
## 455
               id
                      455
                           (Intercept)
                                         -0.636514859
                                                        -0.740497761 2.142843
## 456
               id
                           (Intercept)
                                         -2.735542137
                                                        -2.633992145 1.569668
## 457
                      457
               id
                           (Intercept)
                                         -2.139868895
                                                        -2.162262485 1.886013
                      458
   458
                           (Intercept)
                                                        12.036783039 2.020671
##
               id
                                         11.969253922
##
  459
               id
                      459
                           (Intercept)
                                         -6.645754747
                                                        -6.784900512 2.103799
##
  460
               id
                           (Intercept)
                                          4.823433354
                                                         4.692089553 2.536349
## 461
                      461
                           (Intercept)
               id
                                          8.348073957
                                                         8.322816517 2.272086
  462
                           (Intercept)
##
               id
                      462
                                         -6.765196109
                                                        -6.884750152 1.813700
                           (Intercept)
## 463
               id
                      463
                                                        -2.948104333 2.238380
                                         -2.731730272
                           (Intercept)
  464
               id
                                         -3.934556322
                                                        -4.023946910 3.120912
  465
                      465
                           (Intercept)
##
               id
                                          4.938816211
                                                         4.721037552 2.094303
##
  466
               id
                      466
                           (Intercept)
                                          7.022360609
                                                         6.911272933 1.914526
##
  467
                      467
                           (Intercept)
               id
                                         16.679597396
                                                        16.566672462 2.415353
## 468
               id
                      468
                           (Intercept)
                                          5.417415276
                                                         5.344303372 1.833601
## 469
                                                         2.893376646 2.044754
               id
                      469
                           (Intercept)
                                          3.137400430
## 470
               id
                      470
                           (Intercept)
                                          0.226328445
                                                         0.478098662 2.202820
## 471
               id
                           (Intercept)
                                          8.462904225
                                                         8.670754162 2.302394
## 472
               id
                      472
                           (Intercept)
                                          8.606178439
                                                         8.652075494 2.280788
## 473
               id
                      473
                           (Intercept)
                                         -2.155178680
                                                        -2.185932696 1.904913
## 474
               id
                      474
                           (Intercept)
                                         -4.008987375
                                                        -3.990452957 2.434584
## 475
               id
                           (Intercept)
                                          0.065792758
                                                         0.247729844 2.211369
## 476
               id
                      476
                          (Intercept)
                                          7.759080980
                                                         7.714285264 2.294318
## 477
               id
                      477 (Intercept)
                                          1.139401880
                                                         1.086382963 2.434162
```

