

Estimating the sleep need of adolescents using nonlinear mixed effects modelling

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Introduction

How much sleep is enough sleep? Using changes in lapses during the psychomotor vigilance task (PVT), Van Dongen et al. (2003) estimated that it is close to 8.16h. In their study, participants were split into different sleep restriction conditions and lapses were analysed for each of these conditions across several days. Lapses in a PVT task are when participants miss reacting to a stimulus that they are supposed to. In general, the number of lapses increases as the amount of sleep restriction increases. Van Dongen et al. modelled this alternatively as lapses increasing as the amount of wakefulness during the previous day increase beyond a certain critical value. This was formulated mathematically as follows:

$$lapses = b(excess)^\theta$$

Here, b represents rate of change of lapses per unit change in the nonlinear part of the equation. Excess denotes sleep in excess of the critical waking duration. Theta accomodates nonlinearity in the relationship. Excess can then be formulated as the difference between Cumulative Wake Time (CWT) across a number of days and the critical waking duration multiplied across the number of days.

$$lapses = b(CWT - critical * day)^\theta$$

Van Dongen's study was based on a population of adults between the ages 21 and 38. In this analysis, I use the same approach but for adolescents between the ages of 15 and 19. The data here is from the Need for sleep studies (Lo et al, 2016; 2017; 2019; 2020). There are four different sleep conditions - 5h, 6.5 h, 8h and 9h across the studies. The baseline sleep for all sleep conditions was 9h. Participants took the neurobehavioral tests three times every day across the sleep restriction days. For the analysis, I need the average lapses across days. These studies also had periods of recovery sleep, either inbetween or at the end. However, only the baseline sleep plus the days of sleep restriction until the first sleep recovery period is sufficient for this analysis.

Part 1 - with aggregated test conditions

The Dataset

The dataset for this analysis came from NFS1, NFS2, NFS4 and NFS5. Here is a section of the original dataset. Most of the columns have been omitted for the sake of presentation here.

```
##      subj gender day_num test_num kss pvt_median_rt pvt_sd_rt pvt_lapses
## 1 NFS001 Female      1        1    6           229       78         1
## 2 NFS001 Female      1        2    7           250       90         2
## 3 NFS001 Female      1        3    4           244       68         1
## 4 NFS001 Female      2        1    4           245       59         1
## 5 NFS001 Female      2        2    4           253       44         0
## 6 NFS001 Female      2        3    5           253       52         0
```

Data cleaning

First, I selected only the columns that were required for the analysis.

```
##      subj day_num      group lapses
## 1 NFS001      1 nonap_5hx7      1
## 2 NFS001      1 nonap_5hx7      2
## 3 NFS001      1 nonap_5hx7      1
## 4 NFS001      2 nonap_5hx7      1
## 5 NFS001      2 nonap_5hx7      0
## 6 NFS001      2 nonap_5hx7      0
```

Since participants did the PVT task three times a day, I summarised the results to get the average PVT lapses for each day.

```
## # A tibble: 6 x 4
## # Groups:   subj, group [1]
##   subj   group    day_num lapses
##   <chr> <chr>      <int> <dbl>
## 1 NFS001 nonap_5hx7      1  1.33
## 2 NFS001 nonap_5hx7      2  0.333
## 3 NFS001 nonap_5hx7      3    5
## 4 NFS001 nonap_5hx7      4  6.33
## 5 NFS001 nonap_5hx7      5    7
## 6 NFS001 nonap_5hx7      6 17.3
```

I then imported the TST data.

```
##      subj  TST day_num study
## 1 NFS001 7.17      1  NFS1
## 2 NFS001 3.47      2  NFS1
## 3 NFS001 3.97      3  NFS1
## 4 NFS001 4.20      4  NFS1
## 5 NFS001 4.30      5  NFS1
## 6 NFS001 4.23      6  NFS1
```

Then I merged the TST dataset and the NFS dataset.

```
##      subj day_num      group      lapses  TST study
## 1 NFS001      1 nonap_5hx7  1.3333333 7.17  NFS1
## 2 NFS001      2 nonap_5hx7  0.3333333 3.47  NFS1
## 3 NFS001      3 nonap_5hx7  5.0000000 3.97  NFS1
## 4 NFS001      4 nonap_5hx7  6.3333333 4.20  NFS1
## 5 NFS001      5 nonap_5hx7  7.0000000 4.30  NFS1
## 6 NFS001      6 nonap_5hx7 17.3333333 4.23  NFS1
```

I created a new column that denotes their total bed time during the previous night. On baseline days, they had 9h of sleep and their bed time varies based on their sleep condition on the other days. The day numbers were also made to align across the different studies and start with day 1 being the baseline day.

```
##      subj day_num      group      lapses  TST study TBT condition
## 1 NFS001      1 nonap_5hx7  1.3333333 7.17  NFS1   9          5
## 2 NFS001      2 nonap_5hx7  0.3333333 3.47  NFS1   5          5
## 3 NFS001      3 nonap_5hx7  5.0000000 3.97  NFS1   5          5
## 4 NFS001      4 nonap_5hx7  6.3333333 4.20  NFS1   5          5
## 5 NFS001      5 nonap_5hx7  7.0000000 4.30  NFS1   5          5
## 6 NFS001      6 nonap_5hx7 17.3333333 4.23  NFS1   5          5
```

Finally I calculated the cumulative wake duration for each participant based on the TBT and TST estimates.

```
## # A tibble: 6 x 10
## # Groups:   subj [1]
##      subj  day_num group      lapses  TST study  TBT condition TWT_tbt TWT_tst
##   <chr>    <dbl> <chr>    <dbl> <dbl> <chr> <dbl>    <dbl>    <dbl>
## 1 NFS001      1 nonap_5hx7  1.33  7.17 NFS1     9         5        15    16.8
## 2 NFS001      2 nonap_5hx7  0.333  3.47 NFS1     5         5        34    37.4
## 3 NFS001      3 nonap_5hx7  5      3.97 NFS1     5         5        53    57.4
## 4 NFS001      4 nonap_5hx7  6.33  4.2  NFS1     5         5        72    77.2
## 5 NFS001      5 nonap_5hx7  7      4.3  NFS1     5         5        91    96.9
## 6 NFS001      6 nonap_5hx7 17.3   4.23 NFS1     5         5       110   117.
```

