HW2

Wei_Wang_ww5 March 15, 2019

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Part 1: Randomized trial for strokes (12 points)

Preliminaries

1a.

- Y: What was the definition of the primary outcome in this study?
- What is (are) the variable name(s) for the outcome?

Answer: The definition of the primary outcome is death within 14 days and death or dependency at 6 months The variable names of the outcome is: **DDEAD(Dead on discharge form)** and **FDEAD(Dead at six month follow-up (Y/N))**

• U: what is (are) the variable name(s) for the intervention, and what is (are) their possible values?

The intervention in this study include the what descibe below: Half the patients were allocated unfractionated heparin (5000 or 12500 IU bd [twice daily]) and half were allocated avoid heparin; and, in a factorial design, half were allocated aspirin 300 mg daily and half avoid aspirin?.

Therefore the variables include: - RHEP24 Heparin within 24 hours prior to randomisation (Y/N) - RASP3 Aspirin within 3 days prior to randomisation (Y/N) - DASP14 Aspirin given for 14 days or till death or discharge (Y/N) - DASPLT Discharged on long term aspirin (Y/N) - DLH14 Low dose heparin given for 14 days or till death/discharge (Y/N) - DHH14 Medium dose heparin given for 14 days or till death/discharge (Y/N) - DHH14 Medium dose heparin given for 14 days etc in pilot (combine with above)

• V, W: describe the covariates included and the population being studied. Be specific where possible.

Covariates can be the patients' personal information including Age, sex, and the Final diagnosis of initial event DDIAGISC Ischaemic stroke; DDIAGHA Haemorrhagic stroke; DDIAGUN Indeterminate stroke; DNOSTRK Not a stroke; DNOSTRKX Comment on above.

The population of the study is: 19435 patients with suspected acute ischaemic stroke entering 467 hospitals in 36 countries were randomised within 48 hours of symptom onset.

1b. Provide descriptive statistics for in groups of {aspirin, no aspirin} use, including information on age, gender, systolic blood pressure, and conscious state. In clinical literature, this information is often referred to as "Table 1".

```
#set environment
loadlibs = function(libs) {
  for(lib in libs) {
    class(lib)
    if(!do.call(require,as.list(lib))) {install.packages(lib)}
    do.call(require, as.list(lib))
  }
}
libs = c("dplyr","mice","randomForest","adabag","gbm","pROC","gsubfn","chron")
loadlibs(libs)
## Loading required package: dplyr
## Warning: package 'dplyr' was built under R version 3.5.2
##
## Attaching package: 'dplyr'
## The following objects are masked from 'package:stats':
##
       filter, lag
##
## The following objects are masked from 'package:base':
##
##
       intersect, setdiff, setequal, union
## Loading required package: mice
## Warning: package 'mice' was built under R version 3.5.2
## Loading required package: lattice
##
## Attaching package: 'mice'
## The following objects are masked from 'package:base':
##
       cbind, rbind
##
## Loading required package: randomForest
## Warning: package 'randomForest' was built under R version 3.5.2
```

```
## randomForest 4.6-14
## Type rfNews() to see new features/changes/bug fixes.
##
## Attaching package: 'randomForest'
## The following object is masked from 'package:dplyr':
##
##
       combine
## Loading required package: adabag
## Warning: package 'adabag' was built under R version 3.5.3
## Loading required package: rpart
## Warning: package 'rpart' was built under R version 3.5.2
## Loading required package: caret
## Warning: package 'caret' was built under R version 3.5.2
## Loading required package: ggplot2
## Warning: package 'ggplot2' was built under R version 3.5.2
## Attaching package: 'ggplot2'
## The following object is masked from 'package:randomForest':
##
##
      margin
## Loading required package: foreach
## Loading required package: doParallel
## Warning: package 'doParallel' was built under R version 3.5.3
## Loading required package: iterators
```

```
## Loading required package: parallel
## Loading required package: gbm
## Warning: package 'gbm' was built under R version 3.5.3
## Loaded gbm 2.1.5
## Loading required package: pROC
## Warning: package 'pROC' was built under R version 3.5.2
## Type 'citation("pROC")' for a citation.
##
## Attaching package: 'pROC'
## The following objects are masked from 'package:stats':
##
##
       cov, smooth, var
## Loading required package: gsubfn
## Warning: package 'gsubfn' was built under R version 3.5.3
## Loading required package: proto
## Warning: package 'proto' was built under R version 3.5.3
## Loading required package: chron
## Warning: package 'chron' was built under R version 3.5.3
## Attaching package: 'chron'
## The following object is masked from 'package:foreach':
##
##
       times
```

```
#read dataset
stroke=read.csv("IST_corrected.csv",header = TRUE)
stroke=stroke[stroke$DASP14!="n",]
stroke=stroke[stroke$DASP14!="y",]
```

