Multinomial-GEE-model—osteophyte-syndesmophyte.R

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```
library(tidyverse)
```

```
## -- Attaching core tidyverse packages ------------------------ tidyverse 2.0.0 --
## v dplyr     1.1.3     v readr     2.1.4
## v forcats   1.0.0     v stringr   1.5.0
## v ggplot2   3.4.3     v tibble    3.2.1
## v lubridate 1.9.2     v tidyr     1.3.0
## v purrr     1.0.2
## -- Conflicts ------------------------------------------ tidyverse_conflicts() --
## x dplyr::filter() masks stats::filter()
## x dplyr::lag()    masks stats::lag()
## i Use the conflicted package (<http://conflicted.r-lib.org/>) to force all conflicts to become errors
```

```
library(prettyR)
library(multgee)
```

```
## Loading required package: gnm
```

```
library(dplyr)
library(brms)
```

```
## Warning: package 'brms' was built under R version 4.3.2
```

```
## Loading required package: Rcpp
## Loading 'brms' package (version 2.21.0). Useful instructions
## can be found by typing help('brms'). A more detailed introduction
## to the package is available through vignette('brms_overview').
##
## Attaching package: 'brms'
##
## The following object is masked from 'package:stats':
##
##     ar
```

```
#Import the table
file_path <- "/Users/laurapina-vegas/Desktop/xray_spa_dc_synd_Osteo_vert3s.csv"
xray_spa_dc_synd_Osteo_vert3s <- read.csv(file_path)

#We wished to analyse the association between a syndesmophyte at one time point
#and an osteophyte on an adjacent vertebra (upper or lower) at the subsequent
#time point using a GEE time-lagged and autoregressive model :
```

```
#may have been confused (i.e., vertebral unit with both syndesmophytes
#and osteophytes + vertebral unit in which a syndesmophyte leads to an
#osteophyte or the other way round, over time),
```

```
#(and not the data from each reader) to determine the presence/absence of
#an osteophyte/syndesmophyte,
```

```
#syndesmophytes and osteophytes (only one place can be available:
#either for an osteophyte or for a syndesmophyte in a adjacent vertebra).

#We created the nominal categorical variable Osteo_synm_tot_corr_upp_low_2
#corresponding to the outcome.
#For the main analysis, we considered that if there was a syndesmophyte
#above OR below (even if one side was an osteophyte), the variable
#Osteo_synm_tot_corr_upp_low_2 was coded as the presence of a syndesmophyte
#on the adjacent vertebra ( upper or lower).
#Thus Osteo_synm_tot_corr_upp_low_2 =
# - 2: synm_upp== 1 or synm_low == 1
# - 1:  Osteo_upp == 1 or Osteo_low == 1 : 1
# - 0: Osteo_upp == 0 and Osteo_low == 0 and synm_upp == 0 and synm_low == 0
#with synm = syndesmophyte, Osteo = osteophyte,
#with _upp = upper vertebra, _low = lower vertebra.

#The variable Osteo_synm_tot_corr_upp_low_2_lag is the lag of the
#outcome Osteo_synm_tot_corr_upp_low_2.

#The variable synm_tot_lag is the lag of synm_tot and is the main variable
#of interest corresponding to the presence of a syndesmophyte at a vertebral
#level at the previous time point.

#The variable t_new corresponds to our time variable
#(one point in time per medical visit).

#I created the id_vertebra variable for use in the multilevel analysis.
#It corresponds to the concatenation of the patient identifier
#and the vertebra number.
xray_spa_dc_synd_Osteo_vert3s$vertebra2 <- sprintf("%02d", xray_spa_dc_synd_Osteo_vert3s$vertebra)
xray_spa_dc_synd_Osteo_vert3s$id2 <- sprintf("%05d", xray_spa_dc_synd_Osteo_vert3s$id)
xray_spa_dc_synd_Osteo_vert3s$id_vertebra <- paste0(xray_spa_dc_synd_Osteo_vert3s$id2, xray_spa_dc_synd
xray_spa_dc_synd_Osteo_vert3s$id_vertebra <- as.numeric(as.character(xray_spa_dc_synd_Osteo_vert3s$id_v

#Descriptive analysis :
#In the overall cohort :
table(xray_spa_dc_synd_Osteo_vert3s$Osteo_synm_tot_corr_upp_low_2,useNA="always")
```

```
##
##    0    1    2 <NA>
## 9393  847  280    0
```

```
prop.table(table(xray_spa_dc_synd_Osteo_vert3s$Osteo_synm_tot_corr_upp_low_2))
```

```
##
```

```
##          0          1          2
## 0.89287072 0.08051331 0.02661597
```

```r
#If syndesmophyte at the previous time point (synm_tot_lag) :
synm_previous_time_point <- subset(xray_spa_dc_synd_Osteo_vert3s, synm_tot_lag==1)
table(synm_previous_time_point$Osteo_synm_tot_corr_upp_low_2,useNA="always")
```

```
##
##    0    1    2 <NA>
##   38    5   49    0
```

```r
prop.table(table(synm_previous_time_point$Osteo_synm_tot_corr_upp_low_2))
```

```
##
##          0          1          2
## 0.41304348 0.05434783 0.53260870
```

```r
#Table 2x3 syndesmophyte at previous time point versus outcome
tableau_contingence <- table(
  xray_spa_dc_synd_Osteo_vert3s$synm_tot_lag,
  xray_spa_dc_synd_Osteo_vert3s$Osteo_synm_tot_corr_upp_low_2,
  dnn = c("synm_tot_lag", "Osteo_synm_tot_corr_upp_low_2")
)
print(tableau_contingence)
```

```
##             Osteo_synm_tot_corr_upp_low_2
## synm_tot_lag    0    1    2
##            0 5772  658  152
##            1   38    5   49
```

```r
pourcentages <- prop.table(tableau_contingence,1) * 100

tableau_complet <- addmargins(tableau_contingence)
tableau_pourcentages <- addmargins(pourcentages)

table_final <- matrix(
  paste0(tableau_contingence, " (", round(pourcentages, 2), "%)"),
  nrow = nrow(tableau_contingence),
  ncol = ncol(tableau_contingence),
  dimnames = dimnames(tableau_contingence)
)
print(table_final)
```

```
##             Osteo_synm_tot_corr_upp_low_2
## synm_tot_lag 0               1           2
##            0 "5772 (87.69%)" "658 (10%)" "152 (2.31%)"
##            1 "38 (41.3%)"    "5 (5.43%)" "49 (53.26%)"
```

```r
#I create the table without the missing variables.
xray_spa_dc_synd_Osteo_vert4 <- xray_spa_dc_synd_Osteo_vert3s %>%filter(!is.na(synm_tot_lag))
n_distinct(xray_spa_dc_synd_Osteo_vert4$id) #324 id
```