Clean data

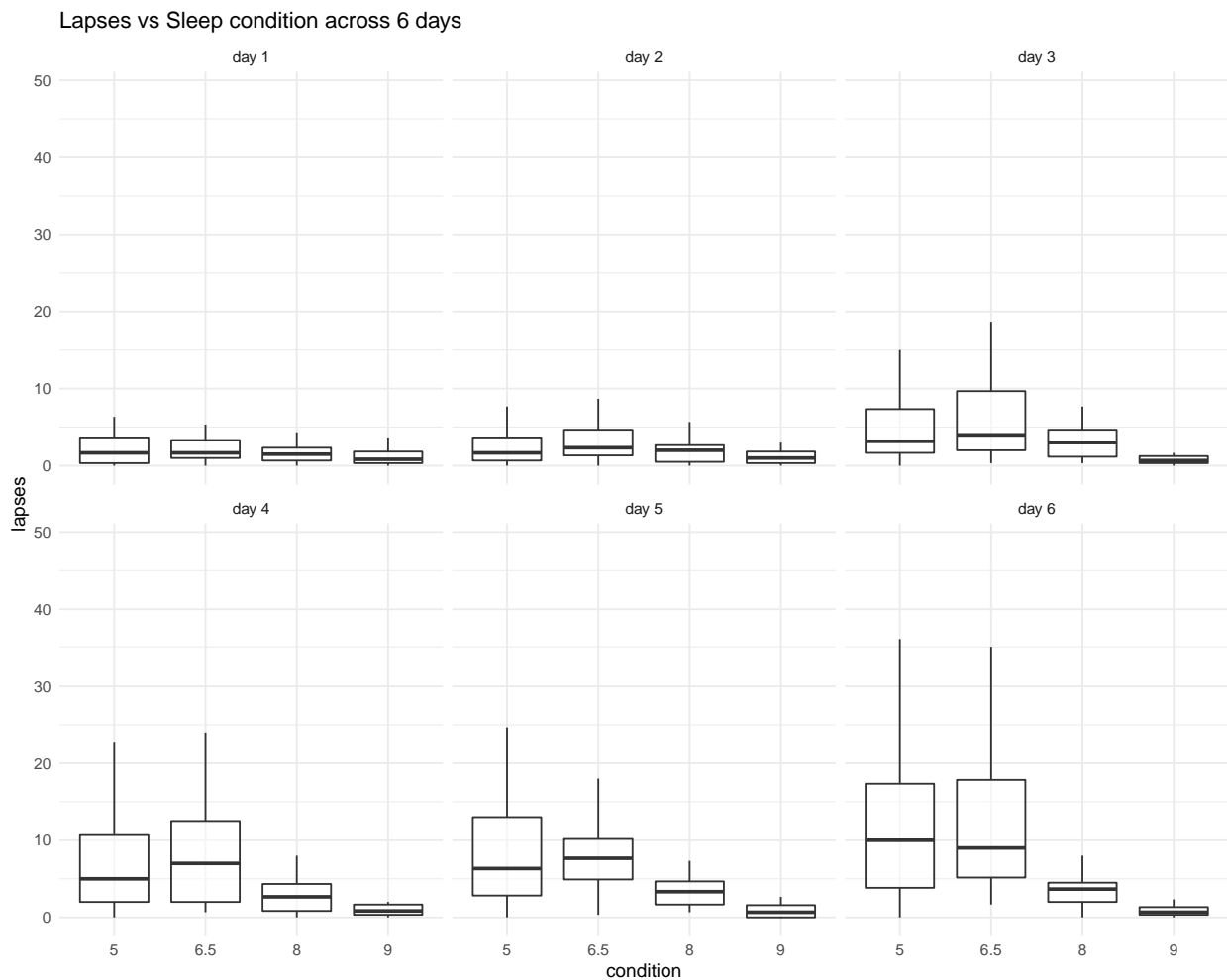
Summing up, the last baseline day plus the first five sleep manipulation days were used for the analysis from the NFS studies. ‘Lapses’ represents mean lapses on a particular day (day_num). TST represents the total sleep time on the previous night. TBT represents the total bed time on the previous night. Total Wake Time was calculated as the cumulative total wakeful duration across days based on both the TST estimate $[(TWT_tst = 24 - TST_tbt) \times day_num]$ and TBT estimate $[(TWT_tbt = 24 - TST_tbt) \times day_num]$. After cleaning, there were 834 observations in total (6 days x 139 subjects).

```
## # A tibble: 6 x 10
## # Groups:   subj [1]
##   subj   day_num group      lapses   TST study   TBT condition TWT_tbt TWT_tst
##   <chr>   <dbl> <chr>      <dbl> <dbl> <chr> <dbl>   <dbl>   <dbl>
## 1 NFS001     1 nonap_5hx7  1.33   7.17 NFS1     9       5       15    16.8
## 2 NFS001     2 nonap_5hx7  0.333  3.47 NFS1     5       5       34    37.4
## 3 NFS001     3 nonap_5hx7   5      3.97 NFS1     5       5       53    57.4
## 4 NFS001     4 nonap_5hx7  6.33   4.2  NFS1     5       5       72    77.2
## 5 NFS001     5 nonap_5hx7   7      4.3  NFS1     5       5       91    96.9
## 6 NFS001     6 nonap_5hx7 17.3   4.23 NFS1     5       5      110   117.
```

Visualising the dataset

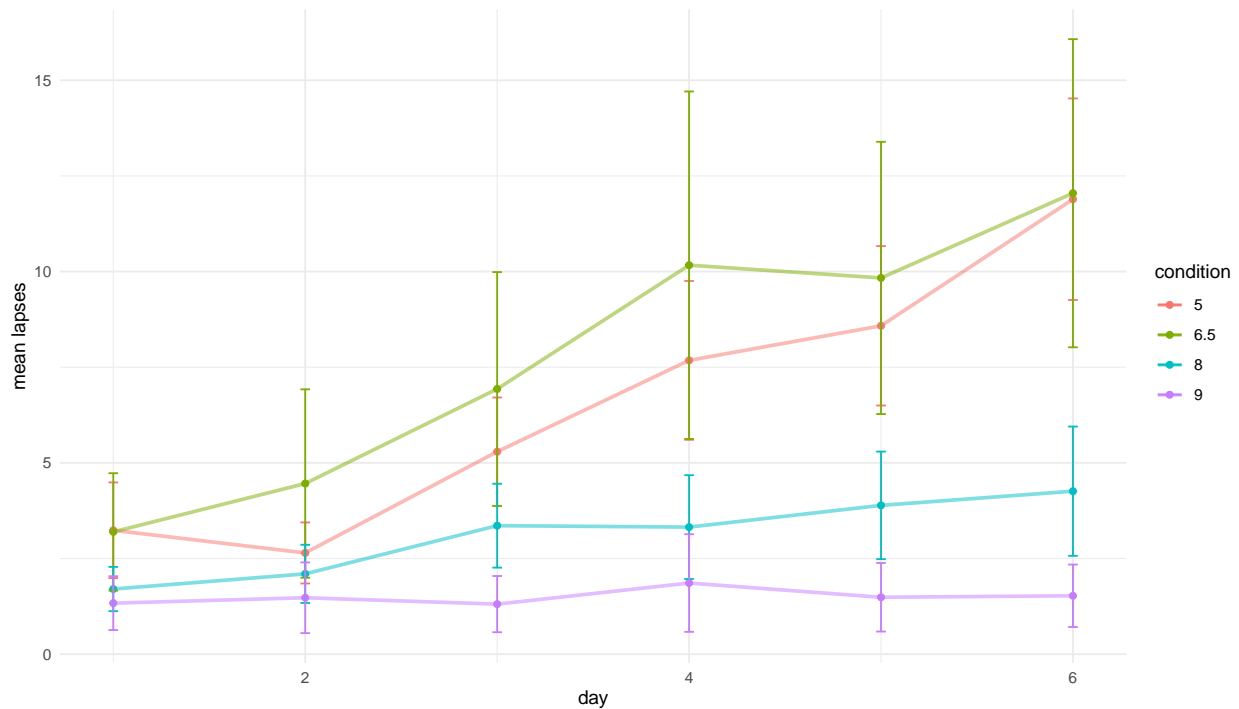
For this analysis, I have mainly focused on no nap conditions. Hence the visualizations below do not include the conditions that had nap time.

Boxplot - Lapses vs Sleep Condition



As it can be seen, the number of lapses increases across the days as the level of sleep restriction increases. This can be noted more clearly in the following charts

Line plot - Lapses vs Day



Estimating Sleep Need

TBT based estimate

Summary I'm using the `nlme()` function from the `nlme` library to fit a nonlinear mixed effects model to my data.

```
library(modelr) #for RMSE
library(nlme)
TBT.nonap.lapses <- nlme(lapses ~ b*(TWT_tbt - crit*day_num)^theta,
  data = data.nonap,
  fixed = b + theta + crit ~ 1,
  random = crit ~ 1,
  groups = ~ subj,
  start = c(b = 1.4, theta = 0.4, crit = 13),
  na.action = na.omit
)
```

```
summary(TBT.nonap.lapses)
```

```
## Nonlinear mixed-effects model fit by maximum likelihood
## Model: lapses ~ b * (TWT_tbt - crit * day_num)^theta
## Data: data.nonap
##      AIC      BIC    logLik
## 4360.464 4384.035 -2175.232
##
```

```
## Random effects:
## Formula: crit ~ 1 | subj
##          crit Residual
## StdDev: 1.696446 2.472632
##
## Fixed effects: b + theta + crit ~ 1
##           Value Std.Error DF t-value p-value
## b          3.276916 0.30539792 683 10.72999      0
## theta      0.667553 0.02602681 683 25.64869      0
## crit      16.213213 0.17853896 683 90.81051      0
## Correlation:
##      b      theta
## theta -0.904
## crit   0.342 -0.222
##
## Standardized Within-Group Residuals:
##      Min      Q1      Med      Q3      Max
## -4.08657132 -0.66240176 -0.01365964  0.60578292  5.07993341
##
## Number of Observations: 824
## Number of Groups: 139
```

RMSE

```
## [1] 3.158632
```

```
intervals(TBT.nonap.lapses)
```

Estimates and their 95% confidence intervals

```
## Approximate 95% confidence intervals
##
## Fixed effects:
##           lower      est.      upper
## b          2.6783772  3.2769161  3.8754551
## theta      0.6165443  0.6675534  0.7185624
## crit      15.8633011 16.2132135 16.5631259
## attr("label")
## [1] "Fixed effects:"
##
## Random Effects:
## Level: subj
##           lower      est.      upper
## sd(crit)  1.42516  1.696446  2.019372
##
## Within-group standard error:
##           lower      est.      upper
## 2.341592  2.472632  2.611006
```

