

Menopause (update)

[B1] TSU NMA software code

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

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1 Sample WinBUGS code

2 Genitourinary symptoms (normal likelihood, identity link 3 function, analysis using SMD)

```

4 # Normal likelihood, identity link: SMD with arm-based means (External SDs for
5 standardising)
6 # Random effects model for multi-arm trials
7 # Fixed class effects
8 model{                                # *** PROGRAM STARTS
9 for(i in 1:ns){                        # LOOP THROUGH STUDIES
10  w[i,1] <- 0 # adjustment for multi-arm trials is zero for control arm
11  delta[i,1] <- 0 # treatment effect is zero for control arm
12  mu[i] ~ dnorm(0,.0001) # vague priors for all trial baselines
13 }
14 # (1) CFB DATA
15 for(i in 1:ns){
16  # calculate pooled.sd and adjustment for SMD
17  df[i] <- sum(n[i,1:na[i]]) - na[i] # denominator for pooled.var
18  #Pooled.var[i] <- sum(nvar[i,1:na[i]])/df[i]
19  #Pooled.sd[i] <- sqrt(Pooled.var[i])
20  H[i] <- 1 - 3/(4*df[i]-1) # use Hedges' g
21  #H[i] <- 1 # use Cohen's d (ie no adjustment)
22  for (k in 1:na[i]){
23    se[i,k] <- sdCFB[i,k]/sqrt(n[i,k])
24    var[i,k] <- pow(se[i,k],2) # calculate variances
25    prec[i,k] <- 1/var[i,k] # set precisions
26    yCFB[i,k] ~ dnorm(phi[i,k], prec[i,k]) # normal likelihood
27    #phi[i,k] <- theta[i,k] * (Pooled.sd[i]/H[i]) # theta is stand mean
28    phi[i,k] <- theta[i,k] * (scalesd[i]/H[i]) # theta is stand mean
29    theta[i,k] <- mu[i] + delta[i,k] # model for linear predictor, delta is SMD
30    dev[i,k] <- (yCFB[i,k]-phi[i,k])*(yCFB[i,k]-phi[i,k])*prec[i,k]
31    #nvar[i,k] <- (n[i,k]-1) * pow(sdCFB[i,k],2) # for pooled.sd
32  }

