

FINAL

Menopause (update)

**[B1] TSU NMA software code inconsistency
model**

NICE guideline NG23

Supplement 5

November 2024

FINAL

*Supplementary material was developed by the
NICE Technical Support Unit*

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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)    # calculate 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])
  }
}
}
```