```
## [1] 324
```

```
n_distinct(xray_spa_dc_synd_Osteo_vert4$id_vert) #3696 id_vert
```

```
## [1] 3696
```

```
xray_spa_dc_synd_Osteo_vert4$Osteo_synm_tot_corr_upp_low_2 <- relevel(as.factor(xray_spa_dc_synd_Osteo_v
xray_spa_dc_synd_Osteo_vert4$Osteo_synm_tot_corr_upp_low_2_lag <- relevel(as.factor(xray_spa_dc_synd_Os
xray_spa_dc_synd_Osteo_vert4$synm_tot_lag <- relevel(as.factor(xray_spa_dc_synd_Osteo_vert4$synm_tot_lag
xray_spa_dc_synd_Osteo_vert4$sexe <- relevel(as.factor(xray_spa_dc_synd_Osteo_vert4$sexe), ref = "0")
xray_spa_dc_synd_Osteo_vert4$hla <- relevel(as.factor(xray_spa_dc_synd_Osteo_vert4$hla), ref = "0")
xray_spa_dc_synd_Osteo_vert4$tabac_10y <- relevel(as.factor(xray_spa_dc_synd_Osteo_vert4$tabac_10y), ref
xray_spa_dc_synd_Osteo_vert4$profession <- relevel(as.factor(xray_spa_dc_synd_Osteo_vert4$profession), r
xray_spa_dc_synd_Osteo_vert4$bdmard_lag <- relevel(as.factor(xray_spa_dc_synd_Osteo_vert4$bdmard_lag), r

#multinomial time-lagged and autoregressive univariate GEE models
summary(nomLORgee(Osteo_synm_tot_corr_upp_low_2 ~ synm_tot_lag,
                  data = xray_spa_dc_synd_Osteo_vert4,
                  id = id_vertebra,
                  repeated = t_new,
                  LORstr = "time.exch"))
```

```
## GEE FOR NOMINAL MULTINOMIAL RESPONSES
## version 1.6.0 modified 2017-07-10
##
## Link : Baseline Category Logit
##
## Local Odds Ratios:
## Structure:         time.exch
## Model:             2way
## Homogenous scores: TRUE
##
## call:
## nomLORgee(formula = Osteo_synm_tot_corr_upp_low_2 ~ synm_tot_lag,
##     data = xray_spa_dc_synd_Osteo_vert4, id = id_vertebra, repeated = t_new,
##     LORstr = "time.exch")
##
## Summary of residuals:
##      Min.   1st Qu.    Median      Mean   3rd Qu.      Max.
## -0.876082 -0.100652 -0.100652 -0.000065  0.123918  0.952439
##
## Number of Iterations: 3
##
## Coefficients:
##                  Estimate   san.se   san.z Pr(>|san.z|)
## beta10            3.62847  0.09808  36.994    < 2.2e-16 ***
## synm_tot_lag1:1 -3.77402  0.24889 -15.163    < 2.2e-16 ***
## beta20            1.46467  0.10817  13.541    < 2.2e-16 ***
## synm_tot_lag1:2 -3.83868  0.55568  -6.908    < 2.2e-16 ***
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Local Odds Ratios Estimates:
```

```
##         [,1]  [,2]    [,3]  [,4]
## [1,]   0.000 0.000 277.879 0.281
## [2,]   0.000 0.000   0.281 1.331
## [3,] 277.879 0.281   0.000 0.000
## [4,]   0.281 1.331   0.000 0.000
##
## p-value of Null model: < 0.0001
```

```
summary(nomLORgee(Osteo_synm_tot_corr_upp_low_2 ~ Osteo_synm_tot_corr_upp_low_2_lag,
                  data = xray_spa_dc_synd_Osteo_vert4,
                  id = id_vertebra,
                  repeated = t_new,
                  LORstr = "time.exch"))
```

```
## GEE FOR NOMINAL MULTINOMIAL RESPONSES
## version 1.6.0 modified 2017-07-10
##
## Link : Baseline Category Logit
##
## Local Odds Ratios:
## Structure:         time.exch
## Model:             2way
## Homogenous scores: TRUE
##
## call:
## nomLORgee(formula = Osteo_synm_tot_corr_upp_low_2 ~ Osteo_synm_tot_corr_upp_low_2_lag,
##     data = xray_spa_dc_synd_Osteo_vert4, id = id_vertebra, repeated = t_new,
##     LORstr = "time.exch")
##
## Summary of residuals:
##       Min.    1st Qu.     Median       Mean    3rd Qu.       Max.
## -0.9231999 -0.0619353 -0.0619353  0.0005776  0.0768001  0.9698357
##
## Number of Iterations: 9
##
## Coefficients:
##                                     Estimate   san.se    san.z Pr(>|san.z|)
## beta10                               4.12885  0.11964  34.5092    < 2.2e-16
## Osteo_synm_tot_corr_upp_low_2_lag1:1 -1.95578  0.40623  -4.8145    < 2.2e-16
## Osteo_synm_tot_corr_upp_low_2_lag2:1 -5.82574  0.28873 -20.1768    < 2.2e-16
## beta20                               1.42709  0.13477  10.5888    < 2.2e-16
## Osteo_synm_tot_corr_upp_low_2_lag1:2  2.09436  0.40752   5.1393    < 2.2e-16
## Osteo_synm_tot_corr_upp_low_2_lag2:2 -4.72930  0.34150 -13.8488    < 2.2e-16
##
## beta10                               ***
## Osteo_synm_tot_corr_upp_low_2_lag1:1 ***
## Osteo_synm_tot_corr_upp_low_2_lag2:1 ***
## beta20                               ***
## Osteo_synm_tot_corr_upp_low_2_lag1:2 ***
## Osteo_synm_tot_corr_upp_low_2_lag2:2 ***
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Local Odds Ratios Estimates:
```

```
##         [,1]       [,2]    [,3]       [,4]
## [1,]   0.000          0 246.637          0
## [2,]   0.000          0   0.000 3505970786
## [3,] 246.637          0   0.000          0
## [4,]   0.000 3505970786   0.000          0
##
## p-value of Null model: < 0.0001
```

```
summary(nomLORgee(Osteo_synm_tot_corr_upp_low_2 ~ sexe,
                  data = xray_spa_dc_synd_Osteo_vert4,
                  id = id_vertebra,
                  repeated = t_new,
                  LORstr = "time.exch"))
```

```
## GEE FOR NOMINAL MULTINOMIAL RESPONSES
## version 1.6.0 modified 2017-07-10
##
## Link : Baseline Category Logit
##
## Local Odds Ratios:
## Structure:         time.exch
## Model:             2way
## Homogenous scores: TRUE
##
## call:
## nomLORgee(formula = Osteo_synm_tot_corr_upp_low_2 ~ sexe, data = xray_spa_dc_synd_Osteo_vert4,
##     id = id_vertebra, repeated = t_new, LORstr = "time.exch")
##
## Summary of residuals:
##       Min.    1st Qu.     Median       Mean    3rd Qu.       Max.
## -0.8746648 -0.1162792 -0.0813656  0.0002197  0.1359894  0.9186344
##
## Number of Iterations: 2
##
## Coefficients:
##         Estimate   san.se   san.z Pr(>|san.z|)
## beta10   4.57041  0.21377 21.3796    < 2.2e-16 ***
## sexe1:1 -1.80929  0.23488 -7.7030    < 2.2e-16 ***
## beta20   2.55256  0.22172 11.5125    < 2.2e-16 ***
## sexe1:2 -2.15408  0.25308 -8.5114    < 2.2e-16 ***
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Local Odds Ratios Estimates:
##         [,1]  [,2]    [,3]  [,4]
## [1,]   0.000 0.000 277.878 0.281
## [2,]   0.000 0.000   0.281 1.331
## [3,] 277.878 0.281   0.000 0.000
## [4,]   0.281 1.331   0.000 0.000
##
## p-value of Null model: < 0.0001
```

```r
summary(nomLORgee(Osteo_synm_tot_corr_upp_low_2 ~ age_m0,
                  data = xray_spa_dc_synd_Osteo_vert4,
                  id = id_vertebra,
                  repeated = t_new,
                  LORstr = "time.exch"))
```