statistics description group by

```
aggregate( . ~ RASP3, data=stroke[c("AGE","RCONSC","RSBP","RASP3")], FUN=range)
```

```
##
     RASP3 AGE.1 AGE.2 RCONSC.1 RCONSC.2 RSBP.1 RSBP.2
## 1
              23
                    99
                               1
                                        3
                                               90
                                                     240
              16
                    98
                                        3
                                               70
                                                     290
## 2
         N
                               1
## 3
         Υ
              26
                    98
                               1
                                        3
                                               71
                                                     295
```

```
aggregate( . ~ RASP3, data=stroke[c("AGE","RSBP","RASP3")], FUN=mean)
```

```
## RASP3 AGE RSBP
## 1 69.96334 159.3564
## 2 N 71.41541 160.2930
## 3 Y 73.25863 159.8614
```

```
stroke %>%
  group_by(RASP3,SEX) %>%
  summarise(Freq = n()) %>%
  filter(RASP3!="")
```

```
## # A tibble: 4 x 3
## # Groups:
               RASP3 [2]
##
    RASP3 SEX
                  Frea
##
   <fct> <fct> <int>
## 1 N
           F
                  6879
## 2 N
           Μ
                  7632
## 3 Y
           F
                  1723
## 4 Y
           Μ
                  2217
```

```
stroke %>%
  group_by(RASP3,RCONSC) %>%
  summarise(Freq = n()) %>%
  filter(RASP3!="")
```

```
## # A tibble: 6 x 3
## # Groups:
              RASP3 [2]
   RASP3 RCONSC Freq
##
    <fct> <fct> <int>
## 1 N
           D
                   3232
## 2 N
           F
                  11066
## 3 N
          U
                    213
## 4 Y
          D
                    824
## 5 Y
          F
                   3080
## 6 Y
                     36
```

Machine learning analysis

```
# split the dataset into 50-50
smp_size <- floor(0.5 * nrow(stroke))
## set the seed to make your partition reproducible
set.seed(123)
train_stroke <- sample(seq_len(nrow(stroke)), size = smp_size)
train <- stroke[train_stroke, ]
test <- stroke[-train_stroke, ]</pre>
```

1c. Let our outcome of interest be "dead or dependent at 6 months", i.e. so that we have a binary classification problem. What percent of patients are dead or dependent at 6 months in your train set and test set?

The variable is chosen to be FDEAD

```
length(train[train$FDEAD=="Y",])/length(train$FDEAD)
```

```
## [1] 0.01152738
```

```
length(test[test$FDEAD=="Y",])/length(test$FDEAD)
```

```
## [1] 0.01152619
```

1d. Choose which variables to include in your model.

The below variables should be removed:

DDEAD, DDEADD, DDEADC, DDEADX, DALIVE, DALIVED, DPLACE, these are all the 14 days variables.

