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 nonlineaerity 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.

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>   <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

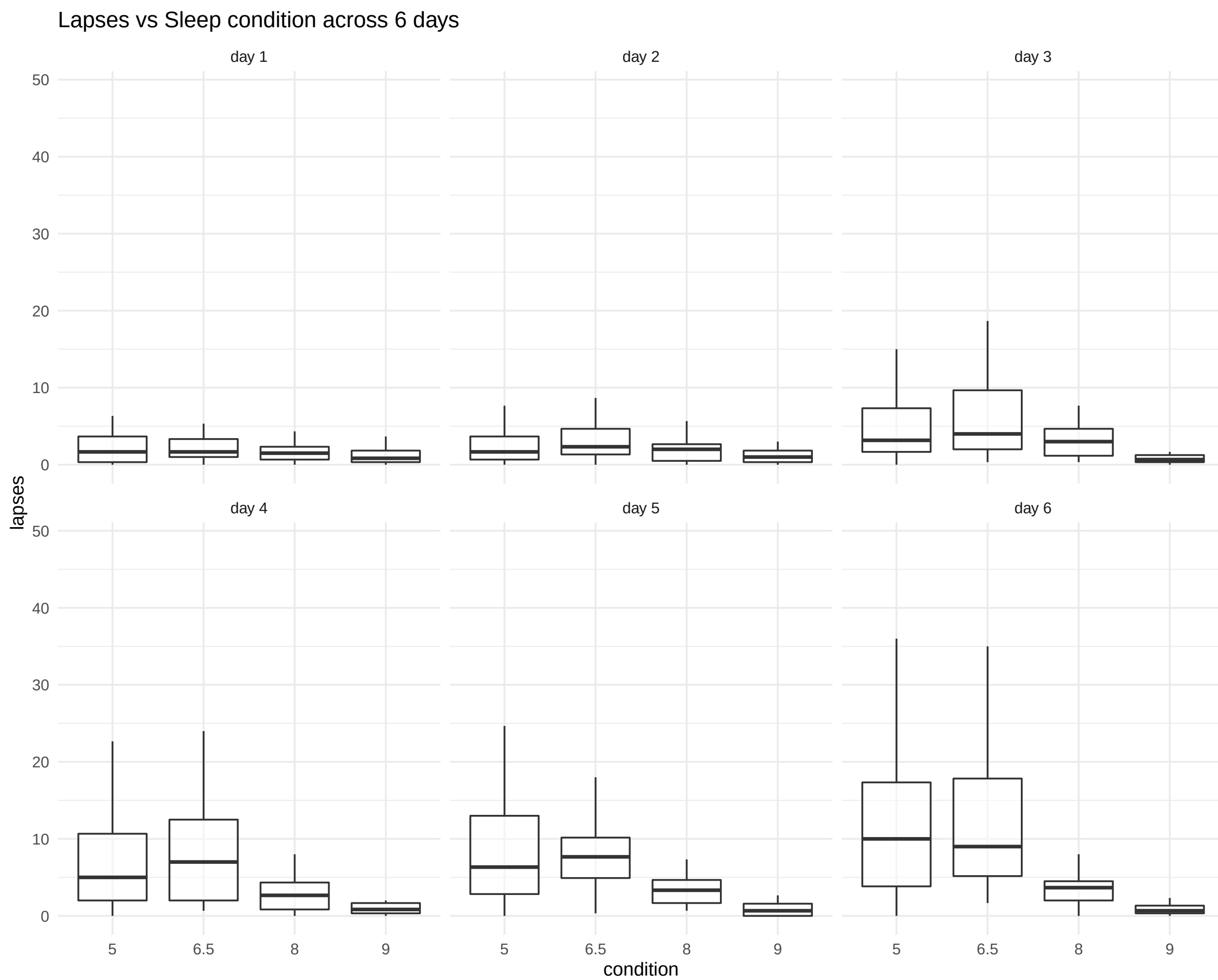
Summing up, the last baseline day plus the first five sleep manipulation days were used for the analysis from the NFS studies. 'Lapses' represents mean lapses on a particular day (day_num). TST represents the total sleep time on the previous night. TBT represents the total bed time on the previous night. Total Wake Time was calculated as the cumulative total wakeful duration across days based on both the TST estimate [(TWT_tst = 24 – TST_tbt) x day_num] and TBT estimate [(TWT_tbt = 24 – TST_tbt) x 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>   <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

