Important notes before you get started

1. This notebook uses SAS Software and R. R is free, SAS is not. You must have a SAS license to run SAS or use SAS onDemand for Academics (free). In addition, you need to install the SAS kernal for jupyter notebook, available here: https://github.com/sassoftware/sas_kernel
2. All file paths in this notebook will need to be revised to the destination you choose to place this notebook and all the datafiles.
3. For those who don't want to install SAS but still want to have a look at the code and its output, we provide a PDF version of the notebook, including all the input and output data files from this analysis.

Dependencies: file locations and libraries

In [13]:

```
%let location =F:\Manuscripts\2021_06_02_Nature_Comm_DSense\GITHUB\data;
libname repo 'F:\Manuscripts\2021_06_02_Nature_Comm_DSense\GITHUB\data';
```

Out[13]:

```
10                                                           The SAS System
     19:55 Monday, June 14, 2021

163        ods listing close;ods html5 (id=saspy_internal) file=_tomods1 options(bitmap_mode='inlin
e') device=svg style=HTMLBlue;
163      ! ods graphics on / outputfmt=png;
NOTE: Writing HTML5(SASPY_INTERNAL) Body file: _TOMODS1
164
165        %let location =F:\Manuscripts\2021_06_02_Nature_Comm_DSense\GITHUB\data;
166        libname repo 'F:\Manuscripts\2021_06_02_Nature_Comm_DSense\GITHUB\data';
NOTE: Libref REPO was successfully assigned as follows:
      Engine:        V9
      Physical Name: F:\Manuscripts\2021_06_02_Nature_Comm_DSense\GITHUB\data
167
168
169        ods html5 (id=saspy_internal) close;ods listing;
170
```

In [14]:

```
setwd("F:\\Manuscripts\\2021_06_02_Nature_Comm_DSense\\GITHUB\\data")
getwd()
```

'F:/Manuscripts/2021_06_02_Nature_Comm_DSense/GITHUB/data'

In [15]:

```
library(rio)
library(corrplot)
library(ggplot2)
library(ggrepel)
library(RColorBrewer)
```

Dataset preparation

Import dataset

In [16]:

```
PROC import out=dsense datafile = "&location\dataset_bubble_plot_final.xlsx"
        DBMS = xlsx replace;
RUN;
```

Out[16]:

```
11                                                           The SAS System
     19:55 Monday, June 14, 2021

173        ods listing close;ods html5 (id=saspy_internal) file=_tomods1 options(bitmap_mode='inlin
e') device=svg style=HTMLBlue;
173      ! ods graphics on / outputfmt=png;
NOTE: Writing HTML5(SASPY_INTERNAL) Body file: _TOMODS1
174
175        PROC import out=dsense datafile = "&location\dataset_bubble_plot_final.xlsx"
176             DBMS = xlsx replace;
177        RUN;

NOTE: The import data set has 70 observations and 22 variables.
NOTE: WORK.DSENSE data set was successfully created.
NOTE: PROCEDURE IMPORT used (Total process time):
      real time           0.26 seconds
      cpu time            0.10 seconds


178
179
180        ods html5 (id=saspy_internal) close;ods listing;
181
```

subset and export datasets for use in R

In [17]:

```
DATA dsense_0 (drop=Patient pat_id Time_to_treatment_month visit);
    set dsense;
    if time_to_treatment_month^=0 then delete;
RUN;

DATA repo.dsense_0;
    set dsense_0;
RUN;


DATA dsense_3 (drop=Patient pat_id Time_to_treatment_month visit);
    set dsense;
    if time_to_treatment_month^=3 then delete;
RUN;

DATA repo.dsense_3;
    set dsense_3;
RUN;

DATA dsense_6 (drop=Patient pat_id Time_to_treatment_month visit);
    set dsense;
    if time_to_treatment_month^=6 then delete;
RUN;

DATA repo.dsense_6;
    set dsense_6;
RUN;



DATA dsense_9 (drop=Patient pat_id Time_to_treatment_month visit);
    set dsense;
    if visit^="revisit" then delete;
RUN;

DATA repo.dsense_9;
    set dsense_9;
RUN;
```

