Cervical Dystonia

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```r
#Loading Libraries
library(haven)
library(data.table)
library(tidyverse)
library(skimr)
library(gridExtra)
library(gtsummary)
library(expss)
library(lme4)
```

```r
#Loading in Data
cerv <- read_dta("cdystonia.dta")

glimpse(cerv)
```

```
Observations: 631
Variables: 7
$ week   <dbl> 0, 2, 4, 8, 12, 16, 0, 2, 4, 8, 12, 16, 0, 2, 4, 8, 12, 16, ...
$ site   <dbl+lbl> 1, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1,...
$ id     <dbl> 1, 1, 1, 1, 1, 1, 2, 2, 2, 2, 2, 2, 3, 3, 3, 3, 3, 3, 4, 4, ...
$ treat  <dbl+lbl> 2, 2, 2, 2, 2, 2, 1, 1, 1, 1, 1, 1, 2, 2, 2, 2, 2, 2, 3,...
$ age    <dbl> 65, 65, 65, 65, 65, 65, 70, 70, 70, 70, 70, 70, 64, 64, 64, ...
$ sex    <dbl+lbl> 1, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1,...
$ twstrs <dbl> 32, 30, 24, 37, 39, 36, 60, 26, 27, 41, 65, 67, 44, 20, 23, ...
```

```r
head(cerv)
```

```
# A tibble: 6 x 7
   week      site    id     treat   age       sex twstrs
  <dbl> <dbl+lbl> <dbl> <dbl+lbl> <dbl> <dbl+lbl>  <dbl>
1     0     1 [1]     1 2 [5000U]    65     1 [F]     32
2     2     1 [1]     1 2 [5000U]    65     1 [F]     30
3     4     1 [1]     1 2 [5000U]    65     1 [F]     24
4     8     1 [1]     1 2 [5000U]    65     1 [F]     37
5    12     1 [1]     1 2 [5000U]    65     1 [F]     39
6    16     1 [1]     1 2 [5000U]    65     1 [F]     36
```

```r
#Mutating the ID variable to capture the Site Location
cerv_dyst <- cerv %>%
            mutate(id = paste0(site, id)) %>%
```

```
            select(-site)

#Mutating the sex variable to numeric, Female = 1
cerv_dyst <- cerv_dyst %>%
            mutate(treat = as.factor(treat), sex = as.numeric(sex)) %>%
            apply_labels(treat = "Treatment", sex = "Sex")
```

Exploratory Analysis

```
#Table recoding
table_cerv <- cerv_dyst %>%
            mutate(
               sex = if_else(sex == 1, "Female", "Male"),
               treat = if_else(treat == 1, "10000U", if_else(
                 treat == 2,"5000U","Placebo")),
               week = paste0("Week ",week),
               week = factor(week, levels = c("Week 0",
                                              "Week 2",
                                              "Week 4",
                                              "Week 8",
                                              "Week 12",
                                              "Week 16")))
#Summary Table by Gender, Week, Treatment
table_cerv %>%
  select(-id, -week, -treat) %>%
  as.data.frame() %>%
  tbl_summary(by = sex) %>%
  add_p() %>%
  bold_p()
```

Characteristic	Female, N = 395[1]	Male, N = 236[1]	p-value[2]
Age [years]	54 (47, 65)	57 (43, 66)	0.9
TWSTRS-total score	44 (34, 52)	40 (31, 50)	0.012

[1]Statistics presented: median (IQR)
[2]Statistical tests performed: Wilcoxon rank-sum test

```
table_cerv %>%
  select(-id, -sex, -week, -age) %>%
  as.data.frame() %>%
  tbl_summary(by = treat) %>%
  add_p() %>%
  bold_p()
```

Characteristic	10000U, N = 213[1]	5000U, N = 211[1]	Placebo, N = 207[1]	p-value[2]
TWSTRS-total score	44 (33, 51)	43 (32, 51)	43 (33, 50)	>0.9

```r
#Histogram of Age and Rating Scales
age_hist <- ggplot(data = cerv_dyst, aes(x = age)) +
            geom_histogram(col = "white", fill = "seagreen3")

twstrs_hist <- ggplot(data = cerv_dyst, aes(x = twstrs)) +
               geom_histogram(col = "white", fill = "seagreen3") +
               labs(x = "Toronto Western Spasmodic Torticollis Rating Scale (TWSTRS)")

set.seed(123)
id_sample <- sample(cerv_dyst$id, 15)