```
## 478
               id
                      478 (Intercept)
                                          1.452080910
                                                         1.250748647 2.137062
               id
## 479
                      479
                          (Intercept)
                                                        -4.172108086 2.583343
                                         -3.772815811
                                                        -3.475919208 2.400876
## 480
               id
                           (Intercept)
                                         -3.459462711
## 481
               id
                           (Intercept)
                                          4.986420509
                                                         5.144164773 2.562584
##
  482
               id
                           (Intercept)
                                         -0.395105323
                                                        -0.436373414 2.468992
  483
##
               id
                      483
                           (Intercept)
                                                         1.609158244 2.506618
                                          1.319323099
## 484
                           (Intercept)
               id
                                         25.446369688
                                                        25.587512665 2.459626
## 485
               id
                      485
                           (Intercept)
                                         -1.611721671
                                                        -1.867470833 2.814399
## 486
               id
                      486
                           (Intercept)
                                          4.461515823
                                                         4.255010517 2.627411
## 487
               id
                      487
                           (Intercept)
                                         -1.965974629
                                                        -2.015832161 3.162190
## 488
               id
                           (Intercept)
                                         -5.954243490
                                                        -6.004860874 1.993310
## 489
                      489
               id
                           (Intercept)
                                          4.376638527
                                                         4.266727085 3.290472
##
  490
                      490
                           (Intercept)
                                                        12.965220730 3.164312
               id
                                         13.028356146
## 491
               id
                           (Intercept)
                                          1.452335473
                                                         1.149352025 2.599997
## 492
               id
                      492
                           (Intercept)
                                          3.123041106
                                                         3.278121325 2.500049
## 493
               id
                      493
                           (Intercept)
                                         -3.970954388
                                                        -3.901938066 2.211268
## 494
               id
                      494
                           (Intercept)
                                                        -1.710532111 3.479248
                                         -1.855383810
## 495
               id
                           (Intercept)
                                                        11.944749314 3.410659
                                         12.025125631
## 496
               id
                                          6.684623354
                      496
                           (Intercept)
                                                         6.852344948 2.043928
## 497
               id
                           (Intercept)
                                         -0.708873540
                                                        -0.679331275 2.002812
##
  498
               id
                      498
                           (Intercept)
                                         -0.292641619
                                                        -0.320281656 2.271521
## 499
                           (Intercept)
               id
                      499
                                         19.547328830
                                                        19.402794978 2.082965
## 500
               id
                      500
                           (Intercept)
                                         -5.002555488
                                                        -4.791454240 3.598830
## 501
                           (Intercept)
               id
                      501
                                          7.949652614
                                                         7.805875296 2.731124
## 502
               id
                      502
                           (Intercept)
                                          1.874799091
                                                         2.059299487 2.495346
## 503
               id
                      503
                           (Intercept)
                                          1.490717357
                                                         1.385291164 2.516980
## 504
                      504
                           (Intercept)
               id
                                          9.031477865
                                                         8.862595700 2.627156
   505
##
               id
                      505
                           (Intercept)
                                          6.121010689
                                                         6.088495914 3.356826
## 506
               id
                      506
                           (Intercept)
                                         -4.582174084
                                                        -4.407574888 3.307578
## 507
                           (Intercept)
                                                        -3.381673138 2.516752
               id
                      507
                                         -3.349854762
## 508
               id
                      508
                           (Intercept)
                                          4.467357614
                                                         4.217376386 2.640596
## 509
               id
                      509
                           (Intercept)
                                         -3.781535378
                                                        -3.823974980 2.704097
## 510
               id
                           (Intercept)
                                         -0.418350048
                                                        -0.652503109 3.630838
## 511
                      511
               id
                           (Intercept)
                                                        -3.780365709 2.714479
                                         -3.802193392
## 512
                      512
                           (Intercept)
                                                         1.851266974 2.490426
               id
                                          1.858189088
## 513
                           (Intercept)
               id
                      513
                                         -2.913182616
                                                        -2.674358084 3.393477
## 514
               id
                           (Intercept)
                                         -4.854170477
                                                        -5.098310857 4.345181
## 515
                      515
                           (Intercept)
               id
                                         11.148982633
                                                        11.174940668 2.739590
## 516
               id
                           (Intercept)
                      516
                                         -3.753906684
                                                        -3.761900898 2.465926
## 517
               id
                           (Intercept)
                      517
                                         -3.464404421
                                                        -3.375644369 3.022528
## 518
               id
                      518
                           (Intercept)
                                         -2.072279253
                                                        -2.013256494 2.731650
## 519
                      519
                           (Intercept)
               id
                                         16.604555920
                                                        16.579913269 2.502551
## 520
               id
                      520
                           (Intercept)
                                         -5.823509763
                                                        -5.919401793 2.559061
## 521
               id
                      521
                           (Intercept)
                                         -8.622978012
                                                        -8.676670994 2.386457
## 522
               id
                      522
                           (Intercept)
                                         14.267293977
                                                        13.900069568 3.205363
## 523
               id
                      523
                           (Intercept)
                                          1.759266400
                                                         1.915204055 2.564081
## 524
               id
                      524
                           (Intercept)
                                         12.329081483
                                                        12.442466084 2.666153
## 525
               id
                           (Intercept)
                                          2.762399996
                                                         2.671572525 2.415492
                      526
## 526
               id
                           (Intercept)
                                         -4.149271068
                                                        -3.957113858 3.295550
## 527
               id
                      527
                           (Intercept)
                                          0.034407550
                                                         0.084545335 2.586000
## 528
               id
                      528
                           (Intercept)
                                                         0.865232824 3.468683
                                          0.726375535
## 529
               id
                           (Intercept)
                                          0.026507715
                                                         0.002559188 3.421044
## 530
               id
                      530
                          (Intercept)
                                         -0.083006647
                                                         0.062516868 3.397505
## 531
               id
                      531 (Intercept)
                                         -2.350444492
                                                        -2.398505792 3.399576
```

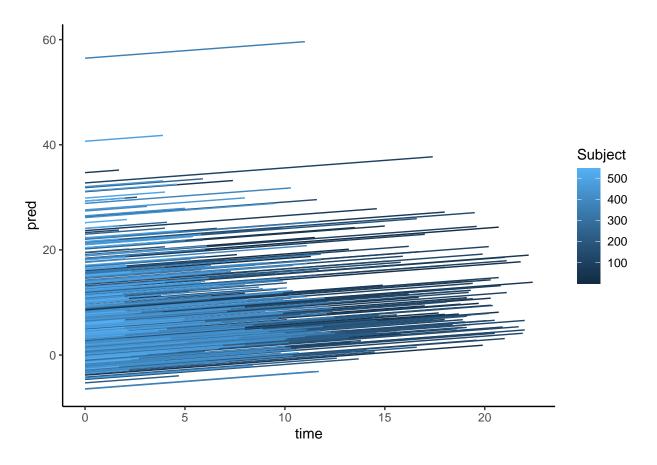
```
## 532
              id
                      532 (Intercept)
                                         5.591358638
                                                       5.601235157 2.519449
                                         9.657712831
## 533
              id
                      533 (Intercept)
                                                       9.623509299 2.400088
## 534
                      534 (Intercept)
              id
                                         4.948004425
                                                       4.845465156 2.957720
## 535
                      535 (Intercept)
              id
                                         1.455846199
                                                       1.936014971 4.388271
## 536
              id
                      536 (Intercept)
                                         7.086432486
                                                       7.248683331 3.235759
## 537
              id
                      537 (Intercept)
                                         3.188657709
                                                       3.291926343 3.377051
## 538
              id
                      538 (Intercept)
                                         1.906564365
                                                       1.792347648 3.529973
## 539
                      539 (Intercept)
              id
                                         0.196363718
                                                       0.148483599 4.337234
## 540
              id
                      540 (Intercept)
                                         7.680163425
                                                       7.524495177 3.433858
## 541
              id
                      541 (Intercept)
                                                       1.506065110 3.532236
                                         1.497987786
## 542
              id
                      542 (Intercept)
                                         7.967057943
                                                       7.991350980 3.184824
## 543
              id
                      543 (Intercept)
                                         4.628916540
                                                       4.924983853 3.726835
                      544 (Intercept)
##
  544
              id
                                         6.495834839
                                                       6.319969910 3.567145
## 545
              id
                      545 (Intercept)
                                                       2.777320396 3.206454
                                         2.437755793
## 546
              id
                      546 (Intercept)
                                       -1.311584553
                                                      -1.679073074 3.539229
```

plotREsim(REsim(db_mixed))

Effect Ranges