FDEADX, comment on death is unrelated

1e. Of the remaining variables, decide whether to exclude variables with missing data, impute them, and/or use indicator variables.

data clean and imputate

```
#check number of Nans in the dataset
null=sapply(train, function(x) sum(is.na(x)))
null=null[null>0]
null
```

```
##
     ONDRUG DMAJNCHD
                        DSIDED
                                DRSISCD
                                            DRSHD
                                                   DRSUNKD
                                                                DPED
                                                                        FLASTD
##
                                             9671
                                                       9598
                                                                9650
                                                                          9687
          1
                 9636
                          9386
                                    9503
##
     FDEADD FU1 RECD FU2 DONE FU1 COMP
                                               TD
##
       7554
                    8
                            48
                                     237
                                                1
```

As we can see from the result, the above columns have high number of NA values, For the date that is missing mostly, I remove the columns. For column **FDEADC**, it relates to the cause of death, for NA record, I replace them with 0, which refers to "unknown". Column **FU1_RECD**, **FU2_DONE**, **FU1_COMP**, **TD** can be impute since it shows some correlation with the outcome

```
##
## iter imp variable
## 1 1 FU1_RECD FU2_DONE FU1_COMP
```

```
train_tmp = mice::complete(mtrain) %>% as_tibble()
# Rename columns to indicate imputation
names(train_tmp) = lapply(names(train_tmp), paste0, "_imputed")
```

```
## Warning: Must use a character vector as names.
## This warning is displayed once per session.
```

```
##
## iter imp variable
## 1 1 FU1_RECD FU2_DONE FU1_COMP
```

```
test tmp = mice::complete(mtest) %>% as tibble()
# Rename columns to indicate imputation
names(test tmp) = lapply(names(test tmp), paste0, " imputed")
#reform the two dataset
delete3=c("FU1 RECD","FU2 DONE","FU1 COMP","TD","ONDRUG")
train=train[, !(colnames(train) %in% delete3), drop=FALSE]
test=test[, !(colnames(test) %in% delete3), drop=FALSE]
train=cbind(train,train_tmp)
test=cbind(test,test_tmp)
#clean dependent variable
train=train[train$FDEAD!="U",]
train=train[train$FDEAD!="",]
train$FDEAD=droplevels(train$FDEAD)
test=test[test$FDEAD!="U",]
test=test[test$FDEAD!="",]
test$FDEAD=droplevels(test$FDEAD)
```

logistic regression

```
mylogit <- glm(FDEAD ~., data = train,family = "binomial")</pre>
```

random forest

```
rf <- randomForest(FDEAD \sim ., data = train, ntree = 500, mtry = 6, importance = TRUE) summary(rf)
```

```
Length Class Mode
##
## call
                      6 -none- call
## type
                         -none- character
## predicted
                   9640 factor numeric
## err.rate
                   1500
                         -none- numeric
## confusion
                       6
                         -none- numeric
## votes
                  19280 matrix numeric
## oob.times
                   9640
                         -none- numeric
## classes
                      2 -none- character
## importance
                    200 -none- numeric
                    150 -none- numeric
## importanceSD
## localImportance
                      0 -none- NULL
## proximity
                      0 -none- NULL
## ntree
                      1 -none- numeric
## mtry
                      1 -none- numeric
## forest
                     14 -none- list
## y
                   9640 factor numeric
                      0 -none- NULL
## test
                      0 -none- NULL
## inbag
## terms
                      3 terms call
```

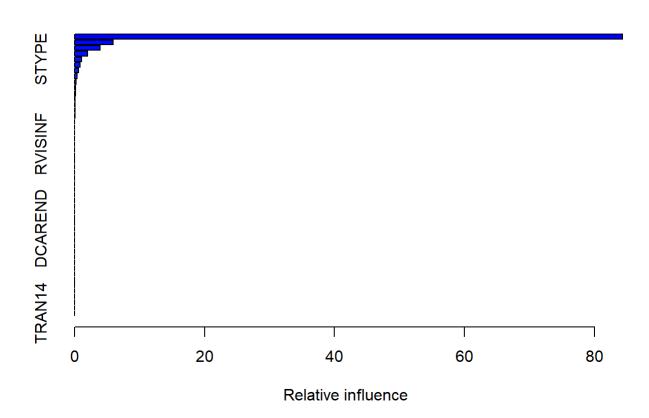
boosting

```
boost <- boosting(FDEAD~., data=train, boos=TRUE, mfinal=3)
summary(boost)</pre>
```

```
##
              Length Class
                             Mode
## formula
                 3 formula call
## trees
                  3
                    -none-
                            list
## weights
                 3
                    -none-
                            numeric
## votes
              19280
                    -none-
                            numeric
## prob
              19280
                    -none-
                            numeric
## class
               9640
                            character
                    -none-
## importance
                 50
                    -none-
                            numeric
## terms
                 3 terms
                             call
## call
                 5
                            call
                    -none-
```

