

## S2 Appendix. Code to fit linear mixed effects models

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#29 May 2018
#Code to fit linear mixed effects models to simulated datasets

require(nlme)
require(MASS)
require(multcomp)

#Code to fit models in R and collect data
setwd("file path")
files <- list.files(path="file path/Sim_Datasets/", pattern="*.csv", full.names=F, recursive=FALSE)

Simulations <- c("0", "00", "000", "0000", "00000", "000000", "0000000", "00000000", seq(1,28,1))
Repeats <- 1000

nSim <- 36 #24 #This is the number of different models used to simulate data
nModels <- 18 #18 #This is the number of different models fitted to the data
Sim_fit_results <- matrix(rep(NA, length = nModels*nSim*Repeats*36), nrow = nModels*nSim*Repeats, ncol = 36)
Sim_fit_results <- as.data.frame(Sim_fit_results)
names(Sim_fit_results) <- c("Model", "Simulation", "Repeat", "AIC", "BIC", "MSE", "Intercept", "Intercep_SE",
"Intercept_p", "Intercep_t3p",
"Time", "Time_SE", "Time_p", "Time_t3p", "Intervention", "Intervention_SE",
"Intervention_p",
"Intervention_t3p", "Interven_time", "Interven_time_SE", "Interven_time_p",
"Intver_time_t3p",
"Exptime", "Exptime_SE", "Exptime_p", "Exptime_t3p", "Timesq", "Timesq_SE", "Timesq_p",
"Estimate", "Estimate_SE", "Estimate_p", "Estimate2", "Estimate2_SE", "Estimate2_p", "Cov_var")
#i = repeated dataset 1 to 1000
#j = model fitted 1 to 20 (1-10 is CS and 11-20 is AR(1))
#Looping through the different repeats

