BST 260 Final Project

Xiao Gu

Introduction

Ischemic heart disease (IHD) has been identified as a leading cause of death globally (Ref). Compelling evidence showed that lifestyle changes could be effective strategies for secondary preventions of IHD (Ref). Therefore, to reduce the burden of IHD mortality, an efficient tool for IHD screening and early diagnosis is warranted. A machine learning algorithm that is developed with serum metabolites, cardiometabolic biomarkers, and self-reported phenotypic data is promising in simplifying the process and reduce the cost of IHD screening/diagnosis. IHD status could be accurately detected with a simple blood draw and metabolomic profiling. In this project, I aim to develop such an algorithm using data from a European population.

I will use data from the MetaCardis consortium that recruited participants aged 18-75 years from Denmark, France, and Germany (Ref). The data was published early this year as the supplementary material of an article on Nature Medicine (Ref). The original study included 372 individuals with IHD. These IHD cases were further classified into acute coronary syndrome (n = 112), chronic ischemic heart disease, (n = 158), and heart failure (n = 102). With a case-control design, the study also included 3 groups of controls matched on varies factors. The raw data includes 1,882 observations including repeated records with the same participant ID but different case-control status.

For this project, I will use records from the 372 IHD cases and 372 controls matched on type 2 diabetes (T2D) status and body mass index (BMI). I will also extract data for age, gender, fasting plasma triglycerides, adiponectin, and CRP, systolic and diastolic blood pressure, left ventricular ejection fraction, physical activity level, and 1,513 log-transformed values of serum metabolites.

Exploratory data analysis

After reading in the data, I first filtered the observations to keep the IHD cases and their controls matched by T2D status and BMI. I then merged metabolites data with cardiometabolic biomarkers and self-reported phenotypic data to create a `main` dataset with 744 rows and 1522 columns. I noticed that several participants do not have any metabolites data, and therefore, need to be removed. Additionally, around 30% of participants had missing values for left ventricular ejection fraction and physical activity level. Many machine learning techniques could not be implemented with that many missing and it would also not be appropriate to replace the missings with any arbitrarily selected value. So I removed these two potential predictors from my analyses. Finally, for variables with less than 10% missing data, I replaced the missing values with the median of the non-missing data. The cleaned `main` dataset had 603 rows and 1522 columns.

I then preprocessed the data to remove non-informative predictors with near-zero variances. Given that I planned to train as least one of my algorithms with regression, it would be better to have more predictors normally distributed so that model efficiencies could be improved. I tested the normality of each predictor with Shapiro-wilks Test and summarized the p-values. I found that only 101 predictors are normally distributed. It is also note-worthy that the metabolite values from the raw data were all log-transformed. Obviously, log-tranformation did not normalize the distributions successfully. So I transformed all metabolite values back to the original scale and used rank-based inverse normal transformation (INT) to normalized the distributions instead. As examples, histograms showing the distributions of oleoylcarnitine (C18:1) and S-methylcysteine sulfoxide before and after the transformation were shown. I ended up having 840 predictors normalized successfully.

Methodologies to use

The outcome that my algorithm aimed to predict is the binary IHD status (non-case = 0, case = 1). Considering that I had 1422 predictors, I would use principle component analysis (PCA) to reduce dimensions. I would keep principle components that account for at least 70% of variability as new predictors, and train a model with logistic regression, and a model with K-nearest neighbor (KNN). Given that the principle components are hard to interpret and algorithms developed based on PCA could be difficult to implement, I would train another KNN model with all 1422 predictors instead. Random forest would be the 4th training method I would use. Finally, I will use ensemble to combine the results of all four algorithms. For all algorithms, I would evaluate the overall accuracy, sensitivity, specificity, F_1 score, and ROC curve. I would use a β of 2 to calculate the F_1 score because higher sensitivity is more important than high specificity when predicting disease. In other words, false positive will be less costly than false negative in this scenario. I would also use cross-validation and bootstrapping to tune the model parameters.

Results

For all the model training and fitting, I partitioned the `main` dataset, which includes IHD case status and all predictors, into a training and a testing dataset. Matrices for predictors and cases were also created. I then train and assess the models with the following 4 approaches: 1) PCA + logistic regression; 2) PCA + KNN; 3) KNN; 4) Random forest.

PCA + logistic regression

The PCA in the training set generated 483 principle components (PC) from 1422 predictors including age, gender, fasting plasma triglycerides, adiponectin, and CRP, systolic and diastolic blood pressure, and 1415 inverse normal transformed serum metabolites. After evaluating the proportion of variance explained by each PC, I selected the first 69 PCs that account for 70% of the total variance as new predictors. I fitted a logistic regression with IHD cases as the dependent variable and the 69 PCs as the independent variables. For the logistic regression, there was no model parameter to tune. To make predictions in the testing set, I used the PC rotations to transform all 1422 predictors in the testing set into 483 PCs and kept the first 69 PCs. The logistic regression estimates were then used to predict the probability of having IHD cases in the testing set. Participants with a predicted probability of having IHD over 0.5 were defined as predicted IHD cases.

The overall accuracy of my predicted IHD cases from the logistic regression was 0.875 with a 95% confidence interval of (0.802, 0.928). This algorithm had a sensitivity of 0.892, a specificity of 0.854, and an F_1 score of 0.890. I also plotted the ROC and observed an area under the curve (AUC) of 0.946, which was very high.

PCA + KNN

I then used KNN to train the model with the 69 PCs as predictors. To select the parameter K that maximize the accuracy, I used 10-fold cross-validation with bootstrapping as the resampling scheme. Given that I have already reduced the dimension to 69 and we only have 603 observations, I did not worry much about the computation time of using 10-fold cross-validation. I fitted the model with K values from 2 to 100 with 20 as the increment. After plotting the model accuracy under different K values, I was not able to identify a clear optimized K given that the curve of accuracy did not go down within the specified K range. Therefore, I fitted the model with K values from 5 to 150 with 10 as the increment instead. I identified 75 as the K for the maximum model accuracy and fitted the model again with this value. The fitted KNN model was then used to predict the IHD cases in the testing set.

Using the combination of PCA and KNN, the overall accuracy of my predicted IHD cases was 0.842 with a 95% confidence interval of (0.764, 0.902). Comparing to the algorithm developed with PCA and logistic regression, this algorithm had a higher sensitivity of 0.923, a lower specificity of 0.746, and a higher F_1 score of 0.898. I plotted the ROC and observed an AUC of 0.889.

