Appendix A – Statistical code

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Dichotomous outcome

```
model{

#Loop through studies
 for(i in 1:NS)  {
#Adjustment for multi-arm trials is zero for control arm
          w[i,1] <- 0
#Treatment effect is zero for control arm
          delta[i,1] <- 0

#Vague priors for trial baselines
          mu[i] ~ dnorm(0,0.0001)

#Binomial likelihood with logit link
 for(k in 1:na[i]){
          x[i,k] ~ dbin(p[i,k],n[i,k])
          logit(p[i,k]) <- mu[i] + delta[i,k]
#Model fit
#Expected value of the numerators
          xhat[i,k] <- p[i,k] * n[i,k]
#Deviance contribution
   dev[i,k] <- 2 * (x[i,k] * (log(x[i,k])-log(xhat[i,k]))
     + (n[i,k]-x[i,k]) * (log(n[i,k]-x[i,k]) - log(n[i,k]-xhat[i,k])))
          }

#Summed residual deviance contribution for each trial
  resdev[i] <- sum(dev[i,1:na[i]])

#Trial-specific log(OR) distributions (random effect)
 for(k in 2:na[i]){
          delta[i,k] ~ dnorm(md[i,k], taud[i,k])

#Mean of log(OR) distributions
          md[i,k] <- d[t[i,k]] - d[t[i,1]] + sw[i,k]

#Precision of log(OR) distributions
          taud[i,k] <- tau*2*(k-1)/k

#Adjustment for multi-arm RCTs
          w[i,k] <- (delta[i,k] - d[t[i,k]] + d[t[i,1]])

#Cumulative adjustment for multi-arm RCTs
          sw[i,k] <- sum(w[i,1:k-1])/(k-1)
                              }
}
```

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```
#Total residual deviance
totresdev <- sum(resdev[])

#Priors for treatment effects
d[1] <- 0 # treatment effect is zero for reference treatment
for(k in 2:NT){
	d[k] ~ dnorm(0,0.0001)
}

#Priors for random effects
#Main analysis
tau <- pow(sd,-2)
sd ~ dunif(0,2)
#Sensitivity analysis (additional uninformative prior)
#tau <- pow(sd,-2)
#sd ~ dnorm(0,1) T(0,)
#Sensitivity analysis (informative prior)
#log.variance ~ dnorm(-3.23,  (1/(1.88*1.88)))
#variance <- exp(log.variance)
#sd <- sqrt(variance)
#tau <- 1/variance

#All pairwise treatment effects
#Probability that each treatment is superior to every other treatment
for(i in 1:NT) {
	for (j in 1:NT) { lor[i,j] <- d[i] - d[j]
			log(OR[i,j]) <- lor[i,j]
			better[i,j] <- step(OR[i,j]-1)
	}}

#Rank the treatments
	rk <- rank(d)

#Baseline treatment effect
for (k in 1:NTpbo){
	xPBO[k] ~ dbin(pPBO[k], nPBO[k])
	logit(pPBO[k]) <- muPBO[k]
	muPBO[k] ~ dnorm(mu0PBO, tauPBO)
}

tauPBO <- pow(sdPBO, -2)
sdPBO ~ dunif(0,2)
mu0PBO ~ dnorm(0,0.001)
```

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Continuous outcome (standardized mean difference)

```
model{
#Loop through studies
 for(i in 1:NS)  {
#Adjustment for multi-arm trials is zero for control arm
          w[i,1] <- 0
#Treatment effect is zero for control arm
          delta[i,1] <- 0

#Vague priors for trial baselines
          mu[i] ~ dnorm(0,0.0001)

#Normal likelihood with identity link
 for(k in 1:na[i]){
          varia[i,k] <- pow(se[i,k],2)
          prec[i,k] <- 1/varia[i,k]
          x[i,k] ~ dnorm(theta[i,k],prec[i,k])
          theta[i,k] <- theta.std[i,k]*pooled.sd[i,k] #Standardization of the means
          theta.std[i,k] <- mu[i] + delta[i,k]

#Model fit
#Deviance contribution
   dev[i,k] <- (x[i,k]-theta[i,k])*(x[i,k]-theta[i,k])*prec[i,k]
          }

#Summed residual deviance contribution for this trial
  resdev[i] <- sum(dev[i,1:na[i]])

#Trial-specific distributions for the random effects
 for(k in 2:na[i]){
          delta[i,k] ~ dnorm(md[i,k], taud[i,k])

#Mean of distributions
          md[i,k] <- d[t[i,k]] - d[t[i,1]] + sw[i,k]

#Precision of distributions
          taud[i,k] <- tau*2*(k-1)/k

#Adjustment for multi-arm trials
          w[i,k] <- (delta[i,k] - d[t[i,k]] + d[t[i,1]])

