Liver Disease Classification

Samuel Higgins

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Introduction

```
library(tidyverse)
## -- Attaching packages ------ tidyverse 1.3.1 --
## v ggplot2 3.3.6
                     v purrr
                               0.3.4
## v tibble 3.1.7
                   v dplyr
                               1.0.9
## v tidyr
          1.2.0
                     v stringr 1.4.0
## v readr
            2.1.2
                     v forcats 0.5.1
## -- Conflicts ----- tidyverse_conflicts() --
## x dplyr::filter() masks stats::filter()
## x dplyr::lag()
                   masks stats::lag()
liverd <- read.csv("C:/Users/samue/Documents/College Notes/PyRe/Data sets/liverdrecords.csv")</pre>
liverd <- liverd %>% rename(Liver_Disease = Dataset) %>% rename(Total_Proteins = Total_Protiens) %>%
 mutate(Liver_Disease = ifelse(Liver_Disease == "1", 1, 0)) %>% na.omit
head(liverd)
    Age Gender Total_Bilirubin Direct_Bilirubin Alkaline_Phosphotase
## 1 65 Female
                          0.7
                                          0.1
                                                              187
                         10.9
                                          5.5
## 2 62
          Male
                                                              699
## 3 62
                          7.3
                                          4.1
                                                              490
          Male
## 4 58
         Male
                          1.0
                                          0.4
                                                              182
## 5 72
         Male
                          3.9
                                          2.0
                                                              195
## 6 46
          Male
                          1.8
                                          0.7
                                                              208
    Alamine_Aminotransferase Aspartate_Aminotransferase Total_Proteins Albumin
## 1
                         16
                                                   18
                                                                6.8
                                                                        3.3
## 2
                         64
                                                  100
                                                                7.5
                                                                        3.2
## 3
                         60
                                                                7.0
                                                                        3.3
                                                   68
                         14
## 4
                                                   20
                                                                6.8
                                                                        3.4
## 5
                                                                7.3
                         27
                                                   59
                                                                        2.4
                                                                7.6
## 6
                         19
                                                   14
                                                                        4.4
    Albumin_and_Globulin_Ratio Liver_Disease
## 1
                         0.90
```

```
## 2
                              0.74
## 3
                              0.89
                                                  1
## 4
                              1.00
                                                  1
## 5
                              0.40
                                                  1
## 6
                              1.30
                                                  1
```

This data set contains 583 observations with 416 liver disease patients and 167 non-afflicted patients. Each numeric variable (except for age) is a measurement relating to a liver protein, enzyme, etc. Categorical variables include liver disease status and sex. Liver patient records were collected from North East of Andhra Pradesh, India. The data was obtained here, however.

Hypothesis Testing

##

##

Response Alamine_Aminotransferase :

```
man1 <- manova(cbind(Total Bilirubin, Direct Bilirubin, Alkaline Phosphotase,
                    Alamine_Aminotransferase, Total_Proteins, Albumin,
                    Albumin_and_Globulin_Ratio, Age) ~ Liver_Disease, data = liverd)
summary(man1)
                 Df Pillai approx F num Df den Df
                  1 0.11601
                              9.3503
                                               570 3.647e-12 ***
## Liver_Disease
                                          8
## Residuals
## ---
## Signif. codes: 0 '***' 0.001 '**' 0.05 '.' 0.1 ' ' 1
summary.aov(man1)
   Response Total_Bilirubin :
##
##
                 Df Sum Sq Mean Sq F value
## Liver_Disease
                 1 1087.2 1087.15 29.408 8.633e-08 ***
## Residuals
                577 21330.3
                              36.97
## ---
## Signif. codes: 0 '***' 0.001 '**' 0.05 '.' 0.1 ' ' 1
##
   Response Direct_Bilirubin :
##
##
                 Df Sum Sq Mean Sq F value
                                              Pr(>F)
                  1 278.1 278.087 37.255 1.903e-09 ***
## Liver_Disease
## Residuals
                577 4307.0
                             7.464
## Signif. codes: 0 '*** 0.001 '** 0.01 '* 0.05 '.' 0.1 ' ' 1
##
##
   Response Alkaline_Phosphotase :
                 \mathtt{Df}
                     Sum Sq Mean Sq F value
                 1 1152846 1152846 20.075 8.982e-06 ***
## Liver Disease
## Residuals
                577 33135491
                               57427
## ---
## Signif. codes: 0 '***' 0.001 '**' 0.05 '.' 0.1 ' ' 1
##
```