KNN

The previous two algorithms developed based on selected PCs already performed well in predicting IHD cases. However, people who wants to implement these two algorithms have to use the PCA rotations to transform their data first. That could increase the burden of using these algorithms, particularly in clinical settings. Also, the PCs no longer have biological meaning, and therefore, could be difficult to interpret. With these concerns, I developed another KNN-based algorithm with the 1422 predictors, including 1415 serum metabolites.

Given that the sample size of my study is not large, I used 10-fold cross-validation with bootstrapping as the resampling scheme to select the parameter K again. I found 65 as the K that maximize the model accuracy after fitting the model with K values from 5 to 150 with 10 as the increment. I then fitted the model in the training set and predicted the IHD cases in the testing set. The overall accuracy of my predicted IHD cases was 0.800 with a 95% confidence interval of (0.717, 0.868). Comparing to the algorithm developed with PCA and KNN, this KNN algorithm had a slightly higher sensitivity of 0.939. But the specificity dropped to 0.636. The F_1 score was 0.894. I plotted the ROC and observed an AUC of 0.897.

Random forest

The last approach I used to train my model is random forest. It is more computationally intensive because predictors have to be randomly selected using bootstrapping to predict a single tree. To stabilize accuracy, hundreds of trees might need to be predicted. Also, I have to change the number of predictors being sampled at each bootstrap iteration to find the one that maximize the accuracy. Therefore, I started training the model with 15 trees and tuning the number of predictors to be sampled between 10 and 1000 with 100 as the increment. I implemented a 5-fold cross-validation. The plot of error against number of trees showed that the accuracy improves as we add more trees and stabilized at around 100 trees. In my second attempt, I changed the number of trees to be predicted to 100. The plot of accuracy by the number of randomly sampled predictors did show a maximum point. However, it seems that the range of 10 to 1000 predictors was too large. So I further tuned the number of predictors to be sampled from 10 to 500 with 20 as the increment. It turned out that randomly sample 150 predictors and predict 100 trees maximized and stabilized the accuracy of model prediction.

The overall accuracy of my predicted IHD cases from the random forest model was 0.900 with a 95% confidence interval of (0.832, 0.947). This algorithm had a high sensitivity of 0.939, a high specificity of 0.855, an high F_1 score of 0.927, and a high AUC of 0.958.

Conclusion

In this project, I aimed to develop an algorithm that uses serum metabolites, cardiometabolic biomarkers, and self-reported phenotypic data to predict ischemic heart disease (IHD) status in a European population. I obtained my data from a paper published early this year on Nature Medicine (Ref). For data preprocessing, I removed observations with missing metabolites measures, and predictors with at least around 30% of missing data. For predictors with small amount of missing data, I replaced the missing values with median values. Additionally, predictors with near-zero variance were also excluded. I used 4 approaches to train my model. The first two approaches used PCA to reduce dimension from 1422 predictors. A logistic regression and a KNN model were trained and fitted with the selected 69 PCs. The 3rd approach was also based on KNN but fitted the model with the 1422 predictors. The last approach used random forest to develop the algorithm. I summarized the sensitivity, specificity, overall accuracy, F_1 score, and AUC of all models in a table. I also conducted an ensemble to combine results from the KNN model and random forest model and showed the performance at the end of the table. ROC curves were plotted on the same figure for comparison.

According to the table, the two models developed with PCs had lower sensitivity than those trained with all predictors. The KNN and random forest models both had a very high sensitivity of 0.938. The two models developed with KNN had lower specificity than the others. The random forest model also had a relatively high specificity of 0.855. The KNN model biologically meaningful predictors had the lowest overall accuracy while the random forest model had the highest overall accuracy. The models with PCs as predictors and used

logistic regression for fitting had an overall accuracy of 0.875 while the model using PCs and KNN had an accuracy of 0.842. When evaluating with F_1 score, the random forest model performed the best while the rest three models performed similarly. Finally, the random forest model had the highest AUC, followed by the PCA + KNN model. It is interesting that ensemble of KNN and random forest did not further improve the model performance. In conclusion, the algorithm developed with random forest performed the best in all measures.

Successful?

