# Homework #3

# Shared Random Effect Joint Models

## Due: Mon, Mar 1, 2021 by 11:59pm

Total possible points: **105**; Max score: **100**

This assignment uses the "aort_new.csv" file in the "Homework" folder on Canvas, as in Homework #1.

As a reminder, the data set contains data from 500 patients who received a human tissue valve in the aortic position. Patients either received a subcoronary implantation (SI) or a root replacement (RR). These patients were followed over time and longitudinal aortic gradient measurements were collected at echo examinations. These patients are at risk of experiencing death following their surgery. The following columns are available in the data set:

- **id** : unique patient id
- **aort.grad**: aortic gradient
- **time**: visit date (years from surgery date)
- **event**: death status (1: dead, 0: patient is alive at end of follow-up)
- **survtime**: years from surgery date until last follow-up
- **oper**: categorical indicator of type of operation (SI or RR)
- **sex**: gender
- **age**: patient age at time of surgery

*Note:* It might be useful to begin by creating a square root transformation of aort.grad and adding it to the data set (*sqrt.aort.grad*).

**Question 1: Simple Joint Model**

a) **(15 pts)** Fit a shared random effect joint model where:
   a. the longitudinal submodel is a linear mixed effects model for sqrt aortic gradient with fixed effects for linear time and operation type and a random intercept, random slope structure
   b. the survival submodel is a proportional hazards model adjusted for operation type and the current value parameterization of sqrt aortic gradient.
   c. the baseline hazard is piecewise-constant
   d. numeric integration is conducted using the (pseudo) adaptive GH rule

b) **(10 pts)** Write out this model formulation in the joint model framework using the notation used in class.

c) **(20 pts)** Interpret all of the parameter estimates from this model (include estimates, 95% confidence intervals, and p-values in your answer).

d) **(15 pts)** Test for three treatment effects: (i) in the longitudinal process, (ii) in the survival process, (iii) in the joint process. Interpret the results from these tests.

**Question 2: Alternative Parameterizations**

a) **(15 pts)** The model in 1(a) assumes that the strength of association between the level of sqrt aortic gradient and the risk of death is the same in the two operation groups (SI and RR). To relax this assumption, we can add an interaction effect in the hazard function between sqrt aortic gradient and operation type (i.e., $m_i(t) \times SI_i$). Update the joint model in 1(a) using the "interFact" argument available for the jointModel() function. This should be a list with two elements:
   a. value: formula with factors for which we want to calculate the interaction terms
   b. data: the data frame used to fit the Cox model

   Take a look at ?jointModel() for more info and an example. Interpret the association parameters from this model. (Hint: Compute the effect of sqrt aortic gradient on risk of death for those who receive SI and for those who receive RR).

b) **(25 pts)** Fit a new joint model to the data where:
   a. the longitudinal submodel is a linear mixed effects model for sqrt aortic gradient with fixed and random effects for linear and quadratic time ($t, t^2$), and adjusted for operation type.
   b. the survival submodel is a proportional hazards model adjusted for operation type and the current value and slope parameterization of sqrt aortic gradient.
   c. the baseline hazard is piecewise-constant
   d. numeric integration is conducted using the (pseudo) adaptive GH rule

   Interpret the association parameter estimates from this model. Fit the model again, but using only the current value parameterization in the survival submodel. Assess which model is a better fit to the data.

c) **(5 pts)** Of all the models fit in the homework, which model provides the best fit to the data? Justify your answer.

**(End of assignment)**