```
## GEE FOR NOMINAL MULTINOMIAL RESPONSES
## version 1.6.0 modified 2017-07-10
##
## Link : Baseline Category Logit
##
## Local Odds Ratios:
## Structure:         time.exch
## Model:             2way
## Homogenous scores: TRUE
##
## call:
## nomLORgee(formula = Osteo_synm_tot_corr_upp_low_2 ~ age_m0, data = xray_spa_dc_synd_Osteo_vert4,
##     id = id_vertebra, repeated = t_new, LORstr = "time.exch")
##
## Summary of residuals:
##       Min.    1st Qu.     Median       Mean    3rd Qu.       Max.
## -0.9758304 -0.0736512 -0.0139124  0.0006703  0.0943502  0.9863777
##
## Number of Iterations: 3
##
## Coefficients:
##          Estimate   san.se   san.z Pr(>|san.z|)
## beta10    5.89208  0.39852 14.7848      < 2e-16 ***
## age_m0:1 -0.07162  0.01024 -6.9966      < 2e-16 ***
## beta20   -0.53380  0.44943 -1.1877      0.23494
## age_m0:2  0.04144  0.01131  3.6626      0.00025 ***
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Local Odds Ratios Estimates:
##         [,1]       [,2]    [,3]       [,4]
## [1,]   0.000          0 246.637          0
## [2,]   0.000          0   0.000 3505969738
## [3,] 246.637          0   0.000          0
## [4,]   0.000 3505969738   0.000          0
##
## p-value of Null model: < 0.0001
```

```r
summary(nomLORgee(Osteo_synm_tot_corr_upp_low_2 ~ bmi,
                  data = xray_spa_dc_synd_Osteo_vert4,
                  id = id_vertebra,
                  repeated = t_new,
                  LORstr = "time.exch"))
```

```
## GEE FOR NOMINAL MULTINOMIAL RESPONSES
## version 1.6.0 modified 2017-07-10
##
```

```
## Link : Baseline Category Logit
##
## Local Odds Ratios:
## Structure:         time.exch
## Model:             2way
## Homogenous scores: TRUE
##
## call:
## nomLORgee(formula = Osteo_synm_tot_corr_upp_low_2 ~ bmi, data = xray_spa_dc_synd_Osteo_vert4,
##     id = id_vertebra, repeated = t_new, LORstr = "time.exch")
##
## Summary of residuals:
##       Min.    1st Qu.     Median       Mean    3rd Qu.       Max.
## -0.9246092 -0.0964504 -0.0681066  0.0000921  0.1216046  0.9383350
##
## Number of Iterations: 3
##
## Coefficients:
##        Estimate   san.se   san.z Pr(>|san.z|)
## beta10  5.91438  0.46366 12.7559       <2e-16 ***
## bmi:1  -0.10480  0.01795 -5.8384       <2e-16 ***
## beta20  2.08115  0.51932  4.0074        6e-05 ***
## bmi:2  -0.03558  0.02010 -1.7708       0.0766 .
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Local Odds Ratios Estimates:
##         [,1]  [,2]    [,3]  [,4]
## [1,]   0.000 0.000 277.878 0.281
## [2,]   0.000 0.000   0.281 1.331
## [3,] 277.878 0.281   0.000 0.000
## [4,]   0.281 1.331   0.000 0.000
##
## p-value of Null model: < 0.0001
```

```
summary(nomLORgee(Osteo_synm_tot_corr_upp_low_2 ~ hla,
                  data = xray_spa_dc_synd_Osteo_vert4,
                  id = id_vertebra,
                  repeated = t_new,
                  LORstr = "time.exch"))
```

```
## GEE FOR NOMINAL MULTINOMIAL RESPONSES
## version 1.6.0 modified 2017-07-10
##
## Link : Baseline Category Logit
##
## Local Odds Ratios:
## Structure:         time.exch
## Model:             2way
## Homogenous scores: TRUE
##
## call:
## nomLORgee(formula = Osteo_synm_tot_corr_upp_low_2 ~ hla, data = xray_spa_dc_synd_Osteo_vert4,
##     id = id_vertebra, repeated = t_new, LORstr = "time.exch")
```

```
##
## Summary of residuals:
##       Min.    1st Qu.     Median       Mean    3rd Qu.       Max.
## -0.8909766 -0.0795645 -0.0795645  0.0001015  0.1090234  0.9204355
##
## Number of Iterations: 2
##
## Coefficients:
##        Estimate   san.se   san.z Pr(>|san.z|)
## beta10  3.25664  0.15393 21.1563      < 2e-16 ***
## hla1:1  0.15268  0.18762  0.8138      0.41578
## beta20  1.46156  0.16782  8.7090      < 2e-16 ***
## hla1:2 -0.46799  0.20895 -2.2397      0.02511 *
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Local Odds Ratios Estimates:
##         [,1]  [,2]    [,3]  [,4]
## [1,]   0.000 0.000 277.879 0.281
## [2,]   0.000 0.000   0.281 1.331
## [3,] 277.879 0.281   0.000 0.000
## [4,]   0.281 1.331   0.000 0.000
##
## p-value of Null model: < 0.0001
```

```
summary(nomLORgee(Osteo_synm_tot_corr_upp_low_2 ~ tabac_10y,
                  data = xray_spa_dc_synd_Osteo_vert4,
                  id = id_vertebra,
                  repeated = t_new,
                  LORstr = "time.exch"))
```

```
## GEE FOR NOMINAL MULTINOMIAL RESPONSES
## version 1.6.0 modified 2017-07-10
##
## Link : Baseline Category Logit
##
## Local Odds Ratios:
## Structure:         time.exch
## Model:             2way
## Homogenous scores: TRUE
##
## call:
## nomLORgee(formula = Osteo_synm_tot_corr_upp_low_2 ~ tabac_10y,
##     data = xray_spa_dc_synd_Osteo_vert4, id = id_vertebra, repeated = t_new,
##     LORstr = "time.exch")
##
## Summary of residuals:
##       Min.    1st Qu.     Median       Mean    3rd Qu.       Max.
## -0.8697799 -0.1048955 -0.0942339  0.0001437  0.1304641  0.9057661
##
## Number of Iterations: 2
##
## Coefficients:
##              Estimate   san.se   san.z Pr(>|san.z|)
```

```
## beta10        3.52660  0.12988 27.1538      < 2e-16 ***
## tabac_10y1:1 -0.34149  0.17680 -1.9315      0.05343 .
## beta20        1.41160  0.14441  9.7748      < 2e-16 ***
## tabac_10y1:2 -0.44896  0.19942 -2.2513      0.02437 *
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Local Odds Ratios Estimates:
##         [,1]  [,2]    [,3]  [,4]
## [1,]   0.000 0.000 277.878 0.281
## [2,]   0.000 0.000   0.281 1.331
## [3,] 277.878 0.281   0.000 0.000
## [4,]   0.281 1.331   0.000 0.000
##
## p-value of Null model: 0.024368
```

```
summary(nomLORgee(Osteo_synm_tot_corr_upp_low_2 ~ profession,
                  data = xray_spa_dc_synd_Osteo_vert4,
                  id = id_vertebra,
                  repeated = t_new,
                  LORstr = "time.exch"))
```

```
## Warning in vglm.fitter(x = x, y = y, w = w, offset = offset, Xm2 = Xm2, : some
## quantities such as z, residuals, SEs may be inaccurate due to convergence at a
## half-step