```
dat_mixed<-data.frame(time=df$TIME,pred=fitted(db_mixed),Subject=df$id)
dat_mixed$Subject<-as.numeric(dat_mixed$Subject)
ggplot(data=dat_mixed,aes(x=time,y=pred,group=Subject,color=Subject))+theme_classic()+geom_line()</pre>
```

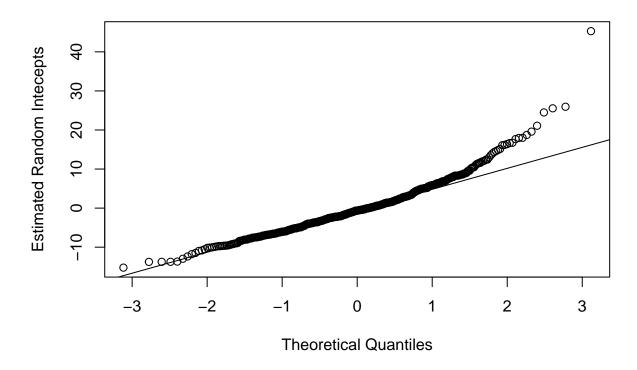


mean(sqrt(resid(db_mixed)^2))

[1] 3.747102

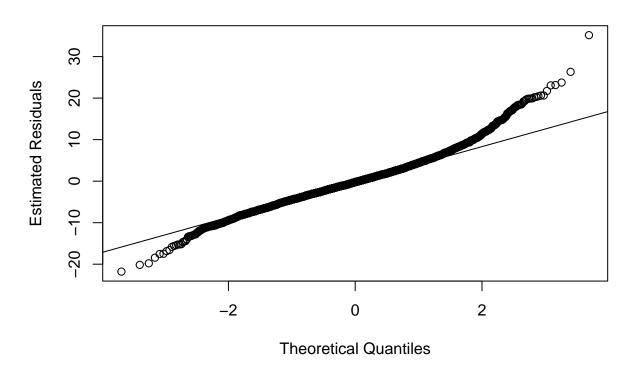
```
#assumptions check
#1. Error terms follow a Normal Distribution
#2. Beta for subject i follows a Normal Distribution
qint<-ranef(db_mixed)$id[["(Intercept)"]]
qres<-residuals(db_mixed)
qqnorm(qint,ylab = "Estimated Random Intecepts",main = "Random Intecepts")
qqline(qint)</pre>
```

Random Intecepts



```
qqnorm(qres,ylab = "Estimated Residuals",main = "Residuals")
qqline(qres)
```

Residuals



```
db_mixed2 = lmer(y ~ age+TIME + (TIME | id), data = df, na.action = na.omit)
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl = control$checkConv, :
## Model failed to converge with max|grad| = 0.0329069 (tol = 0.002, component 1)
summary(db_mixed2)
## Linear mixed model fit by REML ['lmerMod']
## Formula: y ~ age + TIME + (TIME | id)
      Data: df
##
##
## REML criterion at convergence: 28548
## Scaled residuals:
##
                1Q Median
## -4.2434 -0.5595 -0.0475 0.5043 6.9585
##
## Random effects:
    Groups
                         Variance Std.Dev. Corr
##
             Name
##
             (Intercept) 49.3871 7.0276
##
             TIME
                          0.1547 0.3933
                                           -0.17
```

25.6657 5.0661

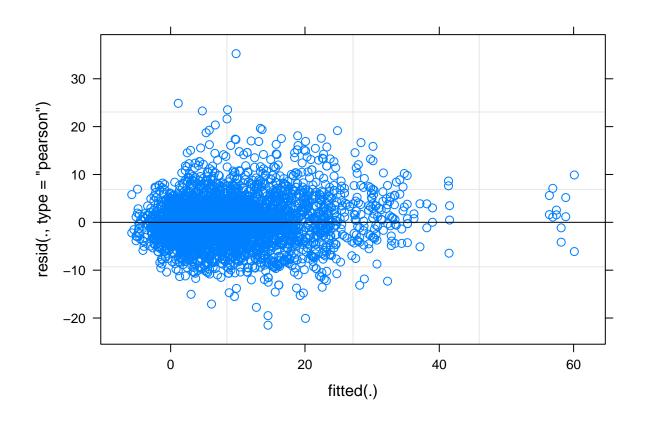
Number of obs: 4419, groups: id, 546

##

##

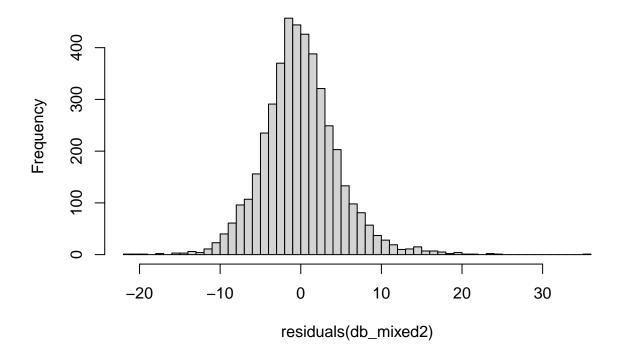
Residual

```
## Fixed effects:
##
               Estimate Std. Error t value
## (Intercept) -5.03542
                           0.93729
                                    -5.372
                           0.01690 14.428
                0.24377
## TIME
                0.28296
                           0.03091
                                     9.153
##
## Correlation of Fixed Effects:
        (Intr) age
##
## age -0.938
## TIME -0.118 0.025
## optimizer (nloptwrap) convergence code: 0 (OK)
## Model failed to converge with max|grad| = 0.0329069 (tol = 0.002, component 1)
plot(db_mixed2)
```

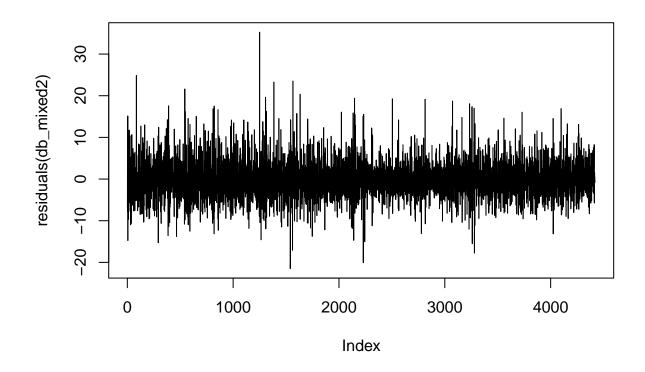


hist(residuals(db_mixed2), breaks = 50)

Histogram of residuals(db_mixed2)



plot(residuals(db_mixed2), type = "1")

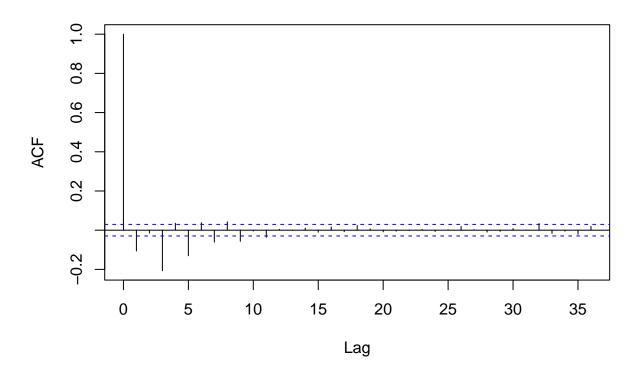


shapiro.test(residuals(db_mixed2))

```
##
## Shapiro-Wilk normality test
##
## data: residuals(db_mixed2)
## W = 0.97582, p-value < 2.2e-16</pre>
```

acf(residuals(db_mixed2))

Series residuals(db_mixed2)



confint(db_mixed2)

Computing profile confidence intervals ...