Pr(>F)

Sum Sq Mean Sq F value

```
## Liver Disease
                 1 516055 516055 15.772 8.049e-05 ***
                577 18879287
## Residuals
                               32720
## Signif. codes: 0 '*** 0.001 '** 0.01 '* 0.05 '.' 0.1 ' 1
##
##
   Response Total Proteins :
                 Df Sum Sq Mean Sq F value Pr(>F)
                 1 0.77 0.76831 0.6527 0.4195
## Liver Disease
## Residuals
                577 679.22 1.17715
##
##
  Response Albumin :
##
                 Df Sum Sq Mean Sq F value
                                             Pr(>F)
## Liver_Disease
                 1 9.31 9.3118 15.114 0.0001129 ***
## Residuals
                577 355.48 0.6161
## ---
## Signif. codes: 0 '*** 0.001 '** 0.01 '* 0.05 '.' 0.1 ' 1
##
   Response Albumin_and_Globulin_Ratio :
##
                 Df Sum Sq Mean Sq F value
                                             Pr(>F)
## Liver Disease
                 1 1.571 1.57107 15.775 8.037e-05 ***
## Residuals
                577 57.465 0.09959
## Signif. codes: 0 '*** 0.001 '** 0.01 '* 0.05 '.' 0.1 ' 1
##
## Response Age :
                 Df Sum Sq Mean Sq F value Pr(>F)
                 1 2697 2697.09 10.416 0.00132 **
## Liver_Disease
                577 149401 258.93
## Residuals
## ---
## Signif. codes: 0 '***' 0.001 '**' 0.05 '.' 0.1 ' ' 1
pairwise.t.test(liverd$Total_Bilirubin, liverd$Liver_Disease, p.adj = "none")
##
## Pairwise comparisons using t tests with pooled SD
## data: liverd$Total_Bilirubin and liverd$Liver_Disease
##
##
    0
## 1 8.6e-08
## P value adjustment method: none
pairwise.t.test(liverd$Direct_Bilirubin, liverd$Liver_Disease, p.adj = "none")
##
## Pairwise comparisons using t tests with pooled SD
##
## data: liverd$Direct_Bilirubin and liverd$Liver_Disease
##
##
    0
## 1 1.9e-09
## P value adjustment method: none
```

```
pairwise.t.test(liverd$Alkaline_Phosphotase, liverd$Liver_Disease, p.adj = "none")
##
##
   Pairwise comparisons using t tests with pooled SD
## data: liverd$Alkaline_Phosphotase and liverd$Liver_Disease
##
     0
## 1 9e-06
##
## P value adjustment method: none
pairwise.t.test(liverd$Alamine_Aminotransferase, liverd$Liver_Disease, p.adj = "none")
##
   Pairwise comparisons using t tests with pooled SD
##
## data: liverd$Alamine_Aminotransferase and liverd$Liver_Disease
##
##
## 1 8e-05
## P value adjustment method: none
pairwise.t.test(liverd$Albumin, liverd$Liver_Disease, p.adj = "none")
##
   Pairwise comparisons using t tests with pooled SD
##
##
## data: liverd$Albumin and liverd$Liver_Disease
##
## 1 0.00011
## P value adjustment method: none
pairwise.t.test(liverd$Albumin_and_Globulin_Ratio, liverd$Liver_Disease, p.adj = "none")
##
## Pairwise comparisons using t tests with pooled SD
## data: liverd$Albumin_and_Globulin_Ratio and liverd$Liver_Disease
##
##
## 1 8e-05
## P value adjustment method: none
pairwise.t.test(liverd$Age, liverd$Liver_Disease, p.adj = "none")
```

