Class 08: Analysis of Breast Cancer Cells

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Background

In today's class we will be employing all the R techniques for data analysis that we have learned thus far - including the machine learning methods of clustering and PCA - to analyze real breast cancer biopsy data.

Data Import

The data is in CSV format:

```
fna.data <- "WisconsinCancer.csv"
```

```
wisc.df <- data.frame(fna.data, row.names=1)
```

```
wisc.df <- read.csv("WisconsinCancer.csv", row.names = 1)
```

wee peak at the data

```r
head(wisc.df, 3)
```

```
         diagnosis radius_mean texture_mean perimeter_mean area_mean
842302           M       17.99        10.38          122.8      1001
842517           M       20.57        17.77          132.9      1326
84300903         M       19.69        21.25          130.0      1203
         smoothness_mean compactness_mean concavity_mean concave.points_mean
842302           0.11840          0.27760         0.3001             0.14710
842517           0.08474          0.07864         0.0869             0.07017
84300903         0.10960          0.15990         0.1974             0.12790
         symmetry_mean fractal_dimension_mean radius_se texture_se perimeter_se
842302          0.2419                0.07871    1.0950     0.9053        8.589
842517          0.1812                0.05667    0.5435     0.7339        3.398
84300903        0.2069                0.05999    0.7456     0.7869        4.585
         area_se smoothness_se compactness_se concavity_se concave.points_se
842302    153.40      0.006399        0.04904      0.05373           0.01587
842517     74.08      0.005225        0.01308      0.01860           0.01340
84300903   94.03      0.006150        0.04006      0.03832           0.02058
         symmetry_se fractal_dimension_se radius_worst texture_worst
842302       0.03003             0.006193        25.38         17.33
842517       0.01389             0.003532        24.99         23.41
84300903     0.02250             0.004571        23.57         25.53
         perimeter_worst area_worst smoothness_worst compactness_worst
842302             184.6       2019           0.1622            0.6656
842517             158.8       1956           0.1238            0.1866
84300903           152.5       1709           0.1444            0.4245
         concavity_worst concave.points_worst symmetry_worst
842302            0.7119               0.2654         0.4601
842517            0.2416               0.1860         0.2750
84300903          0.4504               0.2430         0.3613
         fractal_dimension_worst
842302                   0.11890
842517                   0.08902
84300903                 0.08758
```

Q1. How many observations are in this dataset? 569 observations.

```r
nrow(wisc.df)
```

```
[1] 569
```

Q2. How many of the observations have a malignant diagnosis? 212 observations.

```r
sum( wisc.df$diagnosis == "M" )
```

```
[1] 212
```

```r
table( wisc.df$diagnosis)
```

```

  B   M 
357 212 
```

