

Martel Paper - Daily OA Pain

2024-03-18

Data Wrangling

```
## Load packages
library(tidyverse)
library(ggplot2)
library(tidyr)
library(haven) ## This library provides functions to read sav file into R
library(lme4)
library(lmerTest)

## Read data
data_paper <- read_sav("Dataset; 2024.1.sav")
checkdf3 <- data_paper |>
  subset(ID == 2072) |>
  select(c(ID,
           Level1_Even_DateIn,
           Level1_Even_TimeIn,
           Wave_Day))

## Delete Weird ID 2072 those weird reporting days
data_paper <- data_paper |>
  filter(!(ID == 2072 & Wave_Day >= 7))
```

Adjusting Wave Day

- DT_i combines D_i and T_i : 'DateTime' variable
- DT_0 is the first response 'DateTime' for each patient
- W_i is the adjusted 'Wave_Day' variable
- Add a grace period G for calculating the adjusted W_i , in our case $G = 6$ hours
- Calculate the datetime difference H_i in **hours** from the first response, incorporating the grace period:

$$H_i = DT_i - DT_{i-1}$$

- Then apply the grace period indicator I_i :

$$I_i = \begin{cases} 1 & \text{if } H_i \leq 24 + G \\ \left\lceil \frac{H_i - G}{24} \right\rceil & \text{otherwise} \end{cases}$$

- The initial response for ‘Wave_Day’ is 1, i.e., $W_0 = 1$, then the adjusted ‘Wave_Day’ W_i is

$$W_i = \sum_{i=0}^{i-1} I_i$$

```
## Consecutive Days - Grace Period 6 hours
data_paper <- data_paper |>
  mutate(Lev1_DateTimeIn = as.POSIXct(strptime(paste(Level1_Even_DateIn,
                                                    Level1_Even_TimeIn),
                                                    format="%Y-%m-%d %H:%M:")) |>

  arrange(ID, Lev1_DateTimeIn) |>
  group_by(ID) |>
  mutate(
    TimeDiffHours = as.numeric(difftime(Lev1_DateTimeIn,
                                         lag(Lev1_DateTimeIn,
                                              default = first(Lev1_DateTimeIn)),
                                         units = "hours")), # T diff

    WithinGracePeriod = if_else(TimeDiffHours <= 30,
                                1,
                                ceiling((TimeDiffHours - 6) / 24)), # Check grace perio

    Wave_Day_Adjusted = cumsum(WithinGracePeriod) # Adjusted Wave_Day
  ) |>
  ungroup()

##### Check if the above approach is correct #####
checkdf <- data_paper |> select(c(ID,
                                Lev1_DateTimeIn,
                                TimeDiffHours,
                                WithinGracePeriod,
                                Wave_Day_Adjusted,
                                Baseline_Demog_BMI))
checkdf2 <- checkdf |> subset(ID == 2072) # Weird ID 2072
max(checkdf$Wave_Day_Adjusted, na.rm = TRUE)
```

```
## [1] 21
```

```
## Fill in the gap of Wave_Day
data_paper2 <- data_paper |>
  group_by(ID) |>
  complete(Wave_Day = 1:14) |>
  ungroup()
```

```
## Check the aberrant values
summary(data_paper2$IndexLev1_NegativeAffect_Total) # Lev 1 Negative Affect
summary(data_paper2$IndexLev1_Catastrophizing_Total) # Lev 1 Catas
summary(data_paper2$IndexLev2_QST_BaselinePPTh) # Lev 2 PPTs?
summary(data_paper2$IndexLev2_QST_TSPAve) # Lev 2 TSP?
summary(data_paper2$IndexLev2_QST_CpmTrialAve) # Lev 2 CPM?
summary(data_paper2$IndexLev1_PainAverage) # Lev 1 Pain?

##### Check if lagged value is correct #####
data_paper2_check <- data_paper2 |>
  select(c(ID, Wave_Day_Adjusted, IndexLev1_PainAverage, IndexLev1_PainAverage_Lagged))
```

$$APE(t_i) = I(PAIN(t_i) - PAIN(t_i - 1) \geq 20)$$

```
## APE index
data_paper2 <- data_paper2 |>
  group_by(ID) |>
  mutate(APE = ifelse(IndexLev1_PainAverage - IndexLev1_PainAverage_Lagged >= 20, 1, 0))

##### Check if it is correctly coded #####
data_paper2_check <- data_paper2 |>
  select(c(ID, Wave_Day_Adjusted,
           IndexLev1_PainAverage,
           IndexLev1_PainAverage_Lagged,
           APE))
```

For calculating the RPE based on the within person mean, define the indicator that the pain is above the average pain for person i on day t_i . Note that $n_{t_i} = \max t_i$ for patient i .

$$A(t_i) = I\left(PAIN(t_i) > \frac{1}{n_{t_i}} \sum_{t_i=1}^{n_{t_i}} PAIN(t_i)\right)$$

Then define the RPE given $A(t_i) = 1$ for person i on day t_i .

$$RPE(t_i) = I\left(PAIN(t_i) \leq \frac{1}{n_{t_i}} \sum_{t_i=1}^{n_{t_i}} PAIN(t_i)\right) \times A(t_i - 1)$$

```
## RPE Index using within person mean
data_paper2 <- data_paper2 |>
  group_by(ID) |>
  mutate(AVE = mean(IndexLev1_PainAverage, na.rm = TRUE),
         A = ifelse(IndexLev1_PainAverage > AVE, 1, 0),
         A_lag = lag(A),
         Lev1_RPE_useMean = ifelse(A_lag == 1,
```

```

                                ifelse(IndexLev1_PainAverage <= AVE, 1, 0), 0))

##### Check #####
data_paper2_check <- data_paper2 |>
  select(c(ID, Wave_Day_Adjusted, IndexLev1_PainAverage, IndexLev1_PainAverage_Lagged,
          AVE, A, A_lag, Lev1_RPE_useMean))
# 203 RPEs

```

For calculating the RPE based on the APE,

$$RPE(t_i) = I\left(PAIN(t_i) \leq \frac{1}{n_{t_i}} \sum_{t_i=1}^{n_{t_i}} PAIN(t_i)\right) \times APE(t_i - 1)$$

```

## RPE Index using APE
data_paper2 <- data_paper2 |>
  group_by(ID) |>
  mutate(APE_lag = lag(APE),
         Lev1_RPE_useAPE = ifelse(APE_lag == 1,
                                ifelse(IndexLev1_PainAverage <= 20, 1, 0), 0))

##### Check #####
data_paper2_check <- data_paper2 |>
  select(c(ID, Wave_Day_Adjusted, IndexLev1_PainAverage, IndexLev1_PainAverage_Lagged,
          APE, APE_lag, Lev1_RPE_useAPE))
# 4 RPEs

```

Analysis of APE using the Table in the Manuscript

```

## Unadjusted APE to Negative Affect
model_APE.NA <- glmer(APE ~ IndexLev1_NegativeAffect_Total + (1|ID), family = binomial())
summary(model_APE.NA)

## Unadjusted APE to Catastrophizing
model_APE.Cata <- glmer(APE ~ IndexLev1_Catastrophizing_Total + (1|ID), family = binomial())
summary(model_APE.Cata)

## Unadjusted APE to PPTs
model_APE.PPTs <- glmer(APE ~ IndexLev2_QST_BaselinePPTs + (1|ID), family = binomial())

## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl = control$checkConv, :
## Model failed to converge with max|grad| = 0.00456606 (tol = 0.002, component 1)

## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl = control$checkConv, : Model
## - Rescale variables?;Model is nearly unidentifiable: large eigenvalue ratio
## - Rescale variables?

