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Univariable model for the influence of a single study-level characteristic

Data required:

N_study=no. of studies

N=no. of studies x 2 arms

N_ma=no. of meta-analyses

Study-level:

treat=1 if treatment arm, 0 if control

r=no. of events

n= no. of participants

C1[i] = 1 if the *i*th study has the characteristic of interest, 0 otherwise

ma[i]<- meta-analysis index

s[i]<-study index

Meta-analysis level:

kappa_ok[m] = 1 if there are at least two studies with, and two studies without, the characteristic in the *m*th meta-analysis, 0 otherwise

The WinBUGS model

```
model{
for (i in 1:N) {
        r[i] ~ dbin(p[i],n[i]) # likelihood (binary data r/n=no.of events/no. of participants)
        logit(p[i]) <- alpha[s[i]] +  treat[i]*(theta.minus[i]*+ beta[i] *C1[i])
                # model (treat indicator of treatment group; C1 indicator of study characteristic)
        beta[i]~dnorm(mean[ma[i]],p.k2[ma[i]])I(-10,10)
                # between study, within meta-analysis, variation in difference in effect associated
with characteristic
theta.minus[i]~dnorm(d[ma[i]],p.d[ma[i]])I(-10,10) #RE for intervention effect within meta-analysis

        rhat[i] <- p[i] * n[i]       #calculate residual deviance
        dev[i] <- 2 * (r[i] * (log(r[i])-log(rhat[i]))  +  (n[i]-r[i]) * (log(n[i]-r[i]) - log(n[i]-rhat[i])))
        }
resdev <- sum(dev[])

for (j in 1:N_study) {alpha[j] ~ dnorm(0,.001)}       # priors for study baseline effects - unrelated

for (m in 1:N_ma) {
        mean[m] <- d[m] + b[m]
        d[m] ~ dnorm(0,.001)              # priors for true fixed (unrelated) intervention effects
        b[m] ~ dnorm(b0,p.phi)            # between meta-analysis variation in average difference in
effect associated with characteristic
        var_d[m]~dlnorm(mu,p.tau)       # log-normal distribution for between-study variances
        p.d[m] <- 1/var_d[m]
        p.k2[m] <- equals(kappa_ok[m],1)/(var_d[m]*lambda)
                +equals(kappa_ok[m],0)/(var_d[m]*cut(lambda))
        }
#Prior for unknown parameters
b0 ~ dnorm(0,.001)       # vague prior for overall average difference in effect associated with
characteristic
lambda ~dlnorm(0,1)     # vague prior for change in between-study variation associated with characteristic
```

p.phi1 ~ dgamma(.001,.001)   # vague prior for between meta-analysis variation in average difference in effect associated with characteristic
phi <- pow(p.phi,-0.5)
p.phi <- p.phi1/(1-patom.phi)
patom.phi ~ dbeta(1,1)
mu~dnorm(0,0.001)
p.tau<-1/(sd.tau*sd.tau)
sd.tau~dunif(0,2)

log.tau2.new~dlnorm(mu,p.tau)   # predictive distn for heterogeneity among studies without the characteristic
tau2.new<-exp(log.tau2.new)

# Parameters to monitor
q[1] <- b0
q[2] <- exp(b0)
q[3] <- lambda
q[4] <- phi
q[5]<- log.tau2.new
q[6]<-tau2.new

}

Multivariable model for the influence of three study-level characteristics
Data required:
        N_study=no. of studies
        N=no. of studies x 2 arms
        N_ma=no. of meta-analyses
Study-level:
        treat=1 if treatment arm, 0 if control
        r=no. of events
        n= no. of participants
        C1[i,j] = 1 if the *i*th study has the *j*th characteristic, 0 otherwise
        ma[i]<- meta-analysis index
        s[i]<-study index
Meta-analysis level:
        kappa_ok[m,j] = 1 if there are at least two studies with, and two studies without, the *j*th characteristic in the *m*th meta-analysis, 0 otherwise
        clambda[m,j] = 1 if there are 1, K-1 or K studies with or without the *j*th characteristic in the *m*th meta-analysis, 0 otherwise, where K is the no. of studies in the meta-analysis.
        C0[m,j]=1 if there are no studies in the *m*th meta-analysis with the *j*th characteristic