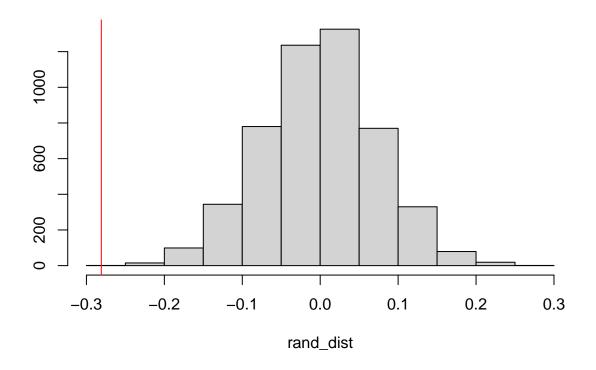
```
##
## Pairwise comparisons using t tests with pooled SD
##
## data: liverd$Age and liverd$Liver_Disease
##
## 0
## 1 0.0013
##
## P value adjustment method: none
.05/16 #Bonferroni correction
```

[1] 0.003125

In total 16 tests were conducted: 1 MANOVA, 8 ANOVAs, and 7 post-hoc t-tests. After a bonferroni adjustment, the probability of making a type I error is .0031. A one-way MANOVA was conducted to determine the effect of liver disease status on all of our numeric variables. Significant differences were found for liver disease status for at least one of our dependent variables, F = 9.350, P < .0001. After running univariate ANOVAs for each of our dependent variables, only "Total Proteins" was found to not be significant (F = 0.652, P = 0.419). Post-hoc t-tests were calculated to determine if liver disease status differed across our variables. Liver disease onset and absence were found to differ from each other significantly in regards to all the variables that were tested.

Randomization Test

```
rand_dist <- vector()</pre>
for(i in 1:5000){
  new <- data.frame(albumin = sample(liverd$Albumin), liver_disease = liverd$Liver_Disease)</pre>
  rand_dist[i] <- mean(new[new$liver_disease == "1" ,]$albumin) -</pre>
    mean(new[new$liver_disease == "0" ,]$albumin)
}
liverd %>% group_by(Liver_Disease) %>% summarise(ldmean = mean(Albumin)) %>%
  summarise(diff_mean = diff(ldmean))
## # A tibble: 1 x 1
     diff_mean
##
##
         <dbl>
## 1
        -0.281
hist(rand_dist, main = NULL, ylab = NULL); abline(v = -0.2809, col = "red")
```

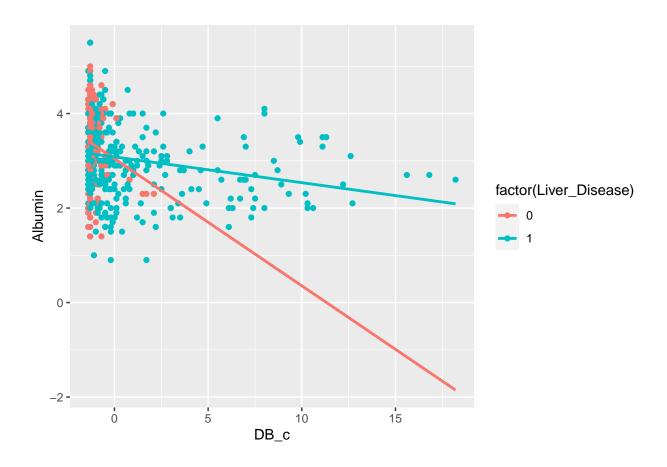


```
mean(rand_dist > .2809 | rand_dist < -.2809)</pre>
## [1] 0
t.test(Albumin ~ Liver_Disease, data = liverd)
##
##
    Welch Two Sample t-test
##
## data: Albumin by Liver_Disease
## t = 3.9067, df = 304.84, p-value = 0.0001153
## alternative hypothesis: true difference in means between group 0 and group 1 is not equal to 0
## 95 percent confidence interval:
   0.1394315 0.4224481
## sample estimates:
## mean in group 0 mean in group 1
##
          3.339394
                           3.058454
```