gradient boosting

```
gbm <- gbm(FDEAD~., data=train,distribution = "gaussian")
#n.trees = 10000,shrinkage = 0.01, interaction.depth = 4
summary(gbm) #Summary gives a table of Variable Importance and a plot of Variable Importance</pre>
```

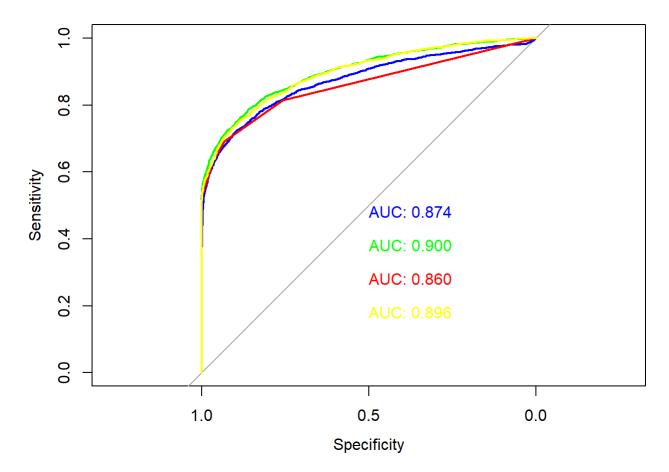


```
##
                                   var
                                           rel.inf
## FU2 DONE imputed FU2 DONE imputed 84.31356287
## AGE
                                   AGE
                                        5.96605271
## RCONSC
                               RCONSC
                                        3.95355940
## DASPLT
                               DASPLT
                                       1.99219721
## STYPE
                                STYPE
                                       1.07983852
## FU1_RECD_imputed FU1_RECD_imputed
                                       0.81934554
## RATRIAL
                              RATRIAL
                                        0.64841877
## DSTER
                                DSTER
                                        0.39546211
## NCB14
                                NCB14
                                        0.22689773
## DOAC
                                 DOAC
                                        0.18157632
## STRK14
                               STRK14
                                        0.14911278
## HOSPNUM
                              HOSPNUM
                                        0.09451329
## CMPLASP
                              CMPLASP
                                        0.07504924
## DLH14
                                 DLH14
                                        0.05239971
## FU1_COMP_imputed FU1_COMP_imputed
                                        0.05201380
## RDELAY
                               RDELAY
                                        0.00000000
## SEX
                                  SEX
                                        0.00000000
## RSLEEP
                               RSLEEP
                                        0.00000000
## RCT
                                   RCT
                                        0.00000000
## RVISINF
                              RVISINF
                                        0.00000000
## RHEP24
                               RHEP24
                                        0.00000000
## RASP3
                                 RASP3
                                        0.00000000
## RSBP
                                 RSBP
                                        0.00000000
## RXASP
                                 RXASP
                                        0.00000000
## RXHEP
                                 RXHEP
                                        0.00000000
## DASP14
                               DASP14
                                        0.00000000
## DMH14
                                 DMH14
                                        0.00000000
## DHH14
                                DHH14
                                        0.00000000
## DSCH
                                 DSCH
                                        0.00000000
## DIVH
                                 DIVH
                                        0.00000000
## DAP
                                  DAP
                                        0.00000000
## DGORM
                                 DGORM
                                        0.00000000
## DCAA
                                 DCAA
                                        0.00000000
## DHAEMD
                               DHAEMD
                                        0.00000000
## DCAREND
                              DCAREND
                                        0.00000000
## DTHROMB
                              DTHROMB
                                        0.00000000
## DMAJNCH
                              DMAJNCH
                                        0.00000000
## DSIDE
                                 DSIDE
                                        0.00000000
## DDIAGISC
                             DDIAGISC
                                        0.00000000
## DDIAGHA
                              DDIAGHA
                                        0.00000000
## DDIAGUN
                              DDIAGUN
                                        0.00000000
## DNOSTRK
                              DNOSTRK
                                        0.00000000
## DRSISC
                               DRSISC
                                        0.00000000
## H14
                                  H14
                                        0.00000000
## ISC14
                                ISC14
                                        0.00000000
## NK14
                                 NK14
                                        0.00000000
## HTI14
                                HTI14
                                        0.00000000
## PE14
                                 PE14
                                        0.00000000
## DVT14
                                DVT14
                                        0.00000000
## TRAN14
                               TRAN14
                                        0.00000000
```

