Compulsory exercise: Team SuperGreat MA8701 Advanced Statistical Learning V2023

Nora Aasen, Elias Angelsen, Jonas Nordstrom

28 mars, 2023

Introduction

In this project we have studied the Framingham Coronary Heart Disease Dataset which can be found on kaggle "Logistic Regression to Predict Heart Disease" (n.d.). This dataset contains patient information for inhabitants in Framingham, Massachusetts, and is typically used to predict the chance of getting coronary heart disease (CHD) within the next 10 years.

For this project, however, we intend to investigate how to handle missing data in combination with lasso and bootstrapping as a method for making inference about the variables. We first do single regression imputation using the package called mice (van Buuren and Groothuis-Oudshoorn (2022)). Our emphasis is on how to avoid data leakage in our procedure. Afterwards we investigate how imputation may affect the subsequent lasso regression, which is done multiple times using bootstrap. Lastly we fit a logistic regression model with the covariates chosen from the lasso procedure using an independent data set, and compare the model based on the imputed and complete data set.

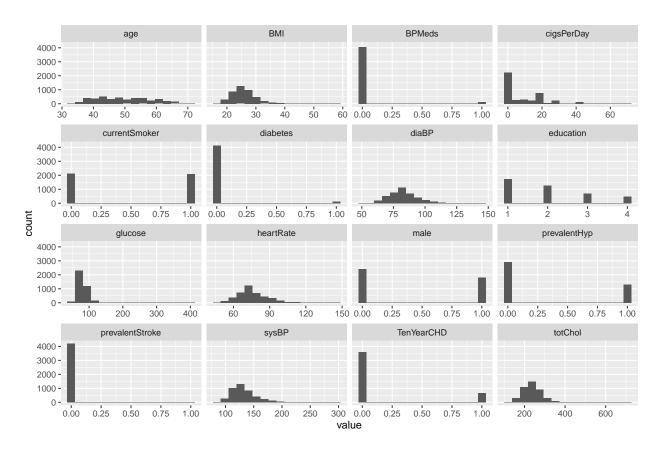
Exploratory Analysis

We start by examining the data set. We use the packages ggplot2 (Wickham et al. (2022)) and tidyr (Wickham and Girlich (2022)) to make the plots.

```
# Load and look at data
data <- read.csv("framingham.csv")
data_dim = dim(data)
pos_response = sum(data$TenYearCHD == 1)

library(ggplot2)
library(tidyr) # gather()

# We visualize the data
ggplot(gather(data), aes(value)) + geom_histogram(bins = 16) + facet_wrap(~key, scales = "free_x")</pre>
```



```
# Code education as a factor variable instead of 1-2-3-4.
data$education = factor(data$education, labels = c("none", "hs", "college", "post-grad"))
```

This data set contains 4238 observations, 15 covariates and a binary response variable TenYearCHD, indicating that a natural model choice is a logistic regression model. The response variable has 644 positive observations, which equals about 15.2% of the total observations. We see from the plot that most of our covariates are either binary, or numeric. However, we note that the variable education is most likely a categorical covariate. We could not find any further elaboration for which four categories the numbers represent, so based on the frequency of each value and qualified guessing, we changed it to a factor variable and defined the four categories as none, hs, college, post-grad.

The next thing we looked at was the number of missing data in our data set. We used the packages ggmice (Oberman (2022)), naniar (Tierney et al. (2023)), and gridExtra (Auguie (2017)) to produce the plots.

```
# Look at the missing data
library(ggmice) # plot_pattern()
library(naniar) # gg_miss_var()
library(gridExtra) # grid.arrange()

gluc_miss = sum(is.na(data$glucose))/length(data$glucose)

plot1 <- plot_pattern(data, rotate = T)
plot2 <- gg_miss_var(data)
grid.arrange(plot1, plot2, ncol=2)</pre>
```

As we can see there are seven covariates that contains missing data: glucose, education, BPMeds, totChol, cigsPerDay, heartRate, and BMI, where glucose is by far the covariate that has the most NA's, with a total