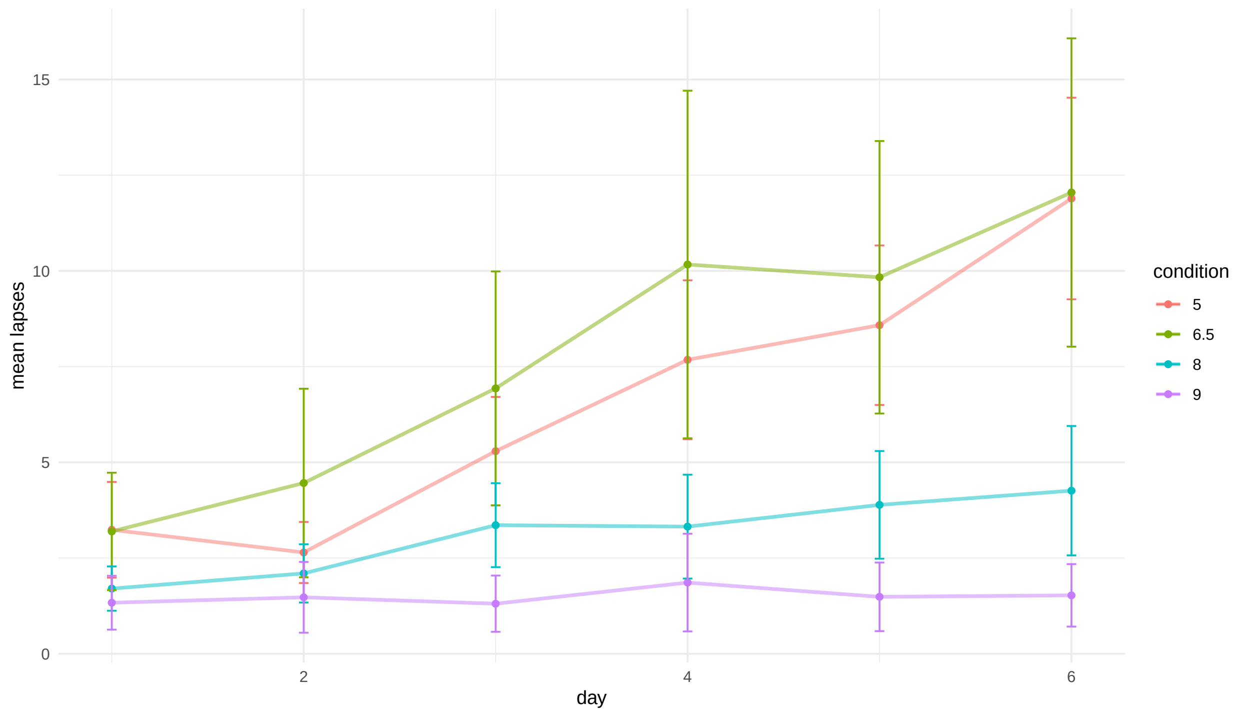
For this analysis, I have mainly focused on no nap conditions. Hence the visualizations below do not include the conditions that had nap time.

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(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
```

Estimates and their 95% confidence intervals

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

```
## 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

Summary

```r
#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)
```

```
## 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
```

