setwd("C:/R files BHMRA")

attach("DS\_11\_6.Rdata")

library(jagsUI)

library(loo)

library(Dowd)

library(e1071)

require(rube)

Sys.setenv(BUGSDIR="c:\\users\\P Congdon\\documents\\WINBUGS14")

**# index for accumulating log-likelihoods over subject-time pairs**

idx=matrix(,201,20)

ndx=0

n=DS\_11\_6$n

J=DS\_11\_6$J

for (i in 1:n) {for (j in 1:J){ndx = ndx+1

idx[i,j]=ndx}}

**# indicators for failing and time spent**

y=matrix(,201,20)

o=matrix(,201,20)

d=DS\_11\_6$d

t=DS\_11\_6$t

a=DS\_11\_6$a

for (i in 1:n) { for (k in 1:J) {# indicator for subject i failing in interval k

y[i,k] = d[i]\*(t[i] >= a[k])\*(a[k+1] >= t[i])

# time at risk in interval k

o[i,k] =(min(t[i], a[k+1]) - a[k])\*(t[i] >= a[k])}}

**# Extend dataset**

DS\_11\_6$o=o

DS\_11\_6$y=y

DS\_11\_6$idx=idx

**#**

**# piecewise exponential model, Normal random effects**

**#**

cat("model {for (i in 1:n) { for (k in 1:J) {

theta[i,k] <- lam[k]\*exp(beta\*trt[i]+e[pat[i]]+u[hos[i]])

mu[i,k] <- o[i,k]\*theta[i,k]

y[i,k] ~ dpois(mu[i,k])

**# likelihood (nu used to avoid logs of zero)**

nu[i,k] <- equals(mu[i,k],0) +(1-equals(mu[i,k],0))\*mu[i,k]

loglik[idx[i,k]] <- y[i,k]\*log(nu[i,k])-mu[i,k]-logfact(y[i,k])}}

**# patient effects**

for (j in 1:L) {e[j] ~ dnorm(0,tau.e)

e.r[j] <- e[j]-mean(e[])}

**# hospital effects**

for (k in 1:M) {u[k] ~ dnorm(0,tau.u)

u.r[k] <- u[k]-mean(u[])}

**# priors for partitioning variance terms**

V ~ dunif(0,100)

r ~ dunif(0,1)

sig2.u <- r\*V

sig2.e <- V-sig2.u

**# within hospital correlation**

within.hosp <- sig2.u/(sig2.u+sig2.e)

tau.e <- 1/sig2.e

tau.u <- 1/sig2.u

**# random effect st devns**

sigma[1] <- 1/sqrt(tau.e)

sigma[2] <- 1/sqrt(tau.u)

**# correlated process prior on baseline hazard**

for (k in 2:J) {lam[k] ~ dgamma(a0, b0[k])

b0[k] <- a0/lam[k-1]}

lam[1] ~ dgamma(0.1,0.1)

a0~ dgamma(0.1,0.1)

**# treatment parameter**

beta ~ dnorm(0, 0.001)

**# Cumulative Hazard**

H0[1] <- lam[1]\*a[1];

for (k in 2:J) {H0[k] <- lam[k]\*(a[k]-a[k-1])}

**# survival with and without treatment**

for (j in 1:J) {S[j,1] <- pow(exp(-sum(H0[1:j])), exp(beta))

S[j,2] <- exp(-sum(H0[1:j]))}}

", file="model1.jag")

**# Initial values and estimation**

inits1 <- list(V=1.4,r=0.2,beta=-1,a0=15)

inits2 <- list(V=1.5,r=0.25,beta=-1.2,a0=10)

inits=list(inits1,inits2)

pars <- c("beta","lam","a0","sigma","S","loglik","e.r","u.r", "within.hosp","V","r")

R1 <- autojags(DS\_11\_6, inits, pars,model.file= "model1.jag",2,iter.increment=2500, n.burnin=500,Rhat.limit=1.1, max.iter=20000, seed=1234, codaOnly= c('loglik'))

R1$summary

**# WAIC and LOO-IC**

loo(R1$sims.list$loglik)

waic(R1$sims.list$loglik)

**# Q-Q plot of random effects**

qqnorm(R1$mean$e.r)

qqnorm(R1$mean$u.r)