Out[17]:

```
12                                                           The SAS System
     19:55 Monday, June 14, 2021

184        ods listing close;ods html5 (id=saspy_internal) file=_tomods1 options(bitmap_mode='inlin
e') device=svg style=HTMLBlue;
184      ! ods graphics on / outputfmt=png;
NOTE: Writing HTML5(SASPY_INTERNAL) Body file: _TOMODS1
185
186        DATA dsense_0 (drop=Patient pat_id Time_to_treatment_month visit);
187            set dsense;
188            if time_to_treatment_month^=0 then delete;
189        RUN;

NOTE: There were 70 observations read from the data set WORK.DSENSE.
NOTE: The data set WORK.DSENSE_0 has 9 observations and 18 variables.
NOTE: DATA statement used (Total process time):
      real time           0.02 seconds
      cpu time            0.03 seconds


190
191        DATA repo.dsense_0;
192            set dsense_0;
193        RUN;

NOTE: There were 9 observations read from the data set WORK.DSENSE_0.
NOTE: The data set REPO.DSENSE_0 has 9 observations and 18 variables.
NOTE: DATA statement used (Total process time):
      real time           1.42 seconds
      cpu time            0.01 seconds


194
195
196        DATA dsense_3 (drop=Patient pat_id Time_to_treatment_month visit);
197            set dsense;
198            if time_to_treatment_month^=3 then delete;
199        RUN;

NOTE: There were 70 observations read from the data set WORK.DSENSE.
NOTE: The data set WORK.DSENSE_3 has 9 observations and 18 variables.
NOTE: DATA statement used (Total process time):
      real time           0.04 seconds
      cpu time            0.03 seconds


200
201        DATA repo.dsense_3;
202            set dsense_3;
203        RUN;

NOTE: There were 9 observations read from the data set WORK.DSENSE_3.
NOTE: The data set REPO.DSENSE_3 has 9 observations and 18 variables.
NOTE: DATA statement used (Total process time):
      real time           1.39 seconds
      cpu time            0.06 seconds


204
205        DATA dsense_6 (drop=Patient pat_id Time_to_treatment_month visit);
206            set dsense;
207            if time_to_treatment_month^=6 then delete;
208        RUN;

NOTE: There were 70 observations read from the data set WORK.DSENSE.
NOTE: The data set WORK.DSENSE_6 has 9 observations and 18 variables.
NOTE: DATA statement used (Total process time):
      real time           0.04 seconds
      cpu time            0.03 seconds


209
210        DATA repo.dsense_6;
211            set dsense_6;
212        RUN;

NOTE: There were 9 observations read from the data set WORK.DSENSE_6.
NOTE: The data set REPO.DSENSE_6 has 9 observations and 18 variables.
NOTE: DATA statement used (Total process time):
      real time           1.37 seconds
      cpu time            0.07 seconds


213
214
215
216        DATA dsense_9 (drop=Patient pat_id Time_to_treatment_month visit);
217            set dsense;
218            if visit^="revisit" then delete;
219        RUN;

NOTE: There were 70 observations read from the data set WORK.DSENSE.
NOTE: The data set WORK.DSENSE_9 has 8 observations and 18 variables.
NOTE: DATA statement used (Total process time):
      real time           0.04 seconds
      cpu time            0.04 seconds


220
221        DATA repo.dsense_9;
222            set dsense_9;
223        RUN;

NOTE: There were 8 observations read from the data set WORK.DSENSE_9.
NOTE: The data set REPO.DSENSE_9 has 8 observations and 18 variables.
NOTE: DATA statement used (Total process time):
      real time           1.52 seconds
      cpu time            0.01 seconds


224
225
226        ods html5 (id=saspy_internal) close;ods listing;
227
```

Analysis and visualization

In [18]:

```
#baseline
dsense<-import("dsense_0.sas7bdat")
dsense<-subset(dsense, select=-c(Paper_code))
names(dsense)[names(dsense) == "timepoint_HbA1c"] <- "HbA1c"

# see ?cor for cor options.  using pairwise.complete.obs because there are cases where all data for a v
ariable is missing for a patient, but we dont want that entire patient point to be deleted
#also decided to use kendalls given the small smaple size, rank nature of method.
m<-cor(dsense, use="pairwise.complete.obs", method="kendall")

#see cor.test function for added parameters that can be used for cor.mtest
#had to use exact=FALSE since their were ties and exact computations could not be performed
#also as a result had to use continuity=TRUE since ties were present
m_sig<-cor.mtest(dsense, method="kendall", conf.level=0.95, , continuity=TRUE, exact=FALSE)

#for sig.level can introduce many different numbers.  used 0 to hide the near perfect correlations (i.
e. they wont receive a star)
#order="AOE" (finding angular order of the eigenvectors) seems to be a good way to group vars related t
o one other more closely together, but does not facilitate comparison between plots
corrplot(m, method="circle",
         order="original",
         type="upper",
         tl.col="black",
         p.mat=m_sig$p, insig = "label_sig",sig.level = c(0, .05), pch.cex = 1.5, pch.col = "white")

mtext("Correlation", side = 1, at=18.5, line=3.3, cex=.85)
mtext("Coefficient", side = 1, at=18.5, line=4.0, cex=.85)
```