Q3. How many variables/features in the data are suffixed with _mean? 10 variables

```r
head(wisc.df)
```

```
         diagnosis radius_mean texture_mean perimeter_mean area_mean
842302           M       17.99        10.38         122.80    1001.0
842517           M       20.57        17.77         132.90    1326.0
84300903         M       19.69        21.25         130.00    1203.0
84348301         M       11.42        20.38          77.58     386.1
84358402         M       20.29        14.34         135.10    1297.0
843786           M       12.45        15.70          82.57     477.1
         smoothness_mean compactness_mean concavity_mean concave.points_mean
842302           0.11840          0.27760         0.3001             0.14710
842517           0.08474          0.07864         0.0869             0.07017
84300903         0.10960          0.15990         0.1974             0.12790
84348301         0.14250          0.28390         0.2414             0.10520
84358402         0.10030          0.13280         0.1980             0.10430
843786           0.12780          0.17000         0.1578             0.08089
         symmetry_mean fractal_dimension_mean radius_se texture_se perimeter_se
842302          0.2419                0.07871    1.0950     0.9053        8.589
842517          0.1812                0.05667    0.5435     0.7339        3.398
84300903        0.2069                0.05999    0.7456     0.7869        4.585
84348301        0.2597                0.09744    0.4956     1.1560        3.445
84358402        0.1809                0.05883    0.7572     0.7813        5.438
843786          0.2087                0.07613    0.3345     0.8902        2.217
         area_se smoothness_se compactness_se concavity_se concave.points_se
842302    153.40      0.006399        0.04904      0.05373           0.01587
842517     74.08      0.005225        0.01308      0.01860           0.01340
84300903   94.03      0.006150        0.04006      0.03832           0.02058
84348301   27.23      0.009110        0.07458      0.05661           0.01867
```

```
84358402   94.44      0.011490        0.02461      0.05688            0.01885
843786     27.19      0.007510        0.03345      0.03672            0.01137
         symmetry_se fractal_dimension_se radius_worst texture_worst
842302       0.03003             0.006193        25.38         17.33
842517       0.01389             0.003532        24.99         23.41
84300903     0.02250             0.004571        23.57         25.53
84348301     0.05963             0.009208        14.91         26.50
84358402     0.01756             0.005115        22.54         16.67
843786       0.02165             0.005082        15.47         23.75
         perimeter_worst area_worst smoothness_worst compactness_worst
842302            184.60     2019.0           0.1622            0.6656
842517            158.80     1956.0           0.1238            0.1866
84300903          152.50     1709.0           0.1444            0.4245
84348301           98.87      567.7           0.2098            0.8663
84358402          152.20     1575.0           0.1374            0.2050
843786            103.40      741.6           0.1791            0.5249
         concavity_worst concave.points_worst symmetry_worst
842302            0.7119               0.2654         0.4601
842517            0.2416               0.1860         0.2750
84300903          0.4504               0.2430         0.3613
84348301          0.6869               0.2575         0.6638
84358402          0.4000               0.1625         0.2364
843786            0.5355               0.1741         0.3985
         fractal_dimension_worst
842302                   0.11890
842517                   0.08902
84300903                 0.08758
84348301                 0.17300
84358402                 0.07678
843786                   0.12440
```

```r
length(grep("_mean", colnames(wisc.df), value=T))
```

```
[1] 10
```

```r
colnames(wisc.df)
```

```
 [1] "diagnosis"               "radius_mean"
 [3] "texture_mean"            "perimeter_mean"
 [5] "area_mean"               "smoothness_mean"
 [7] "compactness_mean"        "concavity_mean"
 [9] "concave.points_mean"     "symmetry_mean"
[11] "fractal_dimension_mean"  "radius_se"
[13] "texture_se"              "perimeter_se"
[15] "area_se"                 "smoothness_se"
[17] "compactness_se"          "concavity_se"
[19] "concave.points_se"       "symmetry_se"
[21] "fractal_dimension_se"    "radius_worst"
[23] "texture_worst"           "perimeter_worst"
[25] "area_worst"              "smoothness_worst"
[27] "compactness_worst"       "concavity_worst"
[29] "concave.points_worst"    "symmetry_worst"
[31] "fractal_dimension_worst"
```

We need to remove the `diagnosis` column before we do any further analysis of this data set - we don't want to pass this to PCA etc. We will save it as a separate wee vector that we can use later to compare our findings to those experts.

```
wisc.data <- wisc.df[,-1]
diagnosis <- wisc.df$diagnosis
```

Principal Component Analysis (PCA)

The main function in base R is called `prcomp()` we will use the optional argument `scale=TRUE` here as the data columns/features/dimensions are on very different scales in the original data set.

```
colMeans(wisc.data)
```

```
            radius_mean            texture_mean          perimeter_mean
           1.412729e+01            1.928965e+01            9.196903e+01
              area_mean         smoothness_mean        compactness_mean
           6.548891e+02            9.636028e-02            1.043410e-01
         concavity_mean     concave.points_mean           symmetry_mean
           8.879932e-02            4.891915e-02            1.811619e-01
 fractal_dimension_mean               radius_se              texture_se
           6.279761e-02            4.051721e-01            1.216853e+00
           perimeter_se                 area_se           smoothness_se
           2.866059e+00            4.033708e+01            7.040979e-03
         compactness_se            concavity_se       concave.points_se
           2.547814e-02            3.189372e-02            1.179614e-02
            symmetry_se    fractal_dimension_se            radius_worst
           2.054230e-02            3.794904e-03            1.626919e+01
          texture_worst         perimeter_worst              area_worst
           2.567722e+01            1.072612e+02            8.805831e+02
       smoothness_worst       compactness_worst         concavity_worst
           1.323686e-01            2.542650e-01            2.721885e-01
   concave.points_worst          symmetry_worst fractal_dimension_worst
           1.146062e-01            2.900756e-01            8.394582e-02
```

```r
apply(wisc.data,2,sd)
```

```
            radius_mean            texture_mean          perimeter_mean
           3.524049e+00            4.301036e+00            2.429898e+01
              area_mean         smoothness_mean        compactness_mean
           3.519141e+02            1.406413e-02            5.281276e-02
         concavity_mean     concave.points_mean           symmetry_mean
           7.971981e-02            3.880284e-02            2.741428e-02
 fractal_dimension_mean               radius_se              texture_se
           7.060363e-03            2.773127e-01            5.516484e-01
           perimeter_se                 area_se           smoothness_se
           2.021855e+00            4.549101e+01            3.002518e-03
         compactness_se            concavity_se       concave.points_se
           1.790818e-02            3.018606e-02            6.170285e-03
            symmetry_se    fractal_dimension_se            radius_worst
           8.266372e-03            2.646071e-03            4.833242e+00
          texture_worst         perimeter_worst              area_worst
           6.146258e+00            3.360254e+01            5.693570e+02
       smoothness_worst       compactness_worst         concavity_worst
           2.283243e-02            1.573365e-01            2.086243e-01
   concave.points_worst          symmetry_worst fractal_dimension_worst
           6.573234e-02            6.186747e-02            1.806127e-02
```

```r
wisc.pr <- prcomp(wisc.data, scale=T)
```

```r
summary(wisc.pr)
```

```
Importance of components:
                          PC1    PC2     PC3     PC4     PC5     PC6     PC7
Standard deviation     3.6444 2.3857 1.67867 1.40735 1.28403 1.09880 0.82172
Proportion of Variance 0.4427 0.1897 0.09393 0.06602 0.05496 0.04025 0.02251
Cumulative Proportion  0.4427 0.6324 0.72636 0.79239 0.84734 0.88759 0.91010
                           PC8    PC9    PC10   PC11    PC12    PC13    PC14
```