1f. Construct an ROC

```
#ROC for multiple model
rf_pred=data.frame(predict(rf, test, type="prob"))
lg_pre=predict(mylogit,newdata=test,type=c("response"))
```

```
## Warning in predict.lm(object, newdata, se.fit, scale = 1, type =
## ifelse(type == : prediction from a rank-deficient fit may be misleading
```



1g. Report the variable importance

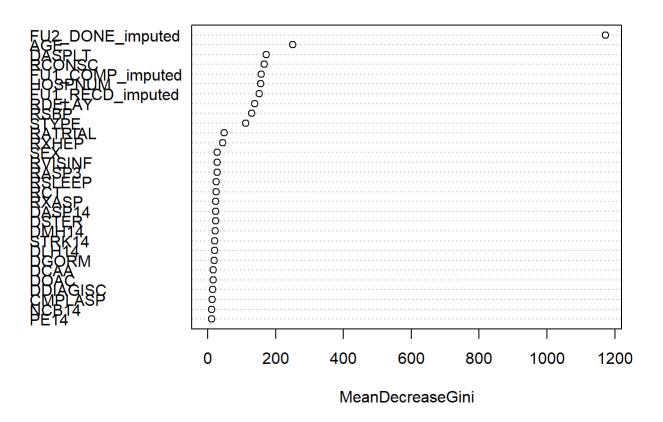
```
# variable importance
importance(rf)
```

##	N	Υ	MeanDecreaseAccuracy	
## HOSPNUM	12.2279584	0.1850410	11.1099578	
## RDELAY	7.1411730	-1.5067412	5.3082822	
## RCONSC	34.0506511	22.5751904	40.0627698	
## SEX	1.8679826	4.6228200	3.8407049	
## AGE	30.9330645	41.1864641	47.7634565	
## RSLEEP	2.4280368	-0.4270501	1.8653519	
## RATRIAL	19.3733298	5.2236866	19.8703742	
## RCT	2.0936229	5.3910411	4.8315323	
## RVISINF	5.2113845	1.7848778	5.6058717	
## RHEP24	4.2023382	-1.1145011	3.3037225	
## RASP3	3.3429257	0.1177898	3.0212864	
## RSBP	7.2336053	2.9784306	7.4755802	
## STYPE	21.7444110	8.7096844	23.1400454	
## RXASP	6.7784216	-1.1269709	5.9885583	
## RXHEP	9.2388762	-2.6926328	7.9722607	
## DASP14	5.6125150	-1.4783907	4.8843067	
## DASPLT	23.1956924	26.1407932	32.4278481	
## DLH14	8.7476914	0.2355522	8.8053785	
## DMH14	5.6060832	-0.4837211	5.4167011	
## DHH14	3.6575119		4.2115200	
		1.9410155		
## DSCH	5.3619374	1.3592752	5.6592254	
## DIVH	7.9306661	-1.5779393	7.0987573	
## DAP	0.1589292	1.5974170	0.8902654	
## DOAC	17.9892238	8.4211391	18.3978770	
## DGORM	6.7530493	-0.1150492	6.1521469	
## DSTER	12.5819108	7.6089452	14.3921243	
## DCAA	2.2255686	-0.1368826	1.9973161	
## DHAEMD	3.3007849	1.1212639	3.4355556	
## DCAREND	3.8541336	0.3748510	3.8654188	
## DTHROMB	1.5573549	-0.4816543	1.2710603	
## DMAJNCH	5.4891457	-2.7526594	4.6850150	
## DSIDE	8.2024467	-1.9052299	7.4681135	
## DDIAGISC	2.1415873	1.3954996	2.6354260	
## DDIAGHA	6.1330119	-2.2682072	4.9100659	
## DDIAGUN	-0.3890229	1.4134316	0.5023799	
## DNOSTRK	0.8164026	6.6539994	4.6501371	
## DRSISC	9.1938318	-4.0552842	8.2336049	
## CMPLASP	0.7907160	2.5486294	1.9704884	
## H14	5.5512914	-1.3211230	4.7161937	
## ISC14	7.1084700	-0.9924735	5.9992698	
## NK14	7.9299684	-1.2469046	6.8882488	
## STRK14	10.1003814	0.3261618	10.3587582	
## HTI14	1.6723738	-0.6370346	1.1619665	
## PE14	12.0565381	1.9522433	12.2006570	
## DVT14	1.6115940	-0.8716831	1.1066048	
## TRAN14	11.7287071	3.0880453	12.4713805	
## NCB14	11.1733332	1.8012520		
## FU1_RECD_imputed	19.6975837			
## FU2_DONE_imputed			117.5243114	
## FU1_COMP_imputed	23.4417308	5.0252253	24.8078678	
			=	
##	MeanDecrease	eGini		