Reference

Appendix

```
library(tidyverse)
library(readxl)
library(caret)
library(RNOmni)
library(pROC)
library(randomForest)
library(kableExtra)

#Read in
meta <- read_excel("/Users/xgu/Documents/Harvard/Fall 2022/BST260/bst260project/41591_2022_1688_MOESM3_
                   sheet = 13, skip = 1, na = "NA", col_types = "guess")
demo <- read_excel("/Users/xgu/Documents/Harvard/Fall 2022/BST260/bst260project/41591_2022_1688_MOESM3_
                   sheet = 10, skip = 1, na = "NA", col_types = c("text", "text", rep("numeric", 22), "

#Selection and filtering
demo_new <- demo %>%
  filter(Status %in% c("IHD372", "MMC372")) %>%
  mutate(case = case_when(Status == "MMC372" ~ 0, TRUE ~ 1),
         Gender = case_when(Gender == "Male" ~ 1, TRUE ~ 0)) %>%
  rename(age = "Age (years)", tag = "Fasting plasma triglycerides (mmol/L)",
         adiponectin = "Fasting plasma adiponectin (mg/L)", crp = "Fasting plasma CRP (mg/L)",
         sbp = "Systolic blood pressure (mmHg)", dbp = "Diastolic blood pressure (mmHg)",
         lvef = "Left ventricular ejection fraction (%)", act = "Physical activity (h/week)") %>%
  select(ID, case, age, tag, adiponectin, crp, sbp, dbp, Gender, lvef, act)

meta_new <- meta %>%
  filter(Status %in% c("IHD372", "MMC372")) %>%
  select(-c(Status))

#Merge
main <- demo_new %>%
  left_join(meta_new, by = "ID")
head(main)
```

```
## # A tibble: 6 x 1,524
##   ID       case   age   tag adipo~1   crp   sbp   dbp Gender  lvef   act acetate
##   <chr>   <dbl> <dbl> <dbl>   <dbl> <dbl> <dbl> <dbl>  <dbl> <dbl> <dbl>   <dbl>
## 1 x14MCx~     0    48 1.00     5.01 0.897  104   60.5      0    60  1.25   -3.91
## 2 x14MCx~     0    49 1.00     4.03 1.11   111   70        0    NA  1.02   -3.91
## 3 x14MCx~     0    54 1.48     6.26 2.05   106.  68.5      1    67  8.75   -3.51
## 4 x14MCx~     0    47 0.787    3.44 0.67   138   78        1    67  4.12   -3.91
## 5 x30MCx~     0    50 0.54     7.82 2.63   154   91.5      0    NA 20.6    NA
```

```
## 6 x30MCx~     0    66 0.59    11.0  0.427  110.  65.5      0    NA 14      -3.91
## # ... with 1,512 more variables: acetone <dbl>, artemisin <dbl>,
## #   `beta-sitosterol` <dbl>, betaine <dbl>, `betaine-aldehyde` <dbl>,
## #   butyrylcarnitine <dbl>, catechol <dbl>, cellotetraose <dbl>, choline <dbl>,
## #   `D-trehalose` <dbl>, `D-lyxose` <dbl>, `D-malate` <dbl>,
## #   `D-sorbitol` <dbl>, `D-threitol` <dbl>, decanoylcarnitine <dbl>,
## #   glyceraldehyde <dbl>, ethanol <dbl>, ethanolamine <dbl>, formate <dbl>,
## #   glucoheptonate <dbl>, glycolate <dbl>, halostachine <dbl>, ...
```

```
#Check missing
pctmiss <- function(x){
  pctmiss <- sum(is.na(x))/length(x)
  return(pctmiss)
}
miss <- as.data.frame(sapply(main, pctmiss))
head(miss)
```

```
##             sapply(main, pctmiss)
## ID                     0.00000000
## case                   0.00000000
## age                    0.00000000
## tag                    0.04704301
## adiponectin            0.05645161
## crp                    0.05779570
```

```
main <- main %>%
  select(-c("lvef", "act")) %>%
  filter(acetate != "NA", spermidine != "NA") %>%
  mutate(tag = case_when(is.na(tag) ~ median(tag, na.rm = TRUE), TRUE ~ tag),
         adiponectin = case_when(is.na(adiponectin) ~ median(adiponectin, na.rm = TRUE), TRUE ~ adipone
         crp = case_when(is.na(crp) ~ median(crp, na.rm = TRUE), TRUE ~ crp),
         sbp = case_when(is.na(sbp) ~ median(sbp, na.rm = TRUE), TRUE ~ sbp),
         dbp = case_when(is.na(dbp) ~ median(dbp, na.rm = TRUE), TRUE ~ dbp))
head(main)
```

```
## # A tibble: 6 x 1,522
##   ID          case   age   tag adipon~1   crp   sbp   dbp Gender acetate acetone
##   <chr>      <dbl> <dbl> <dbl>    <dbl> <dbl> <dbl> <dbl>  <dbl>   <dbl>   <dbl>
## 1 x14MCx1158     0    48 1.00      5.01 0.897  104   60.5      0   -3.91   -3.91
## 2 x14MCx2932     0    49 1.00      4.03 1.11   111   70        0   -3.91   -3.22
## 3 x14MCx2498     0    54 1.48      6.26 2.05   106.  68.5      1   -3.51   -3.51
## 4 x14MCx2237     0    47 0.787     3.44 0.67   138   78        1   -3.91   -4.95
## 5 x30MCx1828     0    66 0.59     11.0  0.427  110.  65.5      0   -3.91   -3.91
## 6 x30MCx1314     0    54 1.41      2.6  1.4    128.  75.5      1   -2.81   -3.91
## # ... with 1,511 more variables: artemisin <dbl>, `beta-sitosterol` <dbl>,
## #   betaine <dbl>, `betaine-aldehyde` <dbl>, butyrylcarnitine <dbl>,
## #   catechol <dbl>, cellotetraose <dbl>, choline <dbl>, `D-trehalose` <dbl>,
## #   `D-lyxose` <dbl>, `D-malate` <dbl>, `D-sorbitol` <dbl>, `D-threitol` <dbl>,
## #   decanoylcarnitine <dbl>, glyceraldehyde <dbl>, ethanol <dbl>,
## #   ethanolamine <dbl>, formate <dbl>, glucoheptonate <dbl>, glycolate <dbl>,
## #   halostachine <dbl>, hydroquinone <dbl>, isovalerylcarnitine <dbl>, ...
```

```
var <- main %>% select(-c("ID", "case"))

#Preprocessing
nzv <- nearZeroVar(var)
```

```r
col_index <- setdiff(1:ncol(var), nzv)
length(col_index)
```

```
## [1] 1422
```

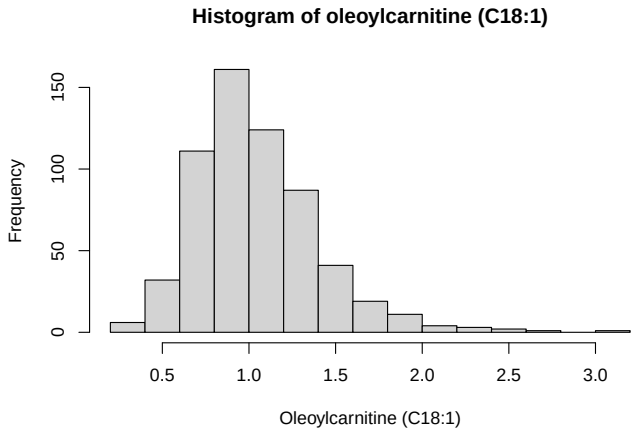
```r
var_proc <- var[,col_index]

#check normality
normality <- data.frame()
for (i in 1:length(colnames(var_proc))){
  normality[i, 1] <- colnames(var_proc)[i]
  normality[i, 2] <- shapiro.test(pull(var_proc[,i]))$p.value
  colnames(normality) <- c("metabolites", "shapiro.p")
}
table(ifelse(normality$shapiro.p >0.05, 1, 0))
```

```
##
##    0    1
## 1321  101
```

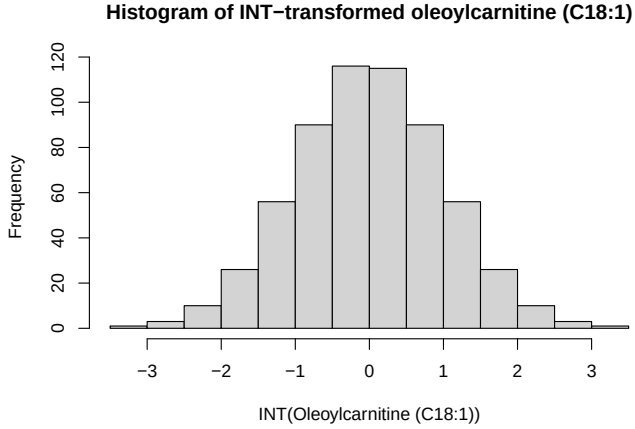
```r
#which(normality$shapiro.p > 0.05)

#Log transformation not work
m <- as.matrix(var_proc[,8:1422])
exp_m <- exp(m)
var_proc_exp <- cbind(var_proc[,1:7], as.data.frame(exp_m))

var_proc_int <- as.data.frame(sapply(var_proc_exp, RankNorm))

#check normality again!
normality_int <- data.frame()
for (i in 1:length(colnames(tibble(var_proc_int)))){
  normality_int[i, 1] <- colnames(tibble(var_proc_int))[i]
  normality_int[i, 2] <- shapiro.test(pull(tibble(var_proc_int)[,i]))$p.value
  colnames(normality_int) <- c("metabolites", "shapiro.p")
}
table(ifelse(normality_int$shapiro.p >0.05, 1, 0))
```

```
##
##   0   1
## 582 840
```