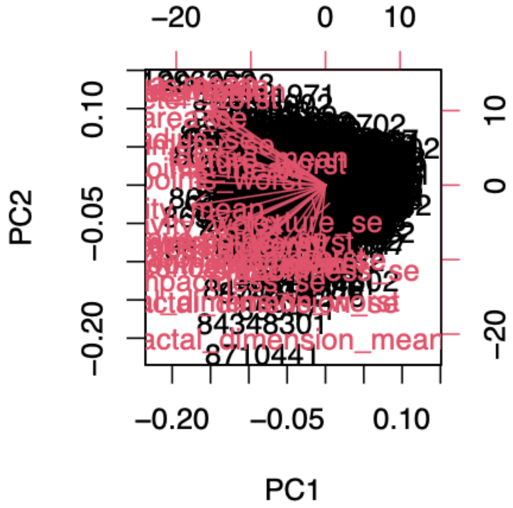
```
Standard deviation     0.69037 0.6457 0.59219 0.5421 0.51104 0.49128 0.39624
Proportion of Variance 0.01589 0.0139 0.01169 0.0098 0.00871 0.00805 0.00523
Cumulative Proportion  0.92598 0.9399 0.95157 0.9614 0.97007 0.97812 0.98335
                          PC15    PC16    PC17    PC18    PC19    PC20   PC21
Standard deviation     0.30681 0.28260 0.24372 0.22939 0.22244 0.17652 0.1731
Proportion of Variance 0.00314 0.00266 0.00198 0.00175 0.00165 0.00104 0.0010
Cumulative Proportion  0.98649 0.98915 0.99113 0.99288 0.99453 0.99557 0.9966
                          PC22    PC23   PC24    PC25    PC26    PC27    PC28
Standard deviation     0.16565 0.15602 0.1344 0.12442 0.09043 0.08307 0.03987
Proportion of Variance 0.00091 0.00081 0.0006 0.00052 0.00027 0.00023 0.00005
Cumulative Proportion  0.99749 0.99830 0.9989 0.99942 0.99969 0.99992 0.99997
                          PC29    PC30
Standard deviation     0.02736 0.01153
Proportion of Variance 0.00002 0.00000
Cumulative Proportion  1.00000 1.00000
```

> Q4. From your results, what proportion of the original variance is captured by the frist principal component (PC1)? 44.27%
>
> Q5. How many principal componetns (PCs) are required to describe at least 70% of the original variance in the data? 3 PCs
>
> Q6. How many principal components (PCs) are required to describe at least 90% of the original variance in the data? 7 PCs

```
attributes(wisc.pr)
```