2019		
##	RDELAY	137.758996
##	RCONSC	165.804265
##	SEX	28.291380
##	AGE	250.890221
##	RSLEEP	25.327855
##	RATRIAL	48.510181
##	RCT	24.805335
##	RVISINF	27.323369
##	RHEP24	9.082253
##	RASP3	27.122339
##	RSBP	129.151219
##	STYPE	111.210348
##	RXASP	23.704629
##	RXHEP	44.572879
	DASP14	23.128638
	DASPLT	171.963370
	DLH14	20.115006
	DMH14	22.274594
	DHH14	4.064133
##	DSCH	10.413337
	DIVH	7.790697
	DAP	6.814847
	DOAC	15.396989
	DGORM	19.164278
	DSTER	22.943997
	DCAA	15.686168
	DHAEMD	10.330789
	DCAREND	3.535490
	DTHROMB	1.568336
	DMAJNCH	3.505411
	DSIDE	9.874953
	DDIAGISC	14.856341
	DDIAGHA	8.031292
	DDIAGUN	9.574251
	DNOSTRK	7.140119
	DRSISC	6.315314
	CMPLASP	12.807783
	H14	4.524180
	ISC14	4.924060
	NK14	9.135068
	STRK14	20.578361
	HTI14	1.339043
	PE14	11.835076
	DVT14	1.441072
	TRAN14	6.633501
	NCB14	11.992205
	FU1_RECD_imputed	152.362931
	FU2_DONE_imputed	1172.662908
	FU1_COMP_imputed	158.004605
пπ	. or_com_rmpaced	170.004007

```
library(caret)
varImpPlot(rf,type=2)
```

rf



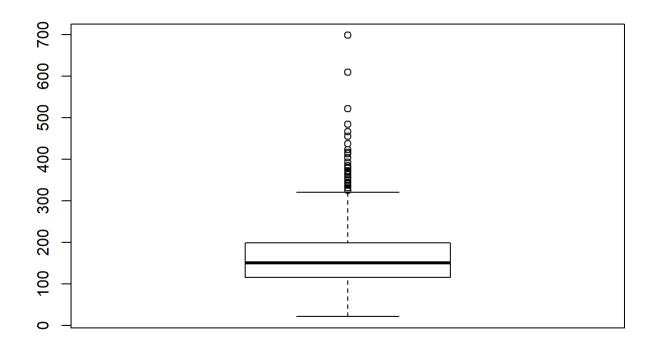
Part 2. Basis functions and regularization for daily glucoses [8 points]

read dataset

```
#read data
item=read.csv("d_labitems.csv",header = TRUE)
events=read.csv("labevents.csv",header = TRUE)
data=events[events$subject_id=="13033",]
data=data[data$itemid=="50112",]
summary(data$valuenum)
```

```
## Min. 1st Qu. Median Mean 3rd Qu. Max.
## 22.0 116.0 151.5 163.5 199.0 698.0
```

boxplot(data\$valuenum)