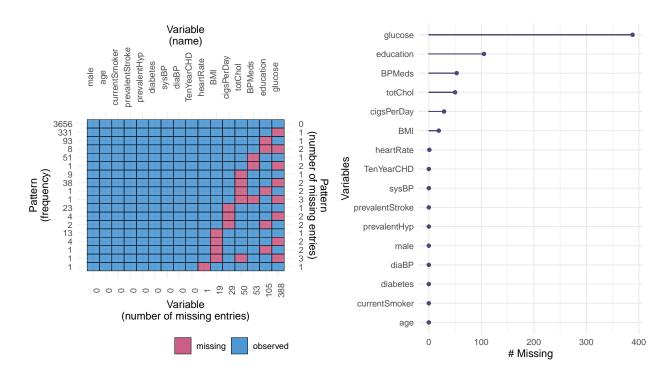


Figure 1: My plot

of 9.2% missing values. We cannot use the rows that contain missing values as is. An option for handling the problem would be to remove all rows that contains NA's, also called *complete case analysis*. In this project we do a method called *single imputation*, and compare it with the complete case analysis to investigate how imputing missing data can affect the subsequent inference.

Before beginning the imputation we have to split the data into two disjoint sets. We call them training and test set here, but because our goal is inference they will serve more as independent sets where one is used for covariate reduction and the other is used for estimating and inference. The same split is used for both the imputation method and complete method.

```
# Split into training and test first to avoid data leakage
set.seed(8701)
tr = 7/10 # train ratio
r = dim(data)[1]
size = round(r*tr)
train = sample(1:r,size = size)

d.train = data[train,]
d.test = data[-train,]

# Make a dataset containing only the complete cases
d.complete <- data[complete.cases(data),]
d.train.complete <- d.train[complete.cases(d.train),]
d.test.complete <- d.test[complete.cases(d.test),]

pos_response_c = sum(data[complete.cases(data),]$TenYearCHD==1)</pre>
```

The complete data set contains 3656 observations and the response variable has 557 positive responses, which equals about 15.2% of the total observations. As we can see, the proportion of positive observations in the

response is the same, which is a good indicator that our data is missing at random (MAR), which we will come back to.

Missing Data

We categorize missing data into one of three categories: missing completely at random (MCAR), missing at random (MAR), or missing not at random (MNAR). If the data is MCAR, we expect no correlation between the missingness of data and the data itself. Consequently, removing data with missing components should cause no loss in information except the loss due to reduction in data quantity. If the data is MAR, then the structure explaining if the data is missing is dependent on the other variables in our data. In this case, naive methods like mean imputing would cause a loss in information, although we expect methods that predict missing data from the rest of the data to compensate for MAR. For MNAR, the missingness is explained by an unknown source, for instance the unobserved data. In the case of MNAR, any imputation method would yield a biased results if one used only the data at hand (Buuren (2018)).

This can be formulated mathematically as follows. Let Z = (X, y) denote the full collection of covariates and responses, respectively, and we let a subscript mis/obs indicate whether we are restricting Z (or X) to the missing or observed parts, respectively. Let R be an indicator matrix indicating missing (0) and observed (1) covariates. Let ψ be the parameters in the distribution of R. We define the data to be:

- Missing completely at random (MCAR) if $P(R|Z, \psi) = P(R|\psi)$.
- Missing at random (MAR) if $P(R|Z, \psi) = P(R|Z_{obs}, \psi)$.
- Missing not at random (MNAR) if $P(R|Z, \psi) = P(R|Z, \psi)$.

Hence, we need to investigate the missingess in our data before imputing. One thing we do is compare the frequency of missing data depending on the wheter the response variable is 0 or 1.

```
d.pos <- subset(data, TenYearCHD == 1)
d.neg <- subset(data, TenYearCHD == 0)
na.pos <- colSums(apply(d.pos, 2, is.na))
na.neg <- colSums(apply(d.neg, 2, is.na))

M = matrix(NA, nrow = 3, ncol = 16)

M[1, ] = round(colSums(is.na(data)), 0)
M[2, ] = round(na.pos/dim(d.pos)[1], 3)
M[3, ] = round(na.neg/dim(d.neg)[1], 3)
colnames(M) = colnames(d.pos)
rownames(M) = c("# miss", "1", "0")
M[, which(colSums(is.na(data)) > 0)]
```

```
##
          education cigsPerDay BPMeds totChol
                                                   BMI heartRate glucose
## # miss
            105.000
                         29.000 53.000
                                        50.000 19.000
                                                           1.000 388.000
## 1
              0.025
                          0.003 0.017
                                         0.014 0.016
                                                           0.002
                                                                    0.078
## 0
              0.025
                          0.008 0.012
                                         0.011 0.003
                                                           0.000
                                                                    0.094
```

Some of our missing data seem dependent on the response, such as BMI, cigsPerDay, and glucose, and this indicates that we should include the response variable in our imputation model. If the goal was prediction, this is not ideal as we use the response to complete the dataset. However, as our aim is inference, we include the response.