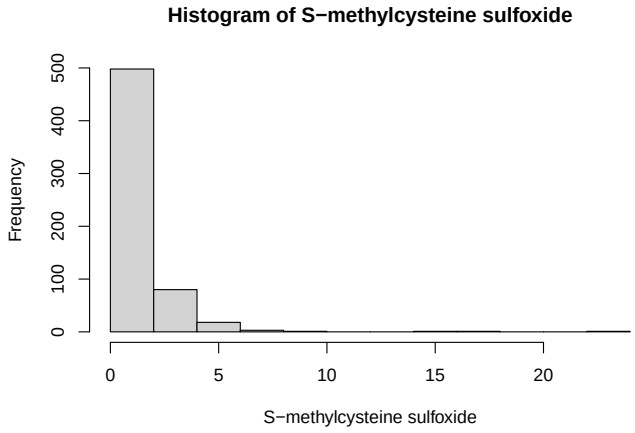
```r
#which(normality_int$shapiro.p > 0.05)

hist(var_proc_exp$`oleoylcarnitine (C18:1)`, main = "Histogram of oleoylcarnitine (C18:1)", xlab = "Ole
```



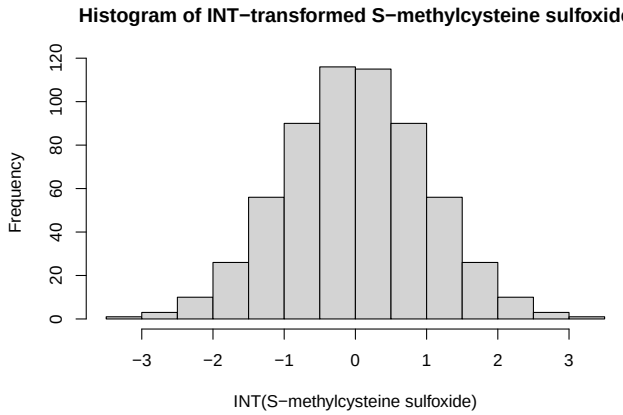

```
hist(var_proc_int$`oleoylcarnitine (C18:1)`, main = "Histogram of INT-transformed oleoylcarnitine (C18:
```




```
hist(var_proc_exp$`S-methylcysteine sulfoxide`, main = "Histogram of S-methylcysteine sulfoxide", xlab =
```




```
hist(var_proc_int$`S-methylcysteine sulfoxide`, main = "Histogram of INT-transformed S-methylcysteine su
```




```
#Split data
set.seed(34324)
main_new <- cbind(main[,1:2], var_proc_int)
train_index <- createDataPartition(main_new$case, times = 1, p = 0.8, list = FALSE)
train_set <- main_new[train_index,]
test_set <- main_new[-train_index,]

#X and Y matrix
x_train <- as.matrix(train_set[,3:1424])
y_train <- factor(train_set$case)
x_test <- as.matrix(test_set[,3:1424])
y_test <- factor(test_set$case)
```

```
#######PCA
col_means <- colMeans(x_train)

pca <- prcomp(x_train)
s_pca_3 <- summary(pca)$importance[3,] ##69 pc
head(s_pca_3, 69)
```

```
##     PC1     PC2     PC3     PC4     PC5     PC6     PC7     PC8     PC9    PC10
## 0.09528 0.14187 0.17858 0.21450 0.24215 0.26855 0.29403 0.31393 0.33268 0.35060
##    PC11    PC12    PC13    PC14    PC15    PC16    PC17    PC18    PC19    PC20
## 0.36595 0.37976 0.39264 0.40522 0.41732 0.42849 0.43910 0.44940 0.45886 0.46815
##    PC21    PC22    PC23    PC24    PC25    PC26    PC27    PC28    PC29    PC30
## 0.47727 0.48587 0.49381 0.50149 0.50892 0.51619 0.52337 0.53013 0.53645 0.54261
##    PC31    PC32    PC33    PC34    PC35    PC36    PC37    PC38    PC39    PC40
## 0.54863 0.55446 0.56017 0.56585 0.57135 0.57666 0.58171 0.58672 0.59164 0.59644
##    PC41    PC42    PC43    PC44    PC45    PC46    PC47    PC48    PC49    PC50
## 0.60116 0.60573 0.61013 0.61444 0.61872 0.62298 0.62701 0.63098 0.63494 0.63877
##    PC51    PC52    PC53    PC54    PC55    PC56    PC57    PC58    PC59    PC60
## 0.64255 0.64624 0.64986 0.65345 0.65694 0.66041 0.66380 0.66717 0.67048 0.67372
##    PC61    PC62    PC63    PC64    PC65    PC66    PC67    PC68    PC69
## 0.67691 0.68005 0.68315 0.68620 0.68922 0.69224 0.69519 0.69808 0.70096
```

```
pc <- 69
x_train_pc <- pca$x[,1:pc]
```

```
#####PCA + glm
glm_tmp <- as.data.frame(cbind(train_set$case, x_train_pc))
glm_tmp <- glm_tmp %>% rename(case = V1)
fit_glm <- glm(case ~., data = glm_tmp, family = "binomial")
```

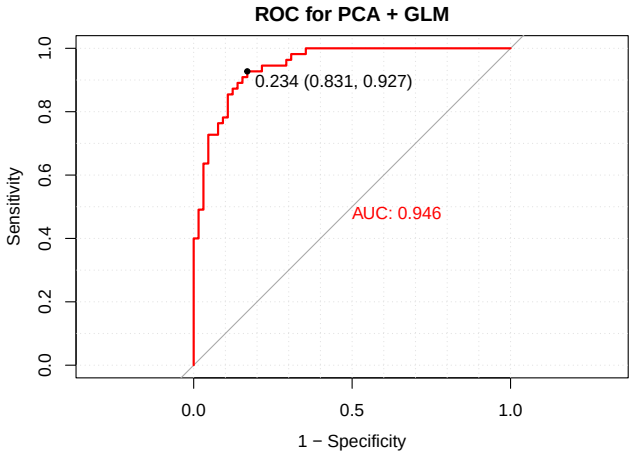
```
x_test_pc_pre <- sweep(x_test,2,col_means) %*% pca$rotation
x_test_pc <- x_test_pc_pre[,1:pc]
y_prob <- predict(fit_glm, as.data.frame(x_test_pc), type = "response")
y_pred_glm <- factor(ifelse(y_prob > 0.5, 1, 0))
confusionMatrix(y_pred_glm, y_test)$overall[["Accuracy"]]
```

```
## [1] 0.875
```