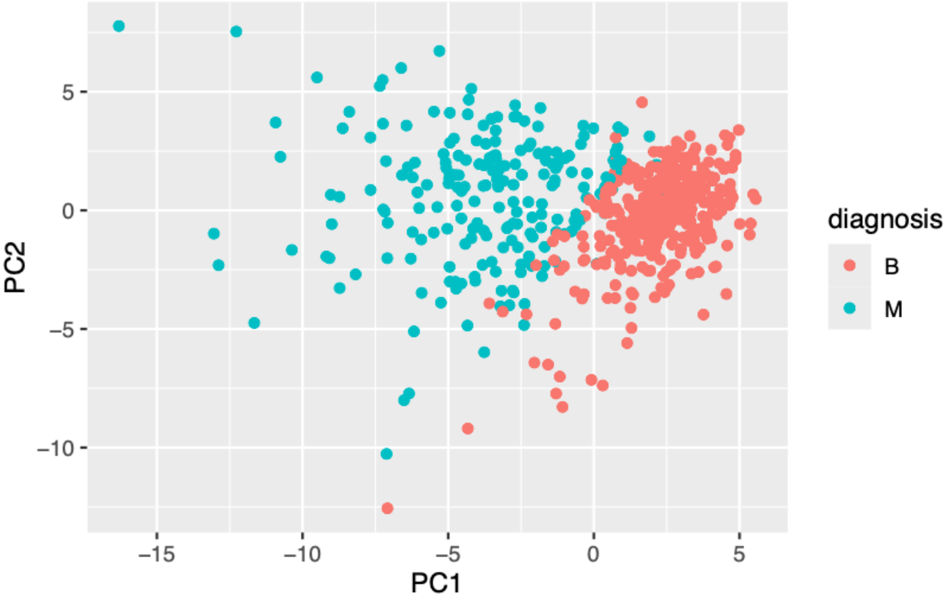
```
$names
[1] "sdev"     "rotation" "center"   "scale"    "x"       

$class
[1] "prcomp"
```

```
biplot(wisc.pr)
```



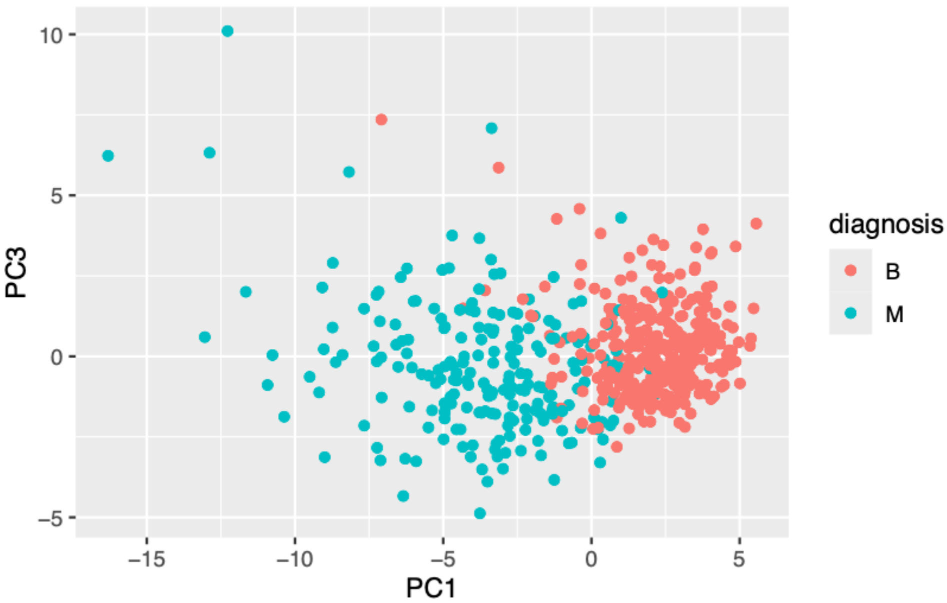
Q7. What stands out to you about this plot? Is it easy or difficult to understand? Why? The plot is extremely poor for visual interpretation and difficult to understand because the row names are plotted which obsecures the data points.

```
library(ggplot2)
ggplot(wisc.pr$x) +
  aes(PC1, PC2, col=diagnosis) +
  geom_point()
```



Q8. Generate a similar plot for principal components 1 and 3. What do you notice about these plots? These plots show how PC1 succesfully captures the visual distinction between the benign (red data points) and malignant (blue data points) cancer samples.

```
ggplot(wisc.pr$x) +
  aes(PC1, PC3, col=diagnosis) +
  geom_point()
```



Calculate variance of each component

```
pr.var <- wisc.pr$sdev^2
head(pr.var)
```