2a. Extract the glucose data

```
library(ggplot2)
library(scales)
library(lubridate)

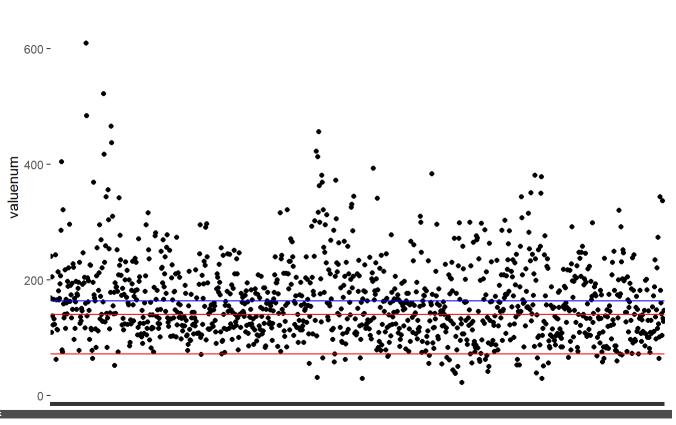
## Warning: package 'lubridate' was built under R version 3.5.2

##
## Attaching package: 'lubridate'

## The following objects are masked from 'package:chron':
##
## days, hours, minutes, seconds, years

## The following object is masked from 'package:base':
##
## date
```

```
data$Date <- as.Date(data$charttime)
data$time <- times(strftime(data$charttime, "%H:%M:%S"))
ggplot(data, aes(charttime, valuenum)) +
   geom_point() +
   #scale_x_datetime(breaks=date_breaks("2 month"), labels="%b-%d-%Y") +
   #theme(axis.text.x=element_text(angle=90))+
   geom_hline(yintercept = mean(data$valuenum), color="blue")+
   geom_hline(yintercept = 72, color="red")+
   geom_hline(yintercept = 140, color="red")</pre>
```



charttime

2b. Split the data into training set and test set

I use period = 0.5, which means 12 hours (24*0.5)

```
#split data
bld test=data[data$Date>"3417-5-1",]
bld_train=data[data$Date<="3417-5-1",]</pre>
#sine consine basic function
period = 0.5
K = 5
# Function for basis expansion of \{\sin(kx),\cos(kx)\}\ for i=1 to K
sincos = function(dat, variable="time", period=2*pi, K=10) {
  data = dat
  for(i in 1:K) {
    data[[paste0("sin_",i)]] = sin(data[[variable]]*i*2*pi/period)
  for(i in 1:K) {
    data[[paste0("cos_",i)]] = cos(data[[variable]]*i*2*pi/period)
  # data$intercept = 1 # not necessary if using with models that use intercepts
  data
}
```

2c. Use cv.glmnet to learn a daily trend for the individual on the training set.

Plot the coefficient profile with lambda on the x-axis. Report the lambda that performed best in CV (use lambda.min for this exercise).

```
bld_train1 = sincos(bld_train, period=period, K=K)
bld_train1 = bld_train1 %>% dplyr::select(-charttime)%>% dplyr::select(-time)%>% dplyr::select(-
Date)

# Learn a linear model, regularized
library(glmnet) # Does regularization with (generalized) linear models
```

```
## Loading required package: Matrix
```