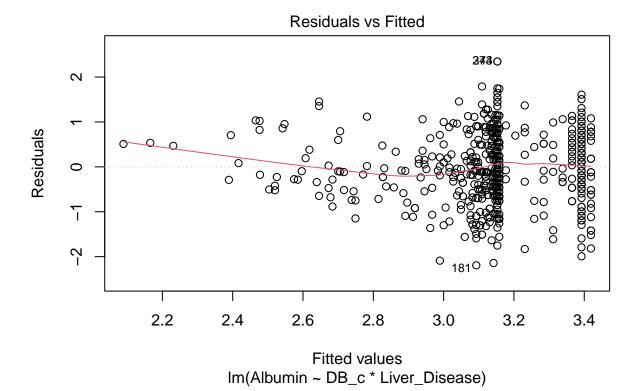
Albumin was chosen because low levels of the protein could indicate the onset of liver disease (more info can be found here). The null hypothesis is that there is no difference between the means of albumin and liver disease status. Likewise, the alternative hypothesis is that there is a difference between the means of albumin and liver disease status. After conducting a randomization test, a p-value of 0 was obtained, leading to a rejection of the null hypothesis and further conclude that there is a significant difference between the true means of albumin and liver disease status (t = 3.907, p = 0).

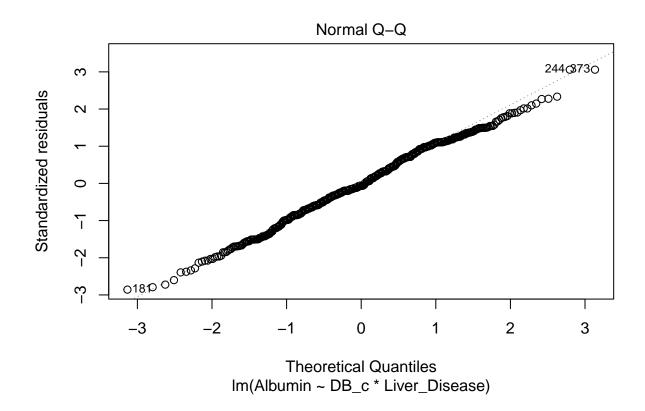
Linear Regression Model

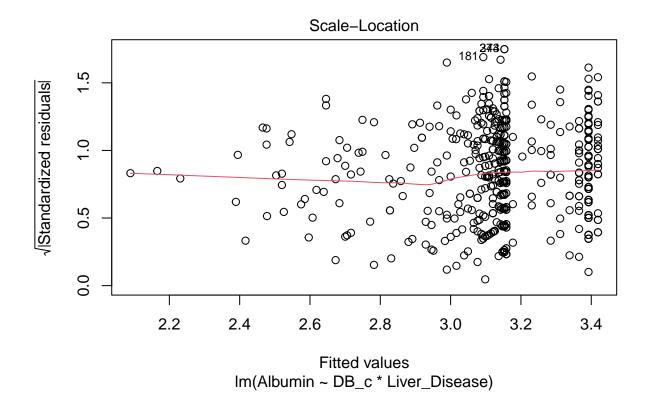
```
library(lmtest)
## Loading required package: zoo
##
## Attaching package: 'zoo'
## The following objects are masked from 'package:base':
##
##
      as.Date, as.Date.numeric
library(sandwich)
## Warning: package 'sandwich' was built under R version 4.2.1
liverd$DB_c <- liverd$Direct_Bilirubin - mean(liverd$Direct_Bilirubin)</pre>
ld_fit <- lm(Albumin ~ DB_c * Liver_Disease, data = liverd)</pre>
summary(ld_fit)
##
## Call:
## lm(formula = Albumin ~ DB_c * Liver_Disease, data = liverd)
##
## Residuals:
                 1Q Median
##
       Min
                                   3Q
## -2.19291 -0.49528 -0.04746 0.57218 2.34709
## Coefficients:
##
                     Estimate Std. Error t value Pr(>|t|)
## (Intercept)
                     ## DB_c
                     -0.26896
                                0.11497 -2.339
                                                  0.0197 *
## Liver_Disease
                      0.03818
                                 0.14478
                                         0.264
                                                  0.7921
## DB_c:Liver_Disease 0.21441
                                0.11557
                                         1.855
                                                 0.0641 .
## ---
## Signif. codes: 0 '*** 0.001 '** 0.01 '* 0.05 '.' 0.1 ' 1
## Residual standard error: 0.7685 on 575 degrees of freedom
## Multiple R-squared: 0.06915,
                                  Adjusted R-squared: 0.06429
\#\# F-statistic: 14.24 on 3 and 575 DF, p-value: 5.819e-09
liverd %>%
 ggplot(aes(x = DB_c, y = Albumin, color = factor(Liver_Disease))) +
 geom_point() +
 stat_smooth(method = "lm", se = F, fullrange = T)
## 'geom_smooth()' using formula 'y ~ x'
```