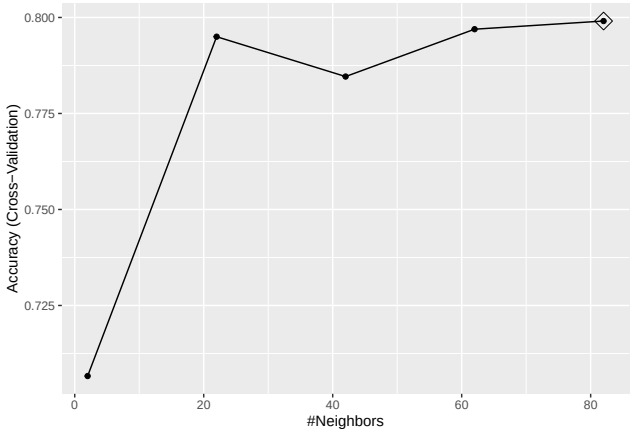
```
F_meas(y_pred_glm, y_test, beta = 2)
```

```
## [1] 0.8895706
```

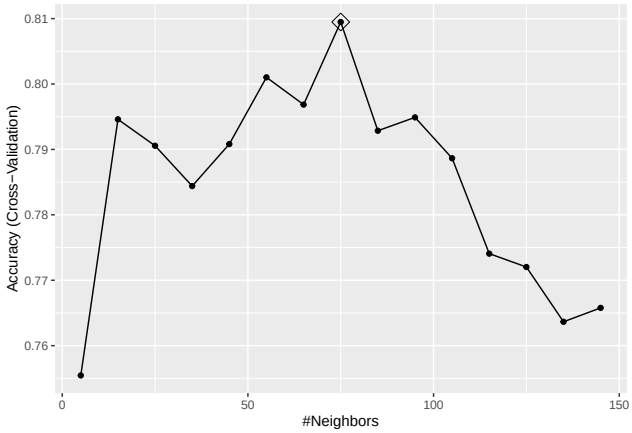
```
#ROC
roc_glm <- roc(as.factor(test_set$case), y_prob)
plot(roc_glm, print.thres="best", type = "line", print.auc = TRUE, legacy.axes = TRUE,
     grid = TRUE, ylim = c(0,1), xlim = c(1,0), col = "Red", main = "ROC for PCA + GLM")
```




```
########PCA + KNN
set.seed(5436)
b <- 10
control_pca <- trainControl(method = "cv", number = b, p = .9)
train_pcaknn <- train(x_train_pc, y_train,
                      method = "knn",
                      tuneGrid = data.frame(k = seq(2,100,20)), #
                      trControl = control_pca)
ggplot(train_pcaknn, highlight = TRUE)
```



```
set.seed(5432)
b <- 10
control_pca <- trainControl(method = "cv", number = b, p = .9)
train_pcaknn2 <- train(x_train_pc, y_train,
                       method = "knn",
                       tuneGrid = data.frame(k = seq(5,150,10)), #
                       trControl = control_pca)
ggplot(train_pcaknn2, highlight = TRUE)
```




```
train_pcaknn2$bestTune
```

```
##    k
## 8 75
```

```
train_pcaknn2$results$Accuracy
```

```
##  [1] 0.7554422 0.7946003 0.7905612 0.7843963 0.7908163 0.8010204 0.7968537
##  [8] 0.8094813 0.7928571 0.7948980 0.7886480 0.7740646 0.7720238 0.7636480
## [15] 0.7657738
```

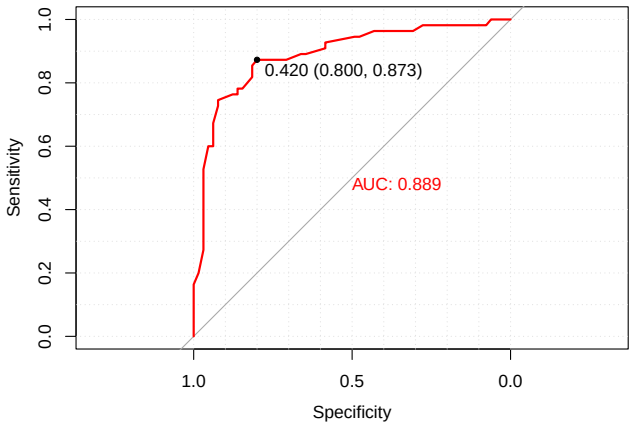
```
fit_pcaknn <- knn3(x_train_pc, y_train, k = train_pcaknn2$bestTune$k)

y_pred_pcaknn <- predict(fit_pcaknn, x_test_pc, type = "class")
y_pred_pcaknn_p <- predict(fit_pcaknn, x_test_pc, type = "prob")
confusionMatrix(y_pred_pcaknn, y_test)$overall["Accuracy"]
```

```
##  Accuracy
## 0.8333333
```

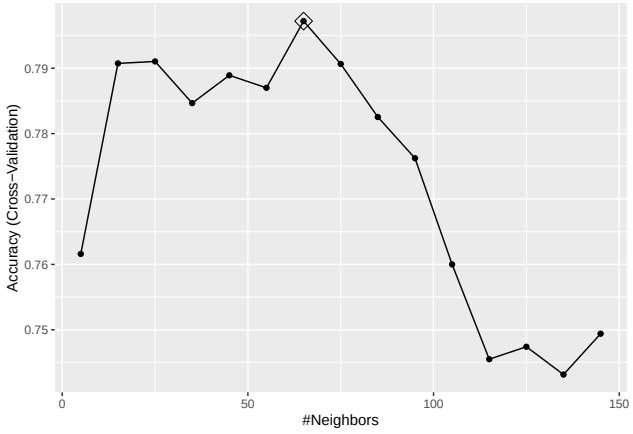
```
F_meas(y_pred_pcaknn, y_test, beta = 2)
```

```
## [1] 0.8955224
```

```
#ROC
roc_pcaknn <- roc(as.factor(test_set$case), y_pred_pcaknn_p[, 2])
plot(roc_pcaknn, print.thres="best", type = "line", print.auc = TRUE, grid = TRUE, ylim = c(0,1), col =
```




```
#####KNN
set.seed(3245)
b <- 10
control_knn <- trainControl(method = "cv", number = b, p = .9)
train_knn <- train(x_train, y_train,
                   method = "knn",
                   tuneGrid = data.frame(k = seq(5,150,10)),
                   trControl = control_knn)
ggplot(train_knn, highlight = TRUE)
```




```
train_knn$bestTune
```

```
##    k
## 7 65
```

```
train_knn$results$Accuracy
```

```
##  [1] 0.7616026 0.7907340 0.7910371 0.7846577 0.7889112 0.7870016 0.7972038
##  [8] 0.7906508 0.7825337 0.7762375 0.7599978 0.7454977 0.7474092 0.7431557
## [15] 0.7494057
```

```
fit_knn <- knn3(x_train, y_train, k = train_knn$bestTune$k)

y_pred_knn <- predict(fit_knn, x_test, type = "class")
y_pred_knn_p <- predict(fit_knn, x_test, type = "prob")
confusionMatrix(y_pred_knn, y_test)
```

```
## Confusion Matrix and Statistics
```

```
##
##           Reference
## Prediction  0  1
##          0 61 20
##          1  4 35
##
##                Accuracy : 0.8
##                  95% CI : (0.7172, 0.8675)
##     No Information Rate : 0.5417
##     P-Value [Acc > NIR] : 3.087e-09
##
##                   Kappa : 0.588
##
##  Mcnemar's Test P-Value : 0.0022
##
##             Sensitivity : 0.9385
##             Specificity : 0.6364
##          Pos Pred Value : 0.7531
##          Neg Pred Value : 0.8974
##              Prevalence : 0.5417
##          Detection Rate : 0.5083
##    Detection Prevalence : 0.6750
##       Balanced Accuracy : 0.7874
##
##        'Positive' Class : 0
##
```