TST based estimate

```
#SLEEP TIME ESTIMATES - no nap
TST.nonap.lapses <- nlme(lapses ~ b*(TWT_tst - crit*day_num)^theta,
  data = data.nonap,
  fixed = b + theta + crit ~ 1,
  random = crit ~ 1,
  groups = ~ subj,
  start = c(b = 1.4, theta = 0.5, crit = 12),
  na.action = na.omit
)

summary(TST.nonap.lapses)
```

Summary

```
## Nonlinear mixed-effects model fit by maximum likelihood
## Model: lapses ~ b * (TWT_tst - crit * day_num)^theta
## Data: data.nonap
##      AIC      BIC    logLik
## 4406.687 4430.258 -2198.344
##
## Random effects:
## Formula: crit ~ 1 | subj
##           crit Residual
## StdDev: 1.402444  2.50208
##
## Fixed effects: b + theta + crit ~ 1
##           Value Std.Error DF   t-value p-value
## b          3.622969 0.31543308 683   11.48570      0
## theta      0.674452 0.02582812 683   26.11308      0
## crit      17.131346 0.14233562 683  120.35881      0
## Correlation:
##      b      theta
## theta -0.889
## crit  0.334 -0.208
##
## Standardized Within-Group Residuals:
##           Min           Q1           Med           Q3           Max
## -4.29474310 -0.62959079 -0.02426273  0.57142563  4.97521379
##
## Number of Observations: 824
## Number of Groups: 139
```

RMSE

```
## [1] 3.084051
```

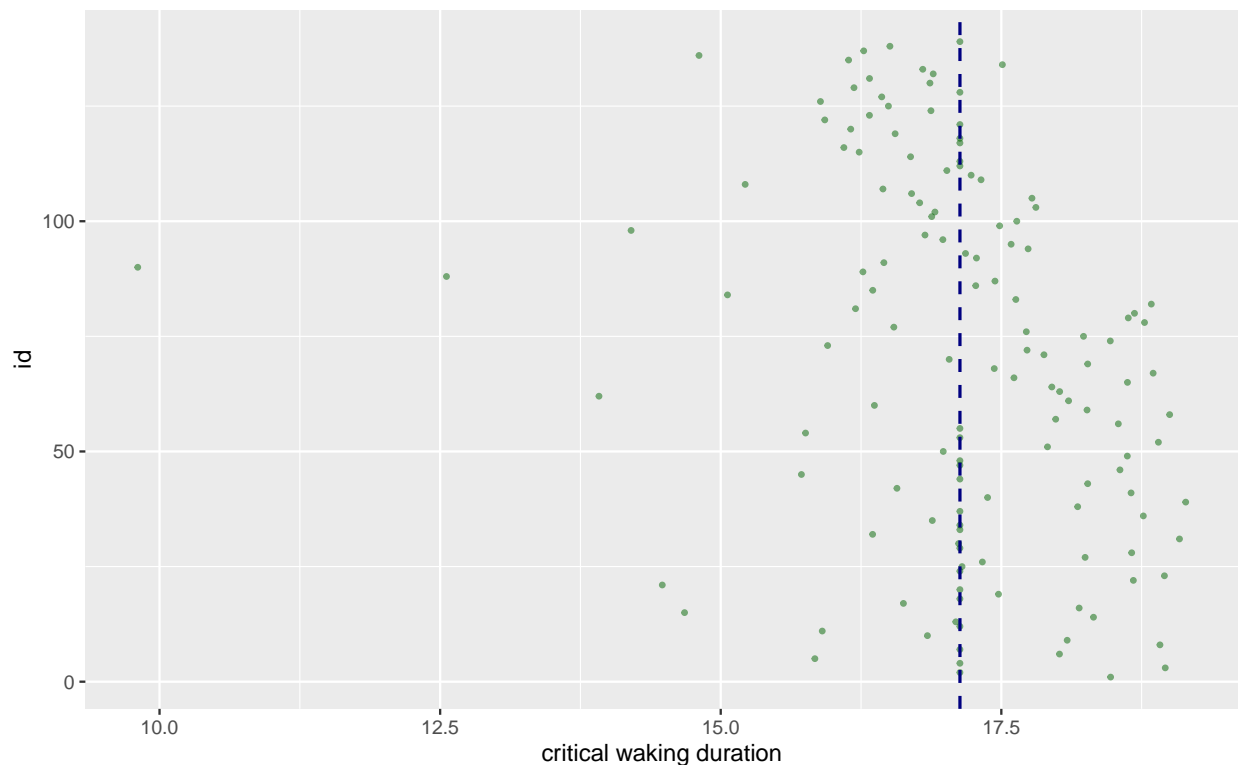
```
intervals(TST.nonap.lapses)
```

Estimates and their 95% confidence intervals

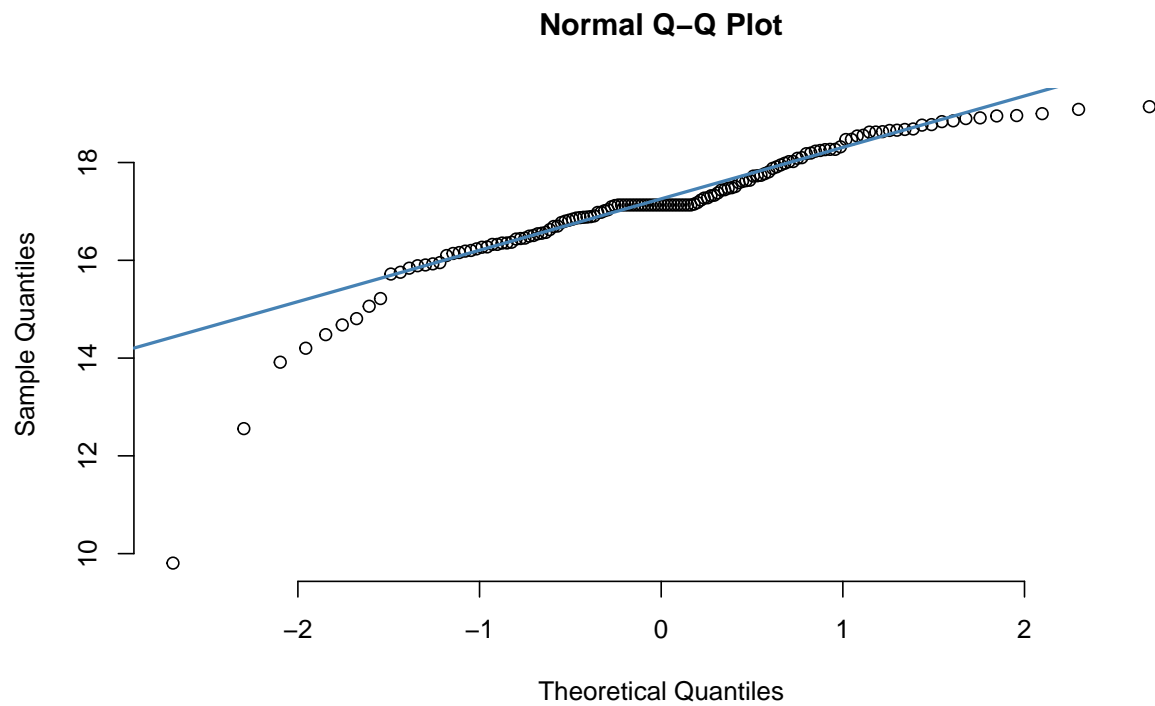
```
## Approximate 95% confidence intervals
##
## Fixed effects:
##      lower      est.      upper
## b      3.0047630  3.6229695  4.2411760
## theta  0.6238322  0.6744519  0.7250715
## crit  16.8523870 17.1313457 17.4103045
## attr("label")
## [1] "Fixed effects:"
##
## Random Effects:
## Level: subj
##      lower      est.      upper
## sd(crit) 1.193168  1.402444  1.648426
##
## Within-group standard error:
##      lower      est.      upper
## 2.369793  2.502080  2.641752
```

