**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 |

```
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 |