for (k in 1:length(Simulations)) {
  print(k)
  #Fitted Model 1
  for (i in 1:Repeats) {
    j=1
    cov_var <- "cs"
```

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data <- read.csv(paste("Sim",Simulations[k],"_",i,".csv", sep ""))
data$Intervention <- as.factor(data$Intervention)
fm1 <- try(lme(HONOS_scores ~ Intervention, random = ~ 1 | Cluster_ID/Patient_ID, data = data, method = "ML",
control=lmeControl(returnObject=TRUE, maxIter=100)), TRUE)
if(isTRUE(class(fm1)=="try-error")) { next } else { fm1=fm1 }
K <- matrix(c(0,1), 1)
t <- glht(fm1, linfct = K)
K2 <- matrix(c(0,1), 1)
t2 <- glht(fm1, linfct = K2)
#Getting AIC
AIC <- AIC(fm1)
BIC <- BIC(fm1)
MSE <- fm1$sigma
#Intercept
intercept <- summary(fm1)$tTable[1,1]
inter_SE <- summary(fm1)$tTable[1,2]
inter_p <- summary(fm1)$tTable[1,5]
inter_t3p <- anova(fm1)[1,4]
#Intervention
interven <- summary(fm1)$tTable[2,1]
interven_SE <- summary(fm1)$tTable[2,2]
interven_p <- summary(fm1)$tTable[2,5]
interven_t3p <- anova(fm1)[2,4]
#Estimate of effect at 6 months
estimate <- summary(t)$test$coefficients[1]
estimate_se <- summary(t)$test$sigma[1]
estimate_p <- summary(t)$test$pvalues[1]
#Estimate of time-averaged effect
estimate2 <- t2[1,2]
estimate2_se <- t2[1,3]
estimate2_p <- t2[1,5]
#Writing out results
Sim_fit_results[(j-1)*nSim*Repeats + (k-1)*Repeats + i,c(1,2,3,4,5,6,7,8,9,10,15,16,17,18,30,31,32,33,34,35,36)]
<- c(j,Simulations[k],i,AIC,BIC,MSE, intercept, inter_SE, inter_p, inter_t3p, interven, interven_SE, interven_p,
interven_t3p, estimate, estimate_se, estimate_p, estimate2, estimate2_se, estimate2_p, cov_var)
}
#Fitted Model 2
for (i in 1:Repeats) {
  j=2

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cov_var <- "cs"
data <- read.csv(paste("Sim",Simulations[k],"_",i,".csv", sep ""))
data$Intervention <- as.factor(data$Intervention)
fm1 <- try(lme(HONOS_scores ~ Time + Intervention, random = ~ 1 | Cluster_ID/Patient_ID, data = data, method =
"ML", control=lmeControl(returnObject=TRUE, maxIter=100)), TRUE)
if(isTRUE(class(fm1)=="try-error")) { next } else { fm1=fm1 }
K <- matrix(c(0,0,1), 1)
t <- glht(fm1, linfct = K)
K2 <- matrix(c(0,0,1), 1)
t2 <- glht(fm1, linfct = K2)
#Getting AIC
AIC <- AIC(fm1)
BIC <- BIC(fm1)
MSE <- fm1$sigma
#Intercept
intercept <- summary(fm1)$tTable[1,1]
inter_SE <- summary(fm1)$tTable[1,2]
inter_p <- summary(fm1)$tTable[1,5]
inter_t3p <- anova(fm1)[1,4]
#Time
time <- summary(fm1)$tTable[2,1]
time_SE <- summary(fm1)$tTable[2,2]
time_p <- summary(fm1)$tTable[2,5]
time_t3p <- anova(fm1)[2,4]
#Intervention
interven <- summary(fm1)$tTable[3,1]
interven_SE <- summary(fm1)$tTable[3,2]
interven_p <- summary(fm1)$tTable[3,5]
interven_t3p <- anova(fm1)[3,4]
#Estimate of effect at 6 months
estimate <- summary(t)$test$coefficients[1]
estimate_se <- summary(t)$test$sigma[1]
estimate_p <- summary(t)$test$pvalues[1]
#Estimate of time-averaged effect
estimate2 <- summary(t2)$test$coefficients[1]
estimate2_se <- summary(t2)$test$sigma[1]
estimate2_p <- summary(t2)$test$pvalues[1]
#Writing out results

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Sim_fit_results[(j-1)*nSim*Repeats + (k-1)*Repeats +
i,c(1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16,17,18,30,31,32,33,34,35,36)] <- c(j,Simulations[k],i,AIC,BIC,MSE,
intercept, inter_SE, inter_p, inter_t3p, time, time_SE, time_p, time_t3p, interven, interven_SE, interven_p,
interven_t3p, estimate, estimate_se, estimate_p, estimate2, estimate2_se, estimate2_p, cov_var)
}
#Fitted Model 3
for (i in 1:Repeats) {
  j=3
  cov_var <- "cs"
  data <- read.csv(paste("Sim",Simulations[k],"_",i,".csv", sep ""))
  data$Intervention <- as.factor(data$Intervention)
  data$Time <- as.factor(data$Time)
  fm1 <- try(lme(HONOS_scores ~ Time + Intervention, random = ~ 1 | Cluster_ID/Patient_ID, data = data, method =
"ML", control=lmeControl(returnObject=TRUE, maxIter=100)), TRUE)
  if(isTRUE(class(fm1)=="try-error")) { next } else { fm1=fm1 }
  K <- matrix(c(0,0,0,0,0,0,0,0,0,0,0,0,0,1), 1)
  t <- glht(fm1, linfct = K)
  K2 <- matrix(c(0,0,0,0,0,0,0,0,0,0,0,0,0,1), 1)
  t2 <- glht(fm1, linfct = K2)
  #Getting AIC
  AIC <- AIC(fm1)
  BIC <- BIC(fm1)
  MSE <- fm1$sigma
  #Intercept
  intercept <- summary(fm1)$tTable[1,1]
  inter_SE <- summary(fm1)$tTable[1,2]
  inter_p <- summary(fm1)$tTable[1,5]
  inter_t3p <- anova(fm1)[1,4]
  #Time
  time <- NA
  time_SE <- NA
  time_p <- NA
  time_t3p <- anova(fm1)[2,4]
  #Intervention
  interven <- summary(fm1)$tTable[14,1]
  interven_SE <- summary(fm1)$tTable[14,2]
  interven_p <- summary(fm1)$tTable[14,5]
  interven_t3p <- anova(fm1)[3,4]
  #Estimate of effect at 6 months

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estimate <- summary(t)$test$coefficients[1]
estimate_se <- summary(t)$test$sigma[1]
estimate_p <- summary(t)$test$pvalues[1]
#Estimate of time-averaged effect
estimate2 <- summary(t2)$test$coefficients[1]
estimate2_se <- summary(t2)$test$sigma[1]
estimate2_p <- summary(t2)$test$pvalues[1]
#Writing out results
Sim_fit_results[(j-1)*nSim*Repeats + (k-1)*Repeats +
i,c(1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16,17,18,30,31,32,33,34,35,36)] <- c(j,Simulations[k],i,AIC,BIC,MSE,
intercept, inter_SE, inter_p, inter_t3p, time, time_SE, time_p, time_t3p, interven, interven_SE, interven_p,
interven_t3p, estimate, estimate_se, estimate_p, estimate2, estimate2_se, estimate2_p, cov_var)
}
#Fitted Model 4
for (i in 1:Repeats) {
  j=4
  cov_var <- "cs"
  data <- read.csv(paste("Sim",Simulations[k],"_",i,".csv", sep ""))
  data$Intervention <- as.factor(data$Intervention)
  fml <- try(lme(HONOS_scores ~ Time + Intervention + Time*Intervention, random = ~ 1 | Cluster_ID/Patient_ID,
  data = data, method = "ML", control=lmeControl(returnObject=TRUE, maxIter=100)), TRUE)
  if(isTRUE(class(fml)=="try-error")) { next } else { fml=fml }
  K <- matrix(c(0,0,1,6), 1)
  t <- glht(fml, linfct = K)
  K2 <- matrix(c(0,0,1,7), 1)
  t2 <- glht(fml, linfct = K2)
  #Getting AIC
  AIC <- AIC(fml)
  BIC <- BIC(fml)
  MSE <- fml$sigma
  #Intercept
  intercept <- summary(fml)$tTable[1,1]
  inter_SE <- summary(fml)$tTable[1,2]
  inter_p <- summary(fml)$tTable[1,5]
  inter_t3p <- anova(fml)[1,4]
  #Time
  time <- summary(fml)$tTable[2,1]
  time_SE <- summary(fml)$tTable[2,2]
  time_p <- summary(fml)$tTable[2,5]

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time_t3p <- anova(fm1)[2,4]
#Intervention
interven <- summary(fm1)$tTable[3,1]
interven_SE <- summary(fm1)$tTable[3,2]
interven_p <- summary(fm1)$tTable[3,5]
interven_t3p <- anova(fm1)[3,4]
#Time*Intervention
time_int <- summary(fm1)$tTable[4,1]
time_int_SE <- summary(fm1)$tTable[4,2]
time_int_p <- summary(fm1)$tTable[4,5]
time_int_t3p <- anova(fm1)[4,4]
#Estimate of effect at 6 months
estimate <- summary(t)$test$coefficients[1]
estimate_se <- summary(t)$test$sigma[1]
estimate_p <- summary(t)$test$pvalues[1]
#Estimate of time-averaged effect
estimate2 <- summary(t2)$test$coefficients[1]
estimate2_se <- summary(t2)$test$sigma[1]
estimate2_p <- summary(t2)$test$pvalues[1]
#Writing out results
Sim_fit_results[(j-1)*nSim*Repeats + (k-1)*Repeats +
i,c(1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16,17,18,19,20,21,22,30,31,32,33,34,35,36)] <-
c(j,Simulations[k],i,AIC,BIC,MSE, intercept, inter_SE, inter_p, inter_t3p, time, time_SE, time_p, time_t3p,
interven, interven_SE, interven_p, interven_t3p, time_int, time_int_SE, time_int_p, time_int_t3p, estimate,
estimate_se, estimate_p, estimate2, estimate2_se, estimate2_p, cov_var)
}
#Fitted Model 5
for (i in 1:Repeats) {
  j=5
  cov_var <- "cs"
  data <- read.csv(paste("Sim",Simulations[k],"_",i,".csv", sep = ""))
  data$Intervention <- as.factor(data$Intervention)
  data$Time <- as.factor(data$Time)
  data$Time_Int <- "IntTime0"
  data$Time_Int[data$Time == "3" & data$Intervention == "1"] <- "IntTime3"
  data$Time_Int[data$Time == "4" & data$Intervention == "1"] <- "IntTime4"
  data$Time_Int[data$Time == "5" & data$Intervention == "1"] <- "IntTime5"
  data$Time_Int[data$Time == "6" & data$Intervention == "1"] <- "IntTime6"
  data$Time_Int[data$Time == "7" & data$Intervention == "1"] <- "IntTime7"

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estimate_se <- summary(t)$test$sigma[1]
estimate_p <- summary(t)$test$pvalues[1]
#Estimate of time-averaged effect
estimate2 <- summary(t2)$test$coefficients[1]
estimate2_se <- summary(t2)$test$sigma[1]
estimate2_p <- summary(t2)$test$pvalues[1]
#Writing out results
Sim_fit_results[(j-1)*nSim*Repeats + (k-1)*Repeats +
i,c(1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16,17,18,19,20,21,22,30,31,32,33,34,35,36)] <-
c(j,Simulations[k],i,AIC,BIC,MSE, intercept, inter_SE, inter_p, inter_t3p, time, time_SE, time_p, time_t3p,
interven, interven_SE, interven_p, interven_t3p, time_int, time_int_SE, time_int_p, time_int_t3p, estimate,
estimate_se, estimate_p, estimate2, estimate2_se, estimate2_p, cov_var)
}
#Fitted Model 6
for (i in 1:Repeats) {
  j=6
  cov_var <- "cs"
  data <- read.csv(paste("Sim",Simulations[k],"_",i,".csv", sep ""))
  data$Intervention <- as.factor(data$Intervention)
  fml <- try(lme(HONOS_scores ~ Time + Intervention + TimeInt, random = ~ 1 | Cluster_ID/Patient_ID, data = data,
method = "ML", control=lmeControl(returnObject=TRUE, maxIter=100)), TRUE)
  if(isTRUE(class(fml)=="try-error")) { next } else { fml=fml }
  K <- matrix(c(0, 0, 1, 6), 1)
  t <- glht(fml, linfct = K)
  K2 <- matrix(c(0, 0, 1, 6), 1)
  t2 <- glht(fml, linfct = K2)
  #Getting AIC
  AIC <- AIC(fml)
  BIC <- BIC(fml)
  MSE <- fml$sigma
  #Intercept
  intercept <- summary(fml)$tTable[1,1]
  inter_SE <- summary(fml)$tTable[1,2]
  inter_p <- summary(fml)$tTable[1,5]
  inter_t3p <- anova(fml)[1,4]
  #Time
  time <- summary(fml)$tTable[2,1]
  time_SE <- summary(fml)$tTable[2,2]
  time_p <- summary(fml)$tTable[2,5]

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time_t3p <- anova(fm1) [2,4]
#Intervention
interven <- summary(fm1)$tTable[3,1]
interven_SE <- summary(fm1)$tTable[3,2]
interven_p <- summary(fm1)$tTable[3,5]
interven_t3p <- anova(fm1) [3,4]
#Time*Intervention
timeint <- summary(fm1)$tTable[4,1]
timeint_SE <- summary(fm1)$tTable[4,2]
timeint_p <- summary(fm1)$tTable[4,5]
timeint_t3p <- anova(fm1) [4,4]
#Estimate of effect at 6 months
estimate <- summary(t)$test$coefficients[1]
estimate_se <- summary(t)$test$sigma[1]
estimate_p <- summary(t)$test$pvalues[1]
#Estimate of time-averaged effect
estimate2 <- summary(t2)$test$coefficients[1]
estimate2_se <- summary(t2)$test$sigma[1]
estimate2_p <- summary(t2)$test$pvalues[1]
#Writing out results
Sim_fit_results[(j-1)*nSim*Repeats + (k-1)*Repeats +
i,c(1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16,17,18,23,24,25,26,30,31,32,33,34,35,36)] <-
c(j,Simulations[k],i,AIC,BIC,MSE, intercept, inter_SE, inter_p, inter_t3p, time, time_SE, time_p, time_t3p,
interven, interven_SE, interven_p, interven_t3p, timeint, timeint_SE, timeint_p, timeint_t3p, estimate, estimate_se,
estimate_p, estimate2, estimate2_se, estimate2_p, cov_var)
}
#Fitted Model 7
for (i in 1:Repeats) {
  j=7
  cov_var <- "cs"
  data <- read.csv(paste("Sim",Simulations[k],"_",i,".csv", sep = ""))
  data$Intervention <- as.factor(data$Intervention)
  fm1 <- try(lme(HONOS_scores ~ Time + TimeInt, random = ~ 1 | Cluster_ID/Patient_ID, data = data, method = "ML",
control=lmeControl(returnObject=TRUE, maxIter=100)), TRUE)
  if(istRUE(class(fm1)=="try-error")) { next } else { fm1=fm1 }
  K <- matrix(c(0, 0, 6), 1)
  t <- glht(fm1, linfct = K)
  K2 <- matrix(c(0, 0, 6), 1)
  t2 <- glht(fm1, linfct = K2)

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```

#Getting AIC
AIC <- AIC(fm1)
BIC <- BIC(fm1)
MSE <- fm1$sigma
#Intercept
intercept <- summary(fm1)$tTable[1,1]
inter_SE <- summary(fm1)$tTable[1,2]
inter_p <- summary(fm1)$tTable[1,5]
inter_t3p <- anova(fm1)[1,4]
#Time
time <- summary(fm1)$tTable[2,1]
time_SE <- summary(fm1)$tTable[2,2]
time_p <- summary(fm1)$tTable[2,5]
time_t3p <- anova(fm1)[2,4]
#Exposure Time
timeint <- summary(fm1)$tTable[3,1]
timeint_SE <- summary(fm1)$tTable[3,2]
timeint_p <- summary(fm1)$tTable[3,5]
timeint_t3p <- anova(fm1)[3,4]
#Estimate of effect at 6 months
estimate <- summary(t)$test$coefficients[1]
estimate_se <- summary(t)$test$sigma[1]
estimate_p <- summary(t)$test$pvalues[1]
#Estimate of time-averaged effect
estimate2 <- summary(t2)$test$coefficients[1]
estimate2_se <- summary(t2)$test$sigma[1]
estimate2_p <- summary(t2)$test$pvalues[1]
#Writing out results
Sim_fit_results[(j-1)*nSim*Repeats + (k-1)*Repeats +
i,c(1,2,3,4,5,6,7,8,9,10,11,12,13,14,23,24,25,26,30,31,32,33,34,35,36)] <- c(j,Simulations[k],i,AIC,BIC,MSE,
intercept, inter_SE, inter_p, inter_t3p, time, time_SE, time_p, time_t3p, timeint, timeint_SE, timeint_p,
timeint_t3p, estimate, estimate_se, estimate_p, estimate2, estimate2_se, estimate2_p, cov_var)
}
#Fitted Model 8
for (i in 1:Repeats) {
  j=8
  cov_var <- "cs"
  data <- read.csv(paste("Sim",Simulations[k],"_",i,".csv", sep = ""))
  data$Intervention <- as.factor(data$Intervention)

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Sim_fit_results[(j-1)*nSim*Repeats + (k-1)*Repeats +
i,c(1,2,3,4,5,6,7,8,9,10,11,12,13,14,23,24,25,26,30,31,32,33,34,35,36)] <- c(j,Simulations[k],i,AIC,BIC,MSE,
intercept, inter_SE, inter_p, inter_t3p, time, time_SE, time_p, time_t3p, timeint, timeint_SE, timeint_p,
timeint_t3p, estimate, estimate_se, estimate_p, estimate2, estimate2_se, estimate2_p, cov_var)
}
#Fitted Model 9
for (i in 1:Repeats) {
  j=9
  cov_var <- "cs"
  data <- read.csv(paste("Sim",Simulations[k],"_",i,".csv", sep ""))
  data$Intervention <- as.factor(data$Intervention)
  fm1 <- try(lme(HONOS_scores ~ Time + Intervention + TimeInt + I(Time^2), random = ~ 1 | Cluster_ID/Patient_ID,
  data = data, method = "ML", control=lmeControl(returnObject=TRUE, maxIter=100)), TRUE)
  if(isTRUE(class(fm1)=="try-error")) { next } else { fm1=fm1 }
  K <- matrix(c(0, 0, 1, 6, 0), 1)
  t <- glht(fm1, linfct = K)
  K2 <- matrix(c(0, 0, 1, 6, 0), 1)
  t2 <- glht(fm1, linfct = K2)
  #Getting AIC
  AIC <- AIC(fm1)
  BIC <- BIC(fm1)
  MSE <- fm1$sigma
  #Intercept
  intercept <- summary(fm1)$tTable[1,1]
  inter_SE <- summary(fm1)$tTable[1,2]
  inter_p <- summary(fm1)$tTable[1,5]
  inter_t3p <- anova(fm1)[1,4]
  #Time
  time <- summary(fm1)$tTable[2,1]
  time_SE <- summary(fm1)$tTable[2,2]
  time_p <- summary(fm1)$tTable[2,5]
  time_t3p <- anova(fm1)[2,4]
  #Intervention
  interven <- summary(fm1)$tTable[3,1]
  interven_SE <- summary(fm1)$tTable[3,2]
  interven_p <- summary(fm1)$tTable[3,5]
  interven_t3p <- anova(fm1)[3,4]
  #Time*Intervention
  timeint <- summary(fm1)$tTable[4,1]

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timeint_SE <- summary(fm1)$tTable[4,2]
timeint_p <- summary(fm1)$tTable[4,5]
timeint_t3p <- anova(fm1)[4,4]
#Timesq
timesq <- summary(fm1)$tTable[5,1]
timesq_SE <- summary(fm1)$tTable[5,2]
timesq_p <- summary(fm1)$tTable[5,5]
timesq_t3p <- anova(fm1)[5,4]
#Estimate of effect at 6 months
estimate <- summary(t)$test$coefficients[1]
estimate_se <- summary(t)$test$sigma[1]
estimate_p <- summary(t)$test$pvalues[1]
#Estimate of time-averaged effect
estimate2 <- summary(t2)$test$coefficients[1]
estimate2_se <- summary(t2)$test$sigma[1]
estimate2_p <- summary(t2)$test$pvalues[1]
#Writing out results
Sim_fit_results[(j-1)*nSim*Repeats + (k-1)*Repeats +
i,c(1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16,17,18,23,24,25,26,27,28,29,30,31,32,33,34,35,36)] <-
c(j,Simulations[k],i,AIC,BIC,MSE, intercept, inter_SE, inter_p, inter_t3p, time, time_SE, time_p, time_t3p,
interven, interven_SE, interven_p, interven_t3p, timeint, timeint_SE, timeint_p, timeint_t3p, timesq, timesq_SE,
timesq_p, estimate, estimate_se, estimate_p, estimate2, estimate2_se, estimate2_p, cov_var)
}
##AR(1)
#Fitted Model 1
for (i in 1:Repeats) {
j=10
cov_var <- "ar1"
data <- read.csv(paste("Sim",Simulations[k],"_",i,".csv", sep = ""))
data$Intervention <- as.factor(data$Intervention)
fm1 <- try(lme(HONOS_scores ~ Intervention, random = ~ 1 | Cluster_ID/Patient_ID, data = data, method = "ML",
correlation = corAR1(), control=lmeControl(returnObject=TRUE, maxIter=100)), TRUE)
if(isTRUE(class(fm1)=="try-error")) { next } else { fm1=fm1 }
K <- matrix(c(0,1), 1)
t <- glht(fm1, linfct = K)
K2 <- matrix(c(0,1), 1)
t2 <- glht(fm1, linfct = K2)
#Getting AIC
AIC <- AIC(fm1)

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BIC <- BIC(fm1)
MSE <- fm1$sigma
#Intercept
intercept <- summary(fm1)$tTable[1,1]
inter_SE <- summary(fm1)$tTable[1,2]
inter_p <- summary(fm1)$tTable[1,5]
inter_t3p <- anova(fm1)[1,4]
#Intervention
interven <- summary(fm1)$tTable[2,1]
interven_SE <- summary(fm1)$tTable[2,2]
interven_p <- summary(fm1)$tTable[2,5]
interven_t3p <- anova(fm1)[2,4]
#Estimate of effect at 6 months
estimate <- summary(t)$test$coefficients[1]
estimate_se <- summary(t)$test$sigma[1]
estimate_p <- summary(t)$test$pvalues[1]
#Estimate of time-averaged effect
estimate2 <- summary(t2)$test$coefficients[1]
estimate2_se <- summary(t2)$test$sigma[1]
estimate2_p <- summary(t2)$test$pvalues[1]
#Writing out results
Sim_fit_results[(j-1)*nSim*Repeats + (k-1)*Repeats + i,c(1,2,3,4,5,6,7,8,9,10,15,16,17,18,30,31,32,33,34,35,36)]
<- c(j,Simulations[k],i,AIC,BIC,MSE, intercept, inter_SE, inter_p, inter_t3p, interven, interven_SE, interven_p,
interven_t3p, estimate, estimate_se, estimate_p, estimate2, estimate2_se, estimate2_p, cov_var)
}
#Fitted Model 2
for (i in 1:Repeats) {
j=11
cov_var <- "ar1"
data <- read.csv(paste("Sim",Simulations[k],"_",i,".csv", sep = ""))
data$Intervention <- as.factor(data$Intervention)
fm1 <- try(lme(HONOS_scores ~ Time + Intervention, random = ~ 1 | Cluster_ID/Patient_ID, data = data, method =
"ML", correlation = corAR1(), control=lmeControl(returnObject=TRUE, maxIter=100)), TRUE)
if(isTRUE(class(fm1)=="try-error")) { next } else { fm1=fm1 }
K <- matrix(c(0,0,1), 1)
t <- glht(fm1, linfct = K)
K2 <- matrix(c(0,0,1), 1)
t2 <- glht(fm1, linfct = K2)
#Getting AIC