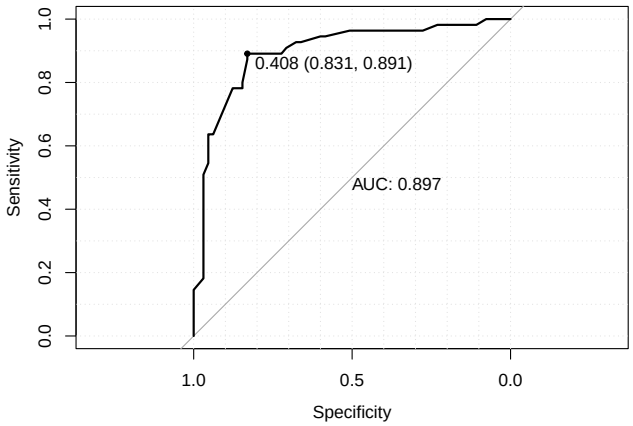
```
confusionMatrix(y_pred_knn, y_test)$overall["Accuracy"]
```

```
## Accuracy
##      0.8
```

```
F_meas(y_pred_knn, y_test, beta = 2)
```

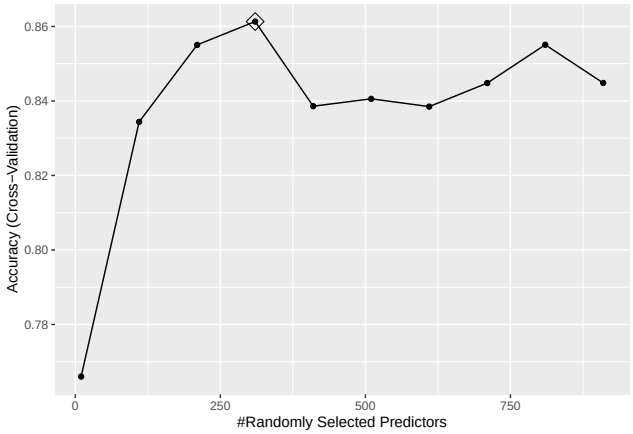
```
## [1] 0.8944282
```

```
#ROC
roc_knn <- roc(as.factor(test_set$case), y_pred_knn_p[, 2])
plot(roc_knn, print.thres="best", type = "line", print.auc = TRUE, grid = TRUE, ylim = c(0,1))
```




```
##########Random forest
set.seed(4536)
```

```
b <- 5
control_rf <- trainControl(method="cv", number = b, p = .9)
train_rf <-  train(x_train, y_train,
                   method = "rf",
                   ntree = 15,
                   trControl = control_rf,
                   tuneGrid = data.frame(mtry = seq(10, 1000, 100)))
ggplot(train_rf, highlight = TRUE)
```



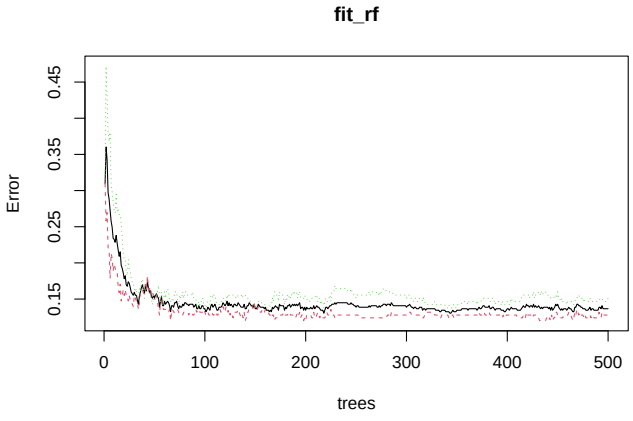

```
train_rf$bestTune
```

```
##   mtry
## 4  310
```

```
train_rf$results$Accuracy
```

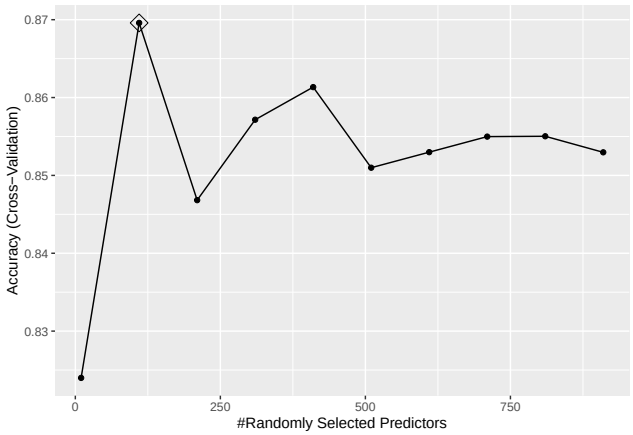
```
##  [1] 0.7660223 0.8343857 0.8550473 0.8613187 0.8385954 0.8405713 0.8384880
##  [8] 0.8448024 0.8550902 0.8448239
```

```
fit_rf <- randomForest(x_train, y_train,
                       mtry = train_rf$bestTune$mtry,
                       minNode = 10)
plot(fit_rf)
```




```
set.seed(6543)
b <- 5
control_rf <- trainControl(method="cv", number = b, p = .9)
train_rf2 <-  train(x_train, y_train,
```

```
                    method = "rf",
                    ntree = 100,
                    trControl = control_rf,
                    tuneGrid = data.frame(mtry = seq(10, 1000, 100)))
ggplot(train_rf2, highlight = TRUE)
```



