SAS syntax to model annual treatment participation accounting for repeated measurement

proc nlmixed empirical data=file;

where y > 0;

parms a0=-.5 b0=0 c=-3.2 d=-.5;

a = exp(a0);

b = exp(b0);

c = exp(c0);

d = exp(d0);

G = (exp(-(a\*y)\*\*b)\*(1-d)+d)\*exp(-c\*y)+u;

model in ~ binary(G);

random u ~ normal(0,0) subject=ID;

estimate 'a' exp(a0);

estimate 'b' exp(b0);

estimate 'c' exp(c0);

estimate 'd' exp(d0);

run;

“empirical”: requests the likelihood-based empirical estimator of the covariance matrix

“file”: the name of the dataset with variables as described below

“where y > 0” selects the years after first treatment

“parms …”: specify parameter names and initial values

“G”: the annual treatment participation function

 “y”: year after first entry in OAT (i.e. y=0 for the first entry year)

“a0”: logarithm of the scale parameter of the nuisance short-term decline

“b0”: logarithm of the shape parameter of the nuisance short-term decline

“c0”: logarithm of the scale parameter of the long-term decline

“d0”: logarithm of the proportion of patients in treatment in the long term (the adjusted treatment participation)

“in”: the observed treatment status of the patient (in=1 if in OAT, in=0 if not)

 “u”: patient specific effect with mean and variance set to 0

“estimate”: taking the antilogarithm of the respective parameters

To additionally estimate the duration of the nuisance short-term decline, e.g. the duration in years until the effect of the nuisance short-term decline has lowered to 0.01 (=1%) of its initial contribution (=1-d) the following line can be added in the SAS syntax:

estimate ‘years until nuisance short-term declined to 1%’ exp(a0)\*exp(log(-log(0.01))/exp(b0));

SAS syntax specification for model 1 to model 4

We tested 4 different models of the annual treatment participation model by setting some of the parameters to fixed values by replacing the following lines as follows:

Model 1:

parms a0=-.5 b0=0 c=-3.2 d=-.5;

Model 2 (the nuisance short-term decline is fixed to an exponential model):

parms a0=-.5 c=-3.2 d=-.5;

b0 = 0;

Model 3 (the nuisance short-term decline is fixed to an exponential model and the long-term decline is fixed to 4 percent a year):

parms a0=-.5 d=-.5;

b0 = 0;

c0 = log(0.04);

Model 4 (the long-term decline is fixed to 4 percent a year):

parms a0=-.5 b0=0 d=-.5;

c0 = log(0.04);

Specification of subgroup effects

The binary predictor variables were coded so that they had a value=1 if the label was true, otherwise value=0. When testing the multivariate effect of ‘NonSwiss’, ‘Female’, and ‘Inject’ on ‘d’ the line:

‘d = exp(d0);’

in the SAS syntax was replaced by:

‘d = exp(d0 + dNonSwiss\*NonSwiss + dFemale\*Female + dInject\*Inject);’.

Rate ratios of subgroup effects

The rate ratios (RR) for the specific subgroup were obtained by adding the following lines in the SAS syntax:

estimate 'RR dNonSwiss' exp(dNonSwiss);

estimate 'RR dFemale' exp(dFemale);

estimate 'RR dInject' exp(dInject);

All models could be estimated with identical starting values (a=-.5 and d=-.5, and all other with 0) in all four data sets and with different complexity (accounting for three independent variables, and with or without imputation). This indicates that the proposed syntax in proc nlmixed seem to provide a robust procedure for analyzing annual treatment participation in OAT. However, adjusting repeated time-to-event is still computer time consuming if 9 parameters with the complete case dataset and the ten imputed datasets are estimated (for example the shortest computer time was 4 minutes for the Czech Republic, and the longest, 1.5 hours for the Netherlands datasets using Windows 7, 3.5 GHz, 64-Bit-System, 32 GB RAM).