```

```

AIC <- AIC(fm1)
BIC <- BIC(fm1)
MSE <- fm1$sigma
#Intercept
intercept <- summary(fm1)$tTable[1,1]
inter_SE <- summary(fm1)$tTable[1,2]
inter_p <- summary(fm1)$tTable[1,5]
inter_t3p <- anova(fm1)[1,4]
#Time
time <- summary(fm1)$tTable[2,1]
time_SE <- summary(fm1)$tTable[2,2]
time_p <- summary(fm1)$tTable[2,5]
time_t3p <- anova(fm1)[2,4]
#Intervention
interven <- summary(fm1)$tTable[3,1]
interven_SE <- summary(fm1)$tTable[3,2]
interven_p <- summary(fm1)$tTable[3,5]
interven_t3p <- anova(fm1)[3,4]
#Estimate of effect at 6 months
estimate <- summary(t)$test$coefficients[1]
estimate_se <- summary(t)$test$sigma[1]
estimate_p <- summary(t)$test$pvalues[1]
#Estimate of time-averaged effect
estimate2 <- summary(t2)$test$coefficients[1]
estimate2_se <- summary(t2)$test$sigma[1]
estimate2_p <- summary(t2)$test$pvalues[1]
#Writing out results
Sim_fit_results[(j-1)*nSim*Repeats + (k-1)*Repeats +
i,c(1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16,17,18,30,31,32,33,34,35,36)] <- c(j,Simulations[k],i,AIC,BIC,MSE,
intercept, inter_SE, inter_p, inter_t3p, time, time_SE, time_p, time_t3p, interven, interven_SE, interven_p,
interven_t3p, estimate, estimate_se, estimate_p, estimate2, estimate2_se, estimate2_p, cov_var)
}
#Fitted Model 3
for (i in 1:Repeats) {
  j=12
  cov_var <- "ar1"
  data <- read.csv(paste("Sim",Simulations[k],"_",i,".csv", sep = ""))
  data$Intervention <- as.factor(data$Intervention)
  data$Time <- as.factor(data$Time)