Visualising the results of TST based estimate

Dot Plot - Critical Wake Durations across participants

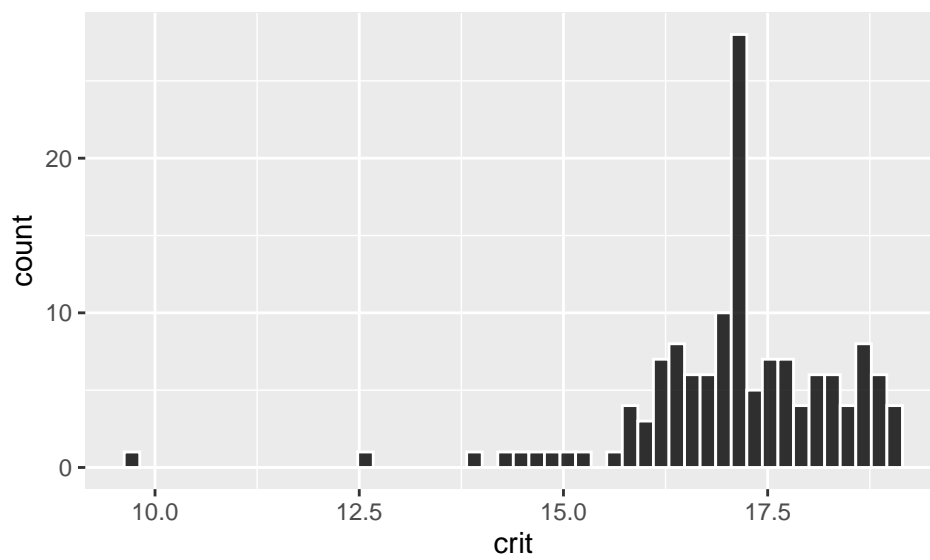


QQ Plot - Normality of distribution

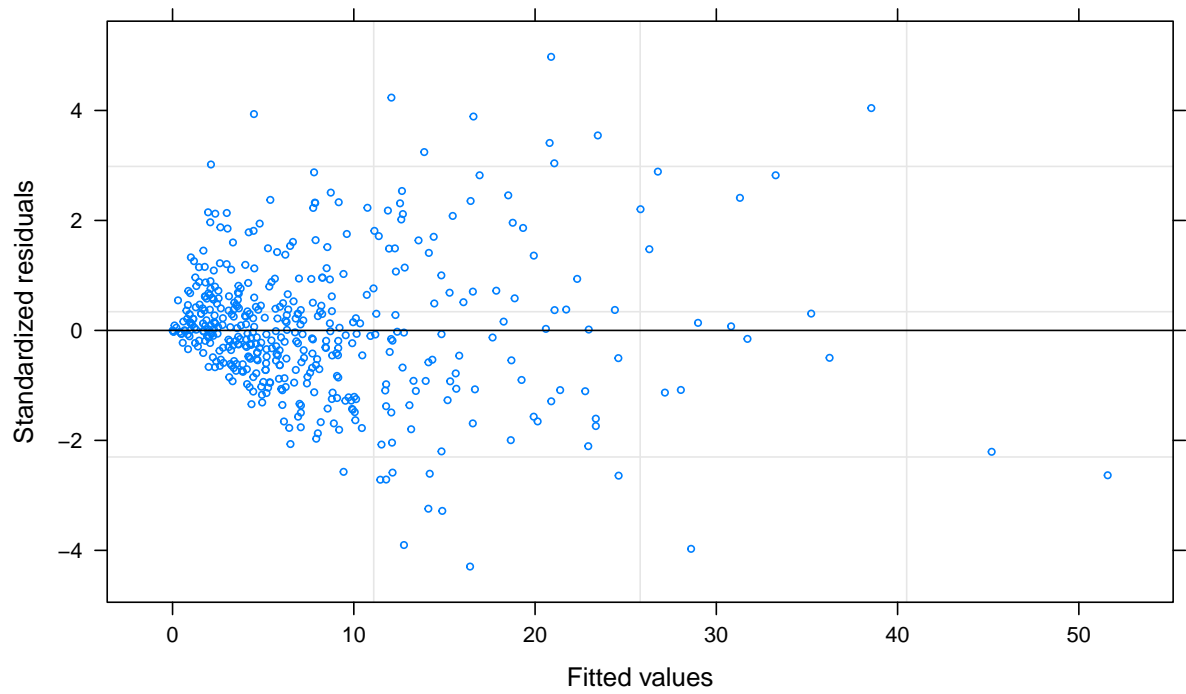


Histogram - Normality of distribution

The plot indicates a left skew. I checked the histogram

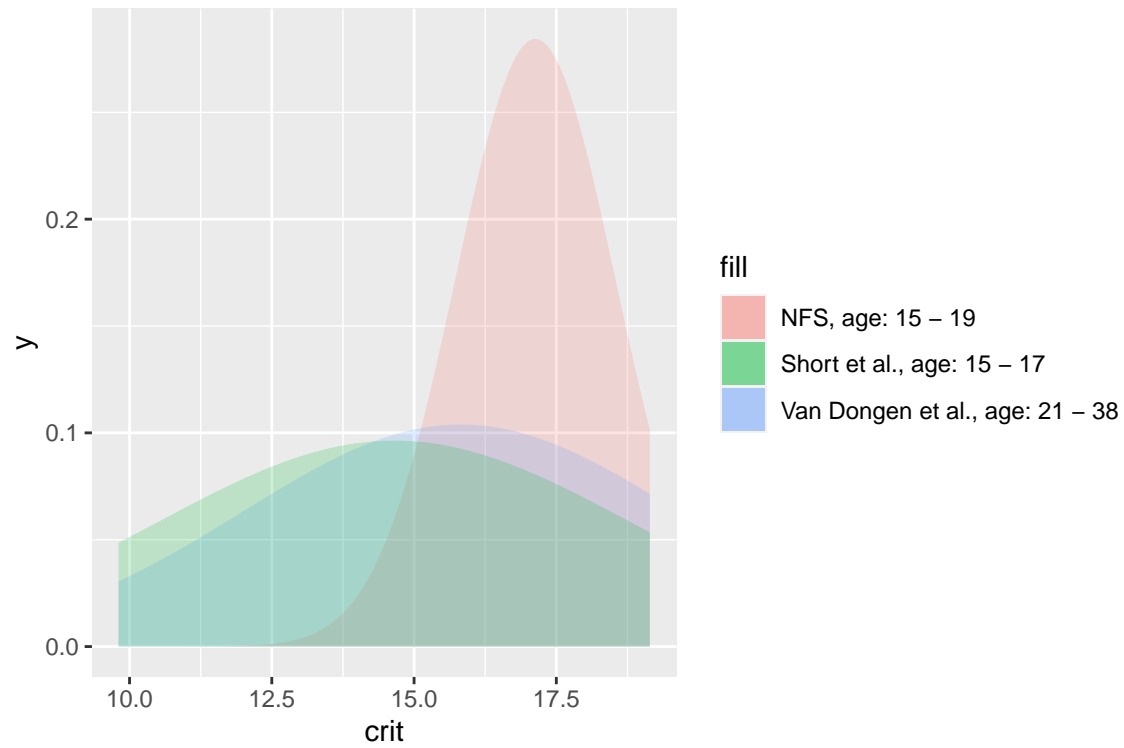


Residuals Plot



Comparison against estimates based on the literature

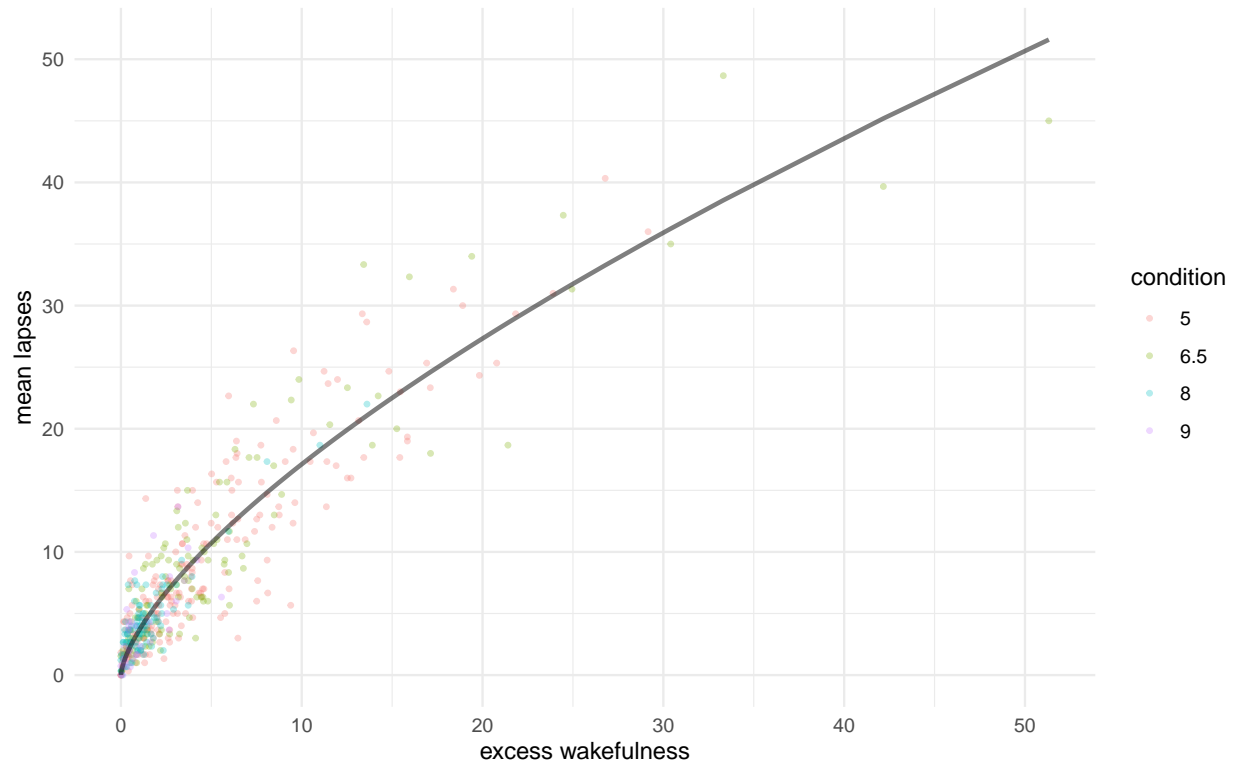
I compared the distribution obtained from this estimate with Van Dongen et al.(2003) and Short et al. (2018) estimates for the critical waking duration



Mean lapses vs excess wakefulness

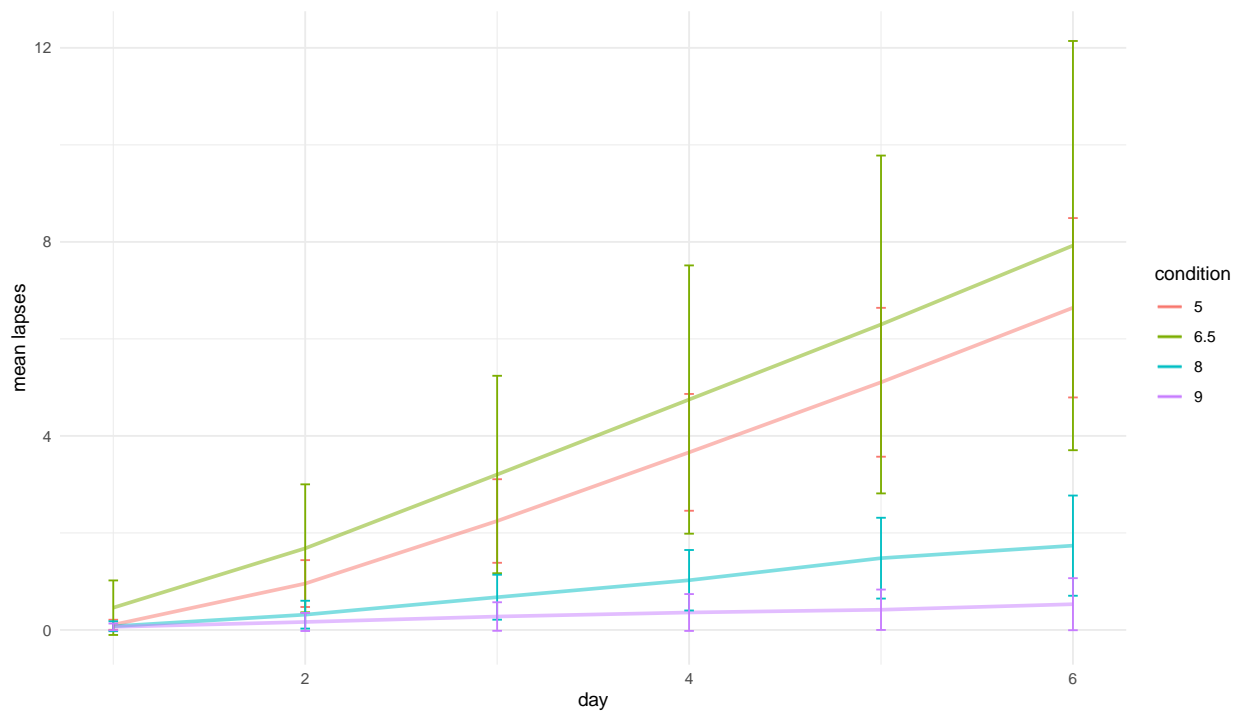
$$lapses = 3.62 * (excess)^{0.67}$$

The line represents predicted number of lapses, dots represent the actual number of lapses observed.



Predicted Lapses vs Day

$$lapses = 3.62 * (CWT - 17.13 * day)^{0.67}$$



To conclude, the estimate of critical waking duration (17.13) was greater than that of Van Dongen's estimate (15.84). Our results seem to suggest that for the average adolescent (based on the sample used for this study), 6.87h of sleep would be sufficient to prevent the build of neurobehavioral deficits at least in the context of the PVT task.

Part 2 - without aggregating test conditions

In this part of the analysis, I won't be aggregating the test results.

The Dataset

I reloaded the nfs dataset again for the analysis.

##	subj	gender	day_num	test_num	kss	pvt_median_rt	pvt_sd_rt	pvt_lapses
## 1	NFS001	Female	1	1	6	229	78	1
## 2	NFS001	Female	1	2	7	250	90	2
## 3	NFS001	Female	1	3	4	244	68	1
## 4	NFS001	Female	2	1	4	245	59	1
## 5	NFS001	Female	2	2	4	253	44	0
## 6	NFS001	Female	2	3	5	253	52	0

Data cleaning

Again, similar to part 1, I selected only the columns that were required for the analysis.

