

#Y-BOC random effects analysis

Code adapted from Program 5(a)

#<http://www.nicesdsu.org.uk/TSD2%20General%20meta%20analysis%20corrected%2015April2014.pdf>

```
model{
for (i in 1:complete){ #loop through studies reporting SD
  for(z in 1:na[i]){
    sd1[i,z]<-sd[i,z]
#calculate the mean and precision of the reported SDs
    sd1[i,z]~dnorm(mu.sd[out[i]],prec.sd[out[i]])
  }
}

for (i in complete+1:ns){#loop through remaining studies (not report SD)
  for (z in 1:na[i]){
    sd1[i,z]~dnorm(mu.sd[out[i]],prec.sd[out[i]])
#SD is equal to estimated SD only for studies that did not report uncertainty
    sd[i,z]<- cut(sd1[i,z])
  }
}

  for (i in 1:ns){ #loop through all studies converting SDs to SEs
    for (z in 1:na[i]){
      se[i,z]<-sd[i,z]/sqrt(n[i,z])
      prec[i,z]<-pow(se[i,z],-2)
    }
  }

#TSD code
for(i in 1:ns){ # LOOP THROUGH STUDIES
  w[i,1] <- 0 # adjustment for multi-arm trials is zero for control arm
  delta[i,1] <- 0 # treatment effect is zero for control arm
  mu[i] ~ dnorm(0,.0001) # vague priors for all trial baselines
  for (k in 1:na[i]) { # LOOP THROUGH ARMS
    y[i,k] ~ dnorm(theta[i,k],prec[i,k]) # normal likelihood
    theta[i,k] <- mu[i] + delta[i,k] # model for linear
predictor
    dev[i,k] <- (y[i,k]-theta[i,k])*(y[i,k]-
theta[i,k])*prec[i,k]
  }

  resdev[i] <- sum(dev[i,1:na[i]]) # summed deviance contribution

for (k in 2:na[i]) { # LOOP THROUGH ARMS
  delta[i,k] ~ dnorm(md[i,k],taud[i,k]) # trial-specific LOR
distributions
  md[i,k] <- d[t[i,k]] - d[t[i,1]] + sw[i,k] # mean of treat effect
distributions (with multi-arm trial correction)
  taud[i,k] <- tau *2*(k-1)/k # precision of treat effects
distributions
  w[i,k] <- (delta[i,k] - d[t[i,k]] + d[t[i,1]]) # adjustment for
multi-arm
  sw[i,k] <- sum(w[i,1:k-1])/(k-1) # cumulative adjustment for
multi-arm
}
}

totresdev <- sum(resdev[1:complete]) #Total Residual Deviance
d[1]<-0 # treatment effect is zero for reference treatment
```

```

D[1]<-0

for (i in 1:n.j1){      #vague prior for trt effects only 1 treatment per
"class"
  d[j1[i]]~dnorm(0,.0001)
  D[class[j1[i]]]<-d[j1[i]]
}

for (i in 1:n.jclass){ #trt effects when multiple treatments form a 'class'
  d[jclass[i]]~dnorm(D[class[jclass[i]]],Prec3[class[jclass[i]]])
}

D[3]~dnorm(0, 0.0001)  #vague prior for 'class' effect

Prec3[3]<- 1/(SD3*SD3)
SD3~dunif(0,10)

# vague priors for treatment effects
sdev ~ dunif(0,10) # vague prior for between-trial SD.
tau <- pow(sdev,-2) # between-trial precision = (1/between-trial
variance)

for (i in 1:2){
  mu.sd[i]~dnorm(0,.0001)I(0,)
}
for (i in 1:2){
  prec.sd[i]~dgamma(.01,.01)
}

# Ranking and probabilities for treatment and class level effects
for(k in 1:nt){
  rk[k]<-rank(d[,k])
  best[k]<-equals(rk[k],1)
  for (h in 1:nt){ prob[h,k]<-equals(rk[k],h)} }

for (q in 1:nclass){
  rk.class[q]<-rank(D[,q])
  best.class[q]<-equals(rk.class[q],1)
  for (x in 1:nclass){
    prob.class[x,q]<-equals(rk.class[x],q)
  }
}

# all MDs for each treatment level comparison
for (c in 1:(nt-1)) {
  for (k in (c+1):nt) {
    treat.mean.diff[c,k] <- (d[k]-d[c]) } }

# all MDs for each class level comparison
for (f in 1:(nclass-1)) {
  for (q in (f+1):nclass) {
    class.mean.diff[f,q] <- (D[q]-D[f]) } }
}