```

```

fm1 <- try(lme(HONOS_scores ~ Time + Intervention, random = ~ 1 | Cluster_ID/Patient_ID, data = data, method =
"ML", correlation = corAR1(), control=lmeControl(returnObject=TRUE, maxIter=100)), TRUE)
if(isTRUE(class(fm1)=="try-error")) { next } else { fm1=fm1 }
K <- matrix(c(0,0,0,0,0,0,0,0,0,0,0,0,0,0,1), 1)
t <- glht(fm1, linfct = K)
K2 <- matrix(c(0,0,0,0,0,0,0,0,0,0,0,0,0,0,1), 1)
t2 <- glht(fm1, linfct = K2)
#Getting AIC
AIC <- AIC(fm1)
BIC <- BIC(fm1)
MSE <- fm1$sigma
#Intercept
intercept <- summary(fm1)$tTable[1,1]
inter_SE <- summary(fm1)$tTable[1,2]
inter_p <- summary(fm1)$tTable[1,5]
inter_t3p <- anova(fm1)[1,4]
#Time
time <- NA
time_SE <- NA
time_p <- NA
time_t3p <- anova(fm1)[2,4]
#Intervention
interven <- summary(fm1)$tTable[14,1]
interven_SE <- summary(fm1)$tTable[14,2]
interven_p <- summary(fm1)$tTable[14,5]
interven_t3p <- anova(fm1)[3,4]
#Estimate of effect at 6 months
estimate <- summary(t)$test$coefficients[1]
estimate_se <- summary(t)$test$sigma[1]
estimate_p <- summary(t)$test$pvalues[1]
#Estimate of time-averaged effect
estimate2 <- summary(t2)$test$coefficients[1]
estimate2_se <- summary(t2)$test$sigma[1]
estimate2_p <- summary(t2)$test$pvalues[1]
#Writing out results
Sim_fit_results[(j-1)*nSim*Repeats + (k-1)*Repeats +
i,c(1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16,17,18,30,31,32,33,34,35,36)] <- c(j,Simulations[k],i,AIC,BIC,MSE,
intercept, inter_SE, inter_p, inter_t3p, time, time_SE, time_p, time_t3p, interven, interven_SE, interven_p,
interven_t3p, estimate, estimate_se, estimate_p, estimate2, estimate2_se, estimate2_p, cov_var)