##	subj	day_num	group	lapses
## 1	NFS001	1	nonap_5hx7	1
## 2	NFS001	1	nonap_5hx7	2
## 3	NFS001	1	nonap_5hx7	1
## 4	NFS001	2	nonap_5hx7	1
## 5	NFS001	2	nonap_5hx7	0
## 6	NFS001	2	nonap_5hx7	0
## 7	NFS001	3	nonap_5hx7	6
## 8	NFS001	3	nonap_5hx7	6

I created a new column called ST that indicated the TBT from the past night

##	subj	day_num	group	lapses	TBT	condition
## 1	NFS001	1	nonap_5hx7	1	9	5
## 2	NFS001	1	nonap_5hx7	2	9	5
## 3	NFS001	1	nonap_5hx7	1	9	5
## 4	NFS001	2	nonap_5hx7	1	5	5
## 5	NFS001	2	nonap_5hx7	0	5	5
## 6	NFS001	2	nonap_5hx7	0	5	5
## 7	NFS001	3	nonap_5hx7	6	5	5
## 8	NFS001	3	nonap_5hx7	6	5	5

Next, I used the TBT data from each night to calculate the cumulative total wake time based on the TBT measures until each test time. For example, if test 1 is at 10 AM and this is day 3, the cumulative wake duration would be the (Total hours since start of first wake time after the end of baseline sleep - cumulative TBT since start of protocol). Additionally, for conditions with nap, I subtracted the nap duration from the cumulative wake duration for test in which participants had a nap preceding the test and during the day.

```
## [1] 3996
```

```
##      subj day_num      group lapses TBT condition test TWT wake_time test_time WD
## 1 NFS001      1 nonap_5h      1   9          5   1  19          6          10   4
## 2 NFS001      1 nonap_5h      2   9          5   2  24          6          15   9
## 3 NFS001      1 nonap_5h      1   9          5   3  29          6          20  14
## 4 NFS001      2 nonap_5h      1   5          5   1  38          6          10   4
## 5 NFS001      2 nonap_5h      0   5          5   2  43          6          15   9
## 6 NFS001      2 nonap_5h      0   5          5   3  48          6          20  14
## 7 NFS001      3 nonap_5h      6   5          5   1  57          6          10   4
## 8 NFS001      3 nonap_5h      6   5          5   2  62          6          15   9
##      type
## 1 no nap
## 2 no nap
## 3 no nap
## 4 no nap
## 5 no nap
## 6 no nap
## 7 no nap
## 8 no nap
```