## GEE FOR NOMINAL MULTINOMIAL RESPONSES
## version 1.6.0 modified 2017-07-10
##
## Link : Baseline Category Logit
##
## Local Odds Ratios:
## Structure:         time.exch
## Model:             2way
## Homogenous scores: TRUE
##
## call:
## nomLORgee(formula = Osteo_synm_tot_corr_upp_low_2 ~ profession,
##     data = xray_spa_dc_synd_Osteo_vert4, id = id_vertebra, repeated = t_new,
##     LORstr = "time.exch")
##
## Summary of residuals:
##       Min.    1st Qu.     Median       Mean    3rd Qu.       Max.
## -0.9198151 -0.1123659 -0.0447477  0.0002042  0.1407345  0.9552523
##
## Number of Iterations: 3
##
## Coefficients:
##               Estimate   san.se   san.z Pr(>|san.z|)
## beta10         3.19446  0.19921 16.0359      < 2e-16 ***
## profession2:1  0.21633  0.22718  0.9522      0.34098
## profession3:1  0.06195  0.29332  0.2112      0.83273
## beta20         0.65790  0.24164  2.7226      0.00648 **
```

```
## profession2:2  0.71857  0.26999  2.6615      0.00778 **
## profession3:2 -0.42463  0.38893 -1.0918      0.27493
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Local Odds Ratios Estimates:
##         [,1]  [,2]    [,3]  [,4]
## [1,]   0.000 0.000 288.641 0.253
## [2,]   0.000 0.000   0.253 1.395
## [3,] 288.641 0.253   0.000 0.000
## [4,]   0.253 1.395   0.000 0.000
##
## p-value of Null model: < 0.0001
```

```
summary(nomLORgee(Osteo_synm_tot_corr_upp_low_2 ~ bdmard_lag,
                  data = xray_spa_dc_synd_Osteo_vert4,
                  id = id_vertebra,
                  repeated = t_new,
                  LORstr = "time.exch"))
```

```
## GEE FOR NOMINAL MULTINOMIAL RESPONSES
## version 1.6.0 modified 2017-07-10
##
## Link : Baseline Category Logit
##
## Local Odds Ratios:
## Structure:         time.exch
## Model:             2way
## Homogenous scores: TRUE
##
## call:
## nomLORgee(formula = Osteo_synm_tot_corr_upp_low_2 ~ bdmard_lag,
##     data = xray_spa_dc_synd_Osteo_vert4, id = id_vertebra, repeated = t_new,
##     LORstr = "time.exch")
##
## Summary of residuals:
##       Min.    1st Qu.     Median       Mean    3rd Qu.       Max.
## -0.8798057 -0.0914722 -0.0914722  0.0000592  0.1201943  0.9085278
##
## Number of Iterations: 3
##
## Coefficients:
##               Estimate   san.se   san.z Pr(>|san.z|)
## beta10         3.42203  0.09836 34.7917      < 2e-16 ***
## bdmard_lag1:1 -0.32573  0.15227 -2.1391      0.03242 *
## beta20         1.15837  0.11189 10.3530      < 2e-16 ***
## bdmard_lag1:2  0.13712  0.17315  0.7919      0.42841
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Local Odds Ratios Estimates:
##         [,1]  [,2]    [,3]  [,4]
## [1,]   0.000 0.000 329.779 0.270
## [2,]   0.000 0.000   0.270 1.345
```

```
## [3,] 329.779 0.270   0.000 0.000
## [4,]   0.270 1.345   0.000 0.000
##
## p-value of Null model: < 0.0001
```

```
#multinomial time-lagged and autoregressive multivariable GEE models adding variable 1 by 1
summary(nomLORgee(Osteo_synm_tot_corr_upp_low_2 ~ synm_tot_lag + Osteo_synm_tot_corr_upp_low_2_lag,
                  data = xray_spa_dc_synd_Osteo_vert4,
                  id = id_vertebra,
                  repeated = t_new,
                  LORstr = "time.exch"))
```