```

```

}
#Fitted Model 4
for (i in 1:Repeats) {
  j=13
  cov_var <- "ar1"
  data <- read.csv(paste("Sim",Simulations[k],"_",i,".csv", sep ""))
  data$Intervention <- as.factor(data$Intervention)
  fm1 <- try(lme(HONOS_scores ~ Time + Intervention + Time*Intervention, random = ~ 1 | Cluster_ID/Patient_ID,
data = data, method = "ML", correlation = corAR1(), control=lmeControl(returnObject=TRUE, maxIter=100)), TRUE)
  if(isTRUE(class(fm1)=="try-error")) { next } else { fm1=fm1 }
  K <- matrix(c(0,0,1,6), 1)
  t <- glht(fm1, linfct = K)
  K2 <- matrix(c(0,0,1,7), 1)
  t2 <- glht(fm1, linfct = K2)
  #Getting AIC
  AIC <- AIC(fm1)
  BIC <- BIC(fm1)
  MSE <- fm1$sigma
  #Intercept
  intercept <- summary(fm1)$tTable[1,1]
  inter_SE <- summary(fm1)$tTable[1,2]
  inter_p <- summary(fm1)$tTable[1,5]
  inter_t3p <- anova(fm1)[1,4]
  #Time
  time <- summary(fm1)$tTable[2,1]
  time_SE <- summary(fm1)$tTable[2,2]
  time_p <- summary(fm1)$tTable[2,5]
  time_t3p <- anova(fm1)[2,4]
  #Intervention
  interven <- summary(fm1)$tTable[3,1]
  interven_SE <- summary(fm1)$tTable[3,2]
  interven_p <- summary(fm1)$tTable[3,5]
  interven_t3p <- anova(fm1)[3,4]
  #Time*Intervention
  time_int <- summary(fm1)$tTable[4,1]
  time_int_SE <- summary(fm1)$tTable[4,2]
  time_int_p <- summary(fm1)$tTable[4,5]
  time_int_t3p <- anova(fm1)[4,4]
  #Estimate of effect at 6 months