We now attempt to predict the missing values using the observed data. A better method for handling missing data is called multiple imputation. However, it is not trivial to combine Rubin's rules with the Lasso, bootstrap and concluding inference. It was therefore not considered for this project.

When doing single imputation mice has as default polynomial regression for the factor variable and predictive mean matching (pmm) for all other. We change to logistic regression for the binary variable BPMeds, keep polynomial regression for education and use linear regression for all other missing variables.

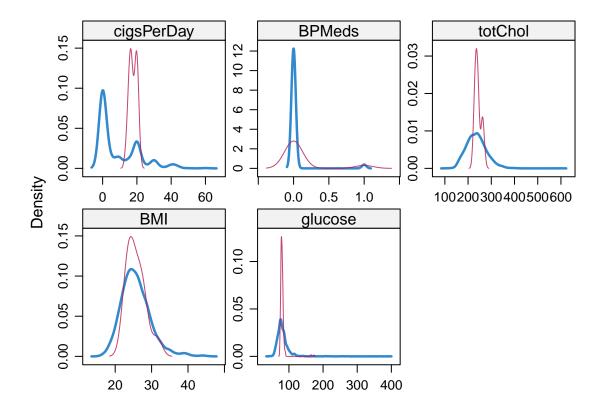
We use the package called mice van Buuren and Groothuis-Oudshoorn (2022) to impute the data. If we wanted to use the test set as normal, we would have to fit the imputation models on the training set, and then reuse these models to impute the test set in order to avoid data leakage. There cannot be correlation in between the samples in the test set when they are used for validation or prediction for instance. This can easily be done using the function mice.reuse from the package NADIA Borowski and Fic (2022). However, since we will use both sets, that we a bit misleadingly called train and test, for model fitting they should be imputed separately with individual models. This is to avoid correlation amongst the data set.

```
library(mice) # mice()

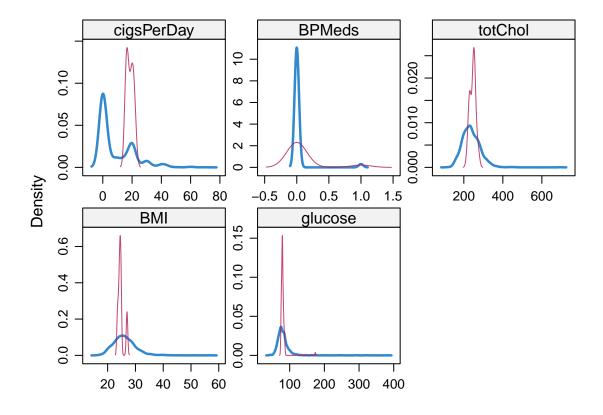
# Change the method for each covariate to our choice
meth = mice(data, maxit = 0)$method
meth[which(meth == "pmm")] = "norm.predict"
meth["BPMeds"] <- "logreg"

# Make a single imputation model using the training data
imp_mod.train = mice(d.train, m = 1, printFlag = F, method = meth)
d.train.imp = complete(imp_mod.train)
imp_mod.test = mice(d.test, m = 1, printFlag = F, method = meth)
d.test.imp = complete(imp_mod.test)

# Compare the density of imputed data vs. actual data in the training set
densityplot(imp_mod.train)</pre>
```