The WinBUGS model

```
model {
for (i in 1:N) {
        r[i] ~ dbin(p[i],n[i]) # likelihood (binary data r/n=no.of events/no. of participants)
        logit(p[i]) <- alpha[s[i]] + theta[i]*treat[i]

        theta[i]<-theta.minus[i]* (1-C1[i,1]) *(1-C1[i,2]) *(1-C1[i,3])  #effect in study without any of  the
characteristics
                        +theta.plus[i]* (1-(1-C1[i,1]) *(1-C1[i,2]) *(1-C1[i,3]))  effect in studies with
one or more characteristics
```

```
        theta.plus[i] ~ dnorm(mean[i], p.k2[i])I(-10,10)

        theta.minus[i]~dnorm(d[ma[i]],p.d[ma[i]])I(-10,10) #RE for treatment effects within meta-analysis

mean[i]<-d[ma[i]]+b[ma[i],1]*C1[i,1]+b[ma[i],2]*C1[i,2]+b[ma[i],3]*C1[i,3]

k2[i]<-  ( (1-C1[i,1]) + # without characteristic 1
        C1[i,1] * kappa_ok[ma[i],1] * lambda[1] + # with characteristic 1 and inform
        C1[i,1] * clambda[ma[i],1] * cut(lambda[1]) + # with characteristic 1 but don't inform
        C1[i,1] * C0[ma[i],1] *1) * # no studies have characteristic 1 in the MA
         ( (1-C1[i,2]) + # without characteristic 2
        C1[i,2] * kappa_ok[ma[i],2] * lambda[2] + # with characteristic 2 and inform
        C1[i,2] * clambda[ma[i],2] * cut(lambda[2]) + # with characteristic 2 but don't inform
        C1[i,2] * C0[ma[i],2] *1) *# no studies have characteristic 2 in the MA
         ( (1-C1[i,3]) + # without characteristic 3
        C1[i,3] * kappa_ok[ma[i],3] * lambda[3] + # with characteristic 3 and inform
        C1[i,3] * clambda[ma[i],3] * cut(lambda[3]) + # with characteristic 3 but don't inform
        C1[i,3] * C0[ma[i],3] *1)* # no studies have characteristic 1 in the MA
        var_d[ma[i]]

p.k2[i]<-1/k2[i]

rhat[i] <- p[i] * n[i]  #calculate residual deviance
dev[i] <- 2 * (r[i] * (log(r[i])-log(rhat[i]))  +  (n[i]-r[i]) * (log(n[i]-r[i]) - log(n[i]-rhat[i])))

            }

resdev <- sum(dev[])


for (j in 1:N_study) {alpha[j] ~ dnorm(0,.01)}       # priors for study baseline effects - unrelated

for(m in 1:N_ma){
        d[m] ~ dnorm(0,0.01)    # priors for true fixed (unrelated) intervention effects
        for(j in 1:3){b[m,j] ~ dnorm(b0[j], p.phi[j])}  # between meta-analysis variation in average
difference in effect associated with characteristic
        var_d[m]~dlnorm(mu,p.tau) # log-normal distribution for between-study variances
        p.d[m] <- 1/var_d[m]
                }

#Prior for unknown parameters
for(j in 1:3){
        b0[j] ~dnorm(0,0.001)    # vague prior for overall average difference in effect associated with
characteristic
        lambda[j] ~ dlnorm(0,0.1) # vague prior for change in between-study variation associated with characteristic j
        p.phi1[j] ~ dgamma(0.001, 0.001)
        phi[j] <- pow(p.phi[j],-0.5)
        p.phi[j] <-p.phi1[j]/(1-patom.phi[j]) # vague prior for between meta-analysis variation in average
difference in effect associated with characteristic
        patom.phi[j] ~ dbeta(1,1)
```

```
        exp.b0[j]<-exp(b0[j])
                }

mu~dnorm(0,0.01)
p.tau<-1/(sd_tau*sd_tau)
sd_tau~dunif(0,2)

log.tau2.new~dlnorm(mu,p.tau)        # predictive distn for heterogeneity among studies without the characteristics
tau2.new<-exp(log.tau2.new)

}
```