**#**

**# Student t(4) Random Effects**

**#**

cat("

model {for (i in 1:n) { for (k in 1:J) {

**# piecewise exponential**

theta[i,k] <- lam[k]\*exp(beta\*trt[i]+e[pat[i]]+u[hos[i]])

mu[i,k] <- o[i,k]\*theta[i,k]

y[i,k] ~ dpois(mu[i,k])

**# likelihood (nu used to avoid logs of zero)**

nu[i,k] <- equals(mu[i,k],0) +(1-equals(mu[i,k],0))\*mu[i,k]

loglik[idx[i,k]] <- y[i,k]\*log(nu[i,k])-mu[i,k]-logfact(y[i,k])}}

**# patient effects**

for (j in 1:L) {e[j] ~ dt(0,tau.e,4)

e.r[j] <- e[j]-mean(e[])}

**# hospital effects**

for (k in 1:M) {u[k] ~ dt(0,tau.u,4)

u.r[k] <- u[k]-mean(u[])}

# priors

V ~ dunif(0,100)

r ~ dunif(0,1)

sig2.u <- r\*V

sig2.e <- V-sig2.u

tau.e <- 1/sig2.e

tau.u <- 1/sig2.u

**# random effect st devns**

sigma[1] <- 1/sqrt(tau.e)

sigma[2] <- 1/sqrt(tau.u)

# correlated process prior on baseline hazard

for (k in 2:J) {lam[k] ~ dgamma(a0, b0[k])

b0[k] <- a0/lam[k-1]}

lam[1] ~ dgamma(0.1,0.1)

# treatment parameter

beta ~ dnorm(0, 0.001)

a0~ dgamma(0.1,0.1)

# Cumulative Hazard

H0[1] <- lam[1]\*a[1];

for (k in 2:J) {H0[k] <- lam[k]\*(a[k]-a[k-1])}

# survival with and without treatment

for (j in 1:J) {S[j,1] <- pow(exp(-sum(H0[1:j])), exp(beta))

S[j,2] <- exp(-sum(H0[1:j]))}}

", file="model2.jag")

**# Initial values and estimation**

inits1 <- list(V=2,r=0.5,beta=0,a0=1)

inits2 <- list(V=3,r=0.3,beta=0,a0=2)

inits=list(inits1,inits2)

pars <- c("beta","lam","a0","sigma","S","loglik","u.r","e.r")

R2 <- autojags(DS\_11\_6, inits, pars,model.file= "model2.jag",2,iter.increment=2000, n.burnin=500,Rhat.limit=1.1, max.iter=10000, seed=1234, codaOnly= c('loglik'))

R2$summary

**# WAIC and LOO-IC**

loo(R2$sims.list$loglik)

waic(R2$sims.list$loglik)

**# quantiles of random effects against quantiles of Student t[4] distribution**

TQQPlot(as.vector(R1$mean$e.r), 4)

TQQPlot(as.vector(R1$mean$u.r), 4)

**#**

**# PEM model, DPP prior on patient effects**

**#**

DS\_11\_6$K=10

DS\_11\_6$KM=9

model3= " model {for (i in 1:n) { for (k in 1:J) {

**# piecewise exponential**

theta[i,k] <- lam[k]\*exp(beta\*trt[i]+e[pat[i]]+u[hos[i]])

mu[i,k] <- o[i,k]\*theta[i,k]

y[i,k] ~ dpois(mu[i,k])

**# likelihood (nu used to avoid logs of zero)**

nu[i,k] <- equals(mu[i,k],0) +(1-equals(mu[i,k],0))\*mu[i,k]

loglik[idx[i,k]] <- y[i,k]\*log(nu[i,k])-mu[i,k]-logfact(y[i,k])}}

**# patient effects**

for (j in 1:L) { e.r[j] <- e[j]-mean(e[])

W[j] ~ dcat(pi[1:K])

e[j] <- estar[W[j]]

for (k in 1:K) {indW[j,k] <- equals(W[j],k)}}

**# centred hospital effects**

for (i in 1:M) { u[i] ~ dnorm(0,tau.u)

u.r[i] <- u[i]-mean(u[])}

**# priors**

tau.e ~ dgamma(1,0.001)

tau.u ~ dgamma(1,0.001)