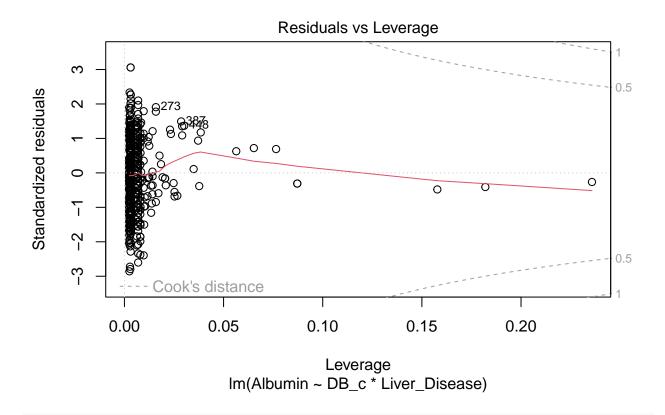


plot(ld_fit) #Assumptions Check









```
coeftest(ld_fit, vcov. = vcovHC(ld_fit))
##
## t test of coefficients:
##
##
                       Estimate Std. Error t value Pr(>|t|)
## (Intercept)
                       3.044144
                                   0.092244 33.0008 < 2.2e-16 ***
## DB c
                       -0.268956
                                   0.075238 -3.5747 0.0003801 ***
## Liver_Disease
                       0.038175
                                   0.099979
                                             0.3818 0.7027252
## DB c:Liver Disease
                       0.214409
                                   0.075949
                                             2.8231 0.0049212 **
```

'***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

Signif. codes:

The predicted albumin level for a non-afflicted patient with an average direct bilirubin level is $3.044~\rm g/dL$. Controlling for liver disease status, for every 1 mg/dL increase in direct bilirubin level, albumin decreases by 0.269 on average. Controlling for direct bilirubin, a patient with liver disease shows a 0.038 g/dL increase in albumin. The slope for direct bilirubin on albumin is 0.214 greater for liver disease afflicted patients than non-afflicted patients. After recomputing the regression with robust standard errors, the interaction between DB and liver disease status become significant, p = 0.0049. Average DB also becomes "more" significant, p = 0.00038 compared to p = 0.0197. Average DB and the interaction between average DB and liver disease status show significant variation in albumin (t = -3.57, p = 0.0003 & t = 2.82, p = 0.0049 respectively).

Bootstrapping

After bootstrapping standard errors, there is an increase in the SE values compared to the robust SEs that were calculated prior. However, compared to the original SEs, the values of the boot SEs are lower.