#Cumulative adjustment for multi-arm RCTs
          sw[i,k] <- sum(w[i,1:k-1])/(k-1)
                          }
}
```

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```
#Total residual deviance
totresdev <- sum(resdev[])

#Priors for treatment effects
d[1] <- 0 # treatment effect is zero for reference treatment
for(k in 2:NT){
        d[k] ~ dnorm(0,0.0001)
}

#Priors for random effects
tau <- pow(sd,-2)
sd ~ dunif(0,2)
#Sensitivity analysis (additional uninformative prior)
#tau <- pow(sd,-2)
#sd ~ dnorm(0,1) T(0,)
#Sensitivity analysis (informative prior)
#log.variance ~ dt(-2.7, (1/(2.46*2.46)) ,5)
#variance <- exp(log.variance)
#sd <- sqrt(variance)
#tau <- 1/variance

#All pairwise treatment effects
#Probability that each treatment is superior to every other treatment
#Convert the SMD into a mean difference, using the pooled SD of the reference scale
for(i in 1:NT) {
        for (j in 1:NT) {       SMD[i,j] <- (d[i] - d[j])
                                better[i,j] <- step(SMD[i,j])
                                diff[i,j] <- SMD[i,j]*mean.pooled.sd.ref
}}

#Rank the treatments
        rk <- rank(d)

#Determine the baseline PBO risk
for(k in 1:NTpbo){
        xPBO[k] ~ dnorm(thetaPBO[k], precPBO[k])
        precPBO[k] <- 1/varPBO[k]
        varPBO[k] <- pow(sePBO[k],2)
        thetaPBO[k] ~ dnorm(mu0PBO, tauPBO)
}

tauPBO <- pow(sdPBO, -2)
sdPBO ~ dunif(0,2)
mu0PBO ~ dnorm(0,0.001)
```

Appendix A – Statistical code

Rate outcome

```
#Loop through studies
model{
 for(i in 1:NS)  {
#Adjustment for multi-arm trials is zero for control arm
        w[i,1] <- 0
#Treatment effect is zero for control arm
        delta[i,1] <- 0

#vague priors for trial baselines
        mu[i] ~ dnorm(0,0.0001)

#Poisson likelihood with log link
 for(k in 1:na[i]){
        x[i,k] ~ dpois(lambda[i,k]*E[i,k])
        log(lambda[i,k]) <- mu[i] + delta[i,k]
#Model fit
#Expected value of the numerators
        xhat[i,k] <- lambda[i,k]*E[i,k]
#Deviance contribution
        x2[i,k] <- max(0.0000001,x[i,k])
   dev[i,k] <- -2*(xhat[i,k] - x2[i,k] + (x2[i,k]*log(xhat[i,k]/x2[i,k])))
        }

#Summed residual deviance contribution for this trial
  resdev[i] <- sum(dev[i,1:na[i]])

# Trial-specific distributions for the random effects
 for(k in 2:na[i]){
        delta[i,k] ~ dnorm(md[i,k], taud[i,k])

# Mean of distributions
        md[i,k] <- d[t[i,k]] - d[t[i,1]] + sw[i,k]

# Precision of distributions
        taud[i,k] <- tau*2*(k-1)/k

#Adjustment multi-arm RCTs
        w[i,k] <- (delta[i,k] - d[t[i,k]] + d[t[i,1]])

#Cumulative adjustment for multi-arm RCTs
        sw[i,k] <- sum(w[i,1:k-1])/(k-1)
                        }
}
#Total residual deviance
```

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```
totresdev <- sum(resdev[])

#Priors for treatment effects
d[1] <- 0
for(k in 2:NT){d[k] ~ dnorm(0,0.0001)}

#Priors for random effects
sd ~ dunif(0, 2)
tau <- pow(sd,-2)
#Sensitivity analysis (additional uninformative prior)
#sd ~ dnorm(0,1) T(0,)
#Sensitivity analysis (informative prior)
#log.variance ~ dnorm(-3.23,  (1/(1.88*1.88)))
#variance <- exp(log.variance)
#sd <- sqrt(variance)
#tau <- 1/variance

# All pairwise treatment effects
# Probability that each treatment is superior to every other treatment
for(i in 1:NT) {
        for (j in 1:NT) { lRR[i,j] <- d[i] - d[j]
                          log(RR[i,j]) <- lRR[i,j]
                          better[i,j] <- step(RR[i,j]-1)
        }}

#Rank the treatments
        rk <- rank(d)

#Determine the baseline PBO risk
for (k in 1:NTpbo){
        xPBO[k] ~ dpois(lambda.pbo[k]*E.PBO[k])
        log(lambda.pbo[k]) <- muPBO[k]
        muPBO[k] ~ dnorm(mu0PBO, tauPBO)
}

tauPBO <- pow(sdPBO, -2)
sdPBO ~ dnorm(0,0.01)
mu0PBO ~ dnorm(0,0.001)
```