In [19]:

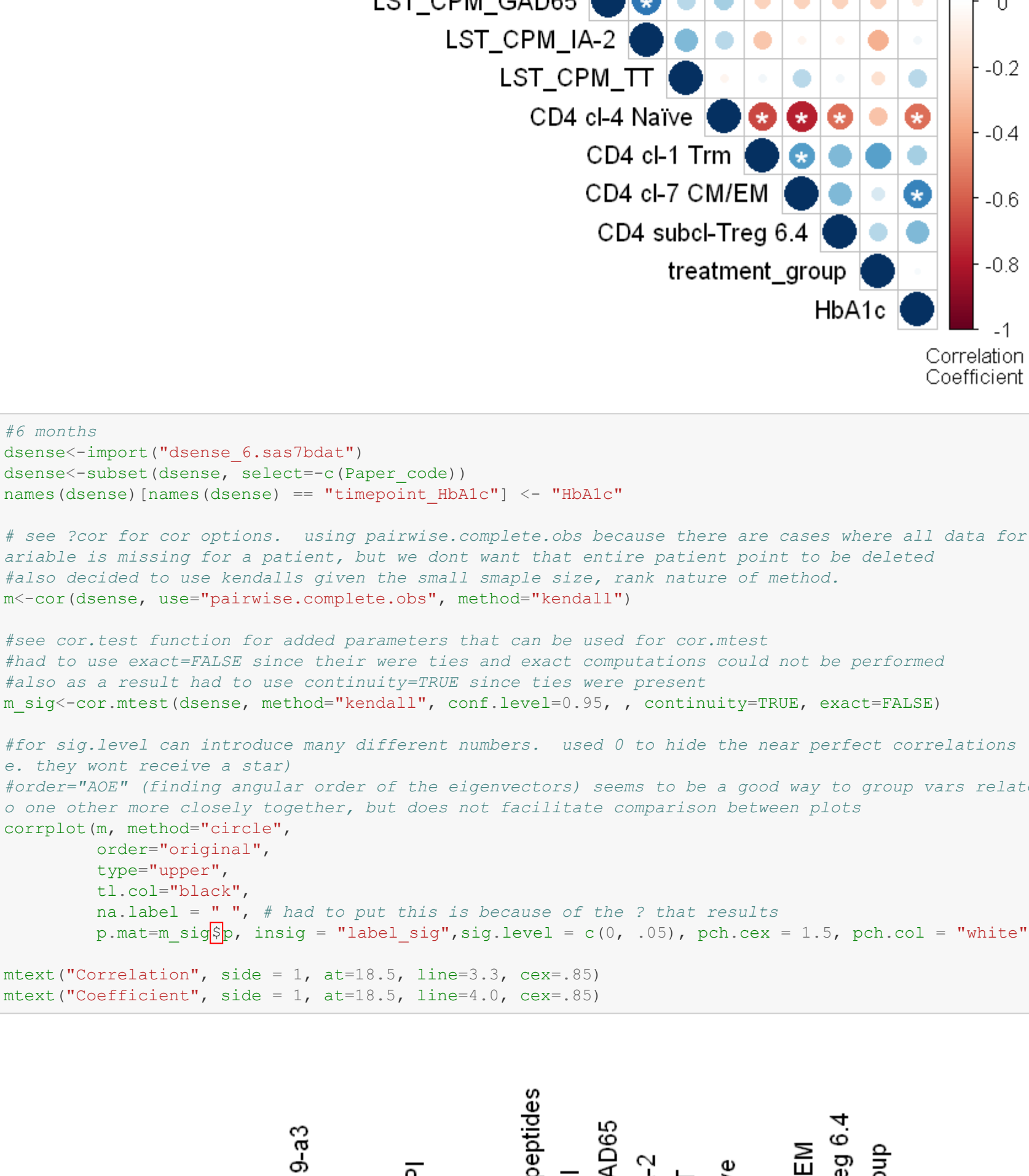
```
#3 months
dsense<-import("dsense_3.sas7bdat")
dsense<-subset(dsense, select=-c(Paper_code))
names(dsense)[names(dsense) == "timepoint_HbA1c"] <- "HbA1c"


# see ?cor for cor options.  using pairwise.complete.obs because there are cases where all data for a v
ariable is missing for a patient, but we dont want that entire patient point to be deleted
#also decided to use kendalls given the small smaple size, rank nature of method.
m<-cor(dsense, use="pairwise.complete.obs", method="kendall")

#see cor.test function for added parameters that can be used for cor.mtest
#had to use exact=FALSE since their were ties and exact computations could not be performed
#also as a result had to use continuity=TRUE since ties were present
m_sig<-cor.mtest(dsense, method="kendall", conf.level=0.95, , continuity=TRUE, exact=FALSE)

#for sig.level can introduce many different numbers.  used 0 to hide the near perfect correlations (i.
e. they wont receive a star)
#order="AOE" (finding angular order of the eigenvectors) seems to be a good way to group vars related t
o one other more closely together, but does not facilitate comparison between plots
corrplot(m, method="circle",
         order="original",
         type="upper",
         tl.col="black",
         na.label = " ", # had to put this is because of the ? that results
         p.mat=m_sig$p, insig = "label_sig",sig.level = c(0, .05), pch.cex = 1.5, pch.col = "white")


mtext("Correlation", side = 1, at=18.5, line=3.3, cex=.85)
mtext("Coefficient", side = 1, at=18.5, line=4.0, cex=.85)
```