# Plots of 15 random sample individuals
ggplot(data = cerv_dyst %>% filter(id %in% id_sample),
       aes(x = week, y = twstrs)) +
  geom_line() +
  facet_wrap(~id, ncol = 5) +
  theme(strip.background = element_rect(colour="white",
                                        fill="skyblue",
                                        size=4,
                                        linetype="solid")) +
  scale_x_continuous(breaks = c(0, 2, 4, 8, 12, 16)) +
  labs(x = "Week",
       y = "TWSTRS")
```
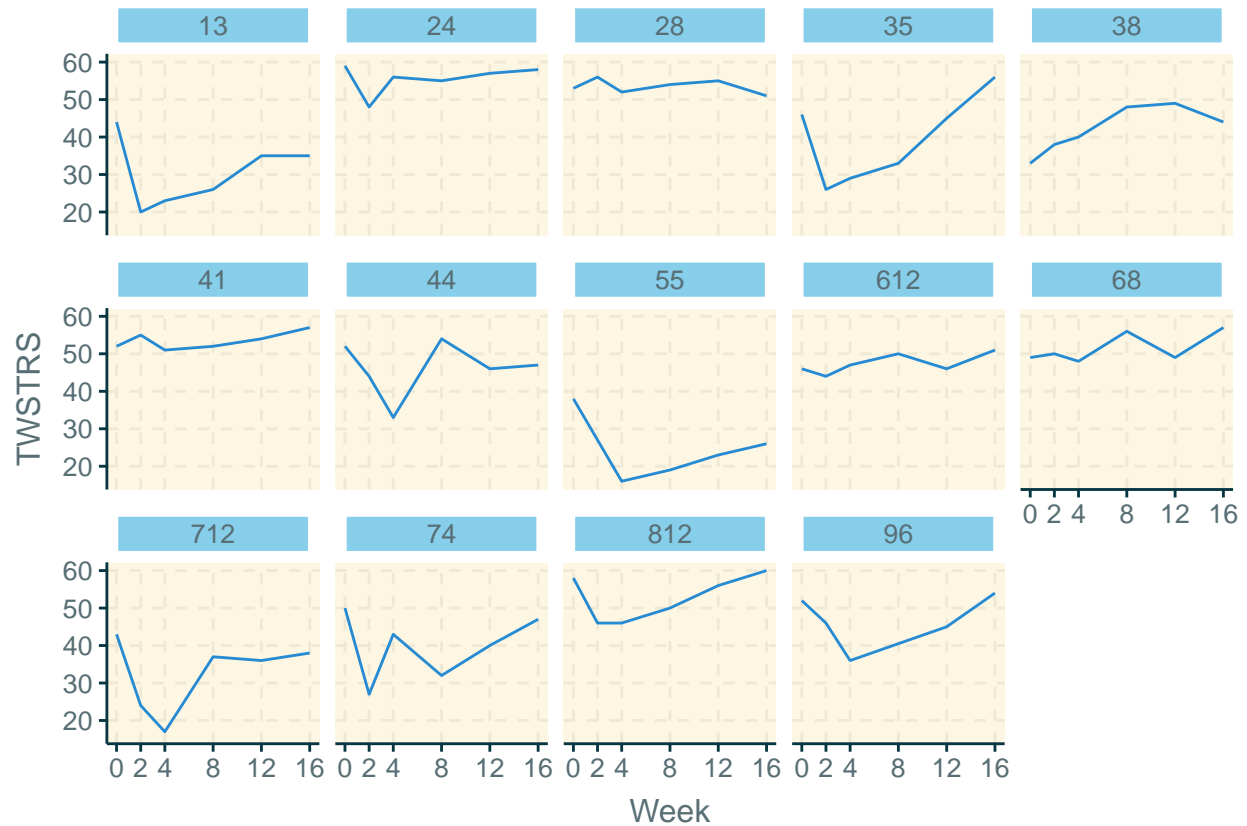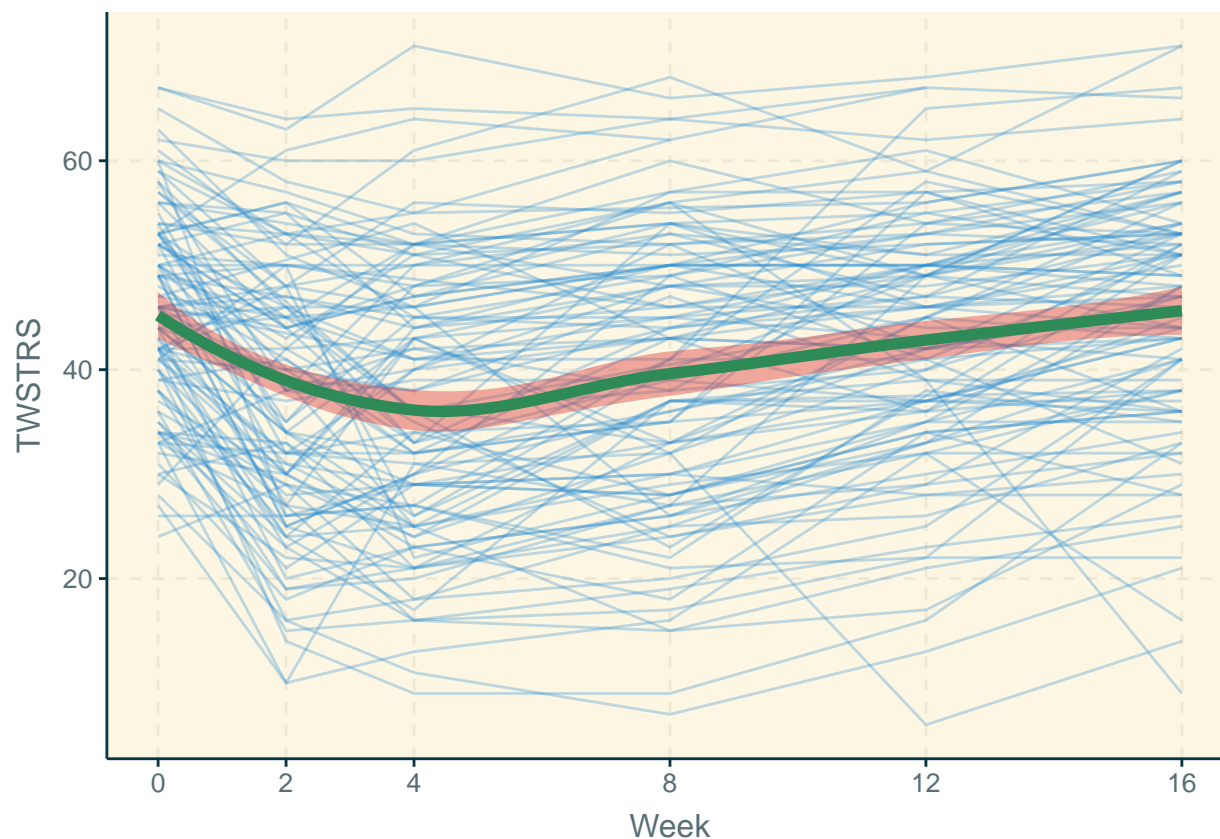
```
# Every individual's change through the weeks with average
ggplot(data = cerv_dyst, aes(x = week, y = twstrs)) +
  geom_line(alpha=0.3, aes(group = id)) +
  geom_smooth(col = "seagreen4", size = 2) +
  scale_x_continuous(breaks = c(0, 2, 4, 8, 12, 16)) +
  labs(x = "Week",
       y = "TWSTRS")
```

`geom_smooth()` using method = 'loess' and formula 'y ~ x'

