National Institute for Health and Care Excellence

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Menopause (update)

[B1] TSU NMA software code inconsistency model

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Sample WinBUGS code

Unrelated Mean Effects (Inconsistency) model – Genitourinary symptoms (normal likelihood, identity link function, analysis using SMD)

```
# Normal likelihood, identity link: SMD with arm-based means
# Random effects model for multi-arm trials
model{                              # *** PROGRAM STARTS
for(i in 1:ns){                     #   LOOP THROUGH STUDIES
  delta[i,1] <- 0                    # treatment effect is zero for control arm
  mu[i] ~ dnorm(0,.0001)            # vague priors for all trial baselines
 }
# (1) CFB DATA
for(i in 1:ns){
  # calculate pooled.sd and adjustment for SMD
  df[i] <- sum(n[i,1:na[i]]) - na[i] # denominator for pooled.var
  H[i] <- 1 - 3/(4*df[i]-1)         # use Hedges' g
  for (k in 1:na[i]){
    se[i,k] <- sdCFB[i,k]/sqrt(n[i,k])
    var[i,k] <- pow(se[i,k],2)       # calcultate variances
    prec[i,k] <- 1/var[i,k]         # set precisions
    yCFB[i,k] ~ dnorm(phi[i,k], prec[i,k]) # normal likelihood
    #phi[i,k] <- theta[i,k] * (Pooled.sd[i]/H[i]) # theta is stand mean
            phi[i,k] <- theta[i,k] * (scalesd[i]/H[i]) # theta is stand mean
    theta[i,k] <- mu[i] + delta[i,k] # model for linear predictor, delta is SMD
    dev[i,k] <- (yCFB[i,k]-phi[i,k])*(yCFB[i,k]-phi[i,k])*prec[i,k]
    #nvar[i,k] <- (n[i,k]-1) * pow(sdCFB[i,k],2) # for pooled.sd
   }
  # summed residual deviance contribution for this trial
  resdev[i] <- sum(dev[i,1:na[i]])
 }
```

```
# RE MODEL (CFB data)
for(i in 1:ns){                    # LOOP THROUGH STUDIES WITH CFB DATA
  for (k in 2:na[i]){              # LOOP THROUGH ARMS
    # trial-specific RE distributions
    delta[i,k] ~ dnorm(md[i,k], tau)
    md[i,k] <- d[t[i,k], t[i,1]]
   }
 }

totresdev <- sum(resdev[])             # Total Residual Deviance (all data)

# treatment effects from Class
for (c in 1:(nt-1)){
            d[c,c] <- 0
            for (k in (c+1):nt) {

                        # Ensures d is fixed if class has 0 variance for ALL comparisons
                        d[c,k] <- m[D[c],D[k]]
                        d[k,c] <- -d[c,k]
            }
}

m[nc,nc] <- 0
for (c1 in 1:(nc-1)){
            m[c1,c1] <- 0
            for (c2 in (c1+1):nc){
                        m[c1,c2] ~ dnorm(0,.0001)
            }
}

sd ~ dunif(0,5)     # vague prior for between-trial SD
tau <- pow(sd,-2)   # between-trial precision = (1/between-trial variance)
```

```
# all pairwise differences
for (c in 1:(nt-1)) {  for (k in (c+1):nt)  { diff[c,k] <- d[c,k] }  }

# pairwise SMDs for all possible class comparisons
for (c in 1:(nc-1)){
  for (k in (c+1):nc){ diffClass[c,k] <- (m[c,k]) }
 }
}                                   # *** PROGRAM ENDS
```

Unrelated Mean Effects (Inconsistency) model – Discontinuation due to adverse events (Binomial likelihood, Logit link function)

```
model{
for(i in 1:ns){
  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]) {
    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
#Deviance contribution
    dev[i,k] <- 2 * (r[i,k] * (log(r[i,k])-log(rhat[i,k])) +  (n[i,k]-r[i,k]) * (log(n[i,k]-r[i,k]) - log(n[i,k]-rhat[i,k])))
   }
#Summed residual deviance contribution for this trial
  resdev[i] <- sum(dev[i,1:na[i]])
  for (k in 2:na[i]) {
    delta[i,k] ~ dnorm(md[i,k],tau)                  # trial-specific LOR distributions
    # mean of LOR distributions (with multi-arm trial correction)
    md[i,k] <-  d[t[i,1], t[i,k]]
   }
```

```
 }
totresdev <- sum(resdev[])          # Total Residual Deviance

# treatment effects from Class
for (c in 1:(nt-1)){
          d[c,c] <- 0
          for (k in (c+1):nt) {

                    # Ensures d is fixed if class has 0 variance for ALL comparisons
                    #d[c,k] <- m[D[c],D[k]] + dvar[c,k]
                    #dvar[c,k] ~ dnorm(0, prec2)
                    #d[k,c] <- -d[c,k]
                    d[c,k] <- m[D[c],D[k]]
                    d[k,c] <- -d[c,k]
          }
}

m[nc,nc] <- 0
for (c1 in 1:(nc-1)){
          m[c1,c1] <- 0
          for (c2 in (c1+1):nc){
                    m[c1,c2] ~ dnorm(0,.0001)
          }
}

sd ~ dunif(0,5)     # vague prior for between-trial SD
tau <- pow(sd,-2)   # between-trial precision = (1/between-trial variance)

# pairwise ORs for all possible pair-wise comparisons
for (c in 1:(nt-1)){
  for (k in (c+1):nt){
    or[c,k] <- exp(d[c,k])
```

```
    }
  }

# Pairwise ORs for all possible pair-wise class combinations
for (c in 1:(nc-1)){
  for (k in (c+1):nc){
    orClass[c,k] <- exp(m[c,k])
    }
  }
}
```