0.08769044

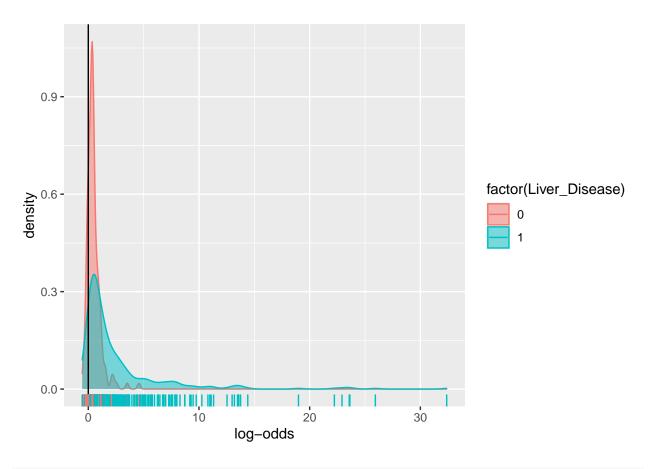
0.1115115

Logistic Regression and Cross Validation

0.1052656 0.08709625

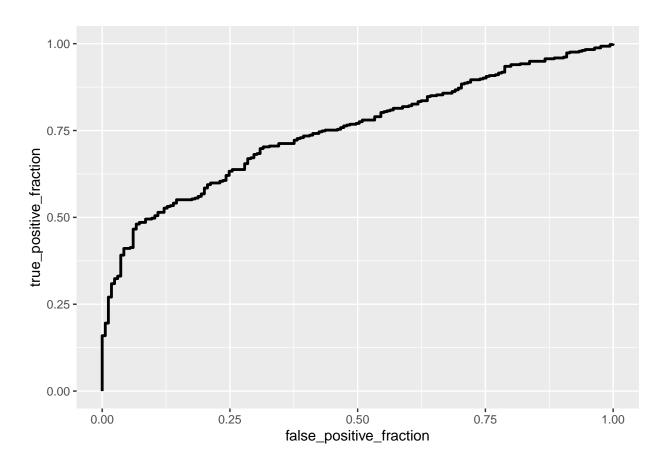
```
library(plotROC)
## Warning: package 'plotROC' was built under R version 4.2.1
ld_fit2 <- glm(Liver_Disease ~ Albumin + Alamine_Aminotransferase +</pre>
               Total_Proteins + Direct_Bilirubin, data = liverd, family = "binomial")
## Warning: glm.fit: fitted probabilities numerically 0 or 1 occurred
summary(ld_fit2)
##
## glm(formula = Liver_Disease ~ Albumin + Alamine_Aminotransferase +
       Total_Proteins + Direct_Bilirubin, family = "binomial", data = liverd)
##
##
## Deviance Residuals:
##
       Min
                 1Q
                     Median
                                   3Q
                                           Max
## -3.0268 -1.1528
                     0.4321
                               0.9331
                                        1.4186
##
## Coefficients:
                             Estimate Std. Error z value Pr(>|z|)
                                        0.641125 -0.751 0.452483
## (Intercept)
                            -0.481666
## Albumin
                            -0.742444
                                        0.245830 -3.020 0.002527 **
                                        0.003876 3.787 0.000153 ***
## Alamine_Aminotransferase 0.014678
## Total Proteins
                             0.415451
                                        0.172685
                                                   2.406 0.016136 *
## Direct_Bilirubin
                             0.578334
                                       0.178999 3.231 0.001234 **
## Signif. codes: 0 '*** 0.001 '** 0.01 '* 0.05 '.' 0.1 ' 1
```

```
##
## (Dispersion parameter for binomial family taken to be 1)
##
##
       Null deviance: 692.01 on 578 degrees of freedom
## Residual deviance: 582.64 on 574 degrees of freedom
## AIC: 592.64
## Number of Fisher Scoring iterations: 7
#Confusion Matrix
ld_prob <- predict(ld_fit2, type = "response")</pre>
table(predict = as.numeric(ld_prob > .5), truth = liverd$Liver_Disease) %>% addmargins
##
          truth
## predict
           0 1 Sum
           33 25 58
##
       0
##
       1
           132 389 521
##
       Sum 165 414 579
liverd$logit <- predict(ld_fit2, type = "link")</pre>
#AUC plot
liverd %>%
  ggplot() +
  geom_density(aes(logit, color = factor(Liver_Disease), fill = factor(Liver_Disease)), alpha = 0.5) +
  geom_vline(xintercept = 0) +
  xlab("log-odds") +
  geom_rug(aes(logit, color = factor(Liver_Disease)))
```



```
#ROC curve

ld_ROC <- liverd %>%
    ggplot() +
    geom_roc(aes(d = Liver_Disease, m = ld_prob), n.cuts = 0)
ld_ROC
```



```
calc_auc(ld_ROC)
```

```
## PANEL group AUC
## 1 1 -1 0.7494071
```