```
fit_1 <- lmer(data = cerv_dyst,
              twstrs ~ week + age + sex + treat +
              (1|id), REML = F)
fit_2 <- lmer(data = cerv_dyst,
              twstrs ~ week + age + sex + treat +
              (week|id), REML = F)
fit_3 <- lmer(data = cerv_dyst,
              twstrs ~ week + age + sex + treat +
              (0+week|id), REML = F)

anova(fit_2, fit_3, fit_1)
```

```
Data: cerv_dyst
Models:
fit_3: twstrs ~ week + age + sex + treat + (0 + week | id)
fit_1: twstrs ~ week + age + sex + treat + (1 | id)
fit_2: twstrs ~ week + age + sex + treat + (week | id)
      Df    AIC    BIC  logLik deviance   Chisq Chi Df Pr(>Chisq)
fit_3  8 4867.0 4902.6 -2425.5   4851.0
fit_1  8 4576.9 4612.4 -2280.4   4560.9 290.1861      0    <2e-16 ***
fit_2 10 4578.4 4622.9 -2279.2   4558.4   2.4695      2    0.2909
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

```
summary(fit_1)
```

```
Linear mixed model fit by maximum likelihood  ['lmerMod']
Formula: twstrs ~ week + age + sex + treat + (1 | id)
   Data: cerv_dyst

     AIC      BIC   logLik deviance df.resid
  4576.9   4612.4  -2280.4   4560.9      623

Scaled residuals:
    Min      1Q  Median      3Q     Max
-5.0739 -0.5463  0.0273  0.5020  2.9917

Random effects:
 Groups   Name        Variance Std.Dev.
 id       (Intercept) 105.72   10.282
 Residual              52.04    7.214
Number of obs: 631, groups:  id, 109

Fixed effects:
            Estimate Std. Error t value
(Intercept) 42.24251    5.78140   7.307
week         0.24571    0.05114   4.805
age          0.01313    0.08560   0.153
sex         -2.52402    2.16712  -1.165
treat2       0.50567    2.57277   0.197
treat3       0.53281    2.54435   0.209

Correlation of Fixed Effects:
       (Intr) week   age    sex    treat2
week   -0.062
age    -0.829  0.000
sex    -0.472  0.002  0.009
treat2 -0.068 -0.004 -0.047 -0.218
treat3 -0.193  0.000  0.059 -0.145  0.503
```

```
fit_4 <- lmer(data = cerv_dyst,
          twstrs ~ week + age + sex + treat + week*age + week*treat +
          (week|id), REML = F)
fit_5 <- lmer(data = cerv_dyst,
          twstrs ~ week + age + sex + treat + week*age + week*treat +
          (0+week|id), REML = F)
fit_6 <- lmer(data = cerv_dyst,
          twstrs ~ week + age + sex + treat + week*age + week*treat +
          (1|id), REML = F)

anova(fit_4, fit_5, fit_6)
```

```
Data: cerv_dyst
Models:
fit_5: twstrs ~ week + age + sex + treat + week * age + week * treat +
fit_5:     (0 + week | id)
```

```
fit_6: twstrs ~ week + age + sex + treat + week * age + week * treat +
fit_6:     (1 | id)
fit_4: twstrs ~ week + age + sex + treat + week * age + week * treat +
fit_4:     (week | id)
      Df    AIC    BIC  logLik deviance   Chisq Chi Df Pr(>Chisq)
fit_5 11 4870.1 4919.0 -2424.1   4848.1
fit_6 11 4568.4 4617.4 -2273.2   4546.4 301.6882      0      <2e-16 ***
fit_4 13 4571.5 4629.3 -2272.7   4545.5   0.9562      2        0.62
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

`summary(fit_6)`

```
Linear mixed model fit by maximum likelihood  ['lmerMod']
Formula: twstrs ~ week + age + sex + treat + week * age + week * treat +
    (1 | id)
   Data: cerv_dyst

     AIC      BIC   logLik deviance df.resid
  4568.4   4617.4  -2273.2   4546.4      620

Scaled residuals:
    Min      1Q  Median      3Q     Max
-4.7955 -0.5571 -0.0030  0.5609  3.1704

Random effects:
 Groups   Name        Variance Std.Dev.
 id       (Intercept) 105.78   10.285
 Residual              50.63    7.116
Number of obs: 631, groups:  id, 109

Fixed effects:
             Estimate Std. Error t value
(Intercept) 45.411719   6.022331   7.541
week        -0.218724   0.247594  -0.883
age         -0.065617   0.090309  -0.727
sex         -2.505553   2.165405  -1.157
treat2       2.019857   2.706821   0.746
treat3       2.591417   2.679656   0.967
week:age     0.011513   0.004179   2.755
week:treat2 -0.223872   0.122905  -1.822
week:treat3 -0.306266   0.123954  -2.471

Correlation of Fixed Effects:
          (Intr) week   age    sex    treat2 treat3 week:g wk:tr2
week      -0.289
age       -0.840  0.302
sex       -0.454  0.004  0.009
treat2    -0.082  0.064 -0.046 -0.205
treat3    -0.204  0.096  0.061 -0.136  0.501
week:age   0.269 -0.937 -0.321 -0.002  0.012 -0.020
week:treat2 0.063 -0.202  0.012 -0.008 -0.313 -0.154 -0.046
week:treat3 0.088 -0.290 -0.020 -0.005 -0.151 -0.316  0.049  0.489
```

```
par(mfrow=c(2,1))
a <- plot(fit_6)
b <- lattice::qqmath(fit_6)
gridExtra::grid.arrange(a,b, heights = 10)
```