```
##
                    2.5 %
                               97.5 %
## .sig01
                6.5406650 7.51789452
## .sig02
               -0.3295534
                           0.00138868
## .sig03
                0.3272181
                           0.46162676
## .sigma
                4.9505555
                          5.18761884
## (Intercept) -6.9147704 -3.15765854
## age
                0.2097636
                           0.27775884
## TIME
                0.2216831 0.34385036
```

ranef(db_mixed2)\$id %>% head(5)

```
## 1 (Intercept) TIME

## 1 5.048471 0.17564946

## 2 -6.345893 0.14793964

## 3 -7.641045 0.07447785

## 4 -8.438962 0.19058724

## 5 -2.095547 0.02042546
```

coef(db_mixed2)\$id %>% head(5)

```
## (Intercept) age TIME

## 1 0.01305382 0.2437696 0.4586055

## 2 -11.38130988 0.2437696 0.4308957

## 3 -12.67646234 0.2437696 0.3574339

## 4 -13.47437975 0.2437696 0.4735433

## 5 -7.13096470 0.2437696 0.3033815
```

REsim(db_mixed2)

```
##
        groupFctr groupID
                                  term
                                                 mean
                                                             median
## 1
               id
                                        5.129393e+00
                                                        4.984581716 1.7719671
                         1 (Intercept)
##
  2
               id
                         2 (Intercept) -6.510582e+00
                                                       -6.358139216 1.8228594
## 3
               id
                         3 (Intercept) -7.085457e+00
                                                       -6.963498593 3.2284619
## 4
               id
                         4 (Intercept) -8.477490e+00
                                                       -8.676919454 1.9333767
## 5
               id
                         5 (Intercept) -2.273333e+00
                                                       -2.081406270 3.3318973
## 6
               id
                         6 (Intercept) -4.600285e+00
                                                       -4.827531140 1.9818907
## 7
                         7 (Intercept) -1.391598e+01 -13.763626756 2.0796228
               id
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##	594	id	48	TIME	-1.952998e-01	-0.202539589	0.1627988
##	595	id	49	TIME	2.270822e-01	0.212942725	
##	596	id	50	TIME	4.543727e-02	0.006574073	
##	597	id	51		-1.316521e-01	-0.107617144	
##	598	id	52		-1.151983e-01	-0.111120713	
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	600	id	54		-3.953936e-02	-0.051439463	
	601	id	55		-1.515746e-01	-0.134960289	
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	604	id	58		-2.554927e-01	-0.274251706	
	605	id	59		-2.282344e-02	-0.030827638	
	606	id	60	TIME	6.583005e-01	0.660474992	
##	607	id	61	TIME	1.701063e-01	0.164025552	
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	611	id	65	TIME	2.981594e-01	0.302843186	
	612	id	66	TIME	6.883348e-01	0.697046902	
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	615	id	68		-1.370994e-01	-0.123840010	
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	625	id	79		-1.067342e-01	-0.112688228	
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	627	id	81	TIME	3.308060e-01	0.337162276	
	628	id	82	TIME	4.163476e-02	0.043190830	
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##	684	id	138	TIME	3.882452e-01	0.386998019	0.1565371
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	729	id	183	TIME		0.017218229	
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	731	id	185	TIME		0.200323689	
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##	858	id	312	TIME	8.521098e-02	0.101254031	0.3796726
##	859	id	313	TIME	4.914274e-02	0.026802533	0.3700910
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##	863	id	317	TIME	2.466623e-02	-0.003836294	0.3829509
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	870	id	324		-3.629525e-05	-0.034727169	
	871	id	325	TIME	5.112911e-03	-0.026269419	
	872	id	326		-8.501912e-02	-0.130191683	
	873	id	327		-8.419478e-02	-0.078249295	
	874	id	328	TIME	4.262446e-01	0.415573585	
	875	id	329	TIME	6.874069e-02	0.084412087	
	876	id	330		-2.220487e-01	-0.219317898	
	877	id	331	TIME	8.995105e-02	0.086769502	
	878	id	332	TIME	1.224264e+00	1.235798861	
	879	id	333		-2.497205e-01	-0.253675093	
##	880	id	334		-1.187087e-01	-0.111875306	
##	881	id	335	TIME	-1.983241e-01	-0.191493283	
##	882	id	336	TIME	2.664111e-01	0.259776988	
	883 884	id	337	TIME	3.698692e-01	0.356880210	
	885	id	338		-3.581195e-01	-0.338639777 -0.048338492	
	886	id	339		-4.266385e-02 -2.603647e-01	-0.266693485	
	887	id id	340 341	TIME	3.974761e-03	-0.26693485	
	888	id	342		-2.500797e-01	-0.020371328	
			343				
	889 890	id id	344	TIME	2.525789e-01 2.480487e-01	0.248941827 0.255603563	
	891	id	345		-1.162366e-01	-0.120659079	
	892	id	346		-1.271683e-01	-0.128290450	
	893	id	347	TIME	7.471956e-02	0.072887886	
	894	id	348	TIME	7.091667e-01	0.701895979	
	895	id	349	TIME	4.139106e-01	0.411786613	
	896	id	350		-3.552425e-01	-0.367636730	
	897	id	351		-5.890291e-02	-0.081654995	
	898	id	352	TIME	9.553309e-02	0.049157015	
	899	id	353	TIME	5.167923e-02	0.054671899	
	900	id	354		-1.406076e-01	-0.126907589	
	901	id	355		-1.579211e-01	-0.141209557	
	902	id	356	TIME	5.226247e-02	0.040484055	
	903	id	357	TIME	3.599211e-01	0.373809408	
	904	id	358	TIME	1.476144e-01	0.139225665	
	905	id	359	TIME	9.653307e-02	0.116133676	