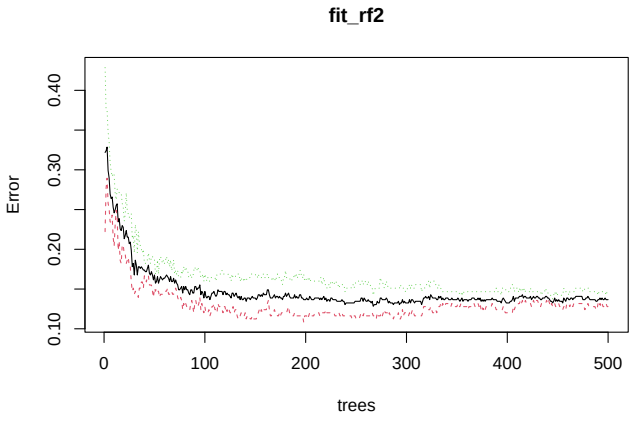

```
train_rf2$bestTune
```

```
##   mtry
## 2  110
```

```
train_rf2$results$Accuracy
```

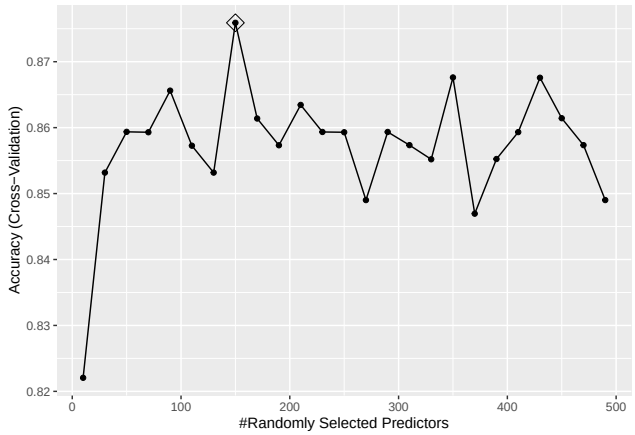
```
##  [1] 0.8239905 0.8695876 0.8468213 0.8571521 0.8613402 0.8509880 0.8529854
##  [8] 0.8549828 0.8550258 0.8529639
```

```
fit_rf2 <- randomForest(x_train, y_train,
                        mtry = train_rf2$bestTune$mtry,
                        minNode = 10)
plot(fit_rf2)
```




```
set.seed(232)
b <- 5
control_rf <- trainControl(method="cv", number = b, p = .9)
train_rf3 <-  train(x_train, y_train,
                    method = "rf",
                    ntree = 100,
                    trControl = control_rf,
```

```
                    tuneGrid = data.frame(mtry = seq(10, 500, 20)))
ggplot(train_rf3, highlight = TRUE)
```



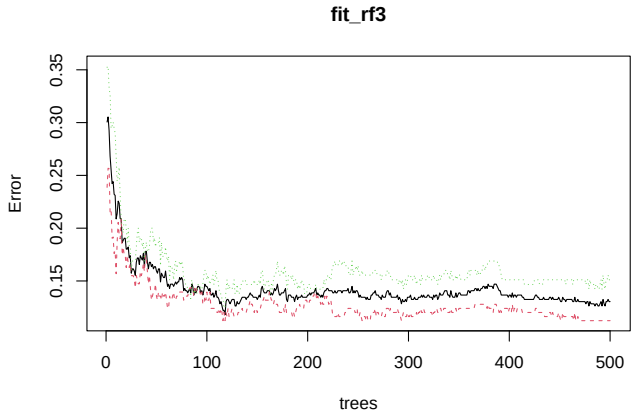

```
train_rf3$bestTune
```

```
##   mtry
## 8  150
```

```
train_rf3$results$Accuracy
```

```
##  [1] 0.8220576 0.8531787 0.8593643 0.8592998 0.8656143 0.8572595 0.8531787
##  [8] 0.8759021 0.8613832 0.8573239 0.8634450 0.8593428 0.8592998 0.8490120
## [15] 0.8593428 0.8573454 0.8551976 0.8676117 0.8469502 0.8552405 0.8593213
## [22] 0.8675687 0.8614261 0.8573454 0.8490120
```

```
fit_rf3 <- randomForest(x_train, y_train,
                        mtry = train_rf3$bestTune$mtry,
                        minNode = 10)
plot(fit_rf3)
```




```
y_pred_rf <- predict(fit_rf3, x_test, type = "class")
y_pred_rf_p <- predict(fit_rf3, x_test, type = "prob")
confusionMatrix(y_pred_rf, y_test)
```

```
## Confusion Matrix and Statistics
##
##           Reference
## Prediction  0  1
```

```
##          0 60  6
##          1  5 49
##
##                Accuracy : 0.9083
##                  95% CI : (0.8419, 0.9533)
##     No Information Rate : 0.5417
##     P-Value [Acc > NIR] : <2e-16
##
##                   Kappa : 0.8151
##
##  Mcnemar's Test P-Value : 1
##
##             Sensitivity : 0.9231
##             Specificity : 0.8909
##          Pos Pred Value : 0.9091
##          Neg Pred Value : 0.9074
##              Prevalence : 0.5417
##          Detection Rate : 0.5000
##    Detection Prevalence : 0.5500
##       Balanced Accuracy : 0.9070
##
##        'Positive' Class : 0
##
```