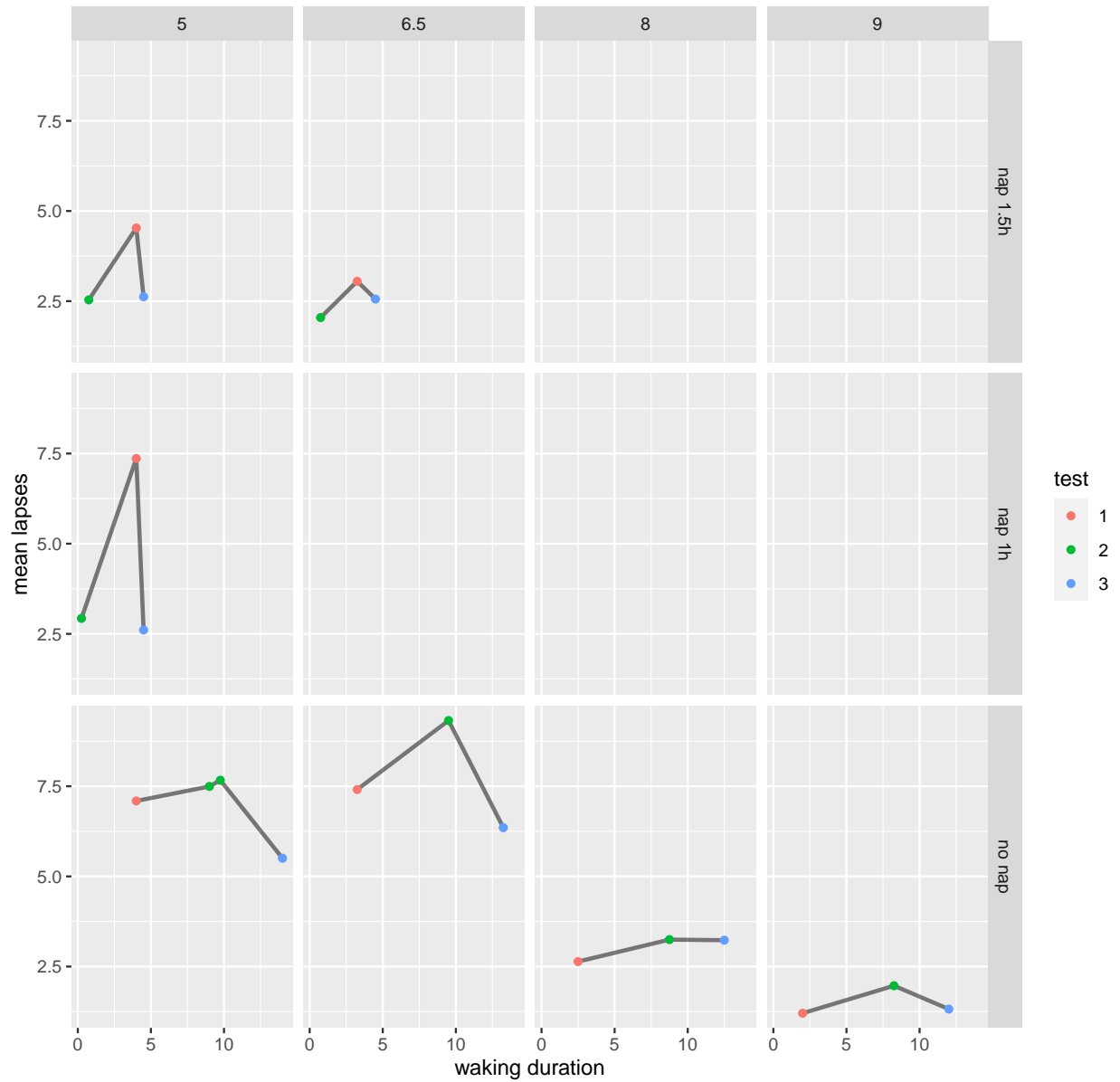
Clean dataset

Final dataset after cleaning

```
##      subj day_num      group lapses TBT condition test TWT wake_time test_time WD
## 1 NFS001      1 nonap_5h      1   9          5   1  19          6          10   4
## 2 NFS001      1 nonap_5h      2   9          5   2  24          6          15   9
## 3 NFS001      1 nonap_5h      1   9          5   3  29          6          20  14
## 4 NFS001      2 nonap_5h      1   5          5   1  38          6          10   4
## 5 NFS001      2 nonap_5h      0   5          5   2  43          6          15   9
## 6 NFS001      2 nonap_5h      0   5          5   3  48          6          20  14
## 7 NFS001      3 nonap_5h      6   5          5   1  57          6          10   4
## 8 NFS001      3 nonap_5h      6   5          5   2  62          6          15   9
##      type
## 1 no nap
## 2 no nap
## 3 no nap
## 4 no nap
## 5 no nap
## 6 no nap
## 7 no nap
## 8 no nap
```

Visualising the Dataset

mean lapses against time awake (from sleep at night or nap)

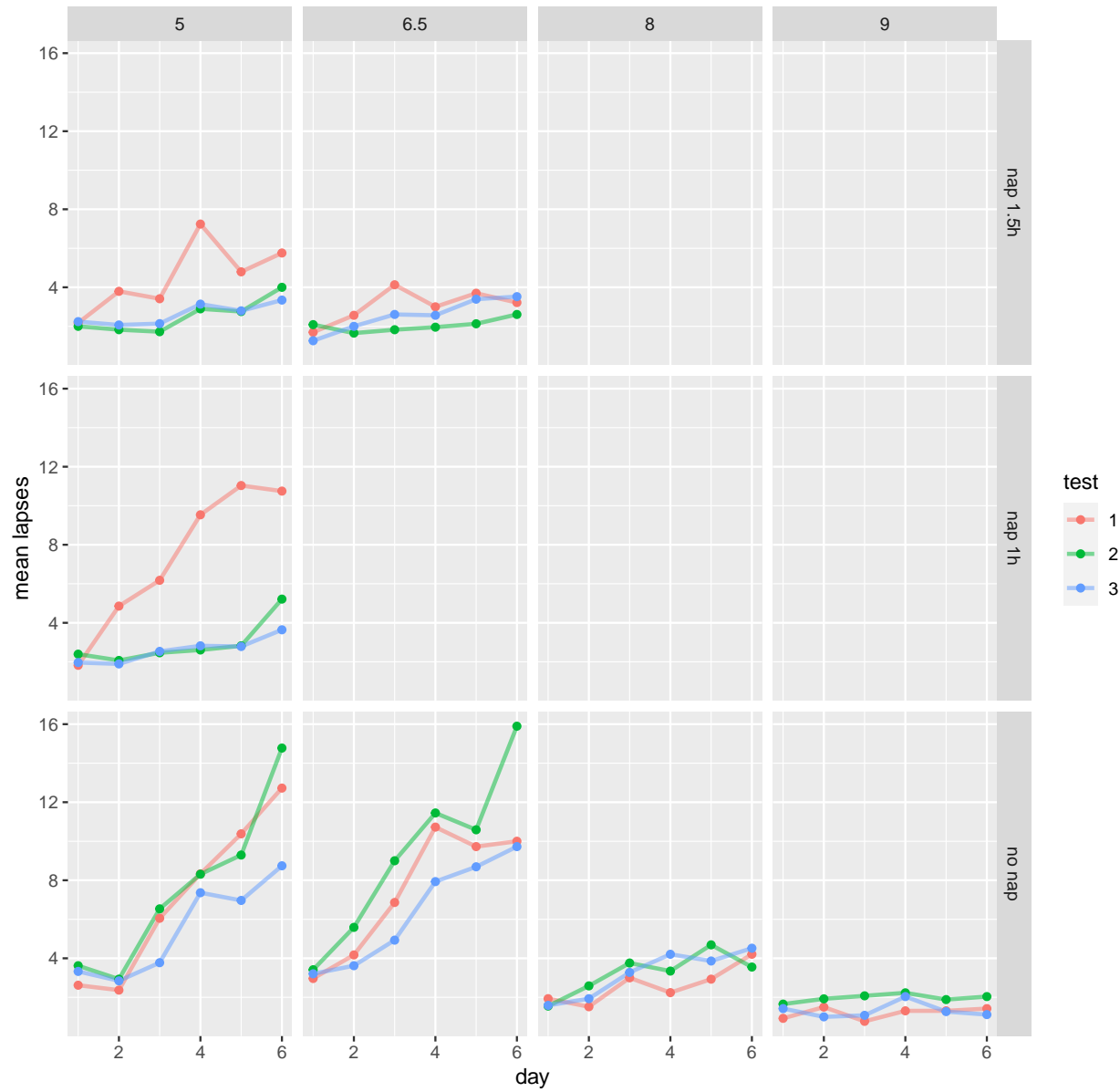


Mean lapses vs Day

#mean lapses vs Day

```
data.nfs %>% mutate(across(group, factor, levels=c("control_9h", "nonap_8h", "nap90_6pt5h", "nonap_6pt5h"),
ggplot(aes(x = day_num, y = lapses, color = as.factor(test))) +
  stat_summary(fun = mean, geom = "line", size = 1, alpha = 0.5) +
  stat_summary(fun = mean, geom = "point") +
```

```
#stat_summary(fun.data = mean_cl_normal, geom = "errorbar", aes(group = as.factor(condition)), width = 1,
labs(x = "day", y = "mean lapses", title = " ", color = "test") +
facet_grid(~ type ~ condition)
```