	906	id	360	TIME	8.743781e-02	0.067208252	
	907	id	361		-8.914237e-02	-0.094571379	
	908	id	362	TIME	3.562289e-01	0.344194143	
	909	id	363		-5.739994e-02	-0.048363943	
##	910	id	364	TIME	-1.178579e-01	-0.123340694	
##	911	id	365	TIME	2.932117e-02	0.047888729	0.2860170
##	912	id	366	TIME	2.048790e-01	0.186314987	0.3186928
##	913	id	367	TIME	-1.451693e-01	-0.119262090	0.4022130
##	914	id	368	TIME	7.072709e-02	0.078652022	0.3544496
##	915	id	369	TIME	-2.777401e-01	-0.296938049	0.2875756
##	916	id	370	TIME	5.589438e-02	0.026558075	0.3195705
##	917	id	371	TIME	5.578649e-01	0.533055980	0.2586571
##	918	id	372	TIME	1.194531e-02	0.036802425	0.3173857
##	919	id	373	TIME	1.001633e-01	0.087657410	0.3824694
##	920	id	374	TIME	-1.525007e-01	-0.114769344	0.3737363
##	921	id	375	TIME	-2.307930e-01	-0.225343719	0.3683191
##	922	id	376	TIME	2.272422e-01	0.254878837	0.3770907
##	923	id	377	TIME	-7.459646e-04	0.002756345	0.2721050
##	924	id	378	TIME	-1.095486e-01	-0.115385648	0.2753794
##	925	id	379	TIME	-2.694123e-01	-0.304130278	0.2655717
##	926	id	380	TIME	2.636174e-02	0.028252852	0.2583024
##	927	id	381	TIME	-1.726510e-01	-0.160805821	0.2732241
##	928	id	382	TIME	-2.469197e-02	0.004253437	0.3504691
##	929	id	383	TIME	8.667900e-02	0.093486217	0.3114709
##	930	id	384	TIME	-1.098910e+00	-1.094112455	0.2730940
##	931	id	385	TIME	1.127825e-01	0.114343356	0.3216239
##	932	id	386	TIME	3.423696e-01	0.352605936	0.3126777
##	933	id	387	TIME	1.733117e-02	0.021253164	0.2818677
##	934	id	388	TIME	8.248927e-03	0.004832423	0.2641456
##	935	id	389	TIME	-5.535671e-02	-0.044750137	0.3029831
	936	id	390	TIME	-1.506447e-01	-0.114627555	
##	937	id	391	TIME	-1.330229e-01	-0.141643404	0.2780476
	938	id	392	TIME	6.869208e-02	0.049031564	
	939	id	393	TIME	1.406180e-01	0.159528486	
	940	id	394	TIME	2.020783e-01	0.186702002	
	941	id	395	TIME	1.435830e-01	0.146510492	
	942	id	396	TIME	1.662481e-02	-0.017806350	
	943	id	397	TIME	2.064657e-01	0.204315738	
	944	id	398	TIME	3.586991e-02	0.007361112	
	945	id	399		-2.045722e-01	-0.244595518	
	946	id	400	TIME	4.972193e-02	0.071386617	
	947	id	401	TIME	1.306527e-01	0.100443484	
	948	id	402	TIME	7.085920e-02	0.086691432	
	949	id	403	TIME	2.788316e-01	0.307431291	
	950	id	404	TIME	3.985183e-01	0.404013471	
	951	id	405		-1.853946e-01	-0.197774610	
	952	id	406		-4.360649e-02	-0.055750653	
	953	id	407		-4.081190e-02	-0.034983210	
	954	id	407	TIME	6.150055e-01	0.608425118	
	955	id	409		-3.063663e-01	-0.310812558	
	956		410		-1.474389e-01	-0.310612556	
	957	id id	410	TIME	5.341861e-02	0.065637450	
	95 <i>1</i> 958	id	411		-9.062318e-02	-0.083280174	
	959		412		-1.480112e-01	-0.147295620	
##	JJJ	id	410	TINE	1.4001126-01	0.14123020	0.2321009