```

```
summary(model_APE.PPThs)

## Unadjusted APE to TSP
model_APE.TSP <- glmer(APE ~ IndexLev2_QST_TSPAve + (1|ID), family = binomial(), data =
summary(model_APE.TSP)

## Unadjusted APE to CPM
model_APE.CPM <- glmer(APE ~ IndexLev2_QST_CpmTrialAve + (1|ID), family = binomial(), da

## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl = control$checkConv, : Model
## - Rescale variables?

summary(model_APE.CPM)

## Adjusted APE
model_APE <- glmer(APE ~ IndexLev1_Catastrophizing_Total + IndexLev1_NegativeAffect_Tota
summary(model_APE)

model_APE_2 <- glmer(APE ~ IndexLev2_QST_CpmTrialAve + IndexLev2_QST_TSPAve + IndexLev2_

## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl = control$checkConv, :
## Model failed to converge with max|grad| = 0.0082882 (tol = 0.002, component 1)

## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl = control$checkConv, : Model
## - Rescale variables?;Model is nearly unidentifiable: large eigenvalue ratio
## - Rescale variables?

summary(model_APE_2)
```

Analysis of RPE using the Table of Manuscript

```
## Unadjusted RPE to Negative Affect
model_RPE.NA <- glmer(Lev1_RPE_useMean ~ IndexLev1_NegativeAffect_Total + (1|ID), family

## boundary (singular) fit: see help('isSingular')

summary(model_RPE.NA)

## Unadjusted RPE to Catastrophizing
model_RPE.Cata <- glmer(Lev1_RPE_useMean ~ IndexLev1_Catastrophizing_Total + (1|ID), fam

## boundary (singular) fit: see help('isSingular')

summary(model_RPE.Cata)

## Unadjusted RPE to PPThs
model_RPE.PPThs <- glmer(Lev1_RPE_useMean ~ IndexLev2_QST_BaselinePPTh + (1|ID), family
```

```
## boundary (singular) fit: see help('isSingular')
summary(model_RPE.PPThs)

## Unadjusted RPE to TSP
model_RPE.TSP <- glmer(Lev1_RPE_useMean ~ IndexLev2_QST_TSPAve + (1|ID), family = binomial)

## boundary (singular) fit: see help('isSingular')
summary(model_RPE.TSP)

## Unadjusted RPE to CPM
model_RPE.CPM <- glmer(Lev1_RPE_useMean ~ IndexLev2_QST_CpmTrialAve + (1|ID), family = binomial)

## boundary (singular) fit: see help('isSingular')
summary(model_RPE.CPM)

## Adjusted RPE
model_RPE <- glmer(Lev1_RPE_useMean ~ IndexLev1_Catastrophizing_Total + IndexLev1_Negative_Affect_Total)

## boundary (singular) fit: see help('isSingular')
summary(model_RPE)

model_RPE_2 <- glmer(Lev1_RPE_useMean ~ IndexLev2_QST_CpmTrialAve + IndexLev2_QST_TSPAve)

## boundary (singular) fit: see help('isSingular')
summary(model_RPE_2)
```

Adjusting more confounding factors

```
## Consider age, sex, BMI,... (Lvl2) for APE
model_APE_2_conf <- glmer(APE ~ IndexLev2_QST_CpmTrialAve + IndexLev2_QST_TSPAve + IndexLev2_QST_CpmTrialAve:IndexLev2_QST_TSPAve)

## boundary (singular) fit: see help('isSingular')
summary(model_APE_2_conf)

## Consider age, sex, BMI,... (Lvl2) for RPE
model_RPE_2_conf <- glmer(Lev1_RPE_useMean ~ IndexLev2_QST_CpmTrialAve + IndexLev2_QST_TSPAve + IndexLev2_QST_CpmTrialAve:IndexLev2_QST_TSPAve)

## boundary (singular) fit: see help('isSingular')
summary(model_RPE_2_conf)
```

These seem to have no confounding effects...

Lev1 and Lev2 Together for APE and RPE

```
model_APE_conf <- glmer(APE ~ IndexLev1_Catastrophizing_Total + IndexLev1_NegativeAffect

## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl = control$checkConv, :
## Model failed to converge with max|grad| = 0.0683676 (tol = 0.002, component 1)

## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl = control$checkConv, : Model
## - Rescale variables?

summary(model_APE_conf)

model_RPE_conf <- glmer(Lev1_RPE_useMean ~ IndexLev1_Catastrophizing_Total + IndexLev1_M

## boundary (singular) fit: see help('isSingular')

summary(model_RPE_conf)
```

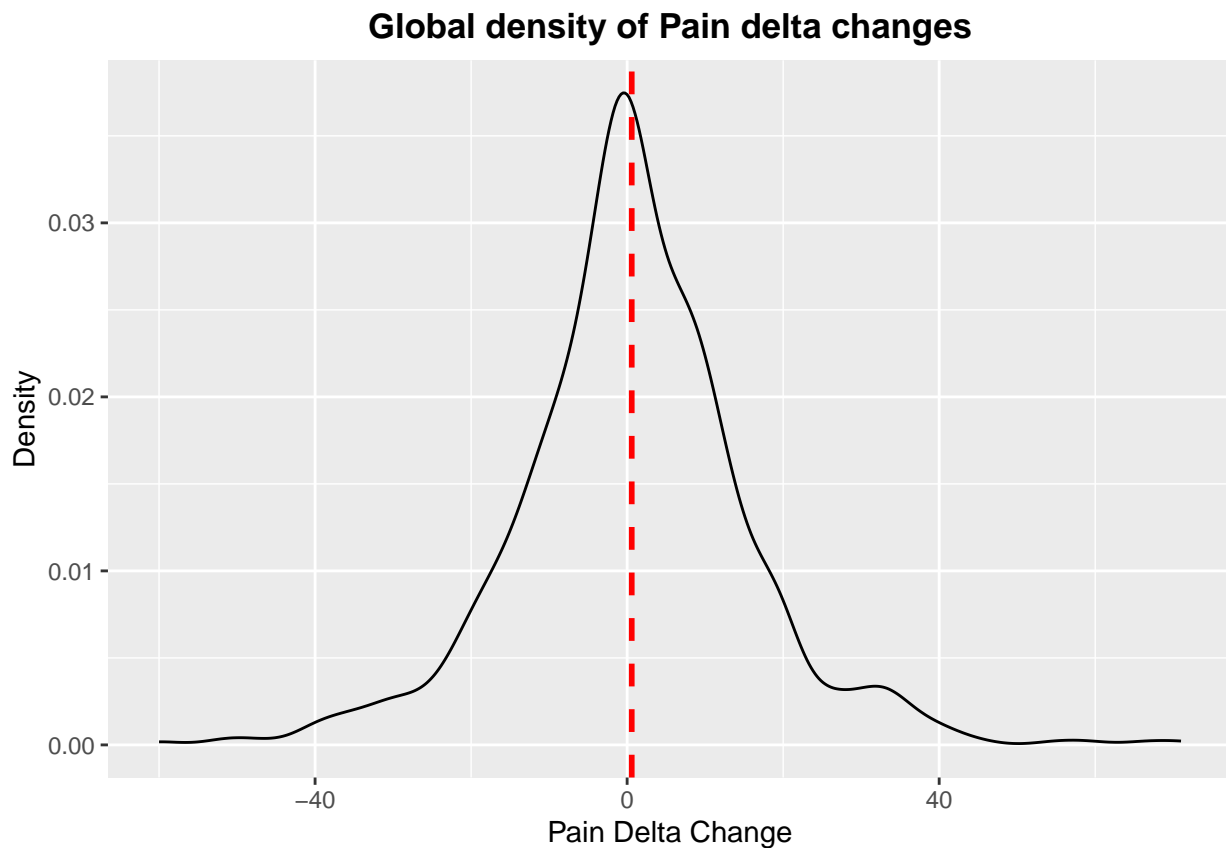
According to the meeting with Dr. Marc O. Martel on Apr. 12, the above results are not sufficient.