```
## GEE FOR NOMINAL MULTINOMIAL RESPONSES
## version 1.6.0 modified 2017-07-10
##
## Link : Baseline Category Logit
##
## Local Odds Ratios:
## Structure:         time.exch
## Model:             2way
## Homogenous scores: TRUE
##
## call:
## nomLORgee(formula = Osteo_synm_tot_corr_upp_low_2 ~ synm_tot_lag +
##     Osteo_synm_tot_corr_upp_low_2_lag, data = xray_spa_dc_synd_Osteo_vert4,
##     id = id_vertebra, repeated = t_new, LORstr = "time.exch")
##
## Summary of residuals:
##       Min.    1st Qu.     Median       Mean    3rd Qu.       Max.
## -0.9230744 -0.0626653 -0.0626653  0.0008823  0.0769256  0.9921701
##
## Number of Iterations: 8
##
## Coefficients:
##                                      Estimate   san.se    san.z Pr(>|san.z|)
## beta10                                4.17023  0.10187  40.9355      < 2e-16
## synm_tot_lag1:1                      -2.77817  0.40011  -6.9434      < 2e-16
## Osteo_synm_tot_corr_upp_low_2_lag1:1 -0.94262  0.51109  -1.8443      0.06513
## Osteo_synm_tot_corr_upp_low_2_lag2:1 -5.62367  0.28347 -19.8384      < 2e-16
## beta20                                1.48032  0.10902  13.5788      < 2e-16
## synm_tot_lag1:2                      -2.34991  0.52895  -4.4426        1e-05
## Osteo_synm_tot_corr_upp_low_2_lag1:2  3.08120  0.51376   5.9973      < 2e-16
## Osteo_synm_tot_corr_upp_low_2_lag2:2 -6.11220  1.37090  -4.4585        1e-05
##
## beta10                                ***
## synm_tot_lag1:1                       ***
## Osteo_synm_tot_corr_upp_low_2_lag1:1 .
## Osteo_synm_tot_corr_upp_low_2_lag2:1 ***
## beta20                                ***
## synm_tot_lag1:2                       ***
## Osteo_synm_tot_corr_upp_low_2_lag1:2 ***
## Osteo_synm_tot_corr_upp_low_2_lag2:2 ***
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

```
##
## Local Odds Ratios Estimates:
##         [,1]  [,2]    [,3]  [,4]
## [1,]   0.000 0.000 277.878 0.281
## [2,]   0.000 0.000   0.281 1.331
## [3,] 277.878 0.281   0.000 0.000
## [4,]   0.281 1.331   0.000 0.000
##
## p-value of Null model: < 0.0001
```

```
summary(nomLORgee(Osteo_synm_tot_corr_upp_low_2 ~ synm_tot_lag + Osteo_synm_tot_corr_upp_low_2_lag + se
                  data = xray_spa_dc_synd_Osteo_vert4,
                  id = id_vertebra,
                  repeated = t_new,
                  LORstr = "time.exch"))
```

```
## GEE FOR NOMINAL MULTINOMIAL RESPONSES
## version 1.6.0 modified 2017-07-10
##
## Link : Baseline Category Logit
##
## Local Odds Ratios:
## Structure:         time.exch
## Model:             2way
## Homogenous scores: TRUE
##
## call:
## nomLORgee(formula = Osteo_synm_tot_corr_upp_low_2 ~ synm_tot_lag +
##     Osteo_synm_tot_corr_upp_low_2_lag + sexe, data = xray_spa_dc_synd_Osteo_vert4,
##     id = id_vertebra, repeated = t_new, LORstr = "time.exch")
##
## Summary of residuals:
##       Min.    1st Qu.     Median       Mean    3rd Qu.       Max.
## -0.9233260 -0.0711291 -0.0530550  0.0008941  0.0772568  0.9952963
##
## Number of Iterations: 8
##
## Coefficients:
##                                      Estimate   san.se    san.z Pr(>|san.z|)
## beta10                                5.11510  0.18263  28.0078      < 2e-16
## synm_tot_lag1:1                      -2.52141  0.40889  -6.1665      < 2e-16
## Osteo_synm_tot_corr_upp_low_2_lag1:1 -1.00413  0.50835  -1.9753      0.04823
## Osteo_synm_tot_corr_upp_low_2_lag2:1 -5.52807  0.31883 -17.3387      < 2e-16
## sexe1:1                              -1.47417  0.20165  -7.3105      < 2e-16
## beta20                                2.55161  0.18870  13.5219      < 2e-16
## synm_tot_lag1:2                      -2.03062  0.53807  -3.7739      0.00016
## Osteo_synm_tot_corr_upp_low_2_lag1:2  3.00125  0.50946   5.8910      < 2e-16
## Osteo_synm_tot_corr_upp_low_2_lag2:2 -5.99852  1.40045  -4.2833        2e-05
## sexe1:2                              -1.76671  0.21381  -8.2631      < 2e-16
##
## beta10                               ***
## synm_tot_lag1:1                      ***
## Osteo_synm_tot_corr_upp_low_2_lag1:1 *
## Osteo_synm_tot_corr_upp_low_2_lag2:1 ***
```

```
## sexe1:1                              ***
## beta20                               ***
## synm_tot_lag1:2                      ***
## Osteo_synm_tot_corr_upp_low_2_lag1:2 ***
## Osteo_synm_tot_corr_upp_low_2_lag2:2 ***
## sexe1:2                              ***
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Local Odds Ratios Estimates:
##         [,1]  [,2]    [,3]  [,4]
## [1,]   0.000 0.000 277.879 0.281
## [2,]   0.000 0.000   0.281 1.331
## [3,] 277.879 0.281   0.000 0.000
## [4,]   0.281 1.331   0.000 0.000
##
## p-value of Null model: < 0.0001
```

```
summary(nomLORgee(Osteo_synm_tot_corr_upp_low_2 ~ synm_tot_lag + Osteo_synm_tot_corr_upp_low_2_lag + se
                  data = xray_spa_dc_synd_Osteo_vert4,
                  id = id_vertebra,
                  repeated = t_new,
                  LORstr = "time.exch"))
```

```
## GEE FOR NOMINAL MULTINOMIAL RESPONSES
## version 1.6.0 modified 2017-07-10
##
## Link : Baseline Category Logit
##
## Local Odds Ratios:
## Structure:         time.exch
## Model:             2way
## Homogenous scores: TRUE
##
## call:
## nomLORgee(formula = Osteo_synm_tot_corr_upp_low_2 ~ synm_tot_lag +
##     Osteo_synm_tot_corr_upp_low_2_lag + sexe + age_m0, data = xray_spa_dc_synd_Osteo_vert4,
##     id = id_vertebra, repeated = t_new, LORstr = "time.exch")
##
## Summary of residuals:
##       Min.    1st Qu.     Median       Mean    3rd Qu.       Max.
## -0.9808523 -0.0528185 -0.0135253  0.0008408  0.0639477  0.9933746
##
## Number of Iterations: 11
##
## Coefficients:
##                                      Estimate   san.se    san.z Pr(>|san.z|)
## beta10                                7.17540  0.48545  14.7808      < 2e-16
## synm_tot_lag1:1                      -2.29613  0.42772  -5.3683      < 2e-16
## Osteo_synm_tot_corr_upp_low_2_lag1:1 -0.54698  0.51103  -1.0704      0.28446
## Osteo_synm_tot_corr_upp_low_2_lag2:1 -5.42353  0.34872 -15.5528      < 2e-16
## sexe1:1                              -1.54189  0.20036  -7.6957      < 2e-16
## age_m0:1                             -0.05785  0.01310  -4.4178        1e-05
## beta20                                1.43203  0.51021   2.8067      0.00500
```

```
## synm_tot_lag1:2                       -1.95034  0.50279  -3.8791      0.00010
## Osteo_synm_tot_corr_upp_low_2_lag1:2   2.84995  0.51470   5.5371      < 2e-16
## Osteo_synm_tot_corr_upp_low_2_lag2:2 -5.95424  1.37524  -4.3296        1e-05
## sexe1:2                               -1.65677  0.21345  -7.7618      < 2e-16
## age_m0:2                               0.02730  0.01368   1.9960      0.04593
##
## beta10                                ***
## synm_tot_lag1:1                       ***
## Osteo_synm_tot_corr_upp_low_2_lag1:1
## Osteo_synm_tot_corr_upp_low_2_lag2:1 ***
## sexe1:1                               ***
## age_m0:1                              ***
## beta20                                **
## synm_tot_lag1:2                       ***
## Osteo_synm_tot_corr_upp_low_2_lag1:2 ***
## Osteo_synm_tot_corr_upp_low_2_lag2:2 ***
## sexe1:2                               ***
## age_m0:2                              *
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Local Odds Ratios Estimates:
##         [,1]  [,2]    [,3]  [,4]
## [1,]   0.000 0.000 277.879 0.281
## [2,]   0.000 0.000   0.281 1.331
## [3,] 277.879 0.281   0.000 0.000
## [4,]   0.281 1.331   0.000 0.000
##
## p-value of Null model: < 0.0001
```

```r
summary(nomLORgee(Osteo_synm_tot_corr_upp_low_2 ~ synm_tot_lag + Osteo_synm_tot_corr_upp_low_2_lag + se
                  data = xray_spa_dc_synd_Osteo_vert4,
                  id = id_vertebra,
                  repeated = t_new,
                  LORstr = "time.exch"))
```

```
## GEE FOR NOMINAL MULTINOMIAL RESPONSES
## version 1.6.0 modified 2017-07-10
##
## Link : Baseline Category Logit
##
## Local Odds Ratios:
## Structure:         time.exch
## Model:             2way
## Homogenous scores: TRUE
##
## call:
## nomLORgee(formula = Osteo_synm_tot_corr_upp_low_2 ~ synm_tot_lag +
##     Osteo_synm_tot_corr_upp_low_2_lag + sexe + age_m0 + bmi,
##     data = xray_spa_dc_synd_Osteo_vert4, id = id_vertebra, repeated = t_new,
##     LORstr = "time.exch")
##
## Summary of residuals:
##       Min.    1st Qu.     Median       Mean    3rd Qu.       Max.
```

```
## -0.9817037 -0.0527818 -0.0115137  0.0008264  0.0647167  0.9935127
##
## Number of Iterations: 11
##
## Coefficients:
##                                      Estimate   san.se    san.z Pr(>|san.z|)
## beta10                                7.52981  0.70521  10.6774      < 2e-16
## synm_tot_lag1:1                      -2.28095  0.43098  -5.2924      < 2e-16
## Osteo_synm_tot_corr_upp_low_2_lag1:1 -0.54574  0.51205  -1.0658      0.28652
## Osteo_synm_tot_corr_upp_low_2_lag2:1 -5.40425  0.34747 -15.5532      < 2e-16
## sexe1:1                              -1.53307  0.19825  -7.7329      < 2e-16
## age_m0:1                             -0.05551  0.01349  -4.1149        4e-05
## bmi:1                                -0.01849  0.02429  -0.7615      0.44638
## beta20                                0.98227  0.72858   1.3482      0.17759
## synm_tot_lag1:2                      -1.95103  0.50140  -3.8912      0.00010
## Osteo_synm_tot_corr_upp_low_2_lag1:2  2.85196  0.51580   5.5291      < 2e-16
## Osteo_synm_tot_corr_upp_low_2_lag2:2 -5.97143  1.36538  -4.3735        1e-05
## sexe1:2                              -1.66863  0.21168  -7.8830      < 2e-16
## age_m0:2                              0.02679  0.01411   1.8984      0.05765
## bmi:2                                 0.01934  0.02512   0.7698      0.44140
##
## beta10                               ***
## synm_tot_lag1:1                      ***
## Osteo_synm_tot_corr_upp_low_2_lag1:1
## Osteo_synm_tot_corr_upp_low_2_lag2:1 ***
## sexe1:1                              ***
## age_m0:1                             ***
## bmi:1
## beta20
## synm_tot_lag1:2                      ***
## Osteo_synm_tot_corr_upp_low_2_lag1:2 ***
## Osteo_synm_tot_corr_upp_low_2_lag2:2 ***
## sexe1:2                              ***
## age_m0:2                             .
## bmi:2
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Local Odds Ratios Estimates:
##         [,1]  [,2]    [,3]  [,4]
## [1,]   0.000 0.000 277.879 0.281
## [2,]   0.000 0.000   0.281 1.331
## [3,] 277.879 0.281   0.000 0.000
## [4,]   0.281 1.331   0.000 0.000
##
## p-value of Null model: < 0.0001
```

```
summary(nomLORgee(Osteo_synm_tot_corr_upp_low_2 ~ synm_tot_lag + Osteo_synm_tot_corr_upp_low_2_lag + se
                  data = xray_spa_dc_synd_Osteo_vert4,
                  id = id_vertebra,
                  repeated = t_new,
                  LORstr = "time.exch"))
```

```
## GEE FOR NOMINAL MULTINOMIAL RESPONSES
```

```
## version 1.6.0 modified 2017-07-10
##
## Link : Baseline Category Logit
##
## Local Odds Ratios:
## Structure:         time.exch
## Model:             2way
## Homogenous scores: TRUE
##
## call:
## nomLORgee(formula = Osteo_synm_tot_corr_upp_low_2 ~ synm_tot_lag +
##     Osteo_synm_tot_corr_upp_low_2_lag + sexe + age_m0 + bmi +
##     hla, data = xray_spa_dc_synd_Osteo_vert4, id = id_vertebra,
##     repeated = t_new, LORstr = "time.exch")
##
## Summary of residuals:
##       Min.    1st Qu.     Median       Mean    3rd Qu.       Max.
## -0.9823508 -0.0508724 -0.0115203  0.0008174  0.0643428  0.9934591
##
## Number of Iterations: 11
##
## Coefficients:
##                                    Estimate   san.se    san.z Pr(>|san.z|)
## beta10                              7.51264  0.78294   9.5954      < 2e-16
## synm_tot_lag1:1                    -2.28234  0.43040  -5.3028      < 2e-16
## Osteo_synm_tot_corr_upp_low_2_lag1:1 -0.55183  0.51067  -1.0806      0.27987
## Osteo_synm_tot_corr_upp_low_2_lag2:1 -5.40630  0.35256 -15.3345      < 2e-16
## sexe1:1                            -1.52907  0.18958  -8.0657      < 2e-16
## age_m0:1                           -0.05548  0.01347  -4.1193        4e-05
## bmi:1                              -0.01793  0.02489  -0.7202      0.47139
## hla1:1                              0.00216  0.18714   0.0116      0.99078
## beta20                              1.22730  0.80251   1.5293      0.12618
## synm_tot_lag1:2                    -1.97379  0.51392  -3.8406      0.00012
## Osteo_synm_tot_corr_upp_low_2_lag1:2  2.83978  0.51428   5.5219      < 2e-16
## Osteo_synm_tot_corr_upp_low_2_lag2:2 -5.99192  1.35822  -4.4116        1e-05
## sexe1:2                            -1.63714  0.20327  -8.0541      < 2e-16
## age_m0:2                            0.02505  0.01407   1.7798      0.07511
## bmi:2                               0.01592  0.02573   0.6189      0.53599
## hla1:2                             -0.18259  0.19801  -0.9221      0.35646
##
## beta10                             ***
## synm_tot_lag1:1                    ***
## Osteo_synm_tot_corr_upp_low_2_lag1:1
## Osteo_synm_tot_corr_upp_low_2_lag2:1 ***
## sexe1:1                            ***
## age_m0:1                           ***
## bmi:1
## hla1:1
## beta20
## synm_tot_lag1:2                    ***
## Osteo_synm_tot_corr_upp_low_2_lag1:2 ***
## Osteo_synm_tot_corr_upp_low_2_lag2:2 ***
## sexe1:2                            ***
## age_m0:2                           .
```

```
## bmi:2
## hla1:2
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Local Odds Ratios Estimates:
##         [,1]  [,2]    [,3]  [,4]
## [1,]   0.000 0.000 277.879 0.281
## [2,]   0.000 0.000   0.281 1.331
## [3,] 277.879 0.281   0.000 0.000
## [4,]   0.281 1.331   0.000 0.000
##
## p-value of Null model: < 0.0001
```

```
summary(nomLORgee(Osteo_synm_tot_corr_upp_low_2 ~ synm_tot_lag + Osteo_synm_tot_corr_upp_low_2_lag + se
                  data = xray_spa_dc_synd_Osteo_vert4,
                  id = id_vertebra,
                  repeated = t_new,
                  LORstr = "time.exch"))
```

```
## GEE FOR NOMINAL MULTINOMIAL RESPONSES
## version 1.6.0 modified 2017-07-10
##
## Link : Baseline Category Logit
##
## Local Odds Ratios:
## Structure:         time.exch
## Model:             2way
## Homogenous scores: TRUE
##
## call:
## nomLORgee(formula = Osteo_synm_tot_corr_upp_low_2 ~ synm_tot_lag +
##     Osteo_synm_tot_corr_upp_low_2_lag + sexe + age_m0 + bmi +
##     hla + tabac_10y, data = xray_spa_dc_synd_Osteo_vert4, id = id_vertebra,
##     repeated = t_new, LORstr = "time.exch")
##
## Summary of residuals:
##       Min.    1st Qu.     Median       Mean    3rd Qu.       Max.
## -0.9821597 -0.0530313 -0.0117665  0.0008569  0.0647327  0.9943153
##
## Number of Iterations: 11
##
## Coefficients:
##                                      Estimate   san.se    san.z Pr(>|san.z|)
## beta10                                7.52136  0.78420   9.5911      < 2e-16
## synm_tot_lag1:1                      -2.31902  0.42130  -5.5044      < 2e-16
## Osteo_synm_tot_corr_upp_low_2_lag1:1 -0.53654  0.50910  -1.0539      0.29193
## Osteo_synm_tot_corr_upp_low_2_lag2:1 -5.44303  0.34494 -15.7797      < 2e-16
## sexe1:1                              -1.55620  0.19090  -8.1518      < 2e-16
## age_m0:1                             -0.05615  0.01342  -4.1830        3e-05
## bmi:1                                -0.02108  0.02504  -0.8417      0.39997
## hla1:1                               -0.05772  0.18140  -0.3182      0.75035
## tabac_10y1:1                          0.36597  0.18364   1.9929      0.04628
## beta20                                1.17589  0.80583   1.4592      0.14450
```