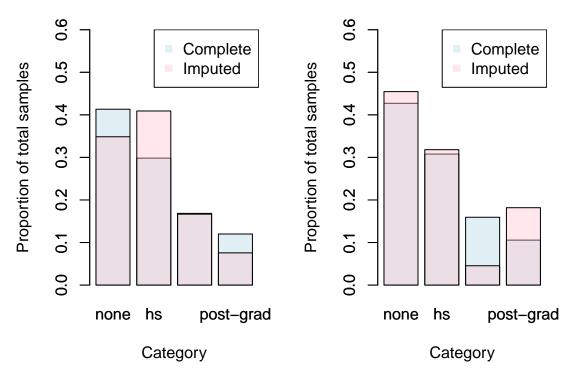


densityplot(imp_mod.test)



```
par(mfrow = c(1, 2))
c1 <- rgb(173, 216, 230, max = 255, alpha = 95, names = "lt.blue")
c2 <- rgb(255, 192, 203, max = 255, alpha = 95, names = "lt.pink")
barplot(prop.table(table(d.train.complete$education)), col = c1, xlab = "Category",
   ylab = "Proportion of total samples", main = "Train Education: Observed and Imputed",
   ylim = c(0, 0.6)) # Plot 1st histogram using a transparent color
barplot(prop.table(table(d.train.imp$education[is.na(d.train$education)])), col = c2,
    add = TRUE)
legend("topright", legend = c("Complete", "Imputed"), cex = 1, pch = 15, col = c(c1,
    c2))
barplot(prop.table(table(d.test.complete$education)), col = c1, xlab = "Category",
   ylab = "Proportion of total samples", main = "Test Education: Observed and Imputed",
   ylim = c(0, 0.6)) # Plot 1st histogram using a transparent color
barplot(prop.table(table(d.test.imp$education[is.na(d.train$education)])), col = c2,
   add = TRUE)
legend("topright", legend = c("Complete", "Imputed"), cex = 1, pch = 15, col = c(c1,
   c2))
```

rain Education: Observed and Imest Education: Observed and Im



As can be seen from the density plots, our imputation is mostly yielding imputations around the mean, but with some added variance. Both sets have some deviance from the observed proportions when it comes to imputation of the categorical variable education, which are unsure how to explain. Furthermore, although the imputation of cigsPerDay may appear strange, it makes sense as all missing observations in that variable also had responded positive to currentSmoker. The imputation of cigsPerDay seems to be about the mean of non-zero values, thus showcasing a similar behavior as the other imputed data.

Model

In this section we fit the same model on both the imputed and complete training data. The two data sets are identical apart from the rows that contained NA's. Since we want to do lasso, we first standardize the data. Secondly, we use bootstrap to calculate the non-zero coefficients multiple times. Lastly, we fit a logistic regression model using the test set.

```
train.imp.sd = attr(x.train.imp, "scaled:scale")
y.train.imp = d.train.imp$TenYearCHD
```

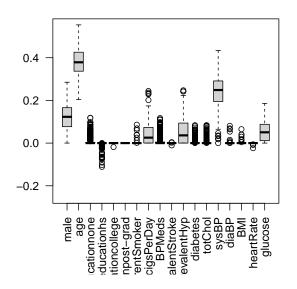
Lasso on complete data

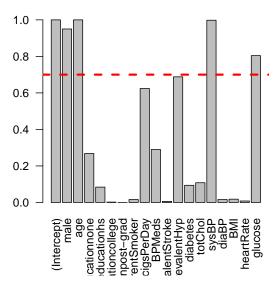
We continue to do the Lasso on the complete case data. This is done by first estimating λ_{min} using cross-validation and then fitting a model with the highest λ within one standard deviation of λ_{min} as penalty term. For easy implementation of the lasso method, we use the package glmnet Friedman et al. (2022).

```
library(glmnet) # implementing lasso
B = 500 # Number of boostrap datasets
B.size.complete = dim(d.train.complete)[1] # Number of samples
# Make a matrix that store the computed coefficients
B.coef.complete = matrix(NA, nrow = B, ncol = length(colnames(x.train.complete)) +
   1)
for (i in 1:B) {
   B.data = sample(1:B.size.complete, size = B.size.complete, replace = TRUE)
   x = x.train.complete[B.data, ]
   y = y.train.complete[B.data]
    cv.out = cv.glmnet(x, y, family = "binomial", alpha = 1)
   lasso_mod = glmnet(x, y, family = "binomial", alpha = 1, intercept = T, lasso = cv.out$lambda.1se)
   B.coef.complete[i, ] <- coef(lasso_mod, s = cv.out$lambda.1se)[, 1]
colnames(B.coef.complete) = names(coef(lasso_mod, s = cv.out$lambda.1se)[, 1])
B.coef.count.complete = ifelse(B.coef.complete == 0, 0, 1)
coef70.complete <- names(apply(B.coef.count.complete, 2, sum)/B)[apply(B.coef.count.complete,</pre>
    2, sum)/B > 0.7
# We do not include intercept as it is always in the model and too large to fit
# in the scaling.
par(mfrow = c(1, 2))
boxplot.matrix(B.coef.complete[, -1], ylim = c(-0.25, 0.55), las = 2, main = "Boxplot of estimated coef
barplot(apply(B.coef.count.complete, 2, sum)/B, las = 2, main = "Percentage of times coefficient was not
abline(h = 0.7, col = "red", lty = 2, lwd = 3)
```

