# 7 R-code for cost-effectiveness analysis and value of information analyses (A8)

```
#Define functions
logit<-function(p){ log(p/(1-p))}
expit<-function(m){ exp(m)/(1+exp(m))}
pCE<-function(effects,costs,WTP){
      NB<-effects*WTP-costs
      rowmax<-apply(NB,1,which.max)
      x<-table(rowmax)
      probCE<-x/sum(x)
      probCE
}
library(mvtnorm)
#Read NMA coda
NMA<- read.table("C:/Users/epnjw/nickyw/ConDuCT-
II/Bluebelle/VOI_Sept2016/EVI Calculation/NMA_All.txt",header=TRUE)
#NMA<- read.table("O:/epnjw/nickyw/ConDuCT-II/Bluebelle/VOI_Sept2016/EVI
Calculation/NMA_BBpop.txt",header=TRUE)
Nops<-1200000 #PHE report, annual non-orthopaedic surgical operations
WoundperOp<- 1.84
Nwounds<- Nops*WoundperOp
lifetime<- 4.673079209  #Liftime horizon of dressing technology


Nsim<-20000
Nn<-55      #No. of different sample sizes evaluated
type<-1     #1=PHE (basecase), 2=Jenks (sens analysis)
Q<-1        #1=SSIQALYloss=0.12 (basecase), 2=SSIQALYloss=0.06,
3=SSIQALYloss=0 (sens analysis)
WTP<-20000  #WTP per QALY

#Baseline risk for Simple
meanSIMPLE<-c(0.137984898, 0.089390519)#mean and se for simple given
surgery type
seSIMPLE<-c(0.001772214, 0.006062126)

#Utility decrement due to SSI
SSIQALYloss<-c(0.12,0.06, 0)
```

```
#Costs
c.dressing<-c(0, 5.25, 13.86, 21.39) #Cost of dressings
(1=exposed,2=simple,3=glue,4=advanced)
c.SSI<-rlnorm(Nsim, 8.972237608, 0.163148238)   #Cost of SSI

#Generate MVNorm relative effects comared with Simple (trt 2)
m.dv2<-c(mean(-NMA$d2),mean(NMA$d3-NMA$d2),mean(NMA$d4-NMA$d2))
cov.dv2<-cov(cbind(-NMA$d2,NMA$d3-NMA$d2,NMA$d4-NMA$d2))

d<-rmvnorm(Nsim,m.dv2,cov.dv2)

#P(SSI)
p.SSI<-matrix(rep(0,Nsim*4), Nsim,4)
p.SSI[,2]<-rnorm(Nsim,meanSIMPLE[type],seSIMPLE[type]) #P(SSI) for simple
dressings
p.SSI[,1]<- expit(logit(p.SSI[,2])+d[,1]) #P(SSI) Exposed
p.SSI[,3]<- expit(logit(p.SSI[,2])+d[,2]) #P(SSI) Glue
p.SSI[,4]<- expit(logit(p.SSI[,2])+d[,3]) #P(SSI) Advanced

#Incremental Net Benefit (positive favours "advanced" dressings
costs<- p.SSI*c.SSI + c.dressing
effects<- -p.SSI*SSIQALYloss[Q]
NB<- effects*WTP - costs
ENB<-apply(NB,2,mean)
tstar<-which.max(ENB)

max.NB<-apply(NB,1,max) - NB[,tstar]
EVPI<-mean(max.NB)
PopEVPI<-Nwounds*lifetime*EVPI

probCE<-pCE(effects,costs,WTP)

#CE-Plane
par(mfrow=c(2,2))
names=c("Exposed v Simple","Glue v Simple","Advanced v Simple")
ind<-c(1,3,4)
for (k in 1:3){
      plot(effects[,ind[k]]-effects[,2],costs[,ind[k]]-
costs[,2],lty=0,main=names[k],ylim=c(-7000,7000),xlim=c(-0.08,0.08),