In [20]:

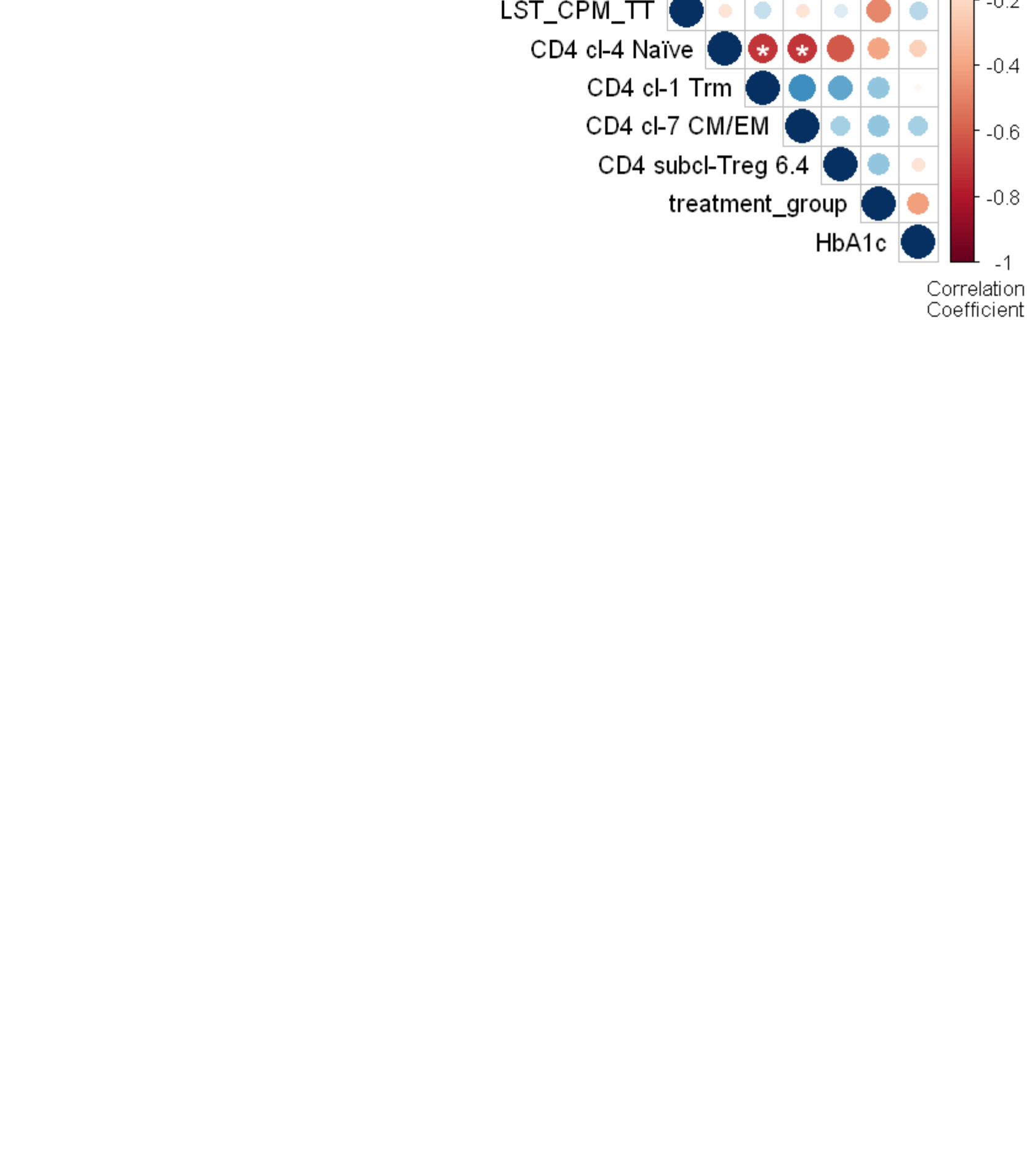
```
#6 months
dsense<-import("dsense_6.sas7bdat")
dsense<-subset(dsense, select=-c(Paper_code))
names(dsense)[names(dsense) == "timepoint_HbA1c"] <- "HbA1c"

# see ?cor for cor options.  using pairwise.complete.obs because there are cases where all data for a v
ariable is missing for a patient, but we dont want that entire patient point to be deleted
#also decided to use kendalls given the small smaple size, rank nature of method.
m<-cor(dsense, use="pairwise.complete.obs", method="kendall")

#see cor.test function for added parameters that can be used for cor.mtest
#had to use exact=FALSE since their were ties and exact computations could not be performed
#also as a result had to use continuity=TRUE since ties were present
m_sig<-cor.mtest(dsense, method="kendall", conf.level=0.95, , continuity=TRUE, exact=FALSE)

#for sig.level can introduce many different numbers.  used 0 to hide the near perfect correlations (i.
e. they wont receive a star)
#order="AOE" (finding angular order of the eigenvectors) seems to be a good way to group vars related t
o one other more closely together, but does not facilitate comparison between plots
corrplot(m, method="circle",
         order="original",
         type="upper",
         tl.col="black",
         na.label = " ", # had to put this is because of the ? that results
         p.mat=m_sig$p, insig = "label_sig",sig.level = c(0, .05), pch.cex = 1.5, pch.col = "white")

mtext("Correlation", side = 1, at=18.5, line=3.3, cex=.85)
mtext("Coefficient", side = 1, at=18.5, line=4.0, cex=.85)
```