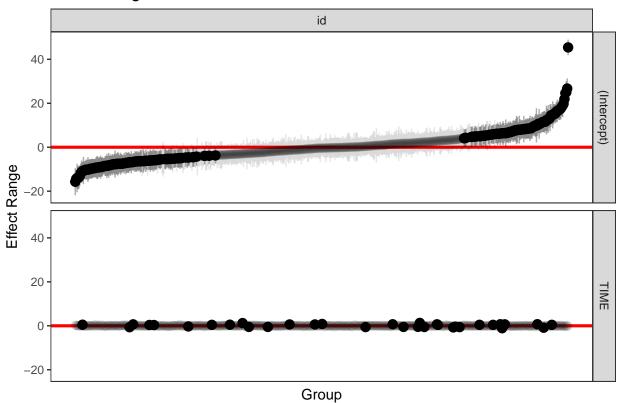
##	960	id	414	TIME	2.880550e-02	0.035805075	0.2993067
##	961	id	415	TIME	1.123022e-02	0.027270805	
##	962	id	416	TIME	5.744776e-02	0.032974865 (
##	963	id	417		-1.404672e-01	-0.141141408 (
##	964	id	418		-1.361647e-01	-0.108170530 (
##	965	id	419	TIME	1.501040e-01	0.132933753 (
##	966	id	420	TIME	2.261956e-02	0.001548755 (
##	967	id	421		-1.719833e-01	-0.175736781	
##	968	id	422	TIME	1.116847e-01	0.125497986 (
##	969	id	423		-5.246142e-02	-0.057410514 (
##	970	id	424	TIME	4.334354e-02	0.032404170 (
##	971	id	425	TIME	1.741620e-02	0.037517800 (
##	972	id	426	TIME	1.018671e-01	0.090672152 (
##	973	id	427		-2.143852e-01	-0.212097806	
	974	id	428		-3.280662e-01	-0.319138095	
##	975	id	429	TIME	6.846910e-02	0.077438282 (
##	976	id	430	TIME	8.055601e-02	0.047848637 (
##	977	id	431		-8.862237e-02	-0.129780211 (
	978	id	431	TIME	2.051971e-02	0.044577607	
	979	id	433	TIME	2.472842e-01	0.044377607 (
##	980	id	434		-5.591535e-02	-0.056498452 (
##	981		435		-3.432837e-02	-0.030290905 (
	982	id	436		-3.432637e-02 -2.764810e-02	-0.030290905 (
		id					
	983	id	437	TIME	3.544971e-02	0.044814775 (
	984	id	438		-6.167656e-02	-0.037425567	
##	985	id	439		-1.857020e-01	-0.186223270 (
##	986	id	440		-9.914264e-02	-0.113562035	
##	987	id	441		-3.951473e-02	-0.046491000 (
##	988	id	442		-2.413010e-02	-0.016181737	
##	989	id	443	TIME	9.902802e-02	0.084439049 (
##	990	id	444		-3.476761e-01	-0.322034981 (
	991	id	445		-3.337061e-02	-0.005834529 (
	992	id	446	TIME	1.054502e-01	0.142204434 (
	993	id	447		-2.795624e-02	-0.030511317 (
	994	id	448	TIME	1.527191e-01	0.132457295 (
	995	id	449	TIME	1.011148e-01	0.111989832 (
	996	id	450		-7.074256e-02	-0.098141521	
	997	id	451	TIME	1.116960e-01	0.126525544 (
	998	id	452		-1.349129e-01	-0.165075270	
	999	id	453	TIME	5.424524e-02	0.038568083 (
	1000	id	454	TIME	6.918681e-02	0.064769628 (
##	1001	id	455		-2.473395e-02	0.004426510 (
##	1002	id	456		-1.305316e-01	-0.149065586	
##	1003	id	457	TIME	9.955161e-02	0.075339353 (
##	1004	id	458		-2.166214e-02	-0.024567161	
##	1005	id	459		-8.348260e-03	0.012270736 (
##	1006	id	460	TIME	8.438717e-02	0.107924936 (
##	1007	id	461		-8.934930e-01	-0.906269783 (
##	1008	id	462		-1.533929e-01	-0.137107884	
##	1009	id	463	TIME	2.130783e-01	0.227184461 (
##	1010	id	464	TIME	3.898344e-02	0.050272487 (
	1011	id	465	TIME	8.760694e-02	0.092437210 (
	1012	id	466	TIME	2.581729e-02	0.029005726	
##	1013	id	467	TIME	2.640703e-02	0.013690355 (0.3470615

##	1014	id	468	TIME -	-1.101534e-01	-0.106778770	0.3125395
	1015	id	469		-6.651511e-02	-0.075046671	
##	1016	id	470	TIME	4.094282e-02	0.057740683	0.3871658
##	1017	id	471	TIME	2.605420e-02	0.048592065	0.3366802
##	1018	id	472	TIME	2.273336e-02	0.040456471	0.3569023
##	1019	id	473	TIME	2.212587e-01	0.207605351	0.3426200
##	1020	id	474	TIME -	-8.126217e-03	-0.028836819	0.4104744
##	1021	id	475	TIME -	-1.599241e-01	-0.163399837	0.3488397
##	1022	id	476	TIME -	-1.111750e-01	-0.120726768	0.3590172
##	1023	id	477	TIME	1.669593e-01	0.181162086	0.3730801
##	1024	id	478	TIME -	-1.209115e-01	-0.102686752	0.3783558
##	1025	id	479	TIME	2.037274e-03	0.020508824	0.3869742
##	1026	id	480	TIME	4.808232e-02	0.049775655	0.3915087
##	1027	id	481	TIME -	-1.950867e-02	-0.047215950	0.3619035
##	1028	id	482	TIME -	-6.762968e-02	-0.094161009	0.3673627
##	1029	id	483	TIME -	-7.796252e-02	-0.092445070	0.3697389
##	1030	id	484	TIME -	-2.456957e-01	-0.253548660	0.3290279
##	1031	id	485	TIME	4.089558e-02	0.033214008	0.3354497
##	1032	id	486	TIME	7.041984e-02	0.062189592	0.3400820
##	1033	id	487	TIME	4.941766e-02	0.050418880	0.4027078
##	1034	id	488	TIME -	-1.056911e-01	-0.112493915	0.3777612
##	1035	id	489		-1.361317e-02	-0.018514869	0.3679237
##	1036	id	490	TIME -	-1.892793e-01	-0.192612159	0.4034936
	1037	id	491	TIME	3.680902e-02	0.040931008	
##	1038	id	492	TIME	8.642932e-02	0.117181442	
##	1039	id	493		-9.962787e-03	-0.003531574	
##	1040	id	494	TIME	4.112236e-02	0.031919571	
##	1041	id	495		-7.851103e-02	-0.082948430	
##	1042	id	496		-1.853004e-01	-0.180251084	
##	1043	id	497	TIME	1.014100e-01	0.102241360	
##	1044	id	498		-4.466566e-02	-0.056709870	
##	1045	id	499		-4.923667e-02	-0.089567612	
##	1046	id	500	TIME	7.411754e-02	0.045020983	
##	1047	id	501		-2.032390e-02	-0.030356538	
## ##	1048 1049	id	502		-1.068330e-01 -9.240835e-02	-0.068498399 -0.111651954	
	1049	id id	503 504		-7.016861e-02	-0.060074987	
	1051 1052	id id	505 506	TIME	-1.176837e-01 2.515388e-02	-0.116464463 0.031673646	
	1053	id	507		-7.357451e-03	-0.031597454	
	1054	id	508	TIME	1.338942e-02	-0.017380361	
	1055	id	509	TIME	1.869163e-02	0.040180888	
	1056	id	510		-1.432458e-02	-0.034816039	
	1057	id	511	TIME	8.260968e-02	0.082423195	
	1058	id	512		-2.399661e-02	-0.049999842	
	1059	id	513	TIME	2.465157e-02	0.009458109	
	1060	id	514	TIME	7.054099e-02	0.058127624	
	1061	id	515		-1.510547e-01	-0.149286881	
##	1062	id	516	TIME	2.355450e-02	0.043008253	0.3576823
##	1063	id	517	TIME	2.708752e-03	-0.008042278	0.3775792
##	1064	id	518	TIME	2.179823e-02	0.033087154	0.3785875
##	1065	id	519	TIME -	-3.354337e-02	-0.077540585	0.3543976
##	1066	id	520	TIME	3.671696e-02	0.028680856	0.3800472
##	1067	id	521	TIME -	-1.494874e-02	-0.010246040	0.3655218