Estimating Sleep Need

All conditions

```
library(nlme)
```



```

#inclusive of nap conditions
sleep.allconditions.lapses <- nlme(lapses ~ b*(TWT - crit*day_num)^theta,
  data = data.nfs,
  fixed = b + crit + theta ~ 1,
  random = crit ~ 1,
  groups = ~ subj,
  start = c(b = 2, crit = 14, theta = 0.5),
  na.action = na.omit
)

summary(sleep.allconditions.lapses)

```

Summary

```

## Nonlinear mixed-effects model fit by maximum likelihood
##   Model: lapses ~ b * (TWT - crit * day_num)^theta
##   Data: data.nfs
##       AIC       BIC    logLik
## 26137.06 26168.53 -13063.53
##
## Random effects:
## Formula: crit ~ 1 | subj
##              crit Residual
## StdDev: 0.000572914 6.366384
##
## Fixed effects: b + crit + theta ~ 1
##              Value Std.Error   DF  t-value p-value
## b           0.205547 0.0461620 3771  4.45272      0
## crit       13.822926 0.3283707 3771 42.09549      0
## theta      1.077504 0.0588213 3771 18.31828      0
## Correlation:
##      b      crit
## crit  0.641
## theta -0.959 -0.412
##
## Standardized Within-Group Residuals:
##      Min      Q1      Med      Q3      Max
## -1.7681189 -0.5314576 -0.1973687  0.2172085  7.9065137
##
## Number of Observations: 3995
## Number of Groups: 222

```

RMSE

```
## [1] 6.366383
```

Estimates and their 95% confidence intervals

```

## Approximate 95% confidence intervals
##
## Fixed effects:
##      lower      est.      upper

```

```
## b      0.1150758  0.2055468  0.2960177
## crit  13.1793665 13.8229262 14.4664858
## theta 0.9622231  1.0775043  1.1927856
## attr("label")
## [1] "Fixed effects:"
```

Only no nap conditions

```
#no nap
sleep.nonap.lapses <- nlme(lapses ~ b*(TWT - crit*day_num)^theta,
  data = data.nonap,
  fixed = b + crit + theta ~ 1,
  random = crit ~ 1,
  groups = ~ subj,
  start = c(b = 1, crit = 12, theta = 0.4),
  na.action = na.omit
)

summary(sleep.nonap.lapses)
```

Summary

```
## Nonlinear mixed-effects model fit by maximum likelihood
## Model: lapses ~ b * (TWT - crit * day_num)^theta
## Data: data.nonap
##      AIC      BIC    logLik
## 17379.7 17408.93 -8684.849
##
## Random effects:
## Formula: crit ~ 1 | subj
##           crit Residual
## StdDev: 0.001138025 7.244334
##
## Fixed effects: b + crit + theta ~ 1
##           Value Std.Error   DF   t-value p-value
## b      0.115809 0.0348742 2411  3.320769  9e-04
## crit 12.440110 0.5334087 2411 23.321908  0e+00
## theta 1.199507 0.0748659 2411 16.022063  0e+00
## Correlation:
##      b      crit
## crit  0.563
## theta -0.953 -0.299
##
## Standardized Within-Group Residuals:
##      Min      Q1      Med      Q3      Max
## -1.7177180 -0.5190705 -0.2433830  0.1732791  6.8882463
##
## Number of Observations: 2555
## Number of Groups: 142
```

RMSE

```
## [1] 7.244333
```

Estimates and their 95% confidence intervals

```
## Approximate 95% confidence intervals
##
## Fixed effects:
##      lower      est.      upper
## b      0.04746279  0.1158091  0.1841554
## crit  11.39473708 12.4401098 13.4854826
## theta  1.05278470  1.1995067  1.3462287
## attr("label")
## [1] "Fixed effects:"
```

Only nap conditions

Summary

```
## Nonlinear mixed-effects model fit by maximum likelihood
## Model: lapses ~ b * (TWT - crit * day_num)^theta
## Data: data.nap
##      AIC      BIC    logLik
## 7669.34 7695.702 -3829.67
##
## Random effects:
## Formula: crit ~ 1 | subj
##      crit Residual
## StdDev: 0.8947836 3.182258
##
## Fixed effects: b + crit + theta ~ 1
##      Value Std.Error   DF   t-value p-value
## b      1.737617 0.18002255 1358    9.65222      0
## crit  17.568085 0.11425575 1358  153.76105      0
## theta  0.734852 0.04226477 1358   17.38686      0
## Correlation:
##      b      crit
## crit  0.341
## theta -0.904 -0.195
##
## Standardized Within-Group Residuals:
##      Min      Q1      Med      Q3      Max
## -3.2553146 -0.5700844 -0.1210714  0.4116992  6.6657784
##
## Number of Observations: 1440
## Number of Groups: 80
```