Boxplot of estimated coefficients

Percentage of times coefficient was nonzero





```
# Fit a logistic model using the test data and chosen covariates
mod.complete <- glm(TenYearCHD ~ age + male + sysBP + glucose, data = d.test.complete,
    family = binomial())</pre>
```

After using lasso on 500 data sets the variables that have nonzero coefficients at least 70% of the time, are (Intercept), male, age, sysBP, glucose. They are also indicated on the right figure above. This cut-off values seems reasonable, but could be altered to include more or fewer coefficients if wanted, as it was chosen a bit arbitrarily. We use the chosen covariates to fit a logistic regression model. To avoid overfitting, we use the independent test data to estimate the coefficients.

We could also investigated the box-plot to determine the covariates that we would like in our model. Here, both cigsPerDay and prevelentHyp has coefficients estimated to be non-zero, although zero is included in their inter-quartile range, which perhaps justifies their exclusion from the final model. However, zero is also included in the inter-quartile range to the coefficient of glucose, which is included in the final model. Since the choice of a 70% cutoff range is somewhat arbitrary, one could perhaps use both plots in combination to determine the most significant covariates.

Lasso on imputed data

We now do the same thing, just using the imputed data instead of the complete case.

```
B = 500  # Number of boostrap datasets
B.size.imp = dim(d.train.imp)[1]  # Number of samples
# Make a matrix that store the computed coefficients
B.coef.imp = matrix(NA, nrow = B, ncol = length(colnames(x.train.imp)) + 1)

for (i in 1:B) {
    B.data = sample(1:B.size.imp, size = B.size.imp, replace = TRUE)
    x = x.train.imp[B.data, ]
    y = y.train.imp[B.data]
    cv.out = cv.glmnet(x, y, family = "binomial", alpha = 1)
    lasso_mod = glmnet(x, y, family = "binomial", alpha = 1, intercept = T, lasso = cv.out$lambda.1se)
```

```
B.coef.imp[i, ] <- coef(lasso_mod, s = cv.out$lambda.1se)[, 1]
}

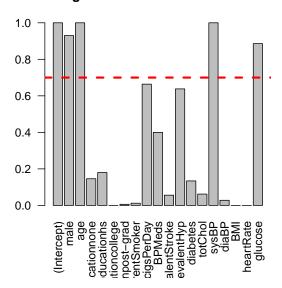
colnames(B.coef.imp) = names(coef(lasso_mod, s = cv.out$lambda.1se)[, 1])
B.coef.count.imp = ifelse(B.coef.imp == 0, 0, 1)
coef70.imp <- names(apply(B.coef.count.imp, 2, sum)/B)[apply(B.coef.count.imp, 2, sum)/B > 0.7]

# We do not include intercept as it is always in the model and too large to fit
# in the scaling.
par(mfrow = c(1, 2))
boxplot.matrix(B.coef.imp[, -1], ylim = c(-0.25, 0.55), las = 2, main = "Boxplot of estimated coefficies barplot(apply(B.coef.count.imp, 2, sum)/B, las = 2, main = "Percentage of times coefficient was nonzero abline(h = 0.7, col = "red", lty = 2, lwd = 3)
```

Boxplot of estimated coefficients

male age cationnone age cationnone ducationhs tioncollege processes and all above as a sysBP of diabetes a college by a college process alentStroke diabetes alentStroke diabetes alentStroke by a college by a colle

Percentage of times coefficient was nonzero



```
# Fit a logistic model using the test data and chosen covariates
mod.imp <- glm(TenYearCHD ~ age + male + sysBP + glucose + cigsPerDay, data = d.test.imp,
    family = binomial())</pre>
```

The Lasso on the imputed data chooses (Intercept), male, age, sysBP, glucoseas the non-zero covariates, here also indicated in the right plot above. The performance of this model is quite similar to that of the complete case, but we note in particular that cigsPerDay, BPMeds and glucose are non-zero more often when using the imputed data. This could perhaps be a sign of correlation in the training data caused by the imputation. As before, we use the chosen covariates to fit a logistic regression model. To avoid overfitting, we use the independent imputed test data to estimate the coefficients. Here we see why it was important to impute the test set using itself, and not the imputation model trained on the training data. However, in a regular train/test situation where the test set is indeed used for testing or validation it is important to reuse the imputation model fitted on the training data, as discussed previously.