Warning: glm.fit: fitted probabilities numerically 0 or 1 occurred

```
## Warning: glm.fit: fitted probabilities numerically 0 or 1 occurred
## Warning: glm.fit: fitted probabilities numerically 0 or 1 occurred
## Warning: glm.fit: fitted probabilities numerically 0 or 1 occurred
## Warning: glm.fit: fitted probabilities numerically 0 or 1 occurred
## Warning: glm.fit: fitted probabilities numerically 0 or 1 occurred
## Warning: glm.fit: fitted probabilities numerically 0 or 1 occurred
summarise_all(diags, mean)
                             spec
                                        ppv
## 1 0.7202057 0.937595 0.1762197 0.7406438 0.7446187
yhat <- predict(cvfit)</pre>
mean((liverd$Liver_Disease - yhat)^2)
## Warning in liverd$Liver_Disease - yhat: longer object length is not a multiple
## of shorter object length
## [1] 11.16522
ld_fit3 <- glm(Liver_Disease ~ Albumin + Alamine_Aminotransferase + Total_Proteins +</pre>
                 Direct_Bilirubin, data = liverd, family = "binomial")
## Warning: glm.fit: fitted probabilities numerically 0 or 1 occurred
summary(ld_fit3)
## Call:
## glm(formula = Liver_Disease ~ Albumin + Alamine_Aminotransferase +
       Total_Proteins + Direct_Bilirubin, family = "binomial", data = liverd)
##
## Deviance Residuals:
       Min
                1Q
                    Median
                                   3Q
                                           Max
## -3.0268 -1.1528
                    0.4321
                                        1.4186
                               0.9331
##
## Coefficients:
##
                             Estimate Std. Error z value Pr(>|z|)
## (Intercept)
                            -0.481666
                                        0.641125 -0.751 0.452483
                                        0.245830 -3.020 0.002527 **
## Albumin
                            -0.742444
## Alamine_Aminotransferase 0.014678
                                        0.003876 3.787 0.000153 ***
                                                   2.406 0.016136 *
## Total_Proteins
                             0.415451
                                        0.172685
## Direct Bilirubin
                             0.578334
                                        0.178999
                                                   3.231 0.001234 **
## Signif. codes: 0 '*** 0.001 '** 0.01 '* 0.05 '.' 0.1 ' 1
##
```

```
## (Dispersion parameter for binomial family taken to be 1)
##
## Null deviance: 692.01 on 578 degrees of freedom
## Residual deviance: 582.64 on 574 degrees of freedom
## AIC: 592.64
##
## Number of Fisher Scoring iterations: 7
```

Controlling for alamine aminotransferase, total proteins, and direct bilirubin, albumin has a significant negative impact on the odds of liver disease onset. Controlling for albumin, total proteins, and direct bilirubin, alamine aminotransferase has a significant positive impact on the odds of liver disease onset. Controlling for albumin, alamine aminotransferase, and direct bilirubin, total proteins has a significant positive impact on the odds of liver disease onset. Controlling for albumin, alamine aminotransferase, and total proteins, direct bilirubin has a significant positive impact on the odds of liver disease onset. After computing a confusion matrix, the sensitivity for the model is 0.929 and the specificity is a value of .169. Calculating the AUC gives a value of 0.740, which tells us that the model is satisfactory, however given the domain (healthcare), the model performance is unacceptable in determining liver disease status among patients. By performing 10-fold cross validation on the model, there is a very miniscule increase in auc (=0.743).