Estimates and their 95% confidence intervals

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

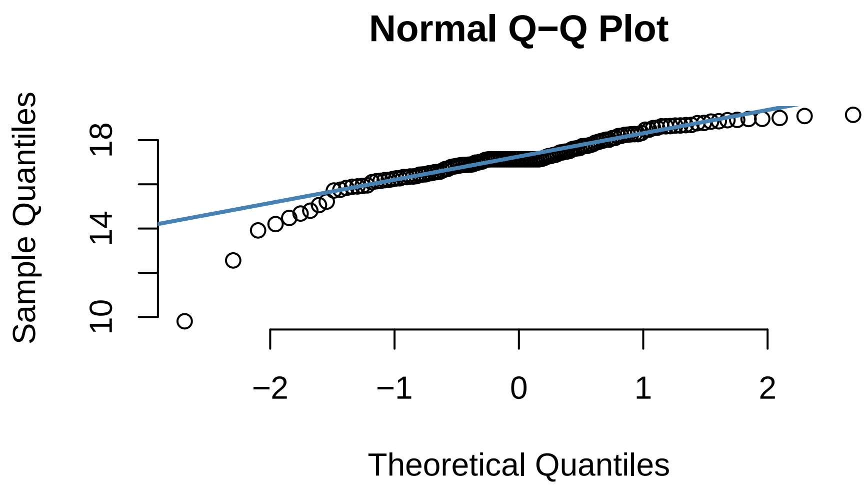
```
## Approximate 95% confidence intervals
##
```

```
##  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

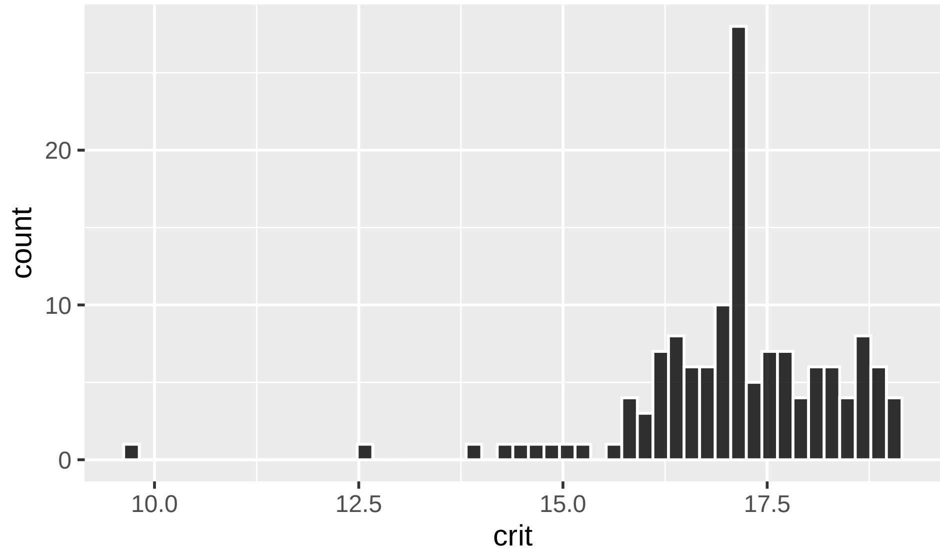
Dot Plot - Critical Wake Durations across participants

QQ Plot - Normality of distribution

