setwd("C:/R files BHMRA")

library(rstan)

library(cmprsk)

library(timereg)

library(memisc)

N=541

data=read.table("DS\_11\_9.txt",header=T)

attach(data)

#

# CAUSE SPECIFIC HAZARDS

#

d1=ifelse(cause==1,1,0)

t.d1=subset(obs\_t,cause==1)

# unique event times

t.d1.unique=unique(t.d1)

NT1=length(t.d1.unique)

t1\_unique=c(sort(t.d1.unique),max(obs\_t)+1)

# define at risk and counting process increments

Y1=dN1=matrix(,N,NT1)

for (i in 1:N) { for (j in 1:NT1) {Y1[i,j] =ifelse(obs\_t[i]>=t1\_unique[j],1,0)}}

for (i in 1:N) { for (j in 1:NT1) {dN1[i, j] =Y1[i, j] \* (t1\_unique[j + 1] > obs\_t[i]) \* d1[i]}}

d2=ifelse(cause==2,1,0)

t.d2=subset(obs\_t,cause==2)

# unique event times

t.d2.unique=unique(t.d2)

NT2=length(t.d2.unique)

t2\_unique=c(sort(t.d2.unique),max(obs\_t)+1)

# define at risk and counting process increments

Y2=dN2=matrix(,N,NT2)

for (i in 1:N) { for (j in 1:NT2) {Y2[i,j] =ifelse(obs\_t[i]>=t2\_unique[j],1,0)}}

for (i in 1:N) { for (j in 1:NT2) {dN2[i, j] =Y2[i, j] \* (t2\_unique[j + 1] > obs\_t[i]) \* d2[i]}}

# dataset

D=list(N=N,

NT1=NT1,t1\_unique=t1\_unique,Y1=Y1,dN1=dN1,

NT2=NT2, t2\_unique=t2\_unique,Y2=Y2,dN2=dN2,

stage=stage,chemo=chemo,age=age,hgb=hgb)

CR.stan ="

data {

int<lower=0> N;

int<lower=0> NT1;

int<lower=0> NT2;

int<lower=0> Y1[N,NT1];

int<lower=0> dN1[N,NT1];

int<lower=0> Y2[N,NT2];

int<lower=0> dN2[N,NT2];

real <lower=0> t1\_unique[NT1 + 1];

real <lower=0> t2\_unique[NT2 + 1];

real stage[N];

real chemo[N];

real age[N];

real hgb[N];

}

transformed data {

real c;

real r;

c = 0.001;

r = 0.1;

}

parameters {

real beta1[4];

real beta2[4];

real<lower=0> dL1[NT1];

real<lower=0> dL2[NT2];

}

model {

real dt1[NT1];

real dt2[NT2];

beta1 ~ normal(0, 10);

beta2 ~ normal(0, 10);

// gamma increments prior

for (j in 1:NT1) {dt1[j] = t1\_unique[j+1] - t1\_unique[j];

dL1[j] ~ gamma(r \* dt1[j] \* c, c);

for (i in 1:N) { if (Y1[i, j] != 0)

target += poisson\_lpmf(dN1[i, j]|

Y1[i, j]\*exp(beta1[1]\*stage[i]+beta1[2]\*chemo[i]+beta1[3]\*age[i]/100+beta1[4]\*hgb[i]/100) \*

dL1[j]); } }

for (j in 1:NT2) {dt2[j] = t2\_unique[j+1] - t2\_unique[j];

dL2[j] ~ gamma(r \* dt2[j] \* c, c);

for (i in 1:N) { if (Y2[i, j] != 0)

target += poisson\_lpmf(dN2[i, j]|

Y2[i, j]\*exp(beta2[1]\*stage[i]+beta2[2]\*chemo[i]+beta2[3]\*age[i]/100+beta2[4]\*hgb[i]/100) \*

dL2[j]); } }

}

generated quantities {

real S1\_nochemo[NT1];

real S1\_chemo[NT1];

for (j in 1:NT1) { // Survival by therapy (includes chemo or not), age and hgb at average levels

real s;

s = 0;

for (i in 1:j)

s = s + dL1[i];