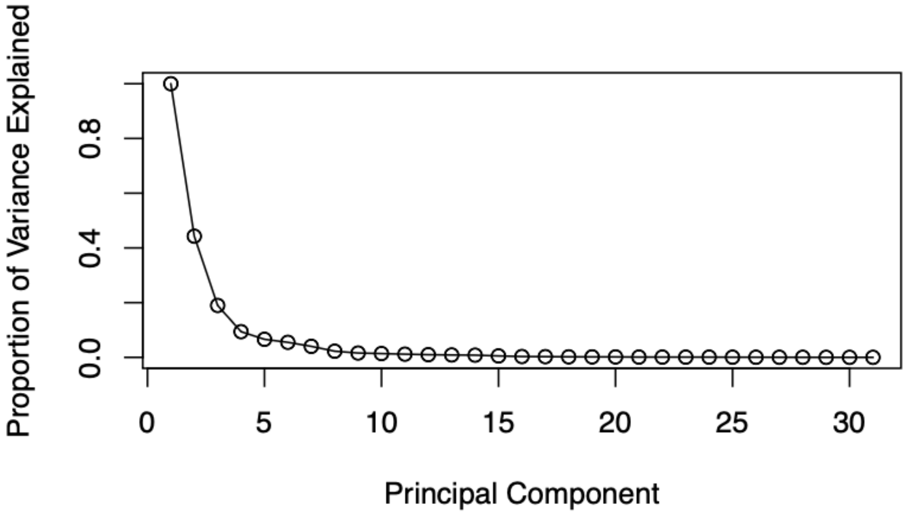
```
[1] 13.281608  5.691355  2.817949  1.980640  1.648731  1.207357
```

Variance explained by each principal component: pve

```
pve <- pr.var / sum(pr.var)
```

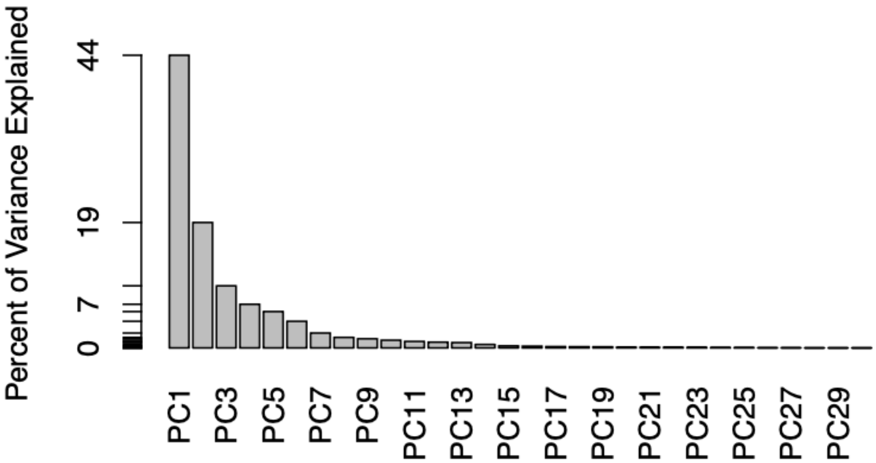
Plot variance explained for each principal component

```
plot(c(1,pve), xlab = "Principal Component",
     ylab = "Proportion of Variance Explained",
     ylim = c(0, 1), type = "o")
```



Alternative scree plot of the same data, note data driven y-axis

```
barplot(pve, ylab = "Percent of Variance Explained",
     names.arg=paste0("PC",1:length(pve)), las=2, axes = FALSE)
axis(2, at=pve, labels=round(pve,2)*100 )
```