Results after Apr. 12

```
## Day-to-day delta change score in pain (From yesterday to today), check normality
ggplot(data_paper2, aes(x = IndexLev1_PainAverage_RawChange)) +
  geom_density() +
  geom_vline(aes(xintercept = mean(IndexLev1_PainAverage_RawChange, na.rm = TRUE)),
             color = "red", linetype = "dashed", size = 1) + # 1399 out of 2212 have mi
  labs(title = "Global density of Pain delta changes",
       x = "Pain Delta Change",
       y = "Density") +
  theme(plot.title = element_text(hjust = 0.5, face = "bold")) # It looks normal to me
```

```
## Warning: Using `size` aesthetic for lines was deprecated in ggplot2 3.4.0.
## i Please use `linewidth` instead.
## This warning is displayed once every 8 hours.
## Call `lifecycle::last_lifecycle_warnings()` to see where this warning was
## generated.

## Warning: Removed 1399 rows containing non-finite outside the scale range
## (`stat_density()`).
```



```
## Shapiro test (Formal test of normality)
normal_check <- data_paper2$IndexLev1_PainAverage_RawChange[!is.na(data_paper2$IndexLev1_PainAverage_RawChange)]
```



```
shapiro.test(normal_check) # Although the formal test does not suggest normality
```

```
##
## Shapiro-Wilk normality test
##
## data: normal_check
## W = 0.97198, p-value = 2.216e-11
```

The below will examine if baseline covairates are associated with the delta pain change individually.

```
## Age
model_age <- lmer(IndexLev1_PainAverage_RawChange ~ Baseline_Demog_Age + (1|ID), data =
```

```
## boundary (singular) fit: see help('isSingular')
```

```
summary(model_age)
```

```
## Linear mixed model fit by REML. t-tests use Satterthwaite's method [
## lmerModLmerTest]
## Formula: IndexLev1_PainAverage_RawChange ~ Baseline_Demog_Age + (1 | ID)
## Data: data_paper2
##
## REML criterion at convergence: 6634.2
##
## Scaled residuals:
##      Min       1Q   Median       3Q      Max
## -4.1109 -0.5294 -0.0235  0.5383  4.7535
##
## Random effects:
## Groups Name Variance Std.Dev.
## ID      (Intercept) 0.0 0.00
## Residual 221.8 14.89
## Number of obs: 805, groups: ID, 155
##
## Fixed effects:
##              Estimate Std. Error      df t value Pr(>|t|)
## (Intercept)    3.80726    4.14557 803.00000  0.918  0.359
## Baseline_Demog_Age -0.04870    0.06225 803.00000 -0.782  0.434
##
## Correlation of Fixed Effects:
##              (Intr)
## Bsln_Dmg_Ag -0.992
## optimizer (nloptwrap) convergence code: 0 (OK)
## boundary (singular) fit: see help('isSingular')
```

Sex

```
model_sex <- lmer(IndexLev1_PainAverage_RawChange ~ Baseline_Demog_Sex + (1|ID), data =
```

```
## boundary (singular) fit: see help('isSingular')
```

```
summary(model_sex)
```

```
## Linear mixed model fit by REML. t-tests use Satterthwaite's method [
## lmerModLmerTest]
## Formula: IndexLev1_PainAverage_RawChange ~ Baseline_Demog_Sex + (1 | ID)
## Data: data_paper2
##
## REML criterion at convergence: 6693.8
##
## Scaled residuals:
##      Min       1Q   Median       3Q      Max
## -4.0760 -0.5161 -0.0313  0.5586  4.7231
##
## Random effects:
## Groups Name Variance Std.Dev.
## ID      (Intercept) 0.0      0.00
## Residual                221.6    14.89
## Number of obs: 813, groups: ID, 157
##
## Fixed effects:
##              Estimate Std. Error      df t value Pr(>|t|)
## (Intercept)    0.2498    1.7464 811.0000   0.143   0.886
## Baseline_Demog_Sex 0.2168    1.0568 811.0000   0.205   0.838
##
## Correlation of Fixed Effects:
##              (Intr)
## Bsln_Dmg_Sx -0.954
## optimizer (nloptwrap) convergence code: 0 (OK)
## boundary (singular) fit: see help('isSingular')
```

BMI

```
model_bmi <- lmer(IndexLev1_PainAverage_RawChange ~ Baseline_Demog_BMI + (1|ID), data =
```

```
## boundary (singular) fit: see help('isSingular')
```

```
summary(model_bmi)
```

```
## Linear mixed model fit by REML. t-tests use Satterthwaite's method [
## lmerModLmerTest]
## Formula: IndexLev1_PainAverage_RawChange ~ Baseline_Demog_BMI + (1 | ID)
## Data: data_paper2
##
```

```
## REML criterion at convergence: 6548.7
##
## Scaled residuals:
##      Min       1Q   Median       3Q      Max
## -4.0854 -0.5285 -0.0161  0.5370  4.6831
##
## Random effects:
##   Groups   Name                Variance Std.Dev.
##   ID       (Intercept)         0.0      0.00
##   Residual                    225.8    15.03
## Number of obs: 793, groups: ID, 153
##
## Fixed effects:
##              Estimate Std. Error      df t value Pr(>|t|)
## (Intercept)    -2.55505     2.70231 791.00000   -0.946    0.345
## Baseline_Demog_BMI  0.10209     0.08595 791.00000    1.188    0.235
##
## Correlation of Fixed Effects:
##              (Intr)
## Bsln_Dm_BMI -0.980
## optimizer (nloptwrap) convergence code: 0 (OK)
## boundary (singular) fit: see help('isSingular')
```