```

#Drop outs (tolerability) consistency model

#Random effects model for multi-arm trials. Binomial link

```
model{ #
for(i in 1:ns){
  w[i,1] <- 0 # adjustment for multi-arm trials is zero for control arm
  delta[i,1] <- 0 # treatment effect is zero for control arm
  mu[i] ~ dnorm(0,.0001) # vague priors for all trial baselines

  for (k in 1:na[i]) { # LOOP THROUGH ARMS
    r[i,k] ~ dbin(p[i,k],n[i,k]) # binomial likelihood
    logit(p[i,k]) <- mu[i] + delta[i,k] # model for linear predictor
    rhat[i,k] <- p[i,k] * n[i,k] # expected value of the numerators
    dev[i,k] <- 2 * (r[i,k] * (log(r[i,k])-log(rhat[i,k]))) #Deviance contribution
    + (n[i,k]-r[i,k]) * (log(n[i,k]-r[i,k]) - log(n[i,k]-rhat[i,k])))
  }

  resdev[i] <- sum(dev[i,1:na[i]]) # summed res.dev contribution per trial

  for (k in 2:na[i]) { # LOOP THROUGH ARMS
    delta[i,k] ~ dnorm(md[i,k],taud[i,k]) # trial-specific LOR distributions
    md[i,k] <- d[t[i,k]] - d[t[i,1]] + sw[i,k] # mean of LOR distributions
    taud[i,k] <- tau *2*(k-1)/k # precision of LOR distributions
    w[i,k] <- (delta[i,k] - d[t[i,k]] + d[t[i,1]]) # adjustment for multi-arm
RCTs
    sw[i,k] <- sum(w[i,1:k-1])/(k-1) # cumulative adjustment for multi-arm trials
  }
}

totresdev <- sum(resdev[]) #Total Residual Deviance
d[1] <- 0 # treatment effect is zero for reference treatment
D[1]<-0

for (i in 1:n.j1){
  d[j1[i]]~dnorm(0,.0001)
  D[class[j1[i]]]<-d[j1[i]]  }

for (i in 1:n.jclass){
  d[jclass[i]]~dnorm(D[class[jclass[i]]],Prec3[class[jclass[i]]])  }

D[3]~dnorm(0, 0.0001)
Prec3[3]<- 1/(SD3*SD3)
SD3~dunif(0,10)
sd ~ dunif(0,5) # vague prior for between-trialSD
tau <- pow(sd,-2) # between-trial precision = (1/between-trial variance)

# Ranking and probabilities for treatment and class level effects
for(k in 1:20){
  rk[k]<-rank(d[,k])
  best[k]<-equals(rk[k],1)
  for (h in 1:20){ prob[h,k]<-equals(rk[k],h) }  }
for (q in 1:15){
  rk.class[q]<-rank(D[,q])
  best.class[q]<-equals(rk.class[q],1)
  for (x in 1:15){
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        prob.class[x,q]<-equals(rk.class[x],q)
    }
}

#Pairwise ORs for treatment level analysis
for (f in 1:14)
  { for (q in (f+1):15)
    { lor.D[f,q] <- D[q] - D[f]
      OR.D[f,q]<-exp(lor.D[f,q])
    }}

#Pairwise ORs for class level analysis
for (c in 1:19) {
for (k in (c+1):20) {
  lor[c,k] <- d[k] - d[c]
  OR[c,k]<-exp(lor[c,k])} }

}}}
```