```



```

t2 <- glht(fm1, linfct = K2)
#Getting AIC
AIC <- AIC(fm1)
BIC <- BIC(fm1)
MSE <- fm1$sigma
#Intercept
intercept <- summary(fm1)$tTable[1,1]
inter_SE <- summary(fm1)$tTable[1,2]
inter_p <- summary(fm1)$tTable[1,5]
inter_t3p <- anova(fm1)[1,4]
#Time
time <- NA
time_SE <- NA
time_p <- NA
time_t3p <- anova(fm1)[2,4]
#Intervention
interven <- summary(fm1)$tTable[14,1]
interven_SE <- summary(fm1)$tTable[14,2]
interven_p <- summary(fm1)$tTable[14,5]
interven_t3p <- anova(fm1)[3,4]
#Time*Intervention
time_int <- NA
time_int_SE <- NA
time_int_p <- NA
time_int_t3p <- anova(fm1)[4,4]
#Estimate of effect at 6 months
estimate <- summary(t)$test$coefficients[1]
estimate_se <- summary(t)$test$sigma[1]
estimate_p <- summary(t)$test$pvalues[1]
#Estimate of time-averaged effect
estimate2 <- summary(t2)$test$coefficients[1]
estimate2_se <- summary(t2)$test$sigma[1]
estimate2_p <- summary(t2)$test$pvalues[1]
#Writing out results
Sim_fit_results[(j-1)*nSim*Repeats + (k-1)*Repeats +
i,c(1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16,17,18,19,20,21,22,30,31,32,33,34,35,36)] <-
c(j,Simulations[k],i,AIC,BIC,MSE, intercept, inter_SE, inter_p, inter_t3p, time, time_SE, time_p, time_t3p,
interven, interven_SE, interven_p, interven_t3p, time_int, time_int_SE, time_int_p, time_int_t3p, estimate,
estimate_se, estimate_p, estimate2, estimate2_se, estimate2_p, cov_var)

