require(jagsUI); require(MCMCpack); require(rube); require(loo)

Sys.setenv(BUGSDIR="c:\\users\\p congdon\\documents\\WINBUGS14")

setwd("C:/R files BHMRA")

set.seed(1234)

attach("DS\_4\_3.Rdata")

attach(DS\_4\_3)

y <- matrix(NA,J,2); S2 <- array(NA,dim=c(J,2,2))

**# define responses and observed covariances**

for (j in 1:J) { y[j,1] <- log(rT[j]/(nT[j]-rT[j]));

y[j,2] <- log(rC[j]/(nC[j]-rC[j]))

S2[j,1,1] <- 1/rT[j] + 1/(nT[j]-rT[j]);

S2[j,1,2] <- 0;

S2[j,2,1] <- 0;

S2[j,2,2] <- 1/rC[j] + 1/(nC[j]-rC[j])}

DS\_4\_3$y <- y

DS\_4\_3$S2 <- S2

**# Wishart prior sensitivity setting, MODEL 1**

# DS\_4\_3$Q <- diag(0.1,2)

Q <- DS\_4\_3$Q

**# MODEL 1 MVN- MVN model**

cat(" model {for (j in 1:J) {# mixed predictions

ynew[j,1:2] ~ dmnorm(bnew[j,1:2],Precy[j,1:2,1:2])

bnew[j,1:2] ~ dmnorm(mu[1:2],Precb[1:2,1:2])

for (k in 1:2) {pred.exc[k,j] <- step(ynew[j,k]-y[j,k])

pfc[j,k] <- pow(ynew[j,k]-y[j,k],2)}

# likelihood

y[j,1:2] ~ dmnorm(b[j,1:2],Precy[j,1:2,1:2])

Precy[j,1:2,1:2] <- inverse(S2[j,1:2,1:2])

# second stage model

b[j,1:2] ~ dmnorm(mu[1:2],Precb[1:2,1:2])}

# second stage inverse variance

Precb[1:2,1:2] ~ dwish(Q[,],2)

Sigma.b[1:2,1:2] <- inverse(Precb[,])

corr.TC <- Sigma.b[1,2]/sqrt(Sigma.b[1,1]\*Sigma.b[2,2]);

slope.TC <- Sigma.b[1,2]/Sigma.b[2,2]

# variation in treatment effects due to baseline risk

V.t <- Sigma.b[1,1]+Sigma.b[2,2]-2\*Sigma.b[1,2]

V.c <- Sigma.b[1,1]-pow(Sigma.b[1,2],2)/Sigma.b[2,2]

r2.base <- 1-V.c/V.t

# gamma : population wide vaccination effect

gamma <- mu[1]-mu[2]

for (j in 1:2) {mu[j] ~ dnorm(0,0.001)}

# predictive fit criterion summary fit

PFC.mix <- sum(pfc[,])}

", file="model1.jag")

**# initial values and estimation**

inits <- function(){list(Precb= rwish(2,Q),mu=rnorm(2,0,0.1))}

pars <- c("mu","Sigma.b","slope.TC","corr.TC","gamma",

"r2.base","pred.exc","PFC.mix")

R1=autojags(DS\_4\_3, inits, pars, "model1.jag",2, n.adapt=100, iter.increment=1000, n.burnin=500,Rhat.limit=1.1, max.iter=5000,seed=1234)

R1$summary

**# MODEL 2 MVN- MVT model (MVT via scale mixing)**

model2= "

model {# 4 degrees of freedom for t-density

for (j in 1:J) {lambda[j] ~ dgamma(2,2)

# predictions

ynew[j,1:2] ~ dmnorm(bnew[j,1:2],Precy[j,1:2,1:2])

bnew[j,1:2] ~ dmnorm(mu[1:2],Preclam[j,1:2,1:2])

for (k in 1:2) {pred.exc[k,j] <- step(ynew[j,k]-y[j,k])

pfc[j,k] <- pow(ynew[j,k]-y[j,k],2)}

# likelihood

y[j,1:2] ~ dmnorm(b[j,1:2],Precy[j,1:2,1:2])

Precy[j,1:2,1:2] <- inverse(S2[j,1:2,1:2])

# second stage model

for (k in 1:2) { for (m in 1:2) {

Preclam[j,k,m] <- Precb[k,m]\*lambda[j]}}

b[j,1:2] ~ dmnorm(mu[1:2], Preclam[j,1:2,1:2])}

# second stage inverse variance

Precb[1:2,1:2] ~ dwish(Q[,],2)

Sigma.b[1:2,1:2] <- inverse(Precb[,])

corr.TC <- Sigma.b[1,2]/sqrt(Sigma.b[1,1]\*Sigma.b[2,2]);

slope.TC <- Sigma.b[1,2]/Sigma.b[2,2]

# variation in treatment effects due to baseline risk

V.t <- Sigma.b[1,1]+Sigma.b[2,2]-2\*Sigma.b[1,2]

V.c <- Sigma.b[1,1]-pow(Sigma.b[1,2],2)/Sigma.b[2,2]

r2.base <- 1-V.c/V.t

# gamma : population wide vaccination effect

gamma <- mu[1]-mu[2]

for (j in 1:2) {mu[j] ~ dnorm(0,0.001)}

# predictive fit criterion summary fit

PFC.mix <- sum(pfc[,])}

"

**# initial values and estimation**

inits <- function(){list(Precb= rwish(2,Q),mu=rnorm(2,0,0.1))}

pars <- c("slope.TC","corr.TC","gamma","r2.base","pred.exc","lambda","PFC.mix")

summary(rube(model2,DS\_4\_3, inits))

R2 = rube(model2, DS\_4\_3, inits, pars, n.burn=500, n.thin=1, n.chains=2,n.iter=5000)

summary(R2,limit=20)