LASSO

```
library(glmnet)

## Warning: package 'glmnet' was built under R version 4.2.1

## Loading required package: Matrix

## Attaching package: 'Matrix'

## The following objects are masked from 'package:tidyr':

## expand, pack, unpack

## Loaded glmnet 4.1-4

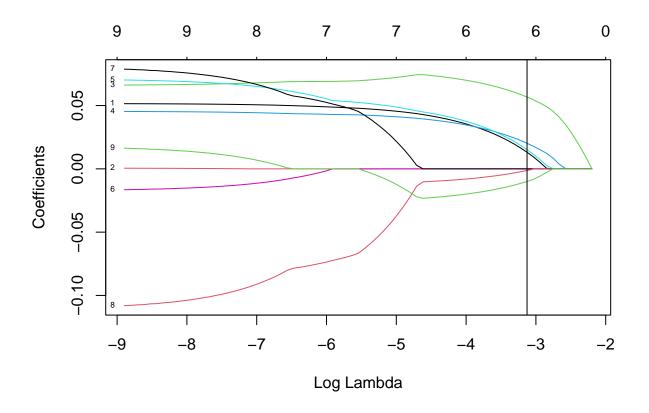
liverd$LD_n <- liverd$Liver_Disease %>% as.numeric #code for orignial LD_n was lost, here for knit

y <- as.matrix(liverd$Liver_Disease)

x <- liverd %>% dplyr::select(-Liver_Disease, -Gender, -DB_c, -LD_n, -logit) %>% mutate_all(scale) %>%

cv <- cv.glmnet(x,y)

plot(cv$glmnet(fit, "lambda", label = T); abline(v = log(cv$lambda.1se)) #Plot looks cool</pre>
```



```
lasso1 <- glmnet(x, y, lambda = cv$lambda.1se)
coef(lasso1)</pre>
```

```
## 10 x 1 sparse Matrix of class "dgCMatrix"
##
## (Intercept)
                               0.715025907
                                0.013123315
## Age
## Total_Bilirubin
                                0.056733246
## Direct_Bilirubin
## Alkaline_Phosphotase
                                0.020210317
## Alamine_Aminotransferase
                                0.015149343
## Aspartate_Aminotransferase
## Total_Proteins
## Albumin
                              -0.001284994
## Albumin_and_Globulin_Ratio -0.009968153
```

```
#LASSO Assisted 10-Fold CV
k = 10

ld_cv2 <- liverd[sample(nrow(liverd)),]
folds2 <- cut(seq(1:nrow(liverd)), breaks = k, labels = F)

diags2 <- NULL
for(i in 1:k){
   train2 <- ld_cv[folds != i,]</pre>
```

```
test2 <- ld_cv[folds == i,]</pre>
  truth2 <- test2$Liver_Disease</pre>
  cvfit2 <- glm(Liver_Disease ~ Albumin + Alkaline_Phosphotase + Age +</pre>
                  Direct_Bilirubin + Alamine_Aminotransferase +
                  Albumin_and_Globulin_Ratio, data = train2, family = "binomial")
  probs2 <- predict(cvfit, newdata = test2, type = "response")</pre>
  diags2 <- rbind(diags, class_diag(probs2, truth2)) #class_diag for convenience
## Warning: glm.fit: fitted probabilities numerically 0 or 1 occurred
## Warning: glm.fit: fitted probabilities numerically 0 or 1 occurred
## Warning: glm.fit: fitted probabilities numerically 0 or 1 occurred
## Warning: glm.fit: fitted probabilities numerically 0 or 1 occurred
summarise_all(diags2, mean)
##
           acc
                    sens
                               spec
                                                     auc
                                          ppv
## 1 0.7205632 0.9432682 0.1783815 0.7372856 0.7537204
yhat2 <- predict(cvfit2)</pre>
mean((liverd$Liver_Disease - yhat2)^2)
## Warning in liverd$Liver_Disease - yhat2: longer object length is not a multiple
## of shorter object length
## [1] 10.02984
```

After performing a LASSO on the data, the variables age, direct bilirubin, alkaline phosphotase, alamine aminotransferase, albumin, and albumin/globulin ratio are retained. The mean-squared error is a value of 12.531, which is larger than the mean-squared error that was obtained prior (1.123).