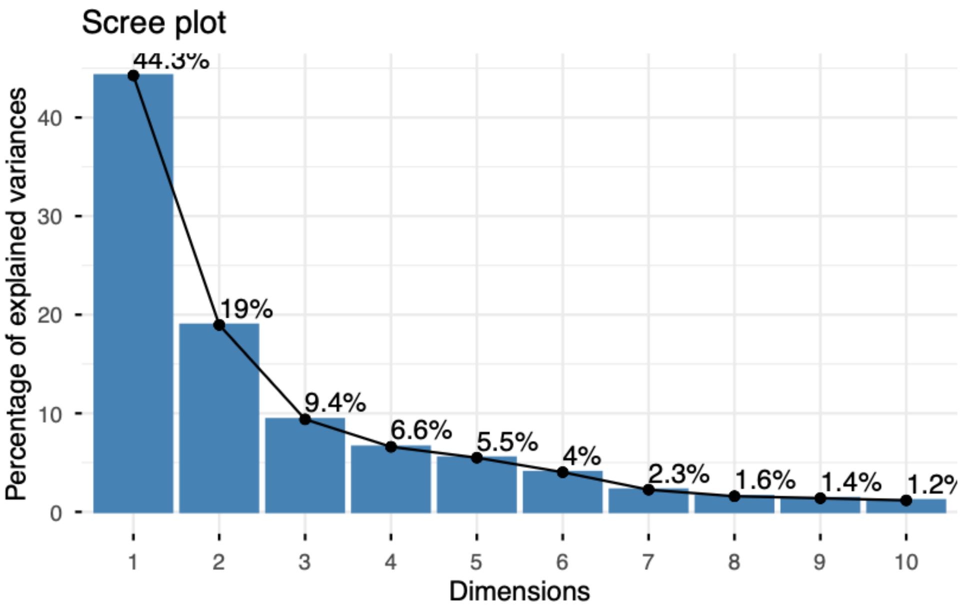


```
library(factoextra)
```

```
Welcome! Want to learn more? See two factoextra-related books at https://goo.gl/ve3WBa
```

```
fviz_eig(wisc.pr, addlabels = TRUE)
```

```
Warning in geom_bar(stat = "identity", fill = barfill, color = barcolor, :
Ignoring empty aesthetic: `width`.
```



```r
wisc.pr$rotation["concave.points_mean", 1]
```

```
[1] -0.2608538
```

```r
pc1_contributions <- wisc.pr$rotation[, 1]
abs(pc1_contributions) > abs(pc1_contributions["concave.points_mean"])
```

```
               radius_mean               texture_mean             perimeter_mean 
                     FALSE                      FALSE                      FALSE 
                 area_mean            smoothness_mean           compactness_mean 
                     FALSE                      FALSE                      FALSE 
            concavity_mean        concave.points_mean              symmetry_mean 
                     FALSE                      FALSE                      FALSE 
 fractional_dimension_mean                  radius_se                 texture_se 
                     FALSE                      FALSE                      FALSE 
              perimeter_se                    area_se              smoothness_se 
                     FALSE                      FALSE                      FALSE 
            compactness_se               concavity_se          concave.points_se 
                     FALSE                      FALSE                      FALSE 
               symmetry_se    fractional_dimension_se               radius_worst 
                     FALSE                      FALSE                      FALSE 
```

```
       texture_worst         perimeter_worst              area_worst 
               FALSE                   FALSE                   FALSE 
    smoothness_worst       compactness_worst         concavity_worst 
               FALSE                   FALSE                   FALSE 
concave.points_worst          symmetry_worst fractal_dimension_worst 
               FALSE                   FALSE                   FALSE 
```

> Q9. For the first principal component, what is the component of the loading vector (i.e. wisc.pr$rotation[,1]) for the feature concave.points_mean? This tells us how much this original feature contributes to the first PC. Are there any features with larger contributions than this one? The component of the loading vector for the feature concave.points_mean is -0.26. There are no features with larger contributions.

Hierarchial Clustering

The goal of this section is to do hierarchical clustering of the original data to see if there is any obvious grouping into malignant and benign clusters.

In short, these results are not good!

First we will scale our `wisc.data`

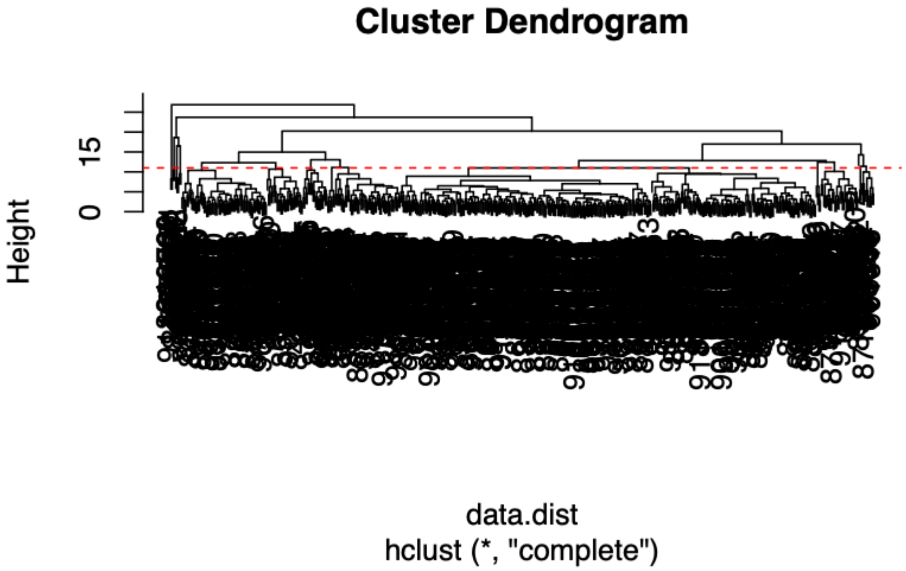
```r
data.scaled <- scale(wisc.data)
```

```r
data.dist <- dist(data.scaled)
```

```r
wisc.hclust <- hclust(data.dist, method = "complete")
```