```

```

}
#Fitted Model 6
for (i in 1:Repeats) {
  j=15
  cov_var <- "ar1"
  data <- read.csv(paste("Sim",Simulations[k],"_",i,".csv", sep ""))
  data$Intervention <- as.factor(data$Intervention)
  fm1 <- try(lme(HONOS_scores ~ Time + Intervention + TimeInt, random = ~ 1 | Cluster_ID/Patient_ID, data = data,
method = "ML", correlation = corAR1(), control=lmeControl(returnObject=TRUE, maxIter=100)), TRUE)
  if(isTRUE(class(fm1)=="try-error")) { next } else { fm1=fm1 }
  K <- matrix(c(0, 0, 1, 6), 1)
  t <- glht(fm1, linfct = K)
  K2 <- matrix(c(0, 0, 1, 6), 1)
  t2 <- glht(fm1, linfct = K2)
  #Getting AIC
  AIC <- AIC(fm1)
  BIC <- BIC(fm1)
  MSE <- fm1$sigma
  #Intercept
  intercept <- summary(fm1)$tTable[1,1]
  inter_SE <- summary(fm1)$tTable[1,2]
  inter_p <- summary(fm1)$tTable[1,5]
  inter_t3p <- anova(fm1)[1,4]
  #Time
  time <- summary(fm1)$tTable[2,1]
  time_SE <- summary(fm1)$tTable[2,2]
  time_p <- summary(fm1)$tTable[2,5]
  time_t3p <- anova(fm1)[2,4]
  #Intervention
  interven <- summary(fm1)$tTable[3,1]
  interven_SE <- summary(fm1)$tTable[3,2]
  interven_p <- summary(fm1)$tTable[3,5]
  interven_t3p <- anova(fm1)[3,4]
  #Time*Intervention
  timeint <- summary(fm1)$tTable[4,1]
  timeint_SE <- summary(fm1)$tTable[4,2]
  timeint_p <- summary(fm1)$tTable[4,5]
  timeint_t3p <- anova(fm1)[4,4]
  #Estimate of effect at 6 months
}

```

```

estimate <- summary(t)$test$coefficients[1]
estimate_se <- summary(t)$test$sigma[1]
estimate_p <- summary(t)$test$pvalues[1]
#Estimate of time-averaged effect
estimate2 <- summary(t2)$test$coefficients[1]
estimate2_se <- summary(t2)$test$sigma[1]
estimate2_p <- summary(t2)$test$pvalues[1]
#Writing out results
Sim_fit_results[(j-1)*nSim*Repeats + (k-1)*Repeats +
i,c(1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16,17,18,23,24,25,26,30,31,32,33,34,35,36)] <-
c(j,Simulations[k],i,AIC,BIC,MSE, intercept, inter_SE, inter_p, inter_t3p, time, time_SE, time_p, time_t3p,
interven, interven_SE, interven_p, interven_t3p, timeint, timeint_SE, timeint_p, timeint_t3p, estimate, estimate_se,
estimate_p, estimate2, estimate2_se, estimate2_p, cov_var)
}
#Fitted Model 7
for (i in 1:Repeats) {
  j=16
  cov_var <- "ar1"
  data <- read.csv(paste("Sim",Simulations[k],"_",i,".csv", sep ""))
  data$Intervention <- as.factor(data$Intervention)
  fm1 <- try(lme(HONOS_scores ~ Time + TimeInt, random = ~ 1 | Cluster_ID/Patient_ID, data = data, method = "ML",
correlation = corAR1(), control=lmeControl(returnObject=TRUE, maxIter=100)), TRUE)
  if(isTRUE(class(fm1)=="try-error")) { next } else { fm1=fm1 }
  K <- matrix(c(0, 0, 6), 1)
  t <- glht(fm1, linfct = K)
  K2 <- matrix(c(0, 0, 6), 1)
  t2 <- glht(fm1, linfct = K2)
  #Getting AIC
  AIC <- AIC(fm1)
  BIC <- BIC(fm1)
  MSE <- fm1$sigma
  #Intercept
  intercept <- summary(fm1)$tTable[1,1]
  inter_SE <- summary(fm1)$tTable[1,2]
  inter_p <- summary(fm1)$tTable[1,5]
  inter_t3p <- anova(fm1)[1,4]
  #Time
  time <- summary(fm1)$tTable[2,1]
  time_SE <- summary(fm1)$tTable[2,2]