Inference

To access the two models we compute the AIC and look at the confidence intervals from the model.

```
data.frame("Complete"=round(summary(mod.complete)$aic,2),
      "Imputed" = round(summary(mod.imp)$aic,2))
     Complete Imputed
      887.96 1020.37
## 1
summary(mod.complete)
##
## Call:
## glm(formula = TenYearCHD ~ age + male + sysBP + glucose, family = binomial(),
##
       data = d.test.complete)
##
## Deviance Residuals:
##
      Min
                1Q
                     Median
                                  3Q
                                          Max
## -1.5252 -0.6070 -0.4669 -0.3512
                                       2.6205
##
## Coefficients:
               Estimate Std. Error z value Pr(>|z|)
## (Intercept) -7.365555
                          0.714477 -10.309 < 2e-16 ***
## age
               0.053072
                         0.010934
                                    4.854 1.21e-06 ***
                          0.175063 2.998 0.00272 **
## male
               0.524847
## sysBP
               0.015454
                          0.003860 4.003 6.25e-05 ***
               0.007395
                          0.002844 2.600 0.00932 **
## glucose
## ---
## Signif. codes: 0 '***' 0.001 '**' 0.05 '.' 0.1 ' ' 1
## (Dispersion parameter for binomial family taken to be 1)
##
##
       Null deviance: 953.22 on 1097 degrees of freedom
## Residual deviance: 877.96 on 1093 degrees of freedom
## AIC: 887.96
## Number of Fisher Scoring iterations: 5
summary(mod.imp)
##
  glm(formula = TenYearCHD ~ age + male + sysBP + glucose + cigsPerDay,
##
       family = binomial(), data = d.test.imp)
##
## Deviance Residuals:
##
      Min
                1Q
                     Median
                                  3Q
                                          Max
## -1.5167 -0.6054 -0.4705 -0.3364
                                       2.6711
##
## Coefficients:
##
               Estimate Std. Error z value Pr(>|z|)
```

```
## (Intercept) -7.547948
                           0.690551 -10.930 < 2e-16 ***
                           0.010543 5.393 6.91e-08 ***
## age
                0.056863
## male
                0.383116
                           0.172167
                                      2.225 0.026064 *
                0.014077
                           0.003617
                                      3.892 9.93e-05 ***
## sysBP
## glucose
                0.007674
                           0.002826
                                      2.716 0.006616 **
                0.022526
                                      3.350 0.000809 ***
## cigsPerDay
                           0.006725
## Signif. codes: 0 '***' 0.001 '**' 0.05 '.' 0.1 ' ' 1
##
##
  (Dispersion parameter for binomial family taken to be 1)
##
##
       Null deviance: 1096.3 on 1270 degrees of freedom
## Residual deviance: 1008.4 on 1265 degrees of freedom
## AIC: 1020.4
##
## Number of Fisher Scoring iterations: 5
confint(mod.complete)
                      2.5 %
                                 97.5 %
## (Intercept) -8.797630570 -5.99288133
                0.031765493 0.07467830
## age
## male
                0.183045486 0.87024058
## sysBP
                0.007921332 0.02308639
## glucose
                0.001797197 0.01315057
confint(mod.imp)
                      2.5 %
                                 97.5 %
## (Intercept) -8.929814820 -6.21947856
## age
                0.036347183 0.07772072
## male
                0.045498113 0.72121913
## sysBP
                0.006992055 0.02119983
## glucose
                0.002132940 0.01338914
## cigsPerDay
                0.009279200 0.03569236
To account for the cherry picking in variables Lasso causes, we may calculate stricter p-values by multiplying
them by the number of covariates chosen for the final model.
summary(mod.complete)$coefficients[, 4] * length(summary(mod.complete)$coefficients[,
    4])
   (Intercept)
                                                  sysBP
                                                             glucose
                         age
## 3.207834e-24 6.050596e-06 1.358597e-02 3.123052e-04 4.660663e-02
summary(mod.imp)$coefficients[, 4] * length(summary(mod.imp)$coefficients[, 4])
## (Intercept)
                                     male
                                                 sysBP
                                                             glucose
                                                                       cigsPerDay
                         age
## 5.273971e-27 4.094036e-07 1.547359e-01 5.935507e-04 4.303852e-02 4.835542e-03
```

All coefficients continue to be significant after the adjustment for the complete model, although glucose are only barely so. For the imputed dataset, only male are no longer significant after the adjustment. This is a somewhat surprising result, since male where almost always included by the Lasso. Perhaps the absence of cigsPerDay and the high correlation between this covariate and male, which is 0.331 weighted male as more significant covarite than what is true.