```
## synm_tot_lag1:2                       -2.01497  0.50690  -3.9751        7e-05
## Osteo_synm_tot_corr_upp_low_2_lag1:2  2.85185  0.51181   5.5721      < 2e-16
## Osteo_synm_tot_corr_upp_low_2_lag2:2 -6.05956  1.34405  -4.5084        1e-05
## sexe1:2                               -1.66821  0.20436  -8.1632      < 2e-16
## age_m0:2                               0.02472  0.01403   1.7618      0.07811
## bmi:2                                  0.01308  0.02580   0.5070      0.61212
## hla1:2                                -0.25540  0.19248  -1.3269      0.18454
## tabac_10y1:2                           0.47433  0.19707   2.4069      0.01609
##
## beta10                                ***
## synm_tot_lag1:1                       ***
## Osteo_synm_tot_corr_upp_low_2_lag1:1
## Osteo_synm_tot_corr_upp_low_2_lag2:1 ***
## sexe1:1                               ***
## age_m0:1                              ***
## bmi:1
## hla1:1
## tabac_10y1:1                          *
## beta20
## synm_tot_lag1:2                       ***
## Osteo_synm_tot_corr_upp_low_2_lag1:2 ***
## Osteo_synm_tot_corr_upp_low_2_lag2:2 ***
## sexe1:2                               ***
## age_m0:2                              .
## bmi:2
## hla1:2
## tabac_10y1:2                          *
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Local Odds Ratios Estimates:
##         [,1]  [,2]    [,3]  [,4]
## [1,]   0.000 0.000 277.878 0.281
## [2,]   0.000 0.000   0.281 1.331
## [3,] 277.878 0.281   0.000 0.000
## [4,]   0.281 1.331   0.000 0.000
##
## p-value of Null model: < 0.0001
```

```
summary(nomLORgee(Osteo_synm_tot_corr_upp_low_2 ~ synm_tot_lag + Osteo_synm_tot_corr_upp_low_2_lag + se
                  data = xray_spa_dc_synd_Osteo_vert4,
                  id = id_vertebra,
                  repeated = t_new,
                  LORstr = "time.exch"))
```

```
## GEE FOR NOMINAL MULTINOMIAL RESPONSES
## version 1.6.0 modified 2017-07-10
##
## Link : Baseline Category Logit
##
## Local Odds Ratios:
## Structure:         time.exch
## Model:             2way
## Homogenous scores: TRUE
```

```
##
## call:
## nomLORgee(formula = Osteo_synm_tot_corr_upp_low_2 ~ synm_tot_lag +
##     Osteo_synm_tot_corr_upp_low_2_lag + sexe + age_m0 + bmi +
##     hla + tabac_10y + profession, data = xray_spa_dc_synd_Osteo_vert4,
##     id = id_vertebra, repeated = t_new, LORstr = "time.exch")
##
## Summary of residuals:
##       Min.    1st Qu.     Median       Mean    3rd Qu.       Max.
## -0.9812826 -0.0509674 -0.0116676  0.0008218  0.0609024  0.9947777
##
## Number of Iterations: 11
##
## Coefficients:
##                                     Estimate   san.se    san.z Pr(>|san.z|)
## beta10                               9.01673  0.87082  10.3543      < 2e-16
## synm_tot_lag1:1                     -2.27822  0.43909  -5.1885      < 2e-16
## Osteo_synm_tot_corr_upp_low_2_lag1:1 -0.43241  0.51236  -0.8440      0.39869
## Osteo_synm_tot_corr_upp_low_2_lag2:1 -5.40316  0.37213 -14.5194      < 2e-16
## sexe1:1                             -1.63360  0.19540  -8.3604      < 2e-16
## age_m0:1                            -0.06612  0.01315  -5.0285      < 2e-16
## bmi:1                               -0.04005  0.02573  -1.5564      0.11960
## hla1:1                               0.02356  0.19126   0.1232      0.90195
## tabac_10y1:1                         0.35448  0.18552   1.9107      0.05605
## profession2:1                       -0.67557  0.24654  -2.7402      0.00614
## profession3:1                       -1.54146  0.36064  -4.2743        2e-05
## beta20                               2.49359  0.89007   2.8016      0.00509
## synm_tot_lag1:2                     -1.90970  0.52501  -3.6374      0.00028
## Osteo_synm_tot_corr_upp_low_2_lag1:2  2.99185  0.51580   5.8004      < 2e-16
## Osteo_synm_tot_corr_upp_low_2_lag2:2 -6.02075  1.45018  -4.1517        3e-05
## sexe1:2                             -1.71544  0.20854  -8.2259      < 2e-16
## age_m0:2                             0.00970  0.01374   0.7061      0.48013
## bmi:2                               -0.00339  0.02635  -0.1287      0.89759
## hla1:2                              -0.21652  0.20160  -1.0740      0.28283
## tabac_10y1:2                         0.42990  0.19897   2.1607      0.03072
## profession2:2                       -0.29539  0.27874  -1.0597      0.28928
## profession3:2                       -1.31177  0.41415  -3.1674      0.00154
##
## beta10                              ***
## synm_tot_lag1:1                     ***
## Osteo_synm_tot_corr_upp_low_2_lag1:1
## Osteo_synm_tot_corr_upp_low_2_lag2:1 ***
## sexe1:1                             ***
## age_m0:1                            ***
## bmi:1
## hla1:1
## tabac_10y1:1                        .
## profession2:1                       **
## profession3:1                       ***
## beta20                              **
## synm_tot_lag1:2                     ***
## Osteo_synm_tot_corr_upp_low_2_lag1:2 ***
## Osteo_synm_tot_corr_upp_low_2_lag2:2 ***
## sexe1:2                             ***
```

```
## age_m0:2
## bmi:2
## hla1:2
## tabac_10y1:2                         *
## profession2:2
## profession3:2                        **
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Local Odds Ratios Estimates:
##         [,1]  [,2]    [,3]  [,4]
## [1,]   0.000 0.000 288.641 0.253
## [2,]   0.000 0.000   0.253 1.395
## [3,] 288.641 0.253   0.000 0.000
## [4,]   0.253 1.395   0.000 0.000
##
## p-value of Null model: < 0.0001
```

```
#multinomial time-lagged and autoregressive GEE complete model
model_gee_multinomial <- summary(nomLORgee(Osteo_synm_tot_corr_upp_low_2 ~ synm_tot_lag + Osteo_synm_to
                                           data = xray_spa_dc_synd_Osteo_vert4,
                                           id = id_vertebra,
                                           repeated = t_new,
                                           LORstr = "time.exch"))
model_gee_multinomial
```

```
## GEE FOR NOMINAL MULTINOMIAL RESPONSES
## version 1.6.0 modified 2017-07-10
##
## Link : Baseline Category Logit
##
## Local Odds Ratios:
## Structure:         time.exch
## Model:             2way
## Homogenous scores: TRUE
##
## call:
## nomLORgee(formula = Osteo_synm_tot_corr_upp_low_2 ~ synm_tot_lag +
##     Osteo_synm_tot_corr_upp_low_2_lag + sexe + age_m0 + bmi +
##     hla + tabac_10y + profession + bdmard_lag, data = xray_spa_dc_synd_Osteo_vert4,
##     id = id_vertebra, repeated = t_new, LORstr = "time.exch")
##
## Summary of residuals:
##      Min.   1st Qu.    Median      Mean   3rd Qu.      Max.
## -0.981307 -0.053012 -0.012291  0.001391  0.061128  0.992902
##
## Number of Iterations: 14
##
## Coefficients:
##                                      Estimate   san.se    san.z Pr(>|san.z|)
## beta10                                8.87880  0.92823   9.5653      < 2e-16
## synm_tot_lag1:1                      -2.09584  0.47000  -4.4592        1e-05
## Osteo_synm_tot_corr_upp_low_2_lag1:1 -2.14008  0.29993  -7.1352      < 2e-16
## Osteo_synm_tot_corr_upp_low_2_lag2:1 -5.50141  0.38498 -14.2902      < 2e-16
```