In [21]:

```r
#final visit (revisit)
dsense<-import("dsense_9.sas7bdat")
#dsense<-subset(dsense, select=-c(Paper_code, `CD4 cl-4 Naïve`, `CD4 cl-1 Trm`, `CD4 cl-7 CM/EM`, `CD4
 subcl-Treg 6.4`))


dsense<-subset(dsense, select=-c(Paper_code))
#assigning missing values 0 so that they appear in the bubble plot
dsense$`CD4 cl-4 Naïve`[is.na(dsense$`CD4 cl-4 Naïve`)] <- 0
dsense$`CD4 cl-1 Trm`[is.na(dsense$`CD4 cl-1 Trm`)] <- 0
dsense$`CD4 cl-7 CM/EM`[is.na(dsense$`CD4 cl-7 CM/EM`)] <- 0
dsense$`CD4 subcl-Treg 6.4`[is.na(dsense$`CD4 subcl-Treg 6.4`)] <- 0
names(dsense)[names(dsense) == "timepoint_HbA1c"] <- "HbA1c"

# see ?cor for cor options.  using pairwise.complete.obs because there are cases where all data for a v
ariable is missing for a patient, but we dont want that entire patient point to be deleted
#also decided to use kendalls given the small smaple size, rank nature of method.
m<-cor(dsense, use="pairwise.complete.obs", method="kendall")

#see cor.test function for added parameters that can be used for cor.mtest
#had to use exact=FALSE since their were ties and exact computations could not be performed
#also as a result had to use continuity=TRUE since ties were present
m_sig<-cor.mtest(dsense, method="kendall", conf.level=0.95, , continuity=TRUE, exact=FALSE)

#for sig.level can introduce many different numbers.  used 0 to hide the near perfect correlations (i.
e. they wont receive a star)
#order="AOE" (finding angular order of the eigenvectors) seems to be a good way to group vars related t
o one other more closely together, but does not facilitate comparison between plots
corrplot(m, method="circle",
         order="original",
         type="upper",
         tl.col="black",
         na.label="square", na.label.col = "darkgrey",
         cl.pos="r", #indicates position of label,
         #cl.cex=1, #legend font size
         #tl.cex=1, #axis font size
         p.mat=m_sig$p, insig = "label_sig",sig.level = c(0, .05), pch.cex = 1.5, pch.col = "white")


mtext("Correlation", side = 1, at=18.5, line=3.3, cex=.85)
mtext("Coefficient", side = 1, at=18.5, line=4.0, cex=.85)
```

```
Warning message in cor(dsense, use = "pairwise.complete.obs", method = "kendall"):
"the standard deviation is zero"Warning message in cor(dsense, use = "pairwise.complete.obs", method
= "kendall"):
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