We see that the AIC evaluates the model fitted on imputed data to be worse. This could be penalty for adding an extra coefficient in our model, so for curiosity we check also a model fitted using the imputed test set, but with the same covariates as chosen by the complete data.

```
# Check the AIC when using the same covariates?
mod.imp2 = glm(TenYearCHD ~ age + male + sysBP + glucose, data = d.test.imp, family = binomial())
summary(mod.imp2)
##
## Call:
##
  glm(formula = TenYearCHD ~ age + male + sysBP + glucose, family = binomial(),
##
       data = d.test.imp)
##
## Deviance Residuals:
##
       Min
                 10
                      Median
                                   3Q
                                           Max
## -1.4771 -0.6098 -0.4754
                             -0.3570
                                         2.5892
##
  Coefficients:
##
                Estimate Std. Error z value Pr(>|z|)
##
## (Intercept) -7.017429
                           0.661384 -10.610 < 2e-16 ***
                0.050017
                           0.010175
                                      4.916 8.85e-07 ***
## age
## male
                0.553023
                           0.162609
                                      3.401 0.000672 ***
                0.014043
                                      3.902 9.56e-05 ***
## sysBP
                           0.003599
                                      2.583 0.009788 **
## glucose
                0.007182
                           0.002780
##
## Signif. codes: 0 '*** 0.001 '** 0.01 '* 0.05 '.' 0.1 ' 1
##
##
  (Dispersion parameter for binomial family taken to be 1)
##
##
       Null deviance: 1096.3 on 1270 degrees of freedom
## Residual deviance: 1019.5 on 1266
                                      degrees of freedom
## AIC: 1029.5
##
## Number of Fisher Scoring iterations: 5
confint(mod.imp2)
##
                      2.5 %
                                 97.5 %
## (Intercept) -8.339200401 -5.74325610
## age
                0.030173778
                             0.07010211
                0.235243686
## male
                             0.87343100
## sysBP
                0.006995738
                             0.02113427
                0.001680692 0.01277382
## glucose
data.frame(Complete = round(summary(mod.complete)$aic, 2), Imputed = round(summary(mod.imp)$aic,
```

2), `Alternative imputed` = round(summary(mod.imp2)\$aic, 2))

```
## Complete Imputed Alternative.imputed
## 1 887.96 1020.52 1029.51
```

```
## Complete 2.80 0.04 0.69 0.02 0.01 NA
## Imputed 2.71 0.04 0.68 0.01 0.01 0.03
## Alternative Imputed 2.60 0.04 0.64 0.01 0.01 NA
```

There is almost no change in AIC between the two models used on the imputed data set, indicating that it is the imputation, despite increasing the size of the data, which causes the AIC to evaluate this model as worse. However, from the table above, which shows the width of the 95% confidence interval for the estimated coefficients, we note that the confidence intervals are slightly smaller for the imputed models. This is likely only due to the fact that the imputed data set is larger, and also that none of our imputed values deviated much from the mean. Therefore, the smaller confidence intervals do not necessarily imply that these are more precise estimates of the true coefficients.

Discussion

When we compare the chosen coefficients from the complete case data compared to the imputed data, we see that they correspond. Thus, in a data-rich situation imputation may only introduce unnecessary variance, without having an immediate effect on the quality of the model or inference. This was exemplified in the bootstrap estimates of the lasso regression on imputed data, where covariates where deemed more significant after imputing than before.

Furthermore, the problem with data leakage, both between independent sets used for fitting models, training and test sets used for fitting and validation, and within a single observation for instance between response and covariates, makes imputation vulnerable for unintended inaccuracies. We also did not use ROC-AUC to evaluate the model as both train and test data had been used to fit the final model. Hence, a third, independent subset would have been needed in order to run ROC-AUC calculations.

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