```
## sexe1:1                                -1.63840  0.21123  -7.7566      < 2e-16
## age_m0:1                               -0.06048  0.01494  -4.0480        5e-05
## bmi:1                                  -0.03358  0.02742  -1.2243      0.22084
## hla1:1                                  0.03668  0.21077   0.1740      0.86185
## tabac_10y1:1                            0.33720  0.19658   1.7153      0.08628
## profession2:1                          -0.81311  0.25790  -3.1528      0.00162
## profession3:1                          -1.36902  0.36757  -3.7245      0.00020
## bdmard_lag1:1                          -0.54980  0.17361  -3.1668      0.00154
## beta20                                  2.57138  0.96856   2.6548      0.00793
## synm_tot_lag1:2                        -2.25943  0.55543  -4.0679        5e-05
## Osteo_synm_tot_corr_upp_low_2_lag1:2    1.48265  0.31551   4.6992      < 2e-16
## Osteo_synm_tot_corr_upp_low_2_lag2:2 -4.60084  0.45572 -10.0957      < 2e-16
## sexe1:2                                -1.80738  0.22746  -7.9459      < 2e-16
## age_m0:2                                0.01185  0.01557   0.7608      0.44675
## bmi:2                                  -0.00173  0.02873  -0.0604      0.95187
## hla1:2                                 -0.22873  0.22867  -1.0003      0.31718
## tabac_10y1:2                            0.37251  0.21660   1.7198      0.08547
## profession2:2                          -0.45873  0.30047  -1.5267      0.12684
## profession3:2                          -1.15102  0.43535  -2.6439      0.00820
## bdmard_lag1:2                          -0.01100  0.17046  -0.0645      0.94854
##
## beta10                                 ***
## synm_tot_lag1:1                        ***
## Osteo_synm_tot_corr_upp_low_2_lag1:1 ***
## Osteo_synm_tot_corr_upp_low_2_lag2:1 ***
## sexe1:1                                ***
## age_m0:1                               ***
## bmi:1
## hla1:1
## tabac_10y1:1                           .
## profession2:1                          **
## profession3:1                          ***
## bdmard_lag1:1                          **
## beta20                                 **
## synm_tot_lag1:2                        ***
## Osteo_synm_tot_corr_upp_low_2_lag1:2 ***
## Osteo_synm_tot_corr_upp_low_2_lag2:2 ***
## sexe1:2                                ***
## age_m0:2
## bmi:2
## hla1:2
## tabac_10y1:2                           .
## profession2:2
## profession3:2                          **
## bdmard_lag1:2
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Local Odds Ratios Estimates:
##         [,1]       [,2]    [,3]       [,4]
## [1,]   0.000          0 291.664          0
## [2,]   0.000          0   0.000 5207137420
## [3,] 291.664          0   0.000          0
## [4,]   0.000 5207137420   0.000          0
```

```
##
## p-value of Null model: < 0.0001
```

```
#OR associated:
coefficients <- coef(model_gee_multinomial)
exp(coefficients)
```

```
##                                          Estimate   san.se        san.z
## beta10                                7.178172e+03 2.530027 1.426109e+04
## synm_tot_lag1:1                       1.229669e-01 1.599994 1.157127e-02
## Osteo_synm_tot_corr_upp_low_2_lag1:1 1.176454e-01 1.349764 7.965904e-04
## Osteo_synm_tot_corr_upp_low_2_lag2:1 4.081013e-03 1.469585 6.220658e-07
## sexe1:1                               1.942907e-01 1.235196 4.279004e-04
## age_m0:1                              9.413126e-01 1.015052 1.745813e-02
## bmi:1                                 9.669775e-01 1.027799 2.939663e-01
## hla1:1                                1.037361e+00 1.234628 1.190079e+00
## tabac_10y1:1                          1.401019e+00 1.217233 5.558621e+00
## profession2:1                         4.434767e-01 1.294209 4.273231e-02
## profession3:1                         2.543561e-01 1.444221 2.412492e-02
## bdmard_lag1:1                         5.770652e-01 1.189592 4.213780e-02
## beta20                                1.308387e+01 2.634149 1.422257e+01
## synm_tot_lag1:2                       1.044100e-01 1.742690 1.711380e-02
## Osteo_synm_tot_corr_upp_low_2_lag1:2 4.404602e+00 1.370958 1.098592e+02
## Osteo_synm_tot_corr_upp_low_2_lag2:2 1.004340e-02 1.577309 4.125740e-05
## sexe1:2                               1.640835e-01 1.255407 3.541146e-04
## age_m0:2                              1.011920e+00 1.015692 2.140073e+00
## bmi:2                                 9.982715e-01 1.029147 9.414256e-01
## hla1:2                                7.955433e-01 1.256927 3.677838e-01
## tabac_10y1:2                          1.451373e+00 1.241847 5.583468e+00
## profession2:2                         6.320859e-01 1.350493 2.172558e-01
## profession3:2                         3.163140e-01 1.545504 7.108564e-02
## bdmard_lag1:2                         9.890603e-01 1.185850 9.374892e-01
##                                      Pr(>|san.z|)
## beta10                                   1.000000
## synm_tot_lag1:1                          1.000010
## Osteo_synm_tot_corr_upp_low_2_lag1:1     1.000000
## Osteo_synm_tot_corr_upp_low_2_lag2:1     1.000000
## sexe1:1                                  1.000000
## age_m0:1                                 1.000050
## bmi:1                                    1.247124
## hla1:1                                   2.367537
## tabac_10y1:1                             1.090112
## profession2:1                            1.001621
## profession3:1                            1.000200
## bdmard_lag1:1                            1.001541
## beta20                                   1.007962
## synm_tot_lag1:2                          1.000050
## Osteo_synm_tot_corr_upp_low_2_lag1:2     1.000000
## Osteo_synm_tot_corr_upp_low_2_lag2:2     1.000000
## sexe1:2                                  1.000000
## age_m0:2                                 1.563223
## bmi:2                                    2.590549
## hla1:2                                   1.373250
## tabac_10y1:2                             1.089229
```

```
## profession2:2                          1.135235
## profession3:2                          1.008234
## bdmard_lag1:2                          2.581937
```

```
#synm_tot_lag when Osteo_synm_tot_corr_upp_low_2=1
#(osteophyte in the adjacent vertebra vs 0: no osteophyte nor syndesmophyte)
#= -2.27553

#synm_tot_lag when Osteo_synm_tot_corr_upp_low_2=2:
#(syndesmophyte in the adjacent vertebra vs 0: no osteophyte nor syndesmophyte)
#= -1.93708

#In this model, the risk of osteophyte AND syndesmophyte would be significantly
#lower in an adjacent vertebra when a syndesmophyte is present.
#This seems to me to be inconsistent with the previous descriptive analyses.

#In addition, the coefficients associated with the
#Osteo_synm_tot_corr_upp_low_2_lag variables (the lag of the outcome) are also
#negative (except Osteo_synm_tot_corr_upp_low_2_lag1:2), which also seems inconsistent to me.
```