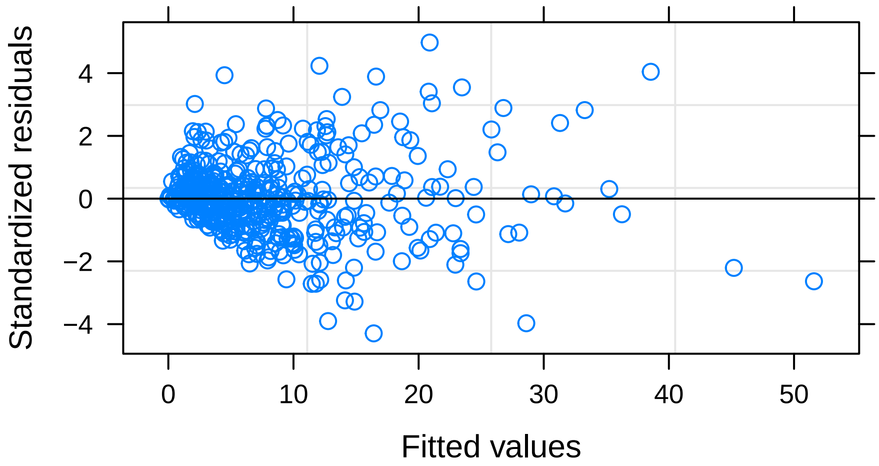


Histogram - Normality of distribution

The plot indicates a left skew. Let's check the histogram

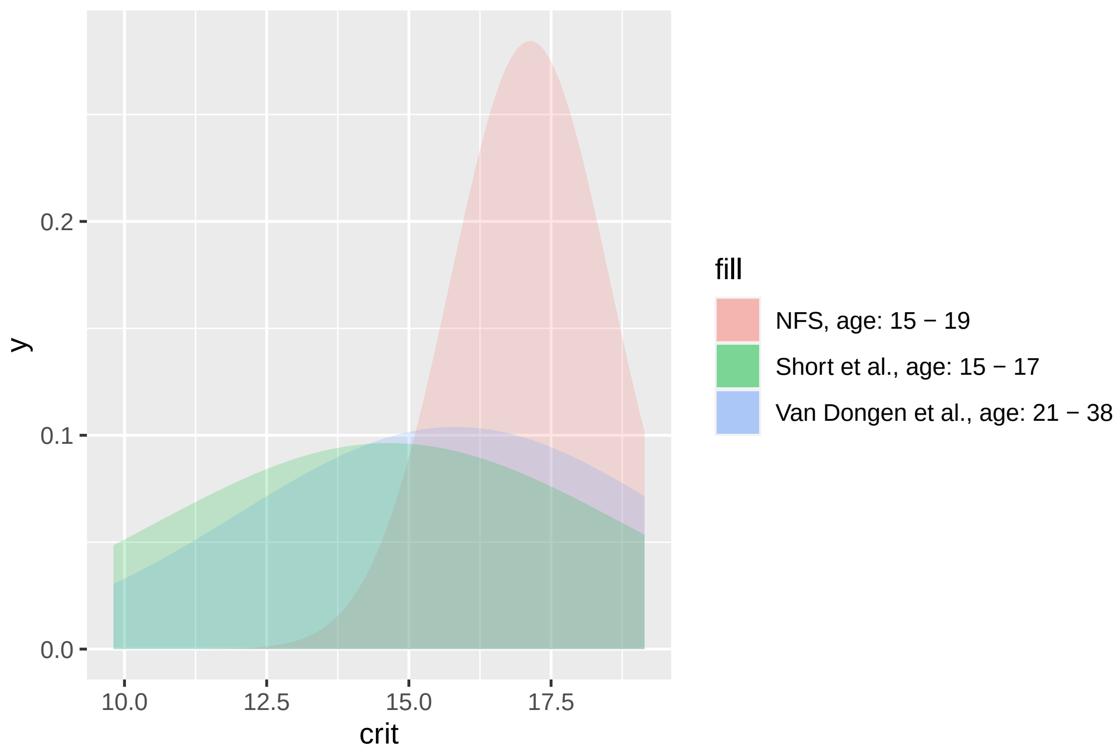


Residuals Plot



Comparison against estimates based on the literature

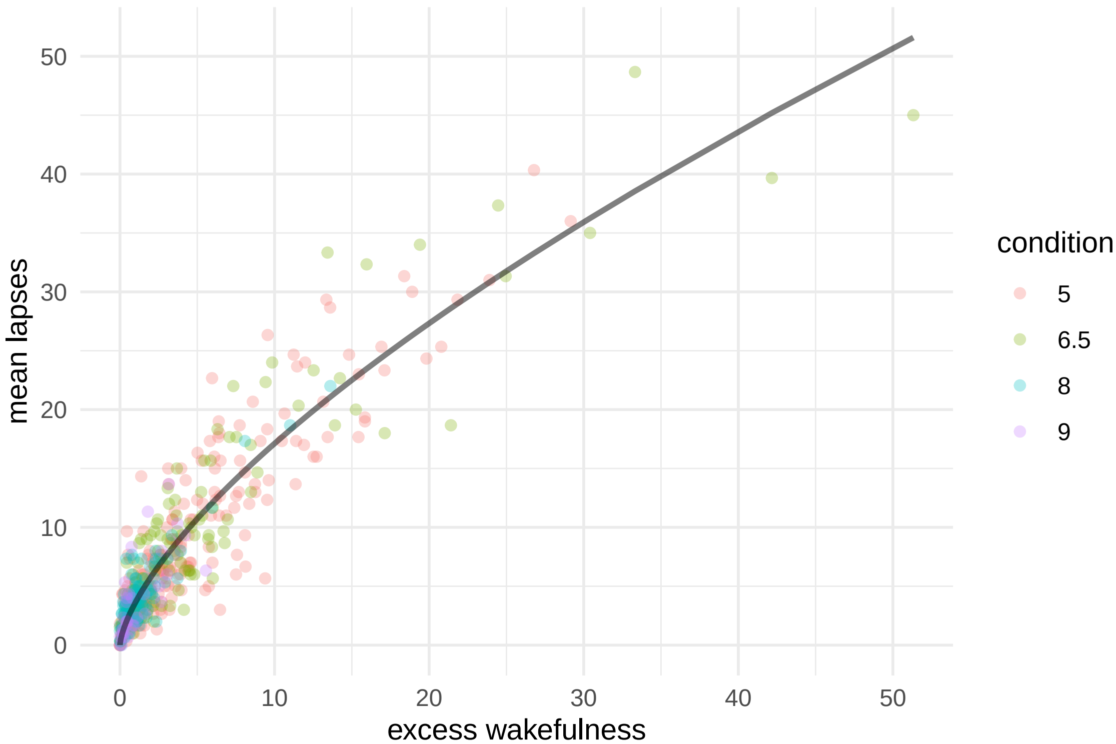
There are clearly some outliers having oversized influence