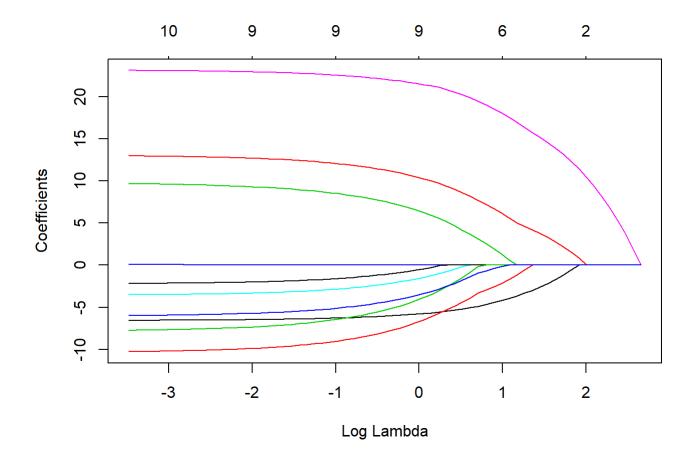
```
## Loaded glmnet 2.0-16
```

```
##
## Attaching package: 'glmnet'
```

```
## The following object is masked from 'package:pROC':
##
## auc
```

```
## [1] 0.5505187
```

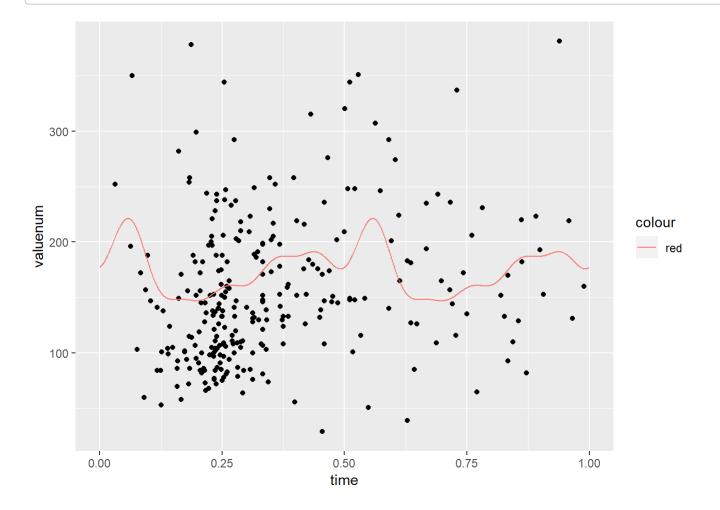
```
plot(lasso$glmnet.fit, "lambda")
```



2d. plot

```
#predict
bld test1 = sincos(bld test, period=period, K=K)
bld_test2 = bld_test1 %>% dplyr::select(-charttime)%>% dplyr::select(-time)%>% dplyr::select(-Da
te)
self_data=data.frame(seq(ISOdate(2000,1,31), by = "min", length.out = 1440))
self_data$time=times(strftime(self_data$seq.ISOdate.2000..1..31...by....min...length.out...144
0., "%H:%M:%S"))
self_data1=sincos(self_data, period=period, K=K)
self_data2=self_data1%>% dplyr::select(-time)%>% dplyr::select(-seq.ISOdate.2000..1..31...by....
min...length.out...1440.)
self_data1[["ylasso"]] = predict(lasso,
                                 self_data2
                                #%>% select(-c(subject_id,hadm_id,icustay_id,itemid,value,valuen
um, valueuom, flag))
                                %>% as.matrix(),
                              s = c(lasso$lambda.min))
# Plot
ggplot(data=bld test1, aes(time,valuenum)) + geom point()+
  geom_line(data = self_data1, aes(x=time,y=ylasso,color="red"))
```

Don't know how to automatically pick scale for object of type times. Defaulting to continuou s.



2e. What percent of the variation is explained by your model compared to using the training set mean?

Based on the claculation below, around 94%

```
train_mean=mean(bld_train$valuenum)
#sum of square error
ssq=sum((bld_test$valuenum-train_mean)^2)
rsq=sum((bld_test1$valuenum-bld_test1$ylasso)^2)
r2=rsq/ssq
r2
```

[1] 0

2f. Make a statement about the daily variation of glucose in this individual. In particular, according to your model, when is it lowest? When is it highest?

It is high in the mid night, and in the morning about 6am, it is low. Until 12:00pm, the value is slowly increasing, and drop to lowest at 6pm.