> Q10. Using the plot() and abline() functions, what is the height at which the clustering model has 4 clusters? At height = 11

```r
plot(wisc.hclust)
abline(h = 11, col="red", lty=2)
```



```r
wisc.hclust.clusters <- cutree(wisc.hclust, k = 4)
table(wisc.hclust.clusters, diagnosis)
```

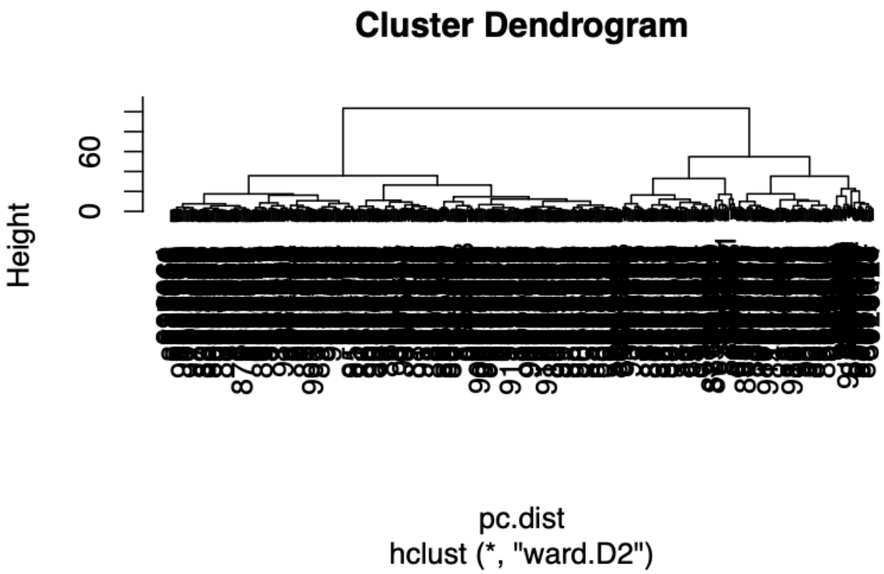
```
                    diagnosis
wisc.hclust.clusters   B   M
                   1  12 165
                   2   2   5
                   3 343  40
                   4   0   2
```

> Q12. Which method gives your favorite results for the same data.dist dataset? Explain your reasoning. The ward.D2 method gives my favorite result. It produces the most well-separated clusters as it minimizes the within-cluster variance.

Combining Methods

The idea here is that I can take my new variables (i.e. the scores on the PCs `wisc.pr$x`) that are better descriptors of the data-set than the original features (i.e. the 30 columns in `wisc.data`) and use these as a basis for the clustering.

```r
pc.dist <- dist(wisc.pr$x[ ,1:3])
wisc.pr.hclust <- hclust(pc.dist, method = "ward.D2")
plot(wisc.pr.hclust)
```



```r
wisc.pr.hclust.clusters <- cutree(wisc.pr.hclust, k=2)
table(wisc.pr.hclust.clusters)
```

```
wisc.pr.hclust.clusters
  1   2 
203 366 
```

```r
table(diagnosis)
```

```
diagnosis
  B   M 
357 212 
```

> Q13. How well does the newly created hclust model with two clusters separate out the two “M” and “B” diagnoses?