Ethnicity

```
model_ethn <- lmer(IndexLev1_PainAverage_RawChange ~ Baseline_Demog_Ethnicity_Rec + (1|ID))
```

```
## boundary (singular) fit: see help('isSingular')
```

```
summary(model_ethn)
```

```
## Linear mixed model fit by REML. t-tests use Satterthwaite's method [
## lmerModLmerTest]
## Formula: IndexLev1_PainAverage_RawChange ~ Baseline_Demog_Ethnicity_Rec +
##      (1 | ID)
##      Data: data_paper2
##
## REML criterion at convergence: 5707.2
##
## Scaled residuals:
##      Min       1Q   Median       3Q      Max
## -4.0600 -0.5292 -0.0100  0.5367  4.6671
##
## Random effects:
##   Groups   Name                Variance Std.Dev.
##   ID       (Intercept)         0.0      0.00
##   Residual                    225.3    15.01
```

```
## Number of obs: 692, groups: ID, 132
##
## Fixed effects:
##               Estimate Std. Error      df t value Pr(>|t|)
## (Intercept)    -0.1436    1.4936 690.0000  -0.096    0.923
## Baseline_Demog_Ethnicity_Rec  1.0869    1.6162 690.0000   0.672    0.502
##
## Correlation of Fixed Effects:
##              (Intr)
## Bsln_Dm_E_R -0.924
## optimizer (nloptwrap) convergence code: 0 (OK)
## boundary (singular) fit: see help('isSingular')

## SmokePerday
model_smoke <- lmer(IndexLev1_PainAverage_RawChange ~ Baseline_Lifestyle_SmokePerday + (

## boundary (singular) fit: see help('isSingular')

summary(model_smoke)

## Linear mixed model fit by REML. t-tests use Satterthwaite's method [
## lmerModLmerTest]
## Formula: IndexLev1_PainAverage_RawChange ~ Baseline_Lifestyle_SmokePerday +
##          (1 | ID)
##      Data: data_paper2
##
## REML criterion at convergence: 6698.1
##
## Scaled residuals:
##      Min       1Q   Median       3Q      Max
## -4.0891 -0.5485 -0.0105  0.5275  4.7640
##
## Random effects:
##  Groups   Name                Variance Std.Dev.
##  ID       (Intercept)         0.0      0.00
##  Residual                    221.1    14.87
## Number of obs: 813, groups: ID, 157
##
## Fixed effects:
##               Estimate Std. Error      df t value Pr(>|t|)
## (Intercept)    0.15585    0.60882 811.00000   0.256    0.798
## Baseline_Lifestyle_SmokePerday  0.06520    0.04699 811.00000   1.387    0.166
##
## Correlation of Fixed Effects:
##              (Intr)
## Bsln_Lfs_SP -0.516
```

```
## optimizer (nloptwrap) convergence code: 0 (OK)
## boundary (singular) fit: see help('isSingular')

## Meds_Acetaminophen
model_acetam <- lmer(IndexLev1_PainAverage_RawChange ~ Baseline_Meds_Acetaminophen + (1|ID), data = data_paper2)

## boundary (singular) fit: see help('isSingular')

summary(model_acetam)

## Linear mixed model fit by REML. t-tests use Satterthwaite's method [
## lmerModLmerTest]
## Formula: IndexLev1_PainAverage_RawChange ~ Baseline_Meds_Acetaminophen +
##      (1 | ID)
##      Data: data_paper2
##
## REML criterion at convergence: 6059.2
##
## Scaled residuals:
##      Min       1Q   Median       3Q      Max
## -4.1575 -0.5174 -0.0367  0.5367  4.8396
##
## Random effects:
##   Groups      Name      Variance Std.Dev.
##   ID          (Intercept)    0      0.00
##   Residual                212      14.56
## Number of obs: 740, groups: ID, 141
##
## Fixed effects:
##              Estimate Std. Error      df t value Pr(>|t|)
## (Intercept)      0.5342    0.6531 738.0000   0.818   0.414
## Baseline_Meds_Acetaminophen -0.1309    1.1397 738.0000  -0.115   0.909
##
## Correlation of Fixed Effects:
##              (Intr)
## Bsln_Mds_Ac -0.573
## optimizer (nloptwrap) convergence code: 0 (OK)
## boundary (singular) fit: see help('isSingular')

## NSAID
model_NSAID <- lmer(IndexLev1_PainAverage_RawChange ~ Baseline_Meds_NSAID + (1|ID), data = data_paper2)

## boundary (singular) fit: see help('isSingular')

summary(model_NSAID)

## Linear mixed model fit by REML. t-tests use Satterthwaite's method [
## lmerModLmerTest]
```

```
## Formula: IndexLev1_PainAverage_RawChange ~ Baseline_Meds_NSAID + (1 | ID)
## Data: data_paper2
##
## REML criterion at convergence: 6105
##
## Scaled residuals:
##      Min       1Q   Median       3Q      Max
## -4.1942 -0.4919 -0.0100  0.5561  4.8245
##
## Random effects:
## Groups   Name                Variance Std.Dev.
## ID       (Intercept)          0         0.00
## Residual                    211        14.53
## Number of obs: 746, groups: ID, 142
##
## Fixed effects:
##              Estimate Std. Error      df t value Pr(>|t|)
## (Intercept)      0.9221    0.7593 744.0000   1.215    0.225
## Baseline_Meds_NSAID -0.7774    1.0638 744.0000  -0.731    0.465
##
## Correlation of Fixed Effects:
##              (Intr)
## Bsl_M_NSAID -0.714
## optimizer (nloptwrap) convergence code: 0 (OK)
## boundary (singular) fit: see help('isSingular')

## Cox2
model_cox2 <- lmer(IndexLev1_PainAverage_RawChange ~ Baseline_Meds_Cox2 + (1|ID), data =
## boundary (singular) fit: see help('isSingular')

summary(model_cox2)

## Linear mixed model fit by REML. t-tests use Satterthwaite's method [
## lmerModLmerTest]
## Formula: IndexLev1_PainAverage_RawChange ~ Baseline_Meds_Cox2 + (1 | ID)
## Data: data_paper2
##
## REML criterion at convergence: 6103
##
## Scaled residuals:
##      Min       1Q   Median       3Q      Max
## -4.1660 -0.5185 -0.0367  0.5827  4.8495
##
## Random effects:
## Groups   Name                Variance Std.Dev.
```

```

## ID (Intercept) 0.0 0.00
## Residual 211.1 14.53
## Number of obs: 746, groups: ID, 142
##
## Fixed effects:
## Estimate Std. Error df t value Pr(>|t|)
## (Intercept) 0.5336 0.5378 744.0000 0.992 0.321
## Baseline_Meds_Cox2 -0.3461 3.6722 744.0000 -0.094 0.925
##
## Correlation of Fixed Effects:
## (Intr)
## Bsln_Mds_C2 -0.146
## optimizer (nloptwrap) convergence code: 0 (OK)
## boundary (singular) fit: see help('isSingular')

## Antidepressants
model_antidep <- lmer(IndexLev1_PainAverage_RawChange ~ Baseline_Meds_Antidepressants +

## boundary (singular) fit: see help('isSingular')

summary(model_antidep)

## Linear mixed model fit by REML. t-tests use Satterthwaite's method [
## lmerModLmerTest]
## Formula: IndexLev1_PainAverage_RawChange ~ Baseline_Meds_Antidepressants +
## (1 | ID)
## Data: data_paper2
##
## REML criterion at convergence: 6104.3
##
## Scaled residuals:
## Min 1Q Median 3Q Max
## -4.1600 -0.5119 -0.0301 0.5326 4.8569
##
## Random effects:
## Groups Name Variance Std.Dev.
## ID (Intercept) 0.0 0.00
## Residual 211.1 14.53
## Number of obs: 746, groups: ID, 142
##
## Fixed effects:
## Estimate Std. Error df t value Pr(>|t|)
## (Intercept) 0.4377 0.5630 744.0000 0.777 0.437
## Baseline_Meds_Antidepressants 0.8248 1.7191 744.0000 0.480 0.632
##
## Correlation of Fixed Effects:

```

```
##          (Intr)
## Bsln_Mds_An -0.327
## optimizer (nloptwrap) convergence code: 0 (OK)
## boundary (singular) fit: see help('isSingular')

## Baseline_Meds_Anxiolytics
model_anxioly <- lmer(IndexLev1_PainAverage_RawChange ~ Baseline_Meds_Anxiolytics + (1|ID))

## boundary (singular) fit: see help('isSingular')

summary(model_anxioly)

## Linear mixed model fit by REML. t-tests use Satterthwaite's method [
## lmerModLmerTest]
## Formula: IndexLev1_PainAverage_RawChange ~ Baseline_Meds_Anxiolytics +
##          (1 | ID)
##      Data: data_paper2
##
## REML criterion at convergence: 6104
##
## Scaled residuals:
##      Min       1Q   Median       3Q      Max
## -4.1661 -0.5186 -0.0369  0.5825  4.8494
##
## Random effects:
##      Groups      Name      Variance Std.Dev.
##      ID          (Intercept)  0.0      0.00
##      Residual                211.1    14.53
## Number of obs: 746, groups: ID, 142
##
## Fixed effects:
##              Estimate Std. Error      df t value Pr(>|t|)
## (Intercept)      0.5357    0.5488 744.0000   0.976   0.329
## Baseline_Meds_Anxiolytics -0.1579    2.2345 744.0000  -0.071   0.944
##
## Correlation of Fixed Effects:
##          (Intr)
## Bsln_Mds_An -0.246
## optimizer (nloptwrap) convergence code: 0 (OK)
## boundary (singular) fit: see help('isSingular')

## MuscleRelaxants
model_musclerelax <- lmer(IndexLev1_PainAverage_RawChange ~ Baseline_Meds_MuscleRelaxants + (1|ID))

## boundary (singular) fit: see help('isSingular')
```



```
summary(model_musclerelax)
```

```
## Linear mixed model fit by REML. t-tests use Satterthwaite's method [
## lmerModLmerTest]
## Formula: IndexLev1_PainAverage_RawChange ~ Baseline_Meds_MuscleRelaxants +
##      (1 | ID)
##      Data: data_paper2
##
## REML criterion at convergence: 6103.9
##
## Scaled residuals:
##      Min       1Q   Median       3Q      Max
## -4.1713 -0.5232 -0.0414  0.5781  4.9182
##
## Random effects:
##   Groups   Name                Variance Std.Dev.
##   ID       (Intercept)          0.0      0.00
##   Residual                    211.1    14.53
## Number of obs: 746, groups: ID, 142
##
## Fixed effects:
##
##              Estimate Std. Error      df t value Pr(>|t|)
## (Intercept)         0.6010     0.5519 744.0000   1.089   0.276
## Baseline_Meds_MuscleRelaxants -1.0538     2.0705 744.0000  -0.509   0.611
##
## Correlation of Fixed Effects:
##              (Intr)
## Bsln_Mds_MR -0.267
## optimizer (nloptwrap) convergence code: 0 (OK)
## boundary (singular) fit: see help('isSingular')
```

```
## Baseline_Meds_Opioids
```

```
model_opioid <- lmer(IndexLev1_PainAverage_RawChange ~ Baseline_Meds_Opioids + (1|ID), d
```

```
## boundary (singular) fit: see help('isSingular')
```

```
summary(model_opioid)
```

```
## Linear mixed model fit by REML. t-tests use Satterthwaite's method [
## lmerModLmerTest]
## Formula: IndexLev1_PainAverage_RawChange ~ Baseline_Meds_Opioids + (1 |
##      ID)
##      Data: data_paper2
##
## REML criterion at convergence: 6104.4
##
```

```
## Scaled residuals:
##      Min       1Q   Median       3Q      Max
## -4.1636 -0.5181 -0.0364  0.5830  4.8498
##
## Random effects:
##   Groups   Name                Variance Std.Dev.
##   ID       (Intercept)         0.0      0.00
##   Residual                    211.1    14.53
## Number of obs: 746, groups: ID, 142
##
## Fixed effects:
##              Estimate Std. Error    df t value Pr(>|t|)
## (Intercept)      0.52868    0.55722 744.00000    0.949    0.343
## Baseline_Meds_Opioids -0.02868    1.87339 744.00000   -0.015    0.988
##
## Correlation of Fixed Effects:
##              (Intr)
## Bsln_Mds_Op -0.297
## optimizer (nloptwrap) convergence code: 0 (OK)
## boundary (singular) fit: see help('isSingular')

## Baseline_Meds_Anticonvulsants
model_anticonv <- lmer(IndexLev1_PainAverage_RawChange ~ Baseline_Meds_Anticonvulsants +
## boundary (singular) fit: see help('isSingular')

summary(model_anticonv)

## Linear mixed model fit by REML. t-tests use Satterthwaite's method [
## lmerModLmerTest]
## Formula: IndexLev1_PainAverage_RawChange ~ Baseline_Meds_Anticonvulsants +
##      (1 | ID)
##      Data: data_paper2
##
## REML criterion at convergence: 6103.3
##
## Scaled residuals:
##      Min       1Q   Median       3Q      Max
## -4.1654 -0.5180 -0.0362  0.5832  4.8500
##
## Random effects:
##   Groups   Name                Variance Std.Dev.
##   ID       (Intercept)         0.0      0.00
##   Residual                    211.1    14.53
## Number of obs: 746, groups: ID, 142
##
```

```
## Fixed effects:
##
##              Estimate Std. Error      df t value Pr(>|t|)
## (Intercept)    0.526207   0.539654 744.000000    0.975    0.330
## Baseline_Meds_Anticonvulsants -0.002397   3.216440 744.000000   -0.001    0.999
##
## Correlation of Fixed Effects:
##              (Intr)
## Bsln_Mds_An -0.168
## optimizer (nloptwrap) convergence code: 0 (OK)
## boundary (singular) fit: see help('isSingular')
```