xlab="Incremental effects",ylab="Incremental costs")
      lines(c(0,0),c(-7000,7000))
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```
	lines(c(-0.08,0.08),c(0,0))
}

#CEAC
#pCEAC<-matrix(rep(0,400),100,4)
#for (k in 1:100){ pCEAC[k,]<-pCE(effects,costs,k*500) }
#matplot(seq(500,50000,500),pCEAC,type="l",lty=1:4)

#EVPPI(c.SSI)
E.pi<- apply(p.SSI,2,mean)
NB.pi<- matrix(rep(0,Nsim*4),Nsim,4)
NB.pi<- -c.SSI%*%t(E.pi) - matrix(rep(c.dressing +
E.pi*SSIQALYloss[Q]*WTP,Nsim),Nsim,4,byrow=T)
max.NB.pi<-apply(NB.pi,1,max)- NB.pi[,tstar]
EVPPI.cSSI<- mean(max.NB.pi)
PopEVPPI.cSSI<-Nwounds*lifetime*EVPPI.cSSI

#EVPPI(d)
E.cSSI<-mean(c.SSI)
E.mu<-mean(logit(p.SSI[,2]))
Var.mu<-var(logit(p.SSI[,2]))
H<-matrix(rep(0,Nsim*4),Nsim,4)
H[,1]<-expit(E.mu + d[,1])
H[,2]<-rep(expit(E.mu),Nsim)
H[,3]<-expit(E.mu + d[,2])
H[,4]<-expit(E.mu + d[,3])
E.pi.d<- H + 0.5*H*(1-H)*(1-2*H)*Var.mu

NB.d<- matrix(rep(0,Nsim*4),Nsim,4)
NB.d<- -E.pi.d*(E.cSSI+SSIQALYloss[Q]*WTP) -
matrix(rep(c.dressing,Nsim),Nsim,4,byrow=T)
max.NB.d<-apply(NB.d,1,max)- NB.d[,tstar]
EVPPI.d<- mean(max.NB.d)
PopEVPPI.d<-Nwounds*lifetime*EVPPI.d

#EVPPI(mu)
mu<-matrix(rep(logit(p.SSI[,2]),4),Nsim,4,byrow=F)
Ed<-rep(0,4); Vd<-rep(0,4)
Ed[1]<- mean(d[,1]); Ed[2]<-0; Ed[3]<- mean(d[,2]); Ed[4]<- mean(d[,3])
Vd[1]<- var(d[,1]); Vd[2]<-0; Vd[3]<- var(d[,2]); Vd[4]<- var(d[,3])
H<-matrix(rep(0,Nsim*4),Nsim,4)
```

```
H<-expit(mu+matrix(rep(Ed,Nsim),Nsim,4,byrow=T))
E.pi.mu<- H + 0.5*H*(1-H)*(1-2*H)*matrix(rep(Vd,Nsim),Nsim,4,byrow=T)

NB.mu<- matrix(rep(0,Nsim*4),Nsim,4)
NB.mu<- -E.pi.mu*(E.cSSI+SSIQALYloss[Q]*WTP) -
matrix(rep(c.dressing,Nsim),Nsim,4,byrow=T)
max.NB.mu<-apply(NB.mu,1,max)- NB.mu[,tstar]
EVPPI.mu<- mean(max.NB.mu)
PopEVPPI.mu<-Nwounds*lifetime*EVPPI.mu

write(c("ENB = ", ENB, "tstar=", tstar, "EVPI=", EVPI, "Population EVPI",
PopEVPI,"ProbCE=",probCE,"EVPPI(c.SSI)",EVPPI.cSSI, "EVPPI(d)",EVPPI.d,
"EVPPI(mu)",EVPPI.mu),"")

#####EVSI#####

#sd<-6.25/2 #sd for new data on log-odds, based on average sd of LOR for
NMA studies, divided by 2 to get log-odds
sd<-3.7     #sd for log-odds for Simple dressings from Cochrane
#Generate data for Nn different total sample sizes (balanced over arms)
y<-array(rep(0,Nsim*Nn*3), c(Nsim,Nn,3))
d.post<-array(rep(0,Nsim*Nn*3), c(Nsim,Nn,3))

n<-c(seq(50,500,50),seq(600,5000,100))
#4-arm (balanced) design
n1<-n/4; n2<-n/4; n3<-n/4; n4<- n/4
#3-arm (balanced) designs
#n1<-n/3; n2<-n/3; n3<-n/3; n4<- c(rep(0.001,Nn)) #EvSvG
