APPENDIX 26:

2009 WINBUGS CODES USED FOR MIXED TREATMENT COMPARISONS IN THE ECONOMIC MODEL OF PHARMACOLOGICAL TREATMENTS FOR RELAPSE PREVENTION

A. Competing risks model for relapse rates, rates of discontinuation because of side effects and rates of discontinuation because of other reasons (random effects model)

```
model{

# code for treatment effects relative to placebo (treatment 1)
for(i in 1:30){ # LOOP OVER ARMS
r[i,1:4] ~ dmulti(p[i,1:4],n[i]) # likelihood
slam[i] <- sum(lam[,i]) # sum of the 3 hazard rates

for (m in 1:3) { # LOOP OVER 3 ENDPOINTS
p[i,m] <- lam[m,i] * (1-exp(-slam[i]*w[i]/52)) / slam[i] # cumulative pr(failed) at
    each end point
log(lam[m,i]) <- theta[m,i] # log rates for each arm, each end point
theta[m,i] <- mu[m,s[i]] + delta[m,i]*(1-equals(t[i],b[i])) # baseline & treatment effects
delta[m,i] ~ dnorm(md[m,i],pr[m]) # random outcome- & trial-specific relative effect
md[m,i] <- d[m,t[i]] - d[m,b[i]] # mean of the random effect
} # END LOOP OVER 3 ENDPOINTS
p[i,4] <- 1- sum(p[i,1:3]) # pr(no failure)
} # END LOOP OVER ARMS

for (m in 1:3) {d[m,1] <- 0
for (k in 2:9) {d[m,k] ~ dnorm(0,.0001) # priors for treatment effects
log(hazr[m,k]) <- d[m,k] # hazard ratios
}
for (j in 1:15) {mu[m,j] ~ dnorm(0,.0001) } # priors for baselines
}

for (m in 1:3) {pr[m] <- pow(sd[m],-2)
sd[m] <- sdb[m] * sqrt(2*(1-rho[m])) }
```

```
# code for absolute effects on baseline (Treatment 1)
for (i in 1:9) { rb[i,1:4] ~ dmulti(pb[i,1:4],nb[i]) # likelihood
for (m in 1:3) { # LOOP OVER 3 ENDPOINTS
pb[i,m] <- lamb[m,i] * (1-exp(-slamb[i]*wb[i]/52)) / slamb[i]
log(lamb[m,i]) <- mub[m,sb[i]]
} # END LOOP OVER 3 ENDPOINTS
slamb[i] <- sum(lamb[,i]) # sum of the 3 hazard rates
pb[i,4] <- 1- sum(pb[i,1:3]) # pr(no failure)
} # END LOOP OVER ARMS
for (m in 1:3) { for (j in 1:9) {mub[m,j] ~ dnorm(mb[m],prb[m]) } # priors for
    outcome- & trial-specific effects
mb[m] ~ dnorm(0,.001) } # common means
for (m in 1:3) {prb[m] ~ dgamma(.1,.1)
sdb[m] <- pow(prb[m],-.5)
rho[m] ~dbeta(1,1) }
u1 <-tb[1]
u2 <-bb[1]

# code for predicted effects at 52 weeks, on a probability scale. baseline risks in
    mub[1:3,9]
for (m in 1:3) {d.new[m,1] <- 0
for (k in 2:9) {d.new[m,k] ~ dnorm(d[m,k],pr[m]) }
for (k in 1:9) {theta52[m,k] <- mub[m,9] + d.new[m,k]
log(lam52[m,k]) <- theta52[m,k]
p52[m,k] <- lam52[m,k] * (1-exp(-slam52[k])) / slam52[k]
}
}
for (k in 1:9) {slam52[k] <- sum(lam52[1:3,k])
p52[4,k] <- 1-sum(p52[1:3,k])
}
for (k in 1:8){
        ind[k] <- k + step(k-6)
        for (m in 1:4){
                p52.rk[m,k] <- p52[m,ind[k]]        #Omits treatment 6, & moves
    treatments 7-9 down to indices 6-8
                rank52[m,k] <- rank(p52.rk[m,],k)   #Smallest is best (i.e. rank 1)
        }
        for (m in 1:3){ best[m,k] <- equals(rank52[m,k],1)}    #Record    whether
    best (rank=1 for outcomes m = 1,2,3)
        best[4,k] <- equals(rank52[4,k],8)    #Record whether best (rank = 8 for
    outcome m = 4)
}
}
```

```
# initial values 1
list(d=structure(.Data=c(NA,0,0,0, 0,0,0,0,0,
     NA,0,0,0, 0,0,0,0,0,
     NA,0,0,0, 0,0,0,0,0),.Dim=c(3,9)),
mu=structure(.Data=c(0,0,0,0,0, 0,0,0,0,0, 0,0,0,0,0,
     0,0,0,0,0, 0,0,0,0,0, 0,0,0,0,0,
     0,0,0,0,0, 0,0,0,0,0, 0,0,0,0,0),.Dim=c(3,15)),
mb=c(0,0,0),prb=c(1,1,1), rho=c(.2,.2,.6)
)

# initial values 2
list(d=structure(.Data=c(NA,-1,-1,-1, -1,-1,-1,-1,-1,
     NA,-1,-1,-1, -1,-1,-1,-1,-1,
     NA,-1,-1,-1, -1,-1,-1,-1,-1),.Dim=c(3,9)),
mu=structure(.Data=c(-1,-1,-1,-1,-1, -1,-1,-1,-1,-1, -1,-1,-1,-1,-1,
     -1,-1,-1,-1,-1, -1,-1,-1,-1,-1, -1,-1,-1,-1,-1,
     -1,-1,-1,-1,-1, -1,-1,-1,-1,-1, -1,-1,-1,-1,-1),.Dim=c(3,15)),
mb=c(-2,-2,-2), prb=c(3,3,3), rho=c(.5,.5,.5)
)
```