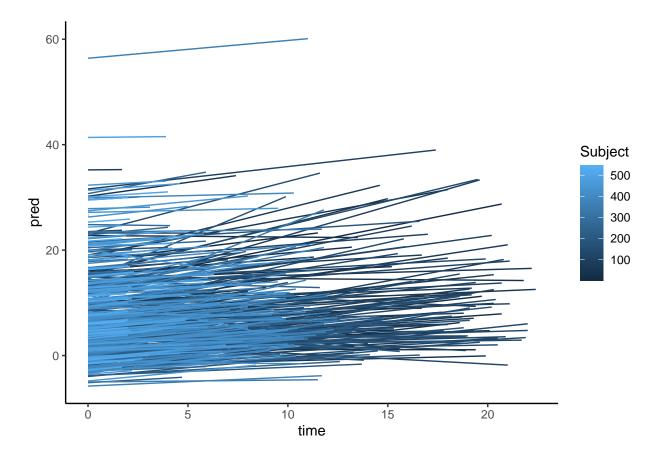
##	1068	id	522	TIME	-1.231096e-01	-0.088174881 0.3863496
##	1069	id	523	TIME	4.689777e-02	0.059276839 0.3804436
##	1070	id	524	TIME	4.065965e-02	0.047050165 0.3727864
##	1071	id	525	TIME	5.862047e-02	0.054975172 0.3846853
##	1072	id	526	TIME	8.267914e-02	0.065307992 0.3736034
##	1073	id	527	TIME	3.880042e-02	0.024980948 0.3690206
##	1074	id	528	TIME	4.958031e-02	0.043423441 0.3968259
##	1075	id	529	TIME	-1.972858e-02	0.018257768 0.3503873
##	1076	id	530	TIME	2.785005e-02	0.022686769 0.4084390
##	1077	id	531	TIME	3.072628e-02	0.048007055 0.3927544
##	1078	id	532	TIME	4.327602e-02	0.055701849 0.3510821
##	1079	id	533	TIME	-9.891108e-03	-0.015034077 0.3778936
##	1080	id	534	TIME	-3.178622e-02	-0.012002817 0.3761102
##	1081	id	535	TIME	-1.927633e-02	-0.012663251 0.4220863
##	1082	id	536	TIME	-1.474515e-01	-0.130918154 0.3786304
##	1083	id	537	TIME	-7.982723e-02	-0.092582707 0.3835059
##	1084	id	538	TIME	-4.189330e-02	-0.057215484 0.4087745
##	1085	id	539	TIME	-5.020666e-02	-0.058207503 0.3687715
##	1086	id	540	TIME	-1.064022e-01	-0.119409510 0.4196486
##	1087	id	541	TIME	-6.996206e-03	0.007952643 0.3481657
##	1088	id	542	TIME	-7.876182e-02	-0.107742718 0.3701339
##	1089	id	543	TIME	-1.451324e-02	-0.020256894 0.3798277
##	1090	id	544	TIME	-8.621476e-02	-0.074513786 0.3995097
##	1091	id	545	TIME	5.817947e-03	0.011274628 0.3849204
##	1092	id	546	TIME	-9.440976e-03	-0.023052688 0.4065739

plotREsim(REsim(db_mixed2))

Effect Ranges



```
dat_mixed2<-data.frame(time=df$TIME,pred=fitted(db_mixed2),Subject=df$id)
dat_mixed2$Subject<-as.numeric(dat_mixed2$Subject)
ggplot(data=dat_mixed2,aes(x=time,y=pred,group=Subject,color=Subject))+theme_classic()+geom_line()</pre>
```

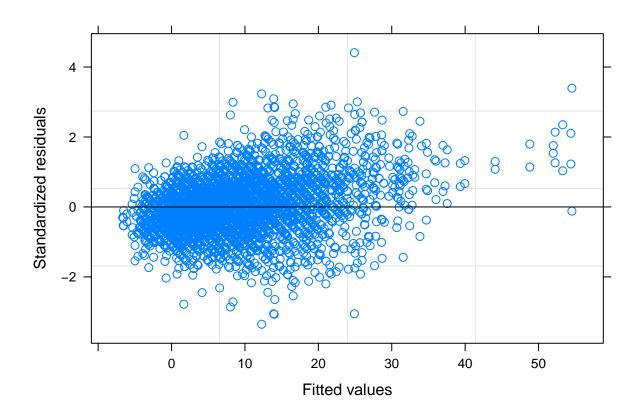


anova(db_mixed,db_mixed2)

```
## refitting model(s) with ML (instead of REML)
## Data: df
## Models:
## db_mixed: y \sim age + TIME + (1 | id)
## db_mixed2: y ~ age + TIME + (TIME | id)
            npar AIC BIC logLik deviance Chisq Df Pr(>Chisq)
               5 28672 28704 -14331
## db_mixed
                                       28662
## db_mixed2
               7 28550 28595 -14268
                                       28536 125.77 2 < 2.2e-16 ***
## ---
## Signif. codes: 0 '*** 0.001 '** 0.01 '* 0.05 '.' 0.1 ' 1
db_mixed5 = lme(y ~ age+TIME ,random=~1|TIME/id, data = df,cor = corAR1())
summary(db_mixed5)
## Linear mixed-effects model fit by REML
    Data: df
##
         AIC
##
                  BIC
                         logLik
##
     30128.64 30173.39 -15057.32
##
## Random effects:
## Formula: ~1 | TIME
```