**# nested random effect st devns**

sigma[1] <- 1/sqrt(tau.e)

sigma[2] <- 1/sqrt(tau.u)

**# correlated process prior on baseline hazard**

for (k in 2:J) {lam[k] ~ dgamma(a0, b0[k])

b0[k] <- a0/lam[k-1]}

**# baseline hazard initial point**

lam[1] ~ dgamma(0.1,0.1)

**# treatment parameter**

beta ~ dnorm(0, 0.001)

a0~ dgamma(0.1,0.1)

**# truncated Dirichlet process**

kappa ~ dgamma(3.5,0.5) I(0.1,)

V[K] <- 1

pi[1] <- V[1]

for (k in 1:KM){ V[k] ~ dbeta(1,kappa)}

for (j in 2:K) {pi[j] <- V[j]\*(1-V[j-1])\*pi[j-1]/V[j-1]}

for (j in 1:K) {estar[j] ~ dnorm(0,tau.e)}

**# Cumulative Hazard**

H0[1] <- lam[1]\*a[1];

for (k in 2:J) {H0[k] <- lam[k]\*(a[k]-a[k-1])}

**# survival with and without treatment**

for (j in 1:J) {S[1,j] <- pow(exp(-sum(H0[1:j])), exp(beta))

S[2,j] <- exp(-sum(H0[1:j]))}

**# total non-empty clusters**

Kstar <- sum(C[])

for (j in 1:K) {C[j] <- step(sum(indW[,j])-1)}}

"

**# Initial values and estimation**

inits1 <- list(tau.u=100,tau.e=100,beta=0,a0=1,W=rep(1,126))

inits2 <- list(tau.u=200,tau.e=200,beta=0,a0=2,W=rep(1,126))

inits=list(inits1,inits2)

pars <- c("beta","lam","a0","sigma","loglik","u.r","e.r","Kstar","kappa")

M3 = rube(model3, DS\_11\_6, inits)

R3= rube(model3, DS\_11\_6, inits, pars, n.burn=1000, n.thin=1, n.chains=2,n.iter=10000)

summary(R3)

**# WAIC and LOO-IC**

loo(R3$sims.list$loglik)

waic(R3$sims.list$loglik)

**#**

**# PEM, Skew-normal random effects**

**#**

cat("

model {for (i in 1:n) { for (k in 1:J) {

**# piecewise exponential**

theta[i,k] <- lam[k]\*exp(beta\*trt[i]+e[pat[i]]+u[hos[i]]

+gam.e\*(e.1[pat[i]]-0.798) +gam.u\*(u.1[hos[i]]-0.798))

mu[i,k] <- o[i,k]\*theta[i,k]

y[i,k] ~ dpois(mu[i,k])

**# likelihood (nu used to avoid logs of zero)**

nu[i,k] <- equals(mu[i,k],0) +(1-equals(mu[i,k],0))\*mu[i,k]

loglik[idx[i,k]] <- y[i,k]\*log(nu[i,k])-mu[i,k]-logfact(y[i,k])}}

**# patient effects**

for (j in 1:L) {e[j] ~ dnorm(0,tau.e)

e.1[j] ~ dnorm(0,1) I(0,)

e.r[j] <- e[j]-mean(e[])}

**# hospital effects**

for (k in 1:M) {u[k] ~ dnorm(0,tau.u)

u.1[k] ~ dnorm(0,1) I(0,)

u.r[k] <- u[k]-mean(u[])}

# skew parameters

gam.e ~ dnorm(0,1)

gam.u ~ dnorm(0,1)

**# Priors on random effects variances**

V ~ dunif(0,100)

r ~ dunif(0,1)

sig2.u <- r\*V

sig2.e <- V-sig2.u

tau.e <- 1/sig2.e

tau.u <- 1/sig2.u

**# random effect st devns**

sigma[1] <- 1/sqrt(tau.e)

sigma[2] <- 1/sqrt(tau.u)

# correlated process prior on baseline hazard

for (k in 2:J) {lam[k] ~ dgamma(a0, b0[k])

b0[k] <- a0/lam[k-1]}

lam[1] ~ dgamma(0.1,0.1)

# treatment parameter

beta ~ dnorm(0, 0.001)

a0~ dgamma(0.1,0.1)