Summary statistics

Node	Mean	SD	MC error	2.5%	Median	97.5%	Start	Sample
d[1,2]	−1.468	0.4232	0.003149	−2.302	−1.474	−0.627	60001	10000
d[1,3]	−0.9755	0.722	0.005072	−2.397	−0.9758	0.4687	60001	10000
d[1,4]	−2.105	0.887	0.005918	−3.91	−2.083	−0.4041	60001	10000
d[1,5]	−0.7272	0.6881	0.004969	−2.104	−0.7243	0.6635	60001	10000
d[1,6]	−1.227	0.5577	0.003978	−2.366	−1.22	−0.1202	60001	10000
d[1,7]	−1.022	0.7104	0.005406	−2.451	−1.024	0.4045	60001	10000
d[1,8]	−0.7058	0.5631	0.004189	−1.804	−0.7139	0.4421	60001	10000
d[1,9]	−1.127	0.6388	0.004798	−2.382	−1.13	0.1351	60001	10000
d[2,2]	−1.167	0.6127	0.005447	−2.317	−1.192	0.1243	60001	10000
d[2,3]	−1.718	1.012	0.008357	−3.807	−1.695	0.1862	60001	10000
d[2,4]	1.147	1.059	0.009187	−0.9445	1.126	3.323	60001	10000
d[2,5]	0.0208	0.9386	0.00601	−1.88	0.0304	1.934	60001	10000
d[2,6]	−1.02	0.7491	0.005658	−2.499	−1.03	0.5075	60001	10000
d[2,7]	1.333	1.679	0.01896	−1.704	1.208	5.037	60001	10000
d[2,8]	−0.8596	0.7718	0.006442	−2.415	−0.8648	0.6964	60001	10000
d[2,9]	−0.9484	0.9093	0.007632	−2.58	−1.01	1.06	60001	10000
d[3,2]	−0.4861	0.3061	0.002925	−1.08	−0.4863	0.1248	60001	10000

Continued

Summary statistics (*Continued*)

Node	Mean	SD	MC error	2.5%	Median	97.5%	Start	Sample
d[3,3]	−0.5919	0.4205	0.003346	−1.435	−0.5906	0.2445	60001	10000
d[3,4]	−0.4769	0.489	0.003619	−1.449	−0.4748	0.4982	60001	10000
d[3,5]	0.2254	0.5352	0.004616	−0.8364	0.2306	1.262	60001	10000
d[3,6]	−0.3937	0.4045	0.003791	−1.175	−0.3992	0.4275	60001	10000
d[3,7]	0.7269	0.5973	0.006136	−0.4142	0.716	1.941	60001	10000
d[3,8]	−0.4185	0.3861	0.003207	−1.189	−0.4155	0.345	60001	10000
d[3,9]	−1.05	0.4485	0.003855	−1.912	−1.058	−0.1139	60001	10000
sd[1]	0.6343	0.1926	9.11E-04	0.324	0.6115	1.078	60001	10000
sd[2]	0.7626	0.3672	0.002587	0.1953	0.7128	1.622	60001	10000
sd[3]	0.3164	0.2131	0.001434	0.0460	0.27	0.8539	60001	10000
sdb[1]	0.6666	0.1996	9.76E-04	0.3884	0.6314	1.147	60001	10000
sdb[2]	0.8122	0.3471	0.002161	0.3387	0.7504	1.662	60001	10000
sdb[3]	0.955	0.2781	0.001428	0.5676	0.9046	1.628	60001	10000