I can now run `table()` with both my clustering `wisc.pr.hclust.clusters` and the expert `diagnoses`

```
table(wisc.pr.hclust.clusters, diagnosis)
```

```
                       diagnosis
wisc.pr.hclust.clusters   B   M
                      1  24 179
                      2 333  33
```

Our cluster "1" has 179 "M" diagnosis Our cluster "2" has 333 "B" diagnosis

179 TP 24 FP 333 TN 33 FN

> Q14. How well do the hierarchical clustering models you created in the previous sections (i.e. without first doing PCA) do in terms of separating the diagnoses? Again, use the table() function to compare the output of each model (wisc.hclust.clusters and wisc.pr.hclust.clusters) with the vector containing the actual diagnoses. The wisc.hclust.clusters model did worse at separating diagnoses compared to the wisc.pr.hclust.clusters model.

```
table(wisc.hclust.clusters, diagnosis)
```

```
                    diagnosis
wisc.hclust.clusters   B   M
                   1  12 165
                   2   2   5
                   3 343  40
                   4   0   2
```

```
table(wisc.pr.hclust.clusters, diagnosis)
```

```
                       diagnosis
wisc.pr.hclust.clusters   B   M
                      1  24 179
                      2 333  33
```

Sensitivity/Specificity

Sensitivity: TP/(TP+FN)

```
179/(179+33)
```

```
[1] 0.8443396
```

Specificity: TN/(TN+FP)

```
333/(333+24)
```

```
[1] 0.9327731
```

> Q15. Which of your analysis procedures resulted in a clustering model with the best specificity? How about sensitivity? The model based on PCA-transsofrmed data resulted in the best specificity (93%) and sensitivity (84%).

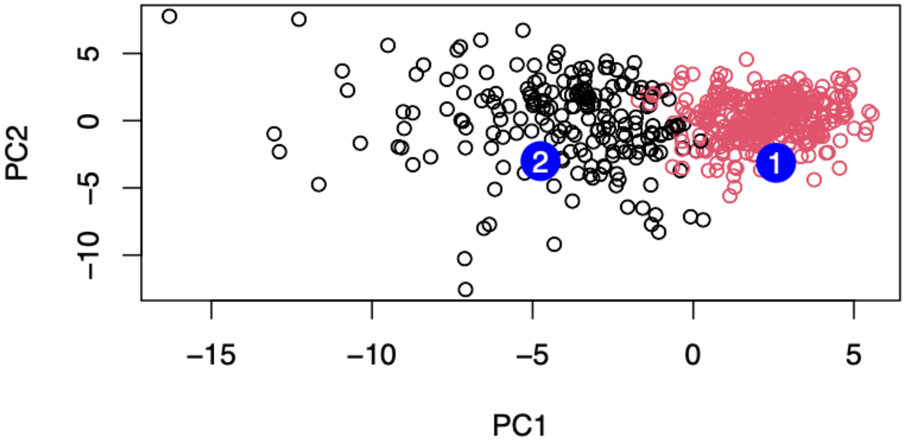
Prediction

We can use our PCA model for prediction of new unseen cases.

```
url <- "https://tinyurl.com/new-samples-CSV"
new <- read.csv(url)
npc <- predict(wisc.pr, newdata=new)
npc
```

```
           PC1       PC2        PC3        PC4       PC5        PC6        PC7
[1,]  2.576616 -3.135913  1.3990492 -0.7631950  2.781648 -0.8150185 -0.3959098
[2,] -4.754928 -3.009033 -0.1660946 -0.6052952 -1.140698 -1.2189945  0.8193031
            PC8       PC9       PC10      PC11      PC12      PC13     PC14
[1,] -0.2307350 0.1029569 -0.9272861 0.3411457  0.375921 0.1610764 1.187882
[2,] -0.3307423 0.5281896 -0.4855301 0.7173233 -1.185917 0.5893856 0.303029
          PC15       PC16        PC17        PC18        PC19       PC20
[1,] 0.3216974 -0.1743616 -0.07875393 -0.11207028 -0.08802955 -0.2495216
[2,] 0.1299153  0.1448061 -0.40509706  0.06565549  0.25591230 -0.4289500
           PC21       PC22       PC23       PC24        PC25         PC26
[1,]  0.1228233 0.09358453 0.08347651  0.1223396  0.02124121  0.078884581
[2,] -0.1224776 0.01732146 0.06316631 -0.2338618 -0.20755948 -0.009833238
             PC27        PC28         PC29         PC30
[1,]  0.220199544 -0.02946023 -0.015620933  0.005269029
[2,] -0.001134152  0.09638361  0.002795349 -0.019015820
```

```
plot(wisc.pr$x[,1:2], col=wisc.pr.hclust.clusters)
points(npc[,1], npc[,2], col="blue", pch=16, cex=3)
text(npc[,1], npc[,2], c(1,2), col="white")
```



Q16. Which of these new patients should we prioritize for follow up based on your results? We should prioritize patient 2 for follow up.