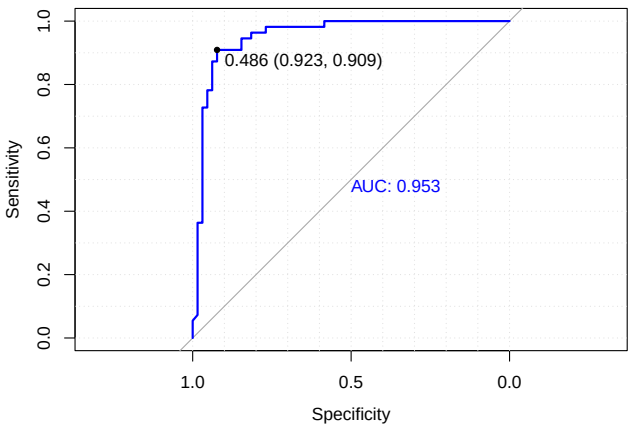
```
confusionMatrix(y_pred_rf, y_test)$overall["Accuracy"]
```

```
##  Accuracy
## 0.9083333
```

```
F_meas(y_pred_rf, y_test, beta = 2)
```

```
## [1] 0.9202454
```

```
roc_rf <- roc(as.factor(test_set$case), y_pred_rf_p[, 2])
plot(roc_rf, print.thres="best", type = "line", print.auc = TRUE, grid = TRUE, ylim = c(0,1), col = "blu
```




```
#Ensemble
p_knn <- y_pred_knn_p
p_rf <- y_pred_rf_p / rowSums(y_pred_rf_p)
p_pcaknn <- y_pred_pcaknn_p
p_glm <- as.matrix(cbind(1-y_prob, y_prob))
colnames(p_glm) <- c(0, 1)
```

```r
p <- (p_rf + p_knn)/2
y_pred <- factor(apply(p, 1, which.max)-1)
confusionMatrix(y_pred, y_test)
```

```
## Confusion Matrix and Statistics
##
##           Reference
## Prediction  0  1
##          0 60  9
##          1  5 46
##
##                Accuracy : 0.8833
##                  95% CI : (0.812, 0.9347)
##     No Information Rate : 0.5417
##     P-Value [Acc > NIR] : 8.505e-16
##
##                   Kappa : 0.7637
##
##  Mcnemar's Test P-Value : 0.4227
##
##             Sensitivity : 0.9231
##             Specificity : 0.8364
##          Pos Pred Value : 0.8696
##          Neg Pred Value : 0.9020
##              Prevalence : 0.5417
##          Detection Rate : 0.5000
##    Detection Prevalence : 0.5750
##       Balanced Accuracy : 0.8797
##
##        'Positive' Class : 0
##
```

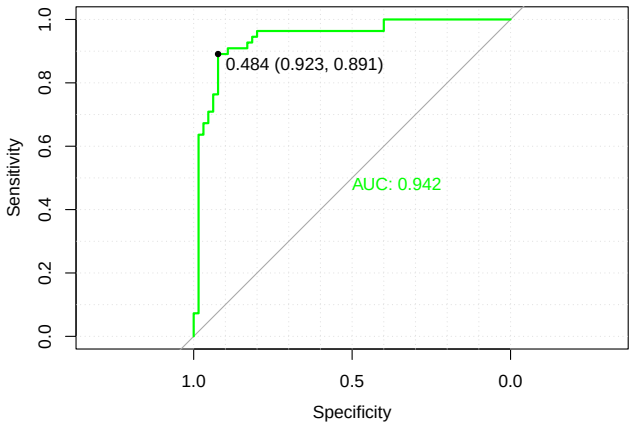
```r
confusionMatrix(y_pred, y_test)$overall["Accuracy"]
```

```
##  Accuracy
## 0.8833333
```

```r
F_meas(y_pred, y_test, beta = 2)
```

```
## [1] 0.9118541
```

```r
roc_es <- roc(as.factor(test_set$case), p[, 2])
plot(roc_es, print.thres="best", type = "line", print.auc = TRUE, grid = TRUE, ylim = c(0,1), col = "gr
```




```
summary <- data.frame()
summary[1,1] <- round(confusionMatrix(y_pred_glm, y_test)$byClass[1], 3)
summary[1,2] <- round(confusionMatrix(y_pred_glm, y_test)$byClass[2], 3)
summary[1,3] <- round(confusionMatrix(y_pred_glm, y_test)$overall["Accuracy"], 3)
summary[1,4] <- round(F_meas(y_pred_glm, y_test, beta = 2), 3)
summary[1,5] <- round(roc_glm$auc, 3)

summary[2,1] <- round(confusionMatrix(y_pred_pcaknn, y_test)$byClass[1], 3)
summary[2,2] <- round(confusionMatrix(y_pred_pcaknn, y_test)$byClass[2], 3)
summary[2,3] <- round(confusionMatrix(y_pred_pcaknn, y_test)$overall["Accuracy"], 3)
summary[2,4] <- round(F_meas(y_pred_pcaknn, y_test, beta = 2), 3)
summary[2,5] <- round(roc_pcaknn$auc, 3)

summary[3,1] <- round(confusionMatrix(y_pred_knn, y_test)$byClass[1], 3)
summary[3,2] <- round(confusionMatrix(y_pred_knn, y_test)$byClass[2], 3)
summary[3,3] <- round(confusionMatrix(y_pred_knn, y_test)$overall["Accuracy"], 3)
summary[3,4] <- round(F_meas(y_pred_knn, y_test, beta = 2), 3)
summary[3,5] <- round(roc_knn$auc, 3)

summary[4,1] <- round(confusionMatrix(y_pred_rf, y_test)$byClass[1], 3)
summary[4,2] <- round(confusionMatrix(y_pred_rf, y_test)$byClass[2], 3)
summary[4,3] <- round(confusionMatrix(y_pred_rf, y_test)$overall["Accuracy"], 3)
summary[4,4] <- round(F_meas(y_pred_rf, y_test, beta = 2), 3)
summary[4,5] <- round(roc_rf$auc, 3)

summary[5,1] <- round(confusionMatrix(y_pred, y_test)$byClass[1], 3)
summary[5,2] <- round(confusionMatrix(y_pred, y_test)$byClass[2], 3)
summary[5,3] <- round(confusionMatrix(y_pred, y_test)$overall["Accuracy"], 3)
summary[5,4] <- round(F_meas(y_pred, y_test, beta = 2), 3)
summary[5,5] <- round(roc_es$auc, 3)

rownames(summary) <- c("PCA + GLM", "PCA + KNN", "KNN", "Random forest", "Ensemble of KNN & RF")
colnames(summary) <- c("Sensitivity", "Specificity", "Overall accuracy", "F_1 score", "AUC")

summary %>%
  kbl() %>%
  kable_material(c("striped"))
```

```
ggroc(list(roc_glm, roc_pcaknn, roc_knn, roc_rf, roc_es), legacy.axes = TRUE) +
  theme_linedraw() +
```

	Sensitivity	Specificity	Overall accuracy	F_1 score	AUC
PCA + GLM	0.892	0.855	0.875	0.890	0.946
PCA + KNN	0.923	0.727	0.833	0.896	0.889
KNN	0.938	0.636	0.800	0.894	0.897
Random forest	0.923	0.891	0.908	0.920	0.953
Ensemble of KNN & RF	0.923	0.836	0.883	0.912	0.942

```
ggtitle("ROC") +
geom_segment(aes(x = 0, xend = 1, y = 0, yend = 1), color="grey", linetype="dashed") +
scale_colour_discrete(labels = c("PCA + Logistic", "PCA + KNN", "KNN", "Random forest", "Ensemble")) +
labs(color = "Models")
```