B. Simple random effects model for rates of weight gain

```
model{
for(i in 1:34){
                    r[i] ~ dbin(p[i],n[i])
                    logit(p[i]) <-mu[s[i]]+delta[i]*(1-equals(t[i],b[i]))
#Random effects model for log-odds ratios
                    delta[i] ~ dnorm(md[i],prec)
                    md[i] <- d[t[i]] - d[b[i]]
#Deviance residuals for data i
rhat[i] <- p[i] * n[i]
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])))
                    }
sumdev <- sum(dev[])

#priors
for(j in 1:17){ mu[j] ~ dnorm(0,.0001)}
prec <- 1/(sd*sd)
sd ~ dunif(0,2)

#Give priors for log-odds ratios
          d[1] <-0
          for (k in 2:7){d[k] ~ dnorm(0,.001) }

#All pairwise odds ratios
for (c in 1:6){
          for (k in (c + 1):7){
                    or[c,k] <- exp(d[k] - d[c]) }}
}

# initial values
list(
d = c(NA,0,0,0,0,0,0),sd = 1,mu = c(0,0,0,0,0, 0,0,0,0,0, 0,0,0,0,0, 0,0),
delta = c(0,0,0,0,0, 0,0,0,0,0, 0,0,0,0,0, 0,0,0,0,0, 0,0,0,0,0, 0,0,0,0,0, 0,0,0,0)
)
```

Summary statistics

Node	Mean	SD	MC error	2.5%	Median	97.5%	Start	Sample
or[1,2]	2.8631	0.7454	0.007843	1.705	2.771	4.509	60001	10000
or[1,3]	0.7373	0.2767	0.003196	0.3498	0.693	1.399	60001	10000
or[1,4]	1.8321	1.009	0.01043	0.7807	1.602	4.284	60001	10000
or[1,5]	1.0779	0.4967	0.005028	0.4405	0.9904	2.164	60001	10000
or[1,6]	1.0895	0.4294	0.004114	0.5214	1.013	2.085	60001	10000
or[1,7]	1.8604	0.989	0.01032	0.7345	1.674	4.036	60001	10000
Sd	0.3218	0.1934	0.002541	0.02308	0.3004	0.7511	60001	10000
sumdev	33.32	7.786	0.0865	19.7	32.77	50.09	60001	10000

C. Full random effects model for rates of acute extrapyramidal side effects

```
model{
sw[1] <- 0
for(i in 1:73){
                    r[i] ~ dbin(p[i],n[i])
                    logit(p[i]) <-mu[s[i]]+delta[i]*(1-equals(t[i],b[i]))

#Random effects model for log-odds ratios
                    delta[i] ~ dnorm(md[i],taud[i])
                    taud[i] <- tau * (1 + equals(m[i],3) /3)
                    md[i] <- d[t[i]] - d[b[i]] + equals(m[i],3) * sw[i]

#Deviance residuals for data i
rhat[i] <- p[i] * n[i]
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])))
                    }
sumdev <- sum(dev[])

#Adjustment for 3 arm trials
for (i in 2:73) { sw[i] <- (delta[i-1] - d[t[i-1]] + d[b[i-1]] ) /2}

#priors
for(j in 1:36){ mu[j]~dnorm(0,.0001)}
tau <- 1/(sd*sd)
sd~dunif(0,2)
#Give priors for log-odds ratios
          d[1] <-0
          for (k in 2:8){d[k] ~ dnorm(0,.001) }

#All pairwise odds ratios
for (c in 1:7){
          for (k in (c+1):8){
                    or[c,k] <- exp(d[k] - d[c]) }}
}

#initial values
list(
d=c(NA,0,0,0,0,0,0,0),sd=1,mu=c(0,0,0,0,0, 0,0,0,0,0, 0,0,0,0,0, 0,0,0,0,0, 0,0,0,0,0,
0,0,0,0,0, 0,0,0,0,0, 0),delta=c(0,0,0,0,0, 0,0,0,0,0, 0,0,0,0,0, 0,0,0,0,0, 0,0,0,0,0,
0,0,0,0,0, 0,0,0,0,0, 0,0,0,0,0, 0,0,0,0,0, 0,0,0,0,0, 0,0,0,0,0, 0,0,0,0,0, 0,0,0,0,0,
0,0,0,0,0, 0,0,0)
)
```

Summary statistics

Node	Mean	SD	MC error	2.5%	Median	97.5%	Start	Sample
or[1,2]	0.4743	0.05824	5.87E-04	0.368	4.72E-01	0.5994	60001	10000
or[1,3]	0.2631	0.04556	4.71E-04	0.1832	2.60E-01	0.3641	60001	10000
or[1,4]	0.1476	0.06829	7.77E-04	0.05171	1.35E-01	0.3132	60001	10000
or[1,5]	0.3993	0.08162	8.73E-04	0.2587	0.3928	0.5836	60001	10000
or[1,6]	0.2405	0.07893	8.70E-04	0.1147	0.2316	0.4221	60001	10000
or[1,7]	0.2517	0.06318	6.28E-04	0.1505	0.2438	0.4002	60001	10000
or[1,8]	0.2983	0.1333	1.26E-03	0.1179	0.2719	0.6214	60001	10000
sd	0.292	0.1132	0.001455	0.08428	0.2859	0.5386	60001	10000
sumdev	75.93	11.79	0.1198	54.13	75.6	100.5	60001	10000