S1\_chemo[j] = pow(exp(-s), exp(beta1[2]+beta1[3]\*0.57+beta1[4]\*1.39));

S1\_nochemo[j] = pow(exp(-s), exp( beta1[3]\*0.57+beta1[4]\*1.39)); }}

"

# Compilation and Estimation

sm = stan\_model(model\_code=CR.stan)

fitCR = sampling(sm,data =D,iter = 1500,warmup=250,chains = 2,seed= 12345)

summaryCR=summary(fitCR, pars = c("S1\_nochemo ", " S1\_chemo ", "beta1", "beta2"), probs = c(0.025,0.05, 0.95, 0.975))$summary

#

# CLASSICAL CAUSE-SPECIFIC

#

age\_sc=age/100

hgb\_sc=hgb/100

d1 <-ifelse(cause==1,1,0)

coxph(Surv(obs\_t,d1)~stage+chemo+age\_sc+hgb\_sc)

d2 <-ifelse(cause==2,1,0)

coxph(Surv(obs\_t,d2)~stage+chemo+age\_sc+hgb\_sc)

#

# SUBDISTRIBUTION HAZARD RISK SET

#

d1=ifelse(cause==1,1,0)

d2=ifelse(cause==2,1,0)

t.d1=subset(obs\_t,cause==1)

# unique event times

t.d1.unique=unique(t.d1)

NT1=length(t.d1.unique)

t1\_unique=c(sort(t.d1.unique),max(obs\_t)+1)

# define at risk and counting process increments

Y1=dN1=matrix(,N,NT1)

# exits from cause 2 retained in risk set

for (i in 1:N) { for (j in 1:NT1) {Y1[i,j] =ifelse(obs\_t[i]>=t1\_unique[j],1,0)+ifelse(d2[i]==1,1,0)}}

for (i in 1:N) { for (j in 1:NT1) {Y1[i,j]=ifelse(Y1[i,j]>0,1,0)}}

for (i in 1:N) { for (j in 1:NT1) {dN1[i, j] =Y1[i, j] \* (t1\_unique[j + 1] > obs\_t[i]) \* d1[i]}}

t.d2=subset(obs\_t,cause==2)

# unique event times

t.d2.unique=unique(t.d2)

NT2=length(t.d2.unique)

t2\_unique=c(sort(t.d2.unique),max(obs\_t)+1)

# define at risk and counting process increments

Y2=dN2=matrix(,N,NT2)

# exits from cause 1 retained in risk set

for (i in 1:N) { for (j in 1:NT2) {Y2[i,j] =ifelse(obs\_t[i]>=t2\_unique[j],1,0)+ifelse(d1[i]==1,1,0)}}

for (i in 1:N) { for (j in 1:NT2) {Y2[i,j]=ifelse(Y2[i,j]>0,1,0)}}

for (i in 1:N) { for (j in 1:NT2) {dN2[i, j] =Y2[i, j] \* (t2\_unique[j + 1] > obs\_t[i]) \* d2[i]}}

# dataset

DSD=list(N=N,NT1=NT1,t1\_unique=t1\_unique,Y1=Y1,dN1=dN1,

NT2=NT2, t2\_unique=t2\_unique,Y2=Y2,dN2=dN2,

stage=stage,chemo=chemo,age=age,hgb=hgb)

fitSD = sampling(sm,data =DSD,iter = 1500,warmup=250,chains = 2,seed= 12345)

summarySD=summary(fitSD, pars = c("beta1","beta2"), probs = c(0.025,0.5, 0.975))$summary

#

# Classical Sub-Distribution Hazard Regression

#

age\_sc=age/100

hgb\_sc=hgb/100

x =cbind(stage, chemo,age\_sc,hgb\_sc)

modSD1=crr(obs\_t, cause, x)

newcause=recode(cause,0<-0,2<-1,1<-2)

modSD2=crr(obs\_t, newcause, x)