setwd("C:/R files BHMRA")

data = read.table("DS\_11\_4.txt",header=T)

require(rube)

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

library(loo)

attach(data)

**# number of subjects**

n=48

**# subjects with time[i]=1**

n1=sum(time==1)+1

time1=numeric(n)

**#**

**# order data according to time survived**

**#**

O <- data[order(time),]

O$time1=O$time-1

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

idx=matrix(,n,max(O$time))

y=matrix(,n,max(O$time))

ndx=0

for (i in 1:n) {for (j in 1:O$time[i]){ndx = ndx+1; idx[i,j]=ndx}}

**#**

**# WEIBULL**

**#**

D= list(n=48, n1=n1,d=O$d,time=O$time,drug=O$drug,age=O$age, idx=idx)

model1= "

model {for (i in 1:n) {y[i,time[i]] <- d[i]}

for (i in 1:n) {for (j in n1:time[i]-1) {y[i,j] <- 0}}

for (i in 1:n) {for (j in 1:time[i]) {y[i,j] ~ dbern(q[i,j])

loglik[idx[i,j]] <- y[i,j]\*log(q[i,j])+(1-y[i,j])\*log(1-q[i,j])

cloglog(q[i,j]) <-

beta[1]+beta[2]\*drug[i]+beta[3]\*age[i]/100+kappa\*log(j)}}

**# Priors on hyperparameters**

for (j in 1:3) {beta[j] ~ dnorm(0,0.01)}

kappa ~ dexp(1)}"

**# Initial values and estimation**

inits1 <- list(beta=c(-8,-2,9),kappa=0.3)

inits2 <- list(beta= c(-7,-2,8),kappa=0.4)

inits=list(inits1,inits2)

pars <- c("beta","kappa","loglik")

**# estimation**

summary(rube(model1, D, inits))

R1=rube(model1, D, inits, pars, n.burn=500, n.thin=1, n.chains=2,n.iter=10000)

summary(R1)

**# WAIC**

waic(R1$sims.list$loglik)

**#**

**# RW1 interval specific intercept**

**#**

D= list(n=48, J=39,n1=3,d=O$d,time=O$time,drug=O$drug,age=O$age, idx=idx)

model2= "

model {for (i in 1:n) {y[i,time[i]] <- d[i]}

for (i in 1:n) {for (j in n1:time[i]-1) {y[i,j] <- 0}}

for (i in 1:n) {for (j in 1:time[i]) {y[i,j] ~ dbern(q[i,j])

cloglog(q[i,j]) <- beta[1]+beta[2]\*drug[i]+beta[3]\*age[i]/100 + alpha0[j]

loglik[idx[i,j]] <- y[i,j]\*log(q[i,j])+(1-y[i,j])\*log(1-q[i,j])}}

**# Priors on hyperparameters**

for (j in 1:3) {beta[j] ~ dnorm(0,0.001)}

tau ~ dgamma(1,0.001)

sigma.alpha <- 1/sqrt(tau)

**# RW1 prior with centred values**

alpha0[1:J] ~ car.normal(adj[],w[],nadj[],tau)

w[1] <- 1

nadj[1] <- 1

w[(J-2)\*2 + 2] <- 1

nadj[J] <- 1

adj[1] <- 2

adj[(J-1)\*2] <- J-1

**# RW1 interior points**

for (j in 2:J-1) {w[2+(j-2)\*2] <- 1; w[3+(j-2)\*2] <- 1;

adj[2+(j-2)\*2] <- j-1; adj[3+(j-2)\*2] <- j+1

nadj[j] <- 2}

**# Baseline hazard including intercept**

for (j in 1:J) {alpha[j] <- beta[1]+alpha0[j]

alphtr[1,j] <- alpha[j]

alphtr[2,j] <- alpha[j]+beta[2]}}

"

**# initial values and parameters**

inits1 <- list(beta=rep(0,3),tau=1,alpha0=rep(0,39))

inits2 <- list(beta=rep(0,3),tau=5,alpha0=rep(0,39))

inits=list(inits1,inits2)

pars <- c("beta","loglik","sigma.alpha","alpha")

**# estimation**

summary(rube(model2, D, inits))

R2=rube(model2, D, inits, pars, n.burn=500, n.thin=1, n.chains=2,n.iter=10000)

summary(R2)

**# fit**

waic(R2$sims.list$loglik)

**#**

**# WEIBULL PLUS FRAILTY**

**#**

D= list(n=48, n1=n1,d=O$d,time=O$time,drug=O$drug,age=O$age, idx=idx)

model3= "model {for (i in 1:n) {y[i,time[i]] <- d[i]}

for (i in 1:n) {for (j in n1:time[i]-1) {y[i,j] <- 0}}

**# subject random effects**

for (i in 1:n) {b[i] ~ dnorm(0,1)

for (j in 1:time[i]) {y[i,j] ~ dbern(q[i,j])

loglik[idx[i,j]] <- y[i,j]\*log(q[i,j])+(1-y[i,j])\*log(1-q[i,j])

cloglog(q[i,j]) <-

beta[1]+beta[2]\*drug[i]+beta[3]\*age[i]/100+kappa\*log(j)+sigma.b\*b[i]}}

**# Priors on hyperparameters**

for (j in 1:3) {beta[j] ~ dnorm(0,0.01)}

sigma.b <- sqrt(1/tau.b)

tau.b ~ dgamma(1,0.01)

kappa ~ dexp(1)}"

**# Initial values and estimation**

inits1 <- list(beta=c(-8,-2,9),kappa=0.3,b=rep(0,48),tau.b=20)

inits2 <- list(beta= c(-7,-2,8),kappa=0.4,b=rep(0,48),tau.b=50)

inits=list(inits1,inits2)

pars <- c("beta","kappa","loglik","sigma.b","b")

**# estimation**

summary(rube(model3, D, inits))

R3=rube(model3, D, inits, pars, n.burn=500, n.thin=1, n.chains=2,n.iter=10000)

summary(R3,limit=48)

**# WAIC**

waic(R3$sims.list$loglik)

**# extreme frailty effects**

b.mn=apply(R3$sims.list$b,2,mean)

sort(b.mn)[1:5]; order(b.mn)[1:5]

sort(b.mn)[44:48]; order(b.mn)[44:48]

hist(b.mn,breaks=20,xlab="Frailties",main="Figure 11.5 Posterior Mean Frailties",col= "gray")