#n1<-n/3; n2<-n/3;  n3<- c(rep(0.001,Nn)); n4<-n/3 #EvSvA
#n1<-c(rep(0.001,Nn)); n2<-n/3; n3<-n/3; n4<-n/3  #SvGvA
#2-arm (balanced) designs
#n1<-n/2; n2<-n/2; n3<-c(rep(0.001,Nn)); n4<- c(rep(0.001,Nn)) #EvS
#n1<-c(rep(0.001,Nn)); n2<-n/2; n3<-n/2; n4<- c(rep(0.001,Nn)) #SvG
#n1<-c(rep(0.001,Nn)); n2<-n/2; n3<-c(rep(0.001,Nn)); n4<- n/2 #SvA
#Unbalanced design as planned in Bluebelle
#n1<-2*n/5; n2<-2*n/5; n3<-n/5; n4<- c(rep(0.001,Nn)) #E2vS2vG1

Prec0<-solve(cov.dv2)
Var.lik<- array(rep(0,Nn*9), c(Nn,3,3))
Prec.lik<- array(rep(0,Nn*9), c(Nn,3,3))
Var.post<- array(rep(0,Nn*9), c(Nn,3,3))
```

```
for (j in 1:Nn){
      Var.lik[j,,]<-
((sd^2)/n2[j])*(matrix(rep(1,9),3,3)+c(n2[j]/n1[j],n2[j]/n3[j],n2[j]/n4[j])
*diag(3))
      Prec.lik[j,,]<-solve(Var.lik[j,,])
      Var.post[j,,]<-solve(Prec0+Prec.lik[j,,])
}

for (i in 1:Nsim){
      for (j in 1:Nn){
                  y[i,j,]<-rmvnorm(1,d[i,],Var.lik[j,,])
                  d.post[i,j,]<- Var.post[j,,]%*%(Prec0%*%m.dv2 +
Prec.lik[j,,]%*%y[i,j,])
      }
}

H.post<-array(rep(0,Nsim*Nn*4),c(Nsim,Nn,4))
E.pi.post<-array(rep(0,Nsim*Nn*4),c(Nsim,Nn,4))
H.post[,,1]<-expit(E.mu + d.post[,,1])
H.post[,,2]<-rep(expit(E.mu),Nsim*Nn)
H.post[,,3]<-expit(E.mu + d.post[,,2])
H.post[,,4]<-expit(E.mu + d.post[,,3])
E.pi.post[,,1]<- H.post[,,1] + 0.5*H.post[,,1]*(1-H.post[,,1])*(1-
2*H.post[,,1])*(Var.mu + matrix(rep(Var.post[,1,1],Nsim),Nsim,Nn,byrow=T))
E.pi.post[,,2]<- H.post[,,2] + 0.5*H.post[,,2]*(1-H.post[,,2])*(1-
2*H.post[,,2])*Var.mu
E.pi.post[,,3]<- H.post[,,3] + 0.5*H.post[,,3]*(1-H.post[,,3])*(1-
2*H.post[,,3])*(Var.mu + matrix(rep(Var.post[,2,2],Nsim),Nsim,Nn,byrow=T))
E.pi.post[,,4]<- H.post[,,4] + 0.5*H.post[,,4]*(1-H.post[,,4])*(1-
2*H.post[,,4])*(Var.mu + matrix(rep(Var.post[,3,3],Nsim),Nsim,Nn,byrow=T))

NB.post<- array(rep(0,Nsim*Nn*4),c(Nsim,Nn,4))
NB.post<- -E.pi.post*(E.cSSI+SSIQALYloss[Q]*WTP) -
array(c(rep(c.dressing[1],Nsim*Nn),rep(c.dressing[2],Nsim*Nn),rep(c.dressin
g[3],Nsim*Nn),rep(c.dressing[4],Nsim*Nn)),c(Nsim,Nn,4))

max.NB.post<-matrix(rep(0,Nsim*Nn),Nsim,Nn)
for (j in 1:Nn){
      max.NB.post[,j]<-apply(NB.post[,j,],1,max)- NB.post[,j,tstar]
}

EVSI<- apply(max.NB.post,2,mean)
PopEVSI<- Nwounds*lifetime*EVSI
```

```
#Opportunity cost and dressing costs for trial with given design

opp.cost<- n1*(ENB[tstar]-ENB[1])+n2*(ENB[tstar]-ENB[2])+n3*(ENB[tstar]-
ENB[3])+n4*(ENB[tstar]-ENB[4])

dress.cost<- n2*c.dressing[2]+n3*c.dressing[3]+n4*c.dressing[4]
```