**# MODEL 3 MVN- MVSkewT model (via scale mixing)**

model3= "

model {

for (j in 1:J) {lambda[j] ~ dgamma(nu.2,nu.2)

# predictions

ynew[j,1:2] ~ dmnorm(bnew[j,1:2],Precy[j,1:2,1:2])

bnew[j,1:2] ~ dmnorm(mu[1:2],Preclam[j,1:2,1:2])

for (k in 1:2) {pred.exc[k,j] <- step(ynew[j,k]-y[j,k])

pfc[j,k] <- pow(ynew[j,k]-y[j,k],2)

# positive skew effects

w[j,k] ~ dt(0,1 ,nu ) I(0,)}

# likelihood

y[j,1:2] ~ dmnorm(b[j,1:2],Precy[j,1:2,1:2])

Precy[j,1:2,1:2] <- inverse(S2[j,1:2,1:2])

# second stage model

for (k in 1:2) { for (m in 1:2) {

Preclam[j,k,m] <- Precb[k,m]\*lambda[j]}}

b[j,1:2] ~ dmnorm(mu.b[j,1:2], Preclam[j,1:2,1:2])

mu.b[j,1] <- mu[1] + delta[1]\*(w[j,1]-mn.w)

mu.b[j,2] <- mu[2] + delta[2]\*(w[j,2]-mn.w)}

# skewness parameters

for (k in 1:K) {delta[k] ~ dnorm(0,0.1)}

# prior parameter settings

nu <- 4

nu.2 <- nu/2

mn.w <- exp(loggam(0.5\*

(nu-1.))-loggam(0.5\*nu))\*sqrt(nu/3.14159)

# second stage inverse variance

Precb[1:2,1:2] ~ dwish(Q[,],2)

Sigma.b[1:2,1:2] <- inverse(Precb[,])

corr.TC <- Sigma.b[1,2]/sqrt(Sigma.b[1,1]\*Sigma.b[2,2]);

slope.TC <- Sigma.b[1,2]/Sigma.b[2,2]

# variation in treatment effects due to baseline risk

V.t <- Sigma.b[1,1]+Sigma.b[2,2]-2\*Sigma.b[1,2]

V.c <- Sigma.b[1,1]-pow(Sigma.b[1,2],2)/Sigma.b[2,2]

r2.base <- 1-V.c/V.t

# gamma : population wide vaccination effect

gamma <- mu[1]-mu[2]

for (j in 1:2) {mu[j] ~ dnorm(0,0.001)}

# predictive fit criterion summary fit

PFC.mix <- sum(pfc[,])}

"

**# initial values and estimation**

C1 <- diag(1,2); C2 <- diag(1.5,2)

w <- b <- bn <- yn <- matrix(0,13,2); lambda=rep(1,13)

init1 = list(Precb=C1,mu=c(0,0),delta=c(0,0),w=w,

lambda=lambda,b=b,bnew=bn,ynew=yn)

init2 = list(Precb=C2,mu=c(-0.2,0.2),delta=c(0,0),w=w,lambda=lambda,b=b,

bnew=bn,ynew=yn)

inits = list(init1,init2)

pars = c("slope.TC","corr.TC","gamma","r2.base","pred.exc",

"lambda","delta","PFC.mix")

C3 = rube(model3,DS\_4\_3, inits)

summary(C3)

M3 = rube(model3, DS\_4\_3, inits, pars, n.burn=500, n.thin=1, n.chains=2,n.iter=25000)

summary(M3,limit=20)

**# MODEL 4 MVN- MVN, Cholesky decomposition of 2nd stage var-cov**

cat(" model {for (j in 1:J) {# likelihood

y[j,1:2] ~ dmnorm(b[j,1:2],Precy[j,1:2,1:2])

Precy[j,1:2,1:2] <- inverse(S2[j,1:2,1:2])

ynew[j,1:2] ~ dmnorm(b[j,1:2],Precy[j,1:2,1:2])

# second stage

b[j,1:2] ~ dmnorm(mu[1:2],Precb[1:2,1:2])}

Precb[1:2,1:2] <- inverse(Sigma.b[,])

**# Cholesky Decomposition**

Sigma.b[1,1] <- sig.b[1]\*sig.b[1]

Sigma.b[2,2] <- sig.b[2]\*sig.b[2]

Sigma.b[2,1] <- rho12\*sig.b[1]\*sig.b[2]

Sigma.b[1,2] <- Sigma.b[2,1]

L12 ~ dunif(-1,1)

rho12 <- L12

for (j in 1:2) {sig.b[j] ~ dunif(0,5)}

V.t <- Sigma.b[1,1]+Sigma.b[2,2]-2\*Sigma.b[1,2]

V.c <- Sigma.b[1,1]-pow(Sigma.b[1,2],2)/Sigma.b[2,2]

**# variation in treatment effects due to baseline risk**

r2.base <- 1-V.c/V.t

corr.TC <- Sigma.b[1,2]/sqrt(Sigma.b[1,1]\*Sigma.b[2,2]);

regslope.TC <- Sigma.b[1,2]/Sigma.b[2,2]

# population wide vaccine effect

gamma <- mu[1]-mu[2];

for (j in 1:2) {mu[j] ~ dnorm(0,0.001)}}",

file="model4.jag")

**# initial values and estimation**

inits <- function(){list(sigb= runif(2,0,2),mu=rnorm(2,0,0.1))}

pars <- c("mu","Sigma.b","slope.TC","corr.TC","gamma","r2.base","pred.exc","PFC.mix")

M4=autojags(DS\_4\_3, inits, pars, "model4.jag",2, n.adapt=100, iter.increment=1000, n.burnin=500,Rhat.limit=1.1, max.iter=5000,seed=1234)

M4$summary