```

```
1 # summed residual deviance contribution for this trial
2 resdev[i] <- sum(dev[i,1:na[i]])
3 }
4
5 # RE MODEL (CFB data)
6 for(i in 1:ns){ # LOOP THROUGH STUDIES WITH CFB DATA
7   for(k in 2:na[i]){ # LOOP THROUGH ARMS
8     # trial-specific RE distributions
9     delta[i,k] ~ dnorm(md[i,k], taud[i,k])
10    md[i,k] <- d[t[i,k]] - d[t[i,1]] + sw[i,k]
11    # precision of RE distributions (with multi-arm trial correction)
12    taud[i,k] <- tau *2*(k-1)/k
13    #adjustment, multi-arm RCTs
14    w[i,k] <- delta[i,k] - d[t[i,k]] + d[t[i,1]]
15    # cumulative adjustment for multi-arm trials
16    sw[i,k] <-sum(w[i,1:k-1])/(k-1)
17  }
18 }
19
20 totesdev <- sum(resdev[]) # Total Residual Deviance (all data)
21
22 # Priors and model assumptions (classes)
23 d[1] <- 0 # treatment effect is zero for reference treatment
24 # treatment effects from Class
25 for(k in 2:nt) {
26   d[k] <- m[D[k]]
27 }
28
29 m[1] <- 0
30 # prior for mean class effect
31 for(k in 2:nc){ m[k] ~ dnorm(0, .0001) }
32
```

```
1 sd ~ dunif(0,4)          # vague prior for between-trial SD
2 tau <- pow(sd,-2)       # between-trial precision
3
4 # all pairwise differences
5 for (c in 1:(nt-1)) { for (k in (c+1):nt) { diff[c,k] <- d[k] - d[c] } }
6
7 # pairwise SMDs for all possible class comparisons
8 for (c in 1:(nc-1)){
9   for (k in (c+1):nc){ diffClass[c,k] <- (m[k]-m[c]) }
10 }
11
12 # treatments of interest to rank
13 for (k in 1:ntR) {
14   dR[k] <- d[tRcode[k]]
15 }
16 # classes of interest to rank
17 for (k in 1:ncR) {
18   mR[k] <- m[cRcode[k]]
19 }
20
21 for (k in 1:ntR){
22   # rk2[k] <- ntR+1-rank(dR[,k])      # lower values are "bad"
23   rk[k] <- rank(dR[,k])      # lower values are "good"
24   best[k] <- equals(rk[k],1) # Smallest is best (i.e. rank 1)
25   # prob treat k is h-th best, prob[1,k]=best[k]
26   for (h in 1:ntR) { prob[h,k] <- equals(rk[k],h) }
27 }
28 #
29 for (k in 1:ncR){
30   rkClass[k] <- rank(mR[,k]) # lower values are "good"
31   bestClass[k] <- equals(rkClass[k],1) # Smallest is best (i.e. rank 1)
32   # prob class k is h-th best, prob[1,k]=best[k]
```

```

1   for (h in 1:ncR) { probClass[h,k] <- equals(rkClass[k],h) }
2   }
3   }          # *** PROGRAM ENDS
4
5   Discontinuation due to adverse events (Binomial
6   likelihood, Logit link function)
7   model{
8   for(i in 1:ns){
9     w[i,1] <- 0          # adjustment for multi-arm trials is zero for control arm
10    delta[i,1] <- 0    # treatment effect is zero for control arm
11    mu[i] ~ dnorm(0,.0001) # vague priors for all trial baselines
12    for (k in 1:na[i]) {
13      r[i,k] ~ dbin(p[i,k],n[i,k])          # binomial likelihood
14      logit(p[i,k]) <- mu[i] + delta[i,k]    # model for linear predictor
15      rhat[i,k] <- p[i,k] * n[i,k]          # expected value of the
16      numerators
17      #Deviance contribution
18      dev[i,k] <- 2 * (r[i,k] * (log(r[i,k])-log(rhat[i,k])))
19        + (n[i,k]-r[i,k]) * (log(n[i,k]-r[i,k]) - log(n[i,k]-rhat[i,k])))
20    }
21    #Summed residual deviance contribution for this trial
22    resdev[i] <- sum(dev[i,1:na[i]])
23    for (k in 2:na[i]) {
24      delta[i,k] ~ dnorm(md[i,k],taud[i,k])    # trial-specific LOR distributions
25      # mean of LOR distributions (with multi-arm trial correction)
26      md[i,k] <- d[t[i,k]] - d[t[i,1]] + sw[i,k]
27      # precision of LOR distributions (with multi-arm trial correction)
28      taud[i,k] <- tau *2*(k-1)/k
29      # adjustment for multi-arm RCTs
30      w[i,k] <- (delta[i,k] - d[t[i,k]] + d[t[i,1]])
31      # cumulative adjustment for multi-arm trials
32      sw[i,k] <- sum(w[i,1:(k-1)])/(k-1)

```



```
1   }
2   }
3   totresdev <- sum(resdev[])      # Total Residual Deviance
4   d[1]<-0    # treatment effect is zero for reference treatment
5
6   for (k in 2:nt) {
7     d[k] <- m[D[k]]
8   }
9
10  m[1] <- 0
11  # prior for mean class effect
12  for (k in 2:nc){ m[k] ~ dnorm(0, .0001) }
13
14  sd ~ dunif(0,5)  # vague prior for between-trial SD
15  tau <- pow(sd,-2) # between-trial precision = (1/between-trial variance)
16  # pairwise ORs and LORs for all possible pair-wise comparisons
17  for (c in 1:(nt-1)){
18    for (k in (c+1):nt){
19      or[c,k] <- exp(d[k] - d[c])
20      lor[c,k] <- (d[k]-d[c])
21    }
22  }
23  # treatments of interest to rank
24  for (k in 1:ntR) {
25    dR[k] <- d[tRcode[k]]
26  }
27  # classes of interest to rank
28  for (k in 1:ncR) {
29    mR[k] <- m[cRcode[k]]
30  }
31  for (k in 1:ntR){
32    rk[k] <- rank(dR[,k])          # assumes events are "bad"
```

```
1 best[k] <- equals(rk[k],1) #calculate probability that treat k is best
2 # calculates probability that treat k is h-th best
3 for (h in 1:ntR){ prob[h,k] <- equals(rk[k],h) }
4 }
5 #
6 # pairwise differences for classes
7 for (c in 1:(nc-1)){
8   for (k in (c+1):nc){
9     lorClass[c,k] <- m[k] - m[c]
10    orClass[c,k] <- exp(m[k] - m[c])
11  }
12 }
13 # rank classes
14 for (k in 1:ncR) {
15   rkClass[k] <- rank(mR[,k])
16   bestClass[k] <- equals(rkClass[k],1) # Smallest is best (i.e. rank 1)
17 # prob class k is h-th best, prob[1,k]=best[k]
18   for (h in 1:ncR) { probClass[h,k] <- equals(rkClass[k],h) }
19 }
20 }
21
22
```