Appendix 3

Examples of R-code with specified DSA and cvDSA algorithms used for the illustrative analysis

A.DSA-selected Treatment Model III

library(DSA)

a<-as.matrix(read.csv("ns1053_glm_FINAL.csv",header = TRUE, sep = ",", quote="\"", dec=".",fill= TRUE,comment.char=""")

b<-as.data.frame(a)

#median-center age

agecen<-b[,1]-70

#replace age variable with age-centered variable

ns<-cbind(agecen,b[,2:9])

"ns" defines a data frame object with single line data (i.e., line for each subject) that
includes baseline covariates used in the selection of the treatment model.
Data should include only variables under consideration for the model. Variable
#names and coding are provided:

#Agecen, Sex (1=F, 0=M), Cardiovascular Disease (Cardio 1=Yes, 0=No), Secondhand #smoke exposure (Total), Body Mass Index (Bmass), Serum cholesterol (Hdl, Ldl), #Diabetes (Diabnm 1=Yes, 0=No). Agecen, Second-hand smoke, Body Mass Index, Hdl, #and Ldl are continuous variables.

result <- DSA(fev1 ~ 1, data = ns, maxsize = 8, maxorderint = 2, maxsumofpow = 2) summary(result)

Arguments:

DSA(formula,data,family=gaussian,maxsize,maxoderint,maxsumofpow)

- "formula" indicates a description of base model which specifies the independent/response variables and all terms forced in the final model. These forced terms might represent part of the model that may be known to the user and incorporated as a "fixed" part of the model. Typically, "formula" is set to 'Y ~ 1' when no terms are forced in the final model.
- 2. *"data"* is a data frame that contains both response variables and candidate covariates for consideration in the procedure.

- 3. *"family"* is currently 'binomial' or 'gaussian'(default)
- 4. "maxsize" specifies the maximum number of terms in the final model
- 5. "maxorderint" specifies the maximum order of interactions in final model
- 6. "*maxsumofpow*" specifies the maximum sum of power for each term of the model (e.g., if set to '2', a term could have a polynomial order of 2 or the term could be an interaction of two variables)

Results with the DSA algorithm can vary because v-fold splits of the data are assigned at random. Options are available in the package for setting the v-fold splits for exact, reproducible results.

B. DSA-Selected MSM 8

library(cvDSA)

a<-as.matrix(read.csv("ns1053_msm_FINAL.csv",header = TRUE, sep = ",", quote="\"", dec=".",fill = TRUE, comment.char=""))

b<-as.data.frame(a)

#median-center age

agecen<-b[,2]-70

#replace age variable with age-centered variable

ns0<-cbind(b[,1],agecen) ns1<-cbind(ns0,b[,3:13])

"ns1" defines a data frame object with multiple lines of data per subject (i.e., single # line for each subject for each 6 month interval of follow-up). #Data can include other variables not considered for inclusion in the model.

```
result1<-cvMSM(y=deathcv, a=fev1, v=cbind(agecen, sex), w=cbind(agecen, sex,BMASS,HDL,LDL,cardio,diabnm,total), data=ns1,yfamily='binomial', afamily='gaussian',model.msm=list(Model=NULL,Size=6,Int=2), model.aw=list(Model="sex+agecen+sex:agecen+BMASS^2+BMASS:sex"), model.av=list(Model="sex+agecen+BMASS"), wt.censor=C_N_WTS, ncv=5, mapping='IPTW', fitting='IPTW', stable.wt=T, rep.ID=T, ID=ID)
```

Arguments:

 "y=deathcv" indicates the outcome variable, "a=fev1" is the treatment variable, "v= cbind(agecen, sex)" and "w=cbind(agecen, sex, ...)" are the covariates in MSM and the baseline covariates, respectively. "data=ns1" is a dataframe with all the variables for analysis as described above.

- 2. *"yfamily*" and *"afamily*" indicate the distribution of the outcome variable and the treatment variable, respectively.
- 3. The following parameters model.msm, model.aw, model.av indicate models for MSM, g(A|W), g(A|V), respectively. If the user wishes to fit a particular causal model, he/she can specify the model---e.g., model. msm=list(Model="agecen+fev1+sex"); otherwise, the cvDSA will select a model given the model search criteria that are provided by the user.
- "wt.censor" is an option to multiply extra weights to the loss function; C_N_WTS is a pre-calculated censoring weight. If "wt.censor=NULL", no extra weight will be used.
- 5. "*ncv*=5" specifies 5-fold cross-validation.
- 6. "stabilized.wt=T" indicates this IPTW estimator uses a stabilized weight -- g(A|V)/g(A|W).
 "cross-validation='IPTW" and "empirical='IPTW" tell the function how the grass validation risk and the ampirical risk are calculated (they could be appreciated with a stabilized value).

the cross-validation risk and the empirical risk are calculated (they could be different). Other options are 'G-comp' and 'DR'.

- 7. "*rep.ID=T*" indicates that the data include observations with repeating IDs --i.e., multiple lines of data per subject.
- 8. "ID=ID" used to identify subject IDs

Documentation ("help" files) for the DSA and cvDSA algorithms are included in the packages and include additional details and options