on the distribution. Let's assume normalty for now and compare the distribution obtained from this estimate with Van Dongen et al.(2003) and Short et al. (2018) estimates for the critical waking duration



Mean lapses vs excess wakefulness

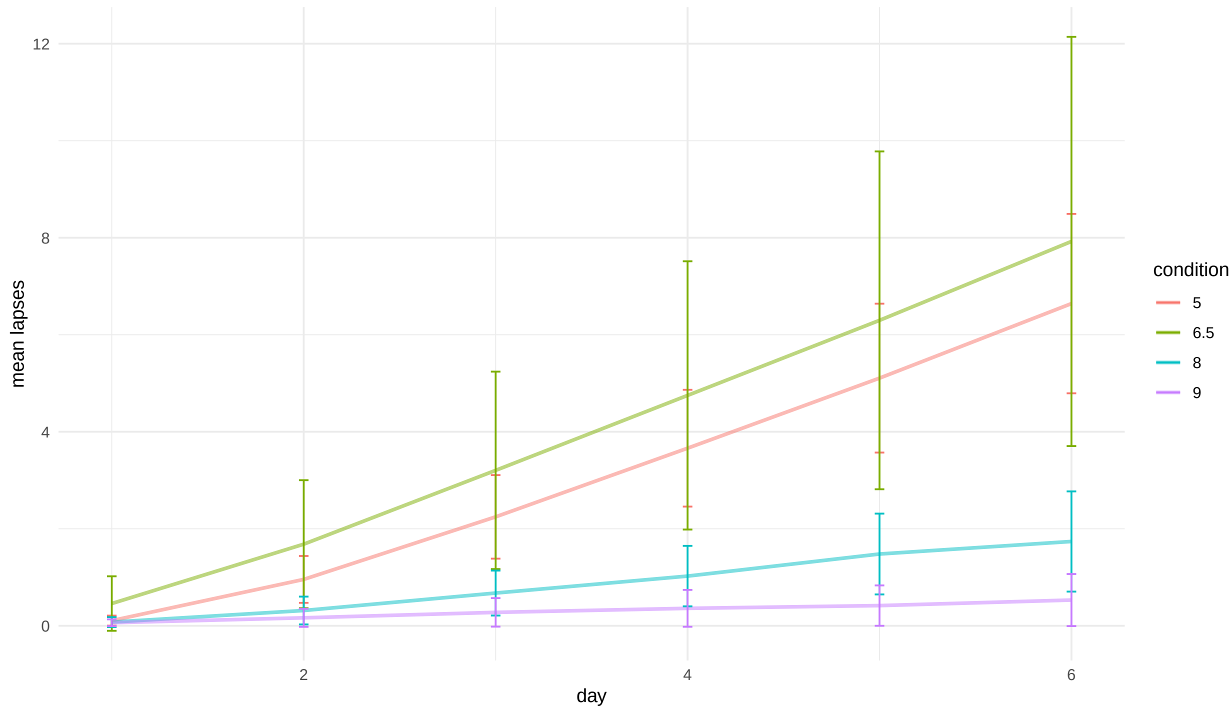
$$lapses = 3.62 * (excess)^{0.67}$$

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.