RMSE

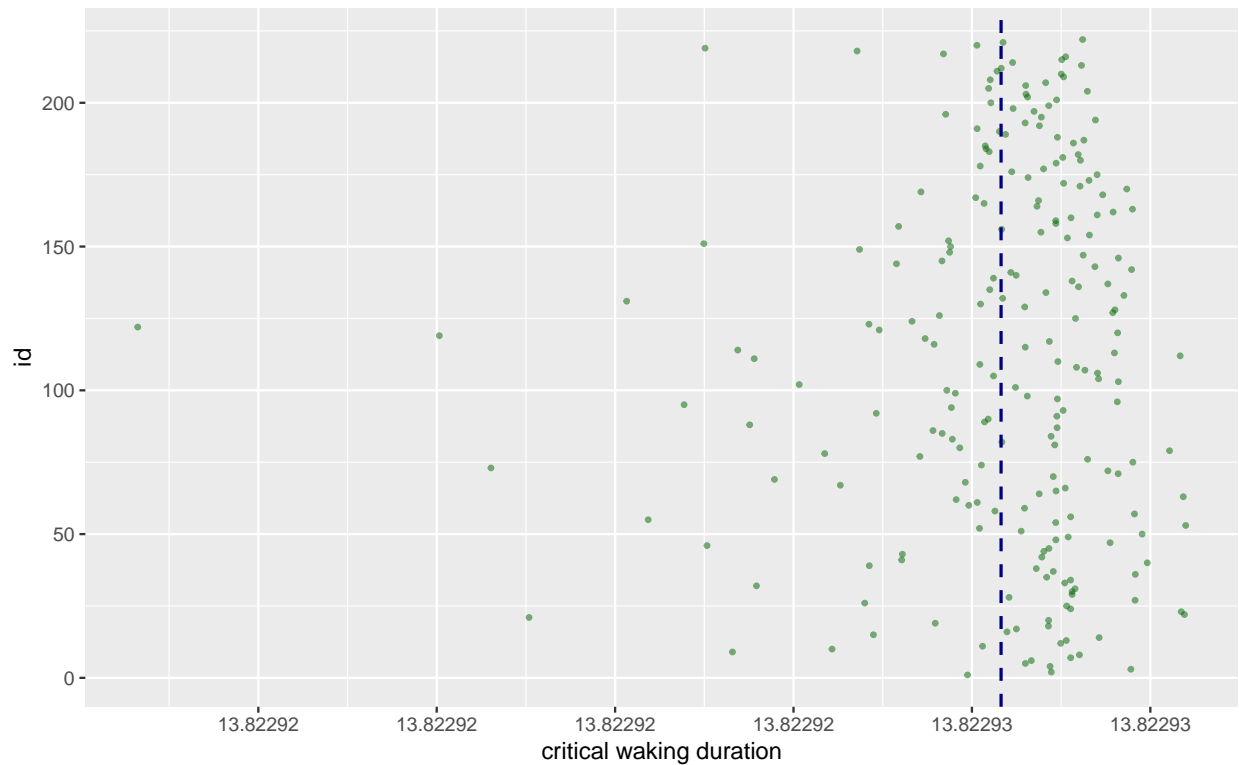
```
## [1] 3.639682
```

Estimates and their 95% confidence intervals

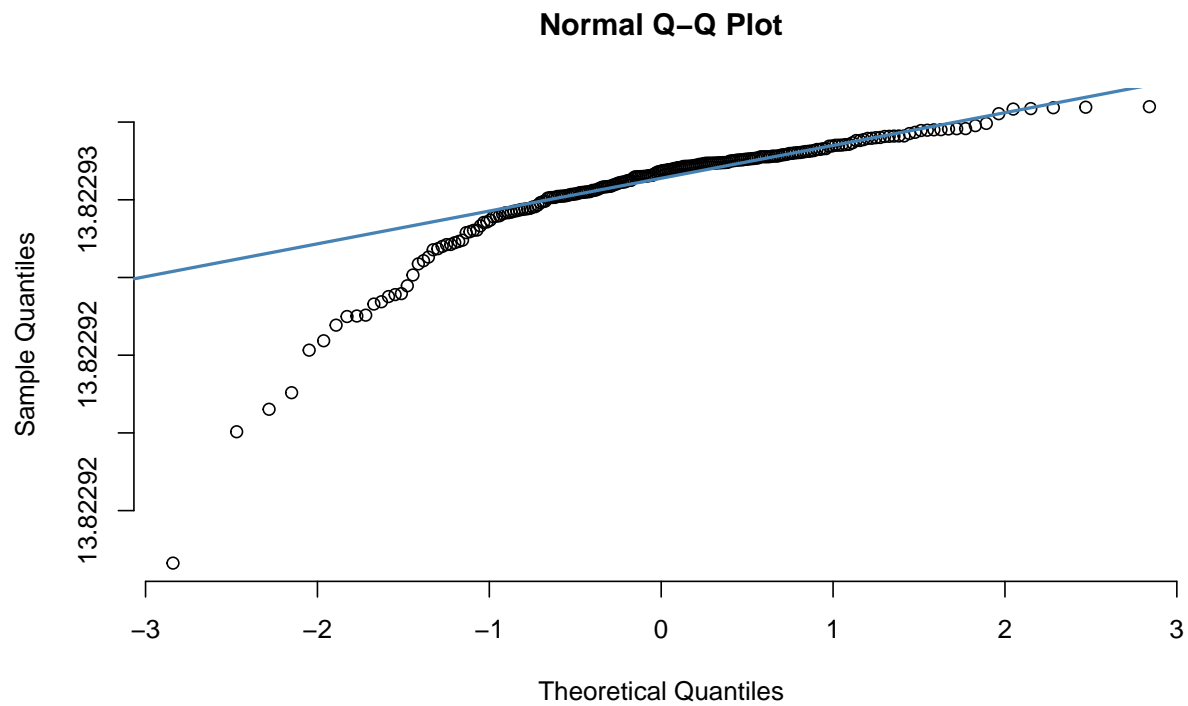
```
## Approximate 95% confidence intervals
##
## Fixed effects:
##           lower      est.      upper
## b      1.3848326  1.7376171  2.0904015
## crit  17.3441815 17.5680848 17.7919881
## theta  0.6520269  0.7348518  0.8176767
## attr(,"label")
## [1] "Fixed effects:"
```

Visualising the results of TBT based estimate - all conditions

Dot Plot - Critical Wake Durations across participants

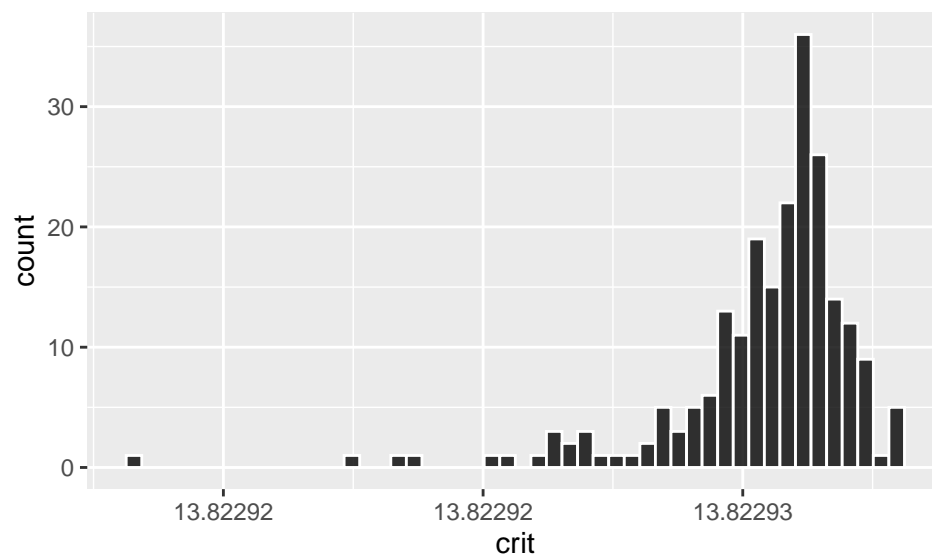


QQ Plot - Normality of distribution

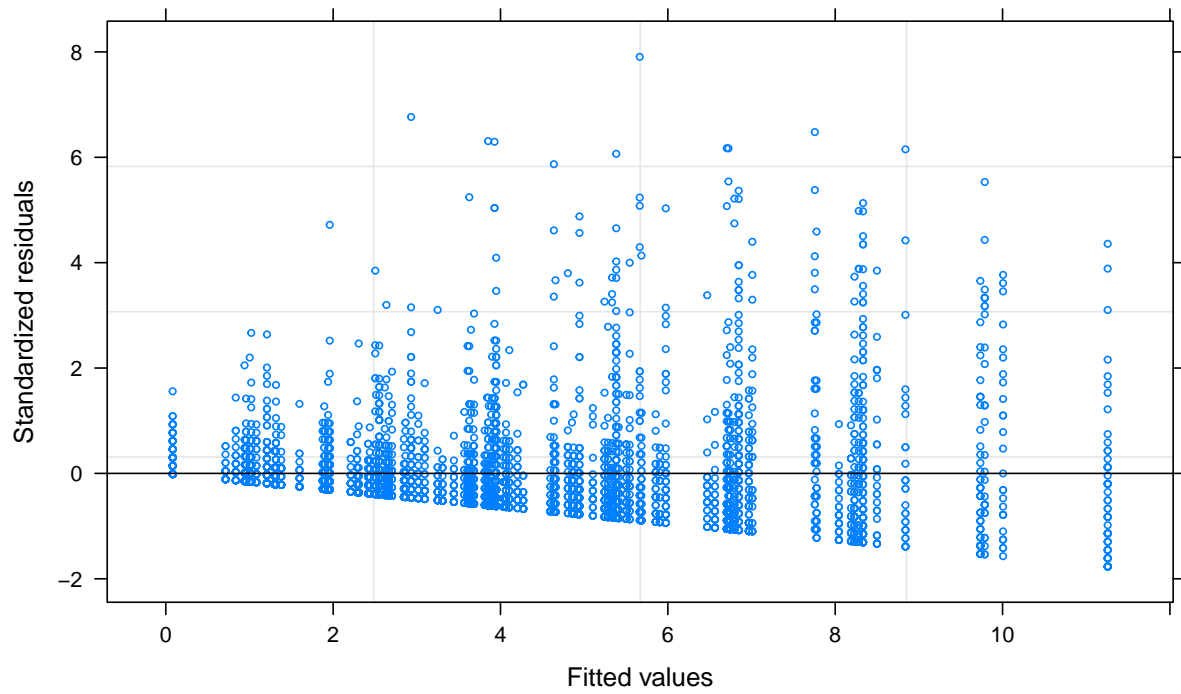


Histogram - Normality of distribution

The plot indicates a left skew. I checked the histogram



Residuals Plot



Comparison of results

##	measure	RMSE	crit.estimate
## 1	aggregated tests (TST) - no nap	3.084051	17.13135
## 2	aggregated tests (TBT) - no nap	3.158632	16.21321
## 3	tests not aggregated (TBT) - no nap	7.244333	12.44011
## 4	tests not aggregated (TBT) - all conditions	6.366383	13.82293
## 5	tests not aggregated (TBT) - nap only	3.639682	17.56808