Level 2 covariates

The below will examine if PPTh, TSP, and CPM are significantly associated with the delta pain change.

```
## PPTh
model_PPTh <- lmer(IndexLev1_PainAverage_RawChange ~ IndexLev2_QST_BaselinePPTh + (1|ID))

## boundary (singular) fit: see help('isSingular')

summary(model_PPTh)
```

```
## Linear mixed model fit by REML. t-tests use Satterthwaite's method [
## lmerModLmerTest]
## Formula: IndexLev1_PainAverage_RawChange ~ IndexLev2_QST_BaselinePPTh +
##          (1 | ID)
##      Data: data_paper2
##
## REML criterion at convergence: 6035.7
##
## Scaled residuals:
##      Min       1Q   Median       3Q      Max
## -4.0198 -0.5541 -0.0301  0.5472  4.6470
##
## Random effects:
##   Groups   Name      Variance Std.Dev.
##   ID       (Intercept)  0.0      0.00
##   Residual                228.5   15.12
## Number of obs: 729, groups: ID, 142
##
## Fixed effects:
##
##              Estimate Std. Error      df t value Pr(>|t|)
## (Intercept)    0.999941   1.202766 727.000000    0.831    0.406
## IndexLev2_QST_BaselinePPTh -0.001204   0.002685 727.000000   -0.448    0.654
##
```

```
## Correlation of Fixed Effects:
##           (Intr)
## IL2_QST_BPP -0.885
## optimizer (nloptwrap) convergence code: 0 (OK)
## boundary (singular) fit: see help('isSingular')

## TSP
model_TSP <- lmer(IndexLev1_PainAverage_RawChange ~ IndexLev2_QST_TSPAve + (1|ID), data

## boundary (singular) fit: see help('isSingular')

summary(model_TSP)

## Linear mixed model fit by REML. t-tests use Satterthwaite's method [
## lmerModLmerTest]
## Formula: IndexLev1_PainAverage_RawChange ~ IndexLev2_QST_TSPAve + (1 | ID)
## Data: data_paper2
##
## REML criterion at convergence: 6283.5
##
## Scaled residuals:
##      Min       1Q   Median       3Q      Max
## -4.0486 -0.5141 -0.0379  0.5535  4.6865
##
## Random effects:
##   Groups   Name                Variance Std.Dev.
##   ID       (Intercept)         0.0      0
##   Residual                    224.9    15
## Number of obs: 761, groups: ID, 146
##
## Fixed effects:
##              Estimate Std. Error      df t value Pr(>|t|)
## (Intercept)    0.71948   0.67826 759.00000   1.061   0.289
## IndexLev2_QST_TSPAve -0.01010   0.02899 759.00000  -0.348   0.728
##
## Correlation of Fixed Effects:
##           (Intr)
## IL2_QST_TSP -0.598
## optimizer (nloptwrap) convergence code: 0 (OK)
## boundary (singular) fit: see help('isSingular')

## CPM
model_CPM <- lmer(IndexLev1_PainAverage_RawChange ~ IndexLev2_QST_CpmTrialAve + (1|ID),

## boundary (singular) fit: see help('isSingular')
```

```
summary(model_CPM)
```

```
## Linear mixed model fit by REML. t-tests use Satterthwaite's method [
## lmerModLmerTest]
## Formula: IndexLev1_PainAverage_RawChange ~ IndexLev2_QST_CpmTrialAve +
##      (1 | ID)
##      Data: data_paper2
##
## REML criterion at convergence: 5966.9
##
## Scaled residuals:
##      Min       1Q   Median       3Q      Max
## -4.0278 -0.5057 -0.0370  0.5571  4.6857
##
## Random effects:
##   Groups      Name            Variance Std.Dev.
##   ID          (Intercept)      0.0      0.00
##   Residual                        226.3    15.04
## Number of obs: 722, groups:  ID, 141
##
## Fixed effects:
##              Estimate Std. Error      df t value Pr(>|t|)
## (Intercept)      0.881281   2.276000 720.000000    0.387    0.699
## IndexLev2_QST_CpmTrialAve -0.002652   0.017876 720.000000   -0.148    0.882
##
## Correlation of Fixed Effects:
##              (Intr)
## IL2_QST_CTA -0.969
## optimizer (nloptwrap) convergence code: 0 (OK)
## boundary (singular) fit: see help('isSingular')
```

```
## Adjusted model
```

```
model_adjusted_lev2 <- lmer(IndexLev1_PainAverage_RawChange ~ IndexLev2_QST_CpmTrialAve
```

```
## boundary (singular) fit: see help('isSingular')
```

```
summary(model_adjusted_lev2)
```

```
## Linear mixed model fit by REML. t-tests use Satterthwaite's method [
## lmerModLmerTest]
## Formula: IndexLev1_PainAverage_RawChange ~ IndexLev2_QST_CpmTrialAve +
##      IndexLev2_QST_TSPAve + IndexLev2_QST_BaselinePPTh + (1 |      ID)
##      Data: data_paper2
##
## REML criterion at convergence: 5683.2
##
```

```
## Scaled residuals:
##      Min       1Q   Median       3Q      Max
## -4.0180 -0.5348 -0.0257  0.5470  4.5886
##
## Random effects:
##   Groups   Name                Variance Std.Dev.
##    ID      (Intercept)          0.0      0.00
## Residual                  232.1     15.23
## Number of obs: 684, groups: ID, 132
##
## Fixed effects:
##              Estimate Std. Error      df t value Pr(>|t|)
## (Intercept)      2.139130   3.138091 680.000000    0.682    0.496
## IndexLev2_QST_CpmTrialAve -0.004746   0.019330 680.000000   -0.246    0.806
## IndexLev2_QST_TSPAve     -0.014221   0.031074 680.000000   -0.458    0.647
## IndexLev2_QST_BaselinePPTh -0.001967   0.003138 680.000000   -0.627    0.531
##
## Correlation of Fixed Effects:
##              (Intr) IL2_QST_C IL2_QST_T
## IL2_QST_CTA -0.879
## IL2_QST_TSP -0.284  0.056
## IL2_QST_BPP -0.643  0.277    0.237
## optimizer (nloptwrap) convergence code: 0 (OK)
## boundary (singular) fit: see help('isSingular')
```

Level 1 covariates

The following will examine if DailyCatastro, DailyNA, Daily PosAffect, DailyPhysExcercise are associated with the delta change in pain

```
## Daily Catastro
model_catastro <- lmer(IndexLev1_PainAverage_RawChange ~ IndexLev1_Catastrophizing_Total

## boundary (singular) fit: see help('isSingular')

summary(model_catastro) # Significant!

## Linear mixed model fit by REML. t-tests use Satterthwaite's method [
## lmerModLmerTest]
## Formula: IndexLev1_PainAverage_RawChange ~ IndexLev1_Catastrophizing_Total +
##          (1 | ID)
##    Data: data_paper2
##
## REML criterion at convergence: 6670.2
##
## Scaled residuals:
```

```

##      Min      1Q  Median      3Q      Max
## -4.0629 -0.5571  0.0302  0.5450  4.6436
##
## Random effects:
##   Groups   Name                Variance Std.Dev.
##   ID       (Intercept)         0.0      0.00
##   Residual                        215.4    14.68
## Number of obs: 812, groups: ID, 157
##
## Fixed effects:
##                                Estimate Std. Error      df t value Pr(>|t|)
## (Intercept)                   -1.69145    0.69735 810.00000   -2.426   0.0155
## IndexLev1_Catastrophizing_Total    0.10163    0.02079 810.00000    4.888 1.23e-06
##
## (Intercept)                    *
## IndexLev1_Catastrophizing_Total ***
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Correlation of Fixed Effects:
##              (Intr)
## IndxLv1_C_T -0.674
## optimizer (nloptwrap) convergence code: 0 (OK)
## boundary (singular) fit: see help('isSingular')
## DailyNA
model_DailyNA <- lmer(IndexLev1_PainAverage_RawChange ~ IndexLev1_NegativeAffect_Total +
## boundary (singular) fit: see help('isSingular')
summary(model_DailyNA) # Significant!

## Linear mixed model fit by REML. t-tests use Satterthwaite's method [
## lmerModLmerTest]
## Formula: IndexLev1_PainAverage_RawChange ~ IndexLev1_NegativeAffect_Total +
##      (1 | ID)
##   Data: data_paper2
##
## REML criterion at convergence: 6686.2
##
## Scaled residuals:
##      Min      1Q  Median      3Q      Max
## -4.0924 -0.5408 -0.0025  0.5375  4.6374
##
## Random effects:
##   Groups   Name                Variance Std.Dev.