# Cumulative Hazard

H0[1] <- lam[1]\*a[1];

for (k in 2:J) {H0[k] <- lam[k]\*(a[k]-a[k-1])}

# survival with and without treatment

for (j in 1:J) {S[j,1] <- pow(exp(-sum(H0[1:j])), exp(beta))

S[j,2] <- exp(-sum(H0[1:j]))}}

", file="model4.jag")

**# Initial values and estimation**

inits1 <- list(V=2,r=0.5,beta=0,a0=1,gam.e=0,gam.u=0)

inits2 <- list(V=3,r=0.3,beta=0,a0=2,gam.e=0,gam.u=0)

inits=list(inits1,inits2)

pars <- c("beta","lam","a0","sigma","S","loglik","u.r","e.r","gam.u","gam.e",

"u.1","e.1")

R4 <- autojags(DS\_11\_6, inits, pars,model.file= "model4.jag",2,

iter.increment=2500, n.burnin=500,Rhat.limit=1.1, max.iter=20000, seed=1234, codaOnly= c('loglik'))

R4$summary

**# WAIC and LOO-IC**

loo(R4$sims.list$loglik)

waic(R4$sims.list$loglik)

**#**

**# PEM, multiplicative patient and hospital effects**

**#**

cat("model {for (i in 1:n) { for (k in 1:J) {

theta[i,k] <- lam[k]\*alpha.p[pat[i]]\*alpha.h[hos[i]]\*exp(beta\*trt[i])

mu[i,k] <- o[i,k]\*theta[i,k]

y[i,k] ~ dpois(mu[i,k])

**# likelihood (nu used to avoid logs of zero)**

nu[i,k] <- equals(mu[i,k],0) +(1-equals(mu[i,k],0))\*mu[i,k]

loglik[idx[i,k]] <- y[i,k]\*log(nu[i,k])-mu[i,k]-logfact(y[i,k])}}

**# patient effects**

for (j in 1:L) {alpha.p[j] ~ dgamma(delta[1],delta[1])

alpha.p.exc[j] <- step(alpha.p[j]-1)}

**# hospital effects**

for (k in 1:M) { alpha.h[k] ~ dgamma(delta[2],delta[2])

alpha.h.exc[k] <- step(alpha.h[k]-1) }

**# priors for gamma parameters**

for (j in 1:2) {delta[j] ~ dgamma(1,0.1)}

sigma2[1] <- 1/delta[1]

sigma2[2] <- 1/delta[2]

**# within hospital correlation**

within.hosp <- sigma2[2]/(sigma2[1]+sigma2[2])

**# correlated process prior on baseline hazard**

for (k in 2:J) {lam[k] ~ dgamma(a0, b0[k])

b0[k] <- a0/lam[k-1]}

lam[1] ~ dgamma(0.1,0.1)

a0~ dgamma(0.1,0.1)

**# treatment parameter**

beta ~ dnorm(0, 0.001)

**# Cumulative Hazard**

H0[1] <- lam[1]\*a[1];

for (k in 2:J) {H0[k] <- lam[k]\*(a[k]-a[k-1])}

**# survival with and without treatment**

for (j in 1:J) {S[j,1] <- pow(exp(-sum(H0[1:j])), exp(beta))

S[j,2] <- exp(-sum(H0[1:j]))}}

", file="model5.jag")

**# Initial values and estimation**

inits1 <- list(delta=c(2,10),beta=0,a0=1)

inits2 <- list(delta=c(2,12),beta=0,a0=2)

inits=list(inits1,inits2)

pars <- c("beta","lam","a0","delta","S","loglik","alpha.p",

"alpha.h","alpha.p.exc","alpha.h.exc")

R5 <- autojags(DS\_11\_6,inits,pars,model.file= "model5.jag",

2,iter.increment=2000, n.burnin=500,Rhat.limit=1.1, max.iter=10000,

seed=1234, codaOnly= c('loglik', 'alpha.p.exc','alpha.h.exc'))

R5$summary

**# WAIC and LOO-IC**

loo(R5$sims.list$loglik)

waic(R5$sims.list$loglik)

**# Histogram of patient effects**

hist(R5$mean$alpha.p,freq=F,breaks=10)

gams=rgamma(1000,R5$mean$delta[1], rate=R5$mean$delta[1])

lines(density(gams),col='red',lwd=2)