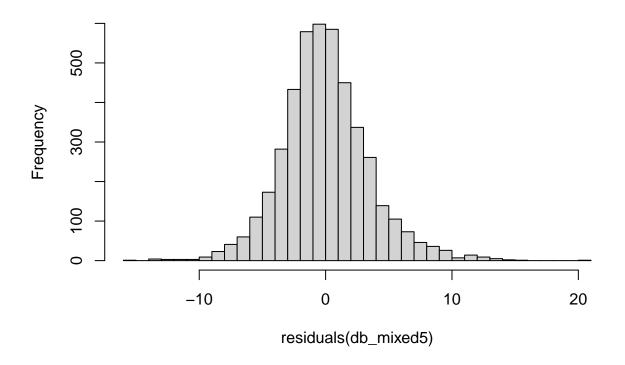
```
## (Intercept)
## StdDev:
            1.575724
##
## Formula: ~1 | id %in% TIME
         (Intercept) Residual
## StdDev: 7.324583 4.554834
## Correlation Structure: AR(1)
## Formula: ~1 | TIME/id
## Parameter estimate(s):
##
         Phi
## -0.01533482
## Fixed effects: y ~ age + TIME
                Value Std.Error DF t-value p-value
## (Intercept) -6.308886 0.7026172 2132 -8.979122
## age 0.259290 0.0101740 1988 25.485653
                                                   0
## TIME
             0.239849 0.0443270 1988 5.410912
## Correlation:
      (Intr) age
## age -0.800
## TIME -0.597 0.117
## Standardized Within-Group Residuals:
                                      Q3
         Min
                     01
                               Med
## -3.35377025 -0.45714697 -0.04599545 0.41175736 4.41035010
## Number of Observations: 4419
## Number of Groups:
        TIME id %in% TIME
##
          297
                     2287
```

plot(db_mixed5)

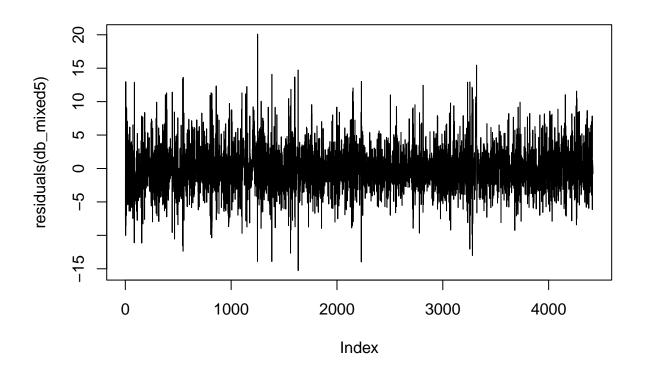


hist(residuals(db_mixed5), breaks = 50)

Histogram of residuals(db_mixed5)



plot(residuals(db_mixed5), type = "1")

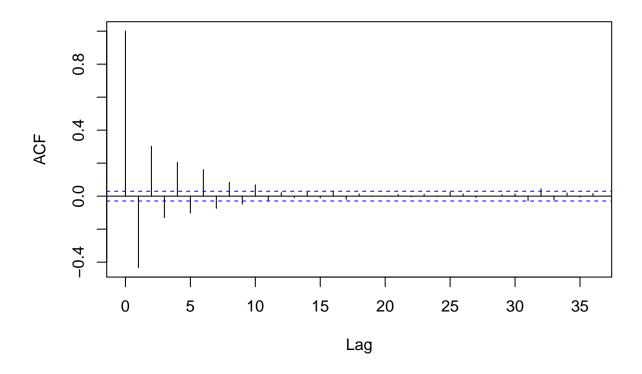


shapiro.test(residuals(db_mixed5))

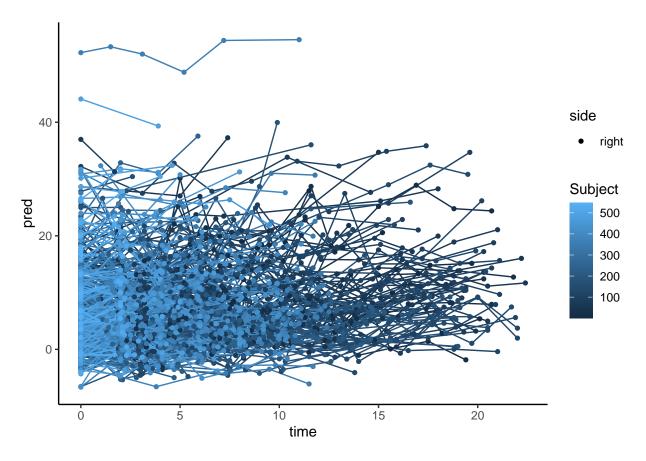
```
##
## Shapiro-Wilk normality test
##
## data: residuals(db_mixed5)
## W = 0.98131, p-value < 2.2e-16</pre>
```

acf(residuals(db_mixed5))

Series residuals(db_mixed5)



```
dat_mixed5<-data.frame(time=df$TIME,pred=fitted(db_mixed5),Subject=df$id,side=df$side)
dat_mixed5$Subject<-as.numeric(dat_mixed5$Subject)
dat_mixed5<-dat_mixed5 %>% filter(side=="right")
ggplot(data=dat_mixed5,aes(x=time,y=pred,color=Subject,shape=side,group=interaction(Subject, side)))+th
    geom_line()+geom_point()
```



Bilder, C. and Loughin, T. (2015). Analysis of Categorical Data with R. CRC Press. Hothorn, T. and Everitt, B. (2014). A Handbook of Statistical Analyses using R. CRC Press, 3rd Edition.