```

```

## ID (Intercept) 0.0 0.00
## Residual 219.8 14.83
## Number of obs: 812, groups: ID, 157
##
## Fixed effects:
## Estimate Std. Error df t value Pr(>|t|)
## (Intercept) -0.92603 0.82773 810.00000 -1.119 0.2636
## IndexLev1_NegativeAffect_Total 0.06144 0.02561 810.00000 2.399 0.0167
##
## (Intercept)
## IndexLev1_NegativeAffect_Total *
## ---
## Signif. codes: 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Correlation of Fixed Effects:
## (Intr)
## IndxL1_NA_T -0.778
## optimizer (nloptwrap) convergence code: 0 (OK)
## boundary (singular) fit: see help('isSingular')

## PosAffect
model_PosAffect <- lmer(IndexLev1_PainAverage_RawChange ~ IndexLev1_PositiveAffect_Total +
## boundary (singular) fit: see help('isSingular')

summary(model_PosAffect)

## Linear mixed model fit by REML. t-tests use Satterthwaite's method [
## lmerModLmerTest]
## Formula: IndexLev1_PainAverage_RawChange ~ IndexLev1_PositiveAffect_Total +
## (1 | ID)
## Data: data_paper2
##
## REML criterion at convergence: 6688.8
##
## Scaled residuals:
## Min 1Q Median 3Q Max
## -4.1242 -0.5363 -0.0145 0.5156 4.6655
##
## Random effects:
## Groups Name Variance Std.Dev.
## ID (Intercept) 0.0 0.00
## Residual 220.5 14.85
## Number of obs: 812, groups: ID, 157
##
## Fixed effects:

```



```

##                                Estimate Std. Error      df t value Pr(>|t|)
## (Intercept)                   3.85909    1.94542 810.00000    1.984    0.0476
## IndexLev1_PositiveAffect_Total -0.04838    0.02798 810.00000   -1.729    0.0842
##
## (Intercept)                    *
## IndexLev1_PositiveAffect_Total .
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Correlation of Fixed Effects:
##              (Intr)
## IndxL1_PA_T -0.963
## optimizer (nloptwrap) convergence code: 0 (OK)
## boundary (singular) fit: see help('isSingular')

## DailyPhysExcercise
model_PhysExercise <- lmer(IndexLev1_PainAverage_RawChange ~ Level1_Even_PhysActiv + (1 |
## boundary (singular) fit: see help('isSingular')

summary(model_PhysExercise) # Significant!

## Linear mixed model fit by REML. t-tests use Satterthwaite's method [
## lmerModLmerTest]
## Formula: IndexLev1_PainAverage_RawChange ~ Level1_Even_PhysActiv + (1 |
##      ID)
##      Data: data_paper2
##
## REML criterion at convergence: 6578.2
##
## Scaled residuals:
##      Min       1Q   Median       3Q      Max
## -3.9409 -0.5310 -0.0294  0.5356  4.8044
##
## Random effects:
##  Groups   Name                Variance Std.Dev.
##  ID       (Intercept)         0.0      0.00
##  Residual                    221.8    14.89
## Number of obs: 798, groups:  ID, 154
##
## Fixed effects:
##                                Estimate Std. Error      df t value Pr(>|t|)
## (Intercept)                   -1.87629    1.26938 796.00000   -1.478    0.1398
## Level1_Even_PhysActiv          0.05115    0.02374 796.00000    2.154    0.0315 *
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

```

```
##
## Correlation of Fixed Effects:
##          (Intr)
## Lvl1_Evn_PA -0.910
## optimizer (nloptwrap) convergence code: 0 (OK)
## boundary (singular) fit: see help('isSingular')
## Adjusted level 1
model_adj_lev1 <- lmer(IndexLev1_PainAverage_RawChange ~ Level1_Even_PhysActiv + IndexLev1_PositiveAffect_Total +
  IndexLev1_NegativeAffect_Total + IndexLev1_Catastrophizing_Total +
  (1 | ID)
  Data: data_paper2
##
## REML criterion at convergence: 6573.5
##
## Scaled residuals:
##      Min       1Q   Median       3Q      Max
## -3.9903 -0.5522  0.0234  0.5361  4.6724
##
## Random effects:
##   Groups   Name                Variance Std.Dev.
##   ID       (Intercept)          0.0      0.00
##   Residual                    216.9    14.73
## Number of obs: 798, groups:  ID, 154
##
## Fixed effects:
##              Estimate Std. Error      df t value Pr(>|t|)
## (Intercept)   -1.31483    2.90515 793.00000   -0.453    0.651
## Level1_Even_PhysActiv    0.03084    0.02426 793.00000    1.271    0.204
## IndexLev1_PositiveAffect_Total -0.02196    0.03421 793.00000   -0.642    0.521
## IndexLev1_NegativeAffect_Total -0.01274    0.03429 793.00000   -0.372    0.710
## IndexLev1_Catastrophizing_Total  0.09698    0.02478 793.00000    3.914 9.85e-05
##
## (Intercept)
## Level1_Even_PhysActiv
## IndexLev1_PositiveAffect_Total
## IndexLev1_NegativeAffect_Total
```

```
## IndexLev1_Catastrophizing_Total ***
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Correlation of Fixed Effects:
##          (Intr) L1_E_P IL1_PA IL1_NA
## Lvl1_Evn_PA -0.235
## IndxL1_PA_T -0.884 -0.143
## IndxL1_NA_T -0.572 -0.080  0.495
## IndxLv1_C_T -0.027 -0.178  0.035 -0.418
## optimizer (nloptwrap) convergence code: 0 (OK)
## boundary (singular) fit: see help('isSingular')
## Both level 1 and level 2
model_adj_all <- lmer(IndexLev1_PainAverage_RawChange ~ Level1_Even_PhysActiv + IndexLev1_PainAverage_RawChange, data = data_paper2)
## boundary (singular) fit: see help('isSingular')
summary(model_adj_all)

## Linear mixed model fit by REML. t-tests use Satterthwaite's method [
## lmerModLmerTest]
## Formula:
## IndexLev1_PainAverage_RawChange ~ Level1_Even_PhysActiv + IndexLev1_PositiveAffect_Total +
##   IndexLev1_NegativeAffect_Total + IndexLev1_Catastrophizing_Total +
##   IndexLev2_QST_CpmTrialAve + IndexLev2_QST_TSPAve + IndexLev2_QST_BaselinePPTth +
##   (1 | ID)
## Data: data_paper2
##
## REML criterion at convergence: 5595.6
##
## Scaled residuals:
##      Min       1Q   Median       3Q      Max
## -3.9453 -0.5351  0.0116  0.5290  4.5073
##
## Random effects:
##   Groups   Name              Variance Std.Dev.
##   ID       (Intercept)       0.0       0.00
##   Residual                    227.6    15.09
## Number of obs: 673, groups: ID, 130
##
## Fixed effects:
##              Estimate Std. Error      df t value
## (Intercept)    0.905046   4.272480 665.000000    0.212
## Level1_Even_PhysActiv    0.029994   0.027298 665.000000    1.099
## IndexLev1_PositiveAffect_Total -0.037847   0.039062 665.000000   -0.969
```

```
## IndexLev1_NegativeAffect_Total -0.021008 0.039652 665.000000 -0.530
## IndexLev1_Catastrophizing_Total 0.102585 0.028395 665.000000 3.613
## IndexLev2_QST_CpmTrialAve -0.001907 0.019226 665.000000 -0.099
## IndexLev2_QST_TSPAve -0.020775 0.031097 665.000000 -0.668
## IndexLev2_QST_BaselinePPTh -0.001197 0.003143 665.000000 -0.381
## Pr(>|t|)
## (Intercept) 0.832303
## Level1_Even_PhysActiv 0.272277
## IndexLev1_PositiveAffect_Total 0.332953
## IndexLev1_NegativeAffect_Total 0.596424
## IndexLev1_Catastrophizing_Total 0.000326 ***
## IndexLev2_QST_CpmTrialAve 0.921021
## IndexLev2_QST_TSPAve 0.504314
## IndexLev2_QST_BaselinePPTh 0.703313
## ---
## Signif. codes: 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Correlation of Fixed Effects:
## (Intr) L1_E_P IL1_PA IL1_NA IL1_C_ IL2_QST_C IL2_QST_T
## Lvl1_Evn_PA -0.135
## IndxL1_PA_T -0.613 -0.151
## IndxL1_NA_T -0.456 -0.072 0.546
## IndxLv1_C_T 0.023 -0.184 -0.044 -0.470
## IL2_QST_CTA -0.589 -0.023 -0.077 -0.025 0.023
## IL2_QST_TSP -0.164 -0.107 -0.028 0.017 -0.017 0.061
## IL2_QST_BPP -0.396 -0.049 -0.102 -0.024 0.031 0.285 0.238
## optimizer (nloptwrap) convergence code: 0 (OK)
## boundary (singular) fit: see help('isSingular')
```