```



```

AIC <- AIC(fm1)
BIC <- BIC(fm1)
MSE <- fm1$sigma
#Intercept
intercept <- summary(fm1)$tTable[1,1]
inter_SE <- summary(fm1)$tTable[1,2]
inter_p <- summary(fm1)$tTable[1,5]
inter_t3p <- anova(fm1)[1,4]
#Time
time <- NA
time_SE <- NA
time_p <- NA
time_t3p <- anova(fm1)[1,4]
#Exposure Time
timeint <- NA
timeint_SE <- NA
timeint_p <- NA
timeint_t3p <- anova(fm1)[2,4]
#Estimate of effect at 6 months
estimate <- summary(t)$test$coefficients[1]
estimate_se <- summary(t)$test$sigma[1]
estimate_p <- summary(t)$test$pvalues[1]
#Estimate of time-averaged effect
estimate2 <- summary(t2)$test$coefficients[1]
estimate2_se <- summary(t2)$test$sigma[1]
estimate2_p <- summary(t2)$test$pvalues[1]
#Writing out results
Sim_fit_results[(j-1)*nSim*Repeats + (k-1)*Repeats +
i,c(1,2,3,4,5,6,7,8,9,10,11,12,13,14,23,24,25,26,30,31,32,33,34,35,36)] <- c(j,Simulations[k],i,AIC,BIC,MSE,
intercept, inter_SE, inter_p, inter_t3p, time, time_SE, time_p, time_t3p, timeint, timeint_SE, timeint_p,
timeint_t3p, estimate, estimate_se, estimate_p, estimate2, estimate2_se, estimate2_p, cov_var)
}
#Fitted Model 9
for (i in 1:Repeats) {
j=18
cov_var <- "ar1"
data <- read.csv(paste("Sim",Simulations[k],"_",i,".csv", sep = ""))
data$Intervention <- as.factor(data$Intervention)

```

```

fm1 <- try(lme(HONOS_scores ~ Time + Intervention + TimeInt + I(Time^2), random = ~ 1 | Cluster_ID/Patient_ID,
data = data, method = "ML", correlation = corAR1(), control=lmeControl(returnObject=TRUE, maxIter=100)), TRUE)
if(isTRUE(class(fm1)=="try-error")) { next } else { fm1=fm1 }
K <- matrix(c(0, 0, 1, 6, 0), 1)
t <- glht(fm1, linfct = K)
K2 <- matrix(c(0, 0, 1, 6, 0), 1)
t2 <- glht(fm1, linfct = K2)
#Getting AIC
AIC <- AIC(fm1)
BIC <- BIC(fm1)
MSE <- fm1$sigma
#Intercept
intercept <- summary(fm1)$tTable[1,1]
inter_SE <- summary(fm1)$tTable[1,2]
inter_p <- summary(fm1)$tTable[1,5]
inter_t3p <- anova(fm1)[1,4]
#Time
time <- summary(fm1)$tTable[2,1]
time_SE <- summary(fm1)$tTable[2,2]
time_p <- summary(fm1)$tTable[2,5]
time_t3p <- anova(fm1)[2,4]
#Intervention
interven <- summary(fm1)$tTable[3,1]
interven_SE <- summary(fm1)$tTable[3,2]
interven_p <- summary(fm1)$tTable[3,5]
interven_t3p <- anova(fm1)[3,4]
#Time*Intervention
timeint <- summary(fm1)$tTable[4,1]
timeint_SE <- summary(fm1)$tTable[4,2]
timeint_p <- summary(fm1)$tTable[4,5]
timeint_t3p <- anova(fm1)[4,4]
#Timesq
timesq <- summary(fm1)$tTable[5,1]
timesq_SE <- summary(fm1)$tTable[5,2]
timesq_p <- summary(fm1)$tTable[5,5]
timesq_t3p <- anova(fm1)[5,4]
#Estimate of effect at 6 months
estimate <- summary(t)$test$coefficients[1]
estimate_se <- summary(t)$test$sigma[1]

```

```

estimate_p <- summary(t)$test$pvalues[1]
#Estimate of time-averaged effect
estimate2 <- summary(t2)$test$coefficients[1]
estimate2_se <- summary(t2)$test$sigma[1]
estimate2_p <- summary(t2)$test$pvalues[1]
#Writing out results
Sim_fit_results[(j-1)*nSim*Repeats + (k-1)*Repeats +
i,c(1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16,17,18,23,24,25,26,27,28,29,30,31,32,33,34,35,36)] <-
c(j,Simulations[k],i,AIC,BIC,MSE, intercept, inter_SE, inter_p, inter_t3p, time, time_SE, time_p, time_t3p,
interven, interven_SE, interven_p, interven_t3p, timeint, timeint_SE, timeint_p, timeint_t3p, timesq, timesq_SE,
timesq_p, estimate, estimate_se, estimate_p, estimate2, estimate2_se, estimate2_p, cov_var)
}
}

```