The following code will examine the count of the APEs per individual using Poisson regression

```
library(pscl)
```

```
## Classes and Methods for R originally developed in the
## Political Science Computational Laboratory
## Department of Political Science
## Stanford University (2002-2015),
## by and under the direction of Simon Jackman.
## hurdle and zeroinfl functions by Achim Zeileis.
```

```
data_paper2_pois <- data_paper2 |>
  select(c(Baseline_Demog_Age, Baseline_Demog_Sex,
           Baseline_Demog_BMI, Baseline_Demog_Ethnicity_Rec,
           Baseline_Lifestyle_SmokePerday, Baseline_Meds_Acetaminophen,
           Baseline_Meds_NSAID, Baseline_Meds_Cox2,
           Baseline_Meds_Antidepressants, Baseline_Meds_Anxiolytics,
```

```

      Baseline_Meds_MuscleRelaxants, Baseline_Meds_Opioids,
      Baseline_Meds_Anticonvulsants, IndexLev2_QST_BaselinePPTh,
      IndexLev2_QST_TSPAve, IndexLev2_QST_CpmTrialAve, APE, ID))
data_paper2_pois2 <- data_paper2_pois |>
  group_by(ID) |>
  summarise(nAPE = sum(APE, na.rm = TRUE))
data_paper2_pois <- merge(data_paper2_pois, data_paper2_pois2, by = "ID")
data_paper2_pois <- data_paper2_pois |>
  group_by(ID) |>
  slice(1) |>
  ungroup()

zinb_model <- zeroinfl(nAPE ~ Baseline_Demog_Age + Baseline_Demog_Sex +
  Baseline_Demog_BMI + Baseline_Demog_Ethnicity_Rec +
  Baseline_Lifestyle_SmokePerday + IndexLev2_QST_BaselinePPTh +
  IndexLev2_QST_TSPAve + IndexLev2_QST_CpmTrialAve, data = data_paper2_pois)
summary(zinb_model)

##
## Call:
## zeroinfl(formula = nAPE ~ Baseline_Demog_Age + Baseline_Demog_Sex + Baseline_Demog_BMI +
##   Baseline_Demog_Ethnicity_Rec + Baseline_Lifestyle_SmokePerday + IndexLev2_QST_Bas
##   IndexLev2_QST_TSPAve + IndexLev2_QST_CpmTrialAve, data = data_paper2_pois)
##
## Pearson residuals:
##      Min      1Q  Median      3Q      Max
## -0.9366 -0.5695 -0.2170  0.2473  3.3475
##
## Count model coefficients (poisson with log link):
##
##              Estimate Std. Error z value Pr(>|z|)
## (Intercept)      3.0728831   2.2391441    1.372  0.16996
## Baseline_Demog_Age -0.0430815   0.0187006   -2.304  0.02124 *
## Baseline_Demog_Sex  0.3009306   0.3561407    0.845  0.39812
## Baseline_Demog_BMI  0.0067367   0.0255358    0.264  0.79192
## Baseline_Demog_Ethnicity_Rec  0.1136111   0.4560741    0.249  0.80328
## Baseline_Lifestyle_SmokePerday  0.0026319   0.0121584    0.216  0.82862
## IndexLev2_QST_BaselinePPTh -0.0006578   0.0014213   -0.463  0.64350
## IndexLev2_QST_TSPAve -0.0319241   0.0110382   -2.892  0.00383 **
## IndexLev2_QST_CpmTrialAve -0.0067122   0.0050443   -1.331  0.18330
##
## Zero-inflation model coefficients (binomial with logit link):
##
##              Estimate Std. Error z value Pr(>|z|)
## (Intercept)    -19.29998  218.94460   -0.088  0.9298
## Baseline_Demog_Age -0.41311   0.30495   -1.355  0.1755

```

```
## Baseline_Demog_Sex          12.05693    7.74287    1.557    0.1194
## Baseline_Demog_BMI          -0.27380    0.22866   -1.197    0.2312
## Baseline_Demog_Ethnicity_Rec 18.23288  217.63519    0.084    0.9332
## Baseline_Lifestyle_SmokePerday -0.73668    0.41205   -1.788    0.0738 .
## IndexLev2_QST_BaselinePPTh    0.05946    0.04044    1.470    0.1415
## IndexLev2_QST_TSPAve         -0.12199    0.09707   -1.257    0.2089
## IndexLev2_QST_CpmTrialAve    -0.05543    0.10067   -0.551    0.5819
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Number of iterations in BFGS optimization: 223
## Log-likelihood: -78.43 on 18 Df
```