BIOS 6611 Homework 5 *Answer Key*

Due Monday, October 8, 2018 by noon to Canvas Assignment Basket

Evaluating Diagnostic Tests*

A new instrument—the Chinese Mini-Mental Status Test (CMMS)—was proposed to identify dementia among people in China. Participants completed the CMMS, alongside an extensive clinical evaluation by psychiatrists and nurses to make a definitive diagnosis of dementia. The table below shows the results for one subgroup of participants (participants with some formal education, who were generally likely to score higher on the CMMS than participants without formal education).

	Clinical Diagnosis	
CMMS Score	**Non-Demented**	**Demented**
0-5	0	2
6-10	0	1
11-15	3	4
16-20	9	5
21-25	16	3
26-30	18	1
Total	46	16

A) Use R to calculate the sensitivity and specificity of the test when a CMMS score of ≤20 is used to identify people with dementia.

Commented [AK1]: 25 points

Sensitivity=0.750 and Specificity=0.739 with cutoff of ≤20. (See R Code for B for these numbers.)

B) The cut-off value of ≤20 is arbitrary. Make a table showing sensitivity and specificity for cut-off values of 5, 10, 15, 20, 25, or 30. Use R to obtain the values. You can use whatever software you like to make the table, but simply printing out a matrix or data frame in R with all the values in it is fine, too.

* Problem adapted from Rosner's *Fundamentals of Biostatistics*. Data from Katzman, R., Zhang, M., Wang, Z., Liu, W.T., Yu, E., Wong, S.C., Salmon, D.P. and Grant, I., 1988. A Chinese version of the Mini-Mental State Examination; impact of illiteracy in a Shanghai dementia survey. *Journal of clinical epidemiology*, *41*(10), pp.971-978.

```
###Parts A and B

##Create dataframe of information from table
cmms <- data.frame(
        d = c(2, 1, 4, 5, 3, 1),
        nd = c(0, 0, 3, 9, 16, 18),
        score = c(5, 10, 15, 20, 25, 30)
)

cmms #print data frame to check values
  d nd score
1 2  0     5
2 1  0    10
3 4  3    15
4 5  9    20
5 3 16    25
6 1 18    30


##Create function to summarize the false positives, true positives, false neg
atives, and true negatives to calculate sensitivity and specificity

test_CMMS <- function(cmms, threshold) {
#cmms: feed in cmms data
#threshold: threshold score to use

   fp <- sum( cmms[cmms$score<=threshold, "nd"] )
   tp <- sum( cmms[cmms$score<=threshold, "d"] )

   tn <- sum( cmms[cmms$score>threshold, "nd"] )
   fn <- sum( cmms[cmms$score>threshold, "d"] )

   res <- c(sensitivity = tp / (tp + fn), specificity = tn / (tn + fp))

   return(res)
}

##Calculate sens and spec for all possible score thresholds

roc <- rbind(cutoff= seq(0,30,by=5), sapply(seq(0,30,by=5), function(x) test_
CMMS(cmms=cmms, threshold=x)) )

roc #print table of results
            [,1]  [,2]    [,3]       [,4]       [,5]       [,6] [,7]
cutoff         0 5.000 10.0000 15.0000000 20.0000000 25.0000000   30
sensitivity    0 0.125  0.1875  0.4375000  0.7500000  0.9375000    1
specificity    1 1.000  1.0000  0.9347826  0.7391304  0.3913043    0
```

C) In the context of this specific diagnostic test—a survey instrument to identify dementia—brainstorm a possible consequence of a false positive, then a possible consequence of a false negative.

Many different consequences could exist, two possibilities are:

A false positive will needlessly raise anxiety in persons and their families.

A false negative would delay potential intervention that could benefit a person.

D) Based on your table in part B, select a cut-off for the CMMS, assuming CMMS false positives and false negatives are equally undesirable (in reality, the errors might not be equally problematic, as we saw in Part C).

Commented [AK2]: 25 points

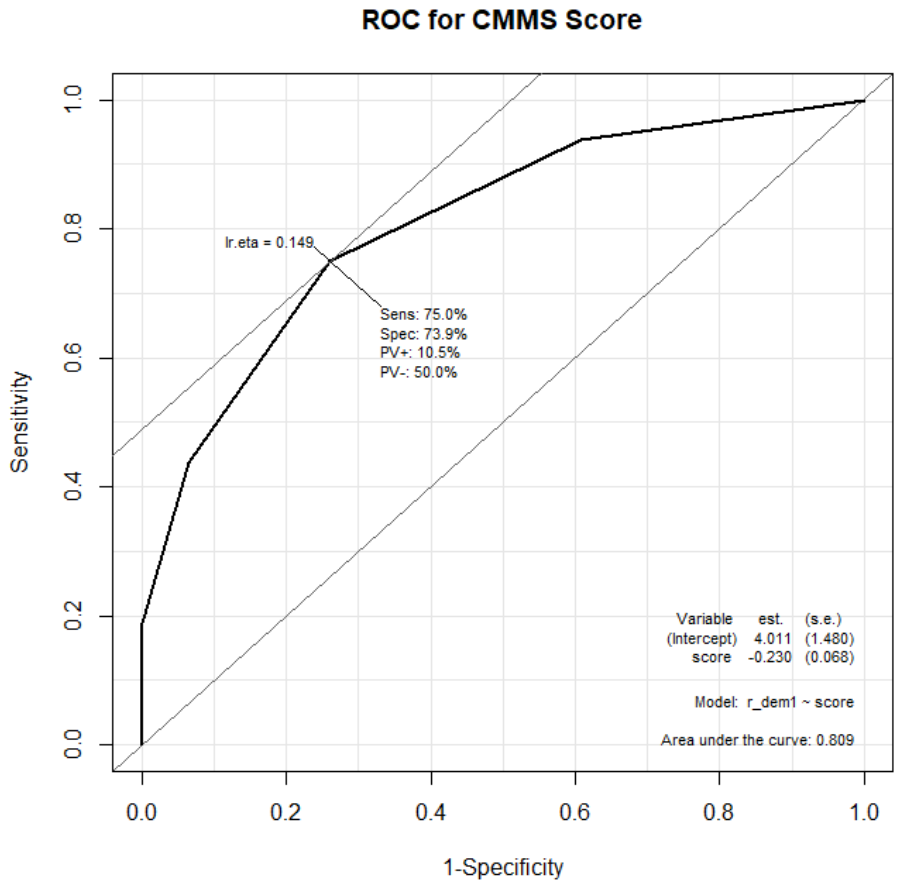
A cutoff of 20 balances false negatives and false positives.

E) Plot the ROC curve and obtain the AUC using R. How well do you think the CMMS discriminates between people with and without dementia?

Commented [AK3]: 25 points

Use data manipulation functions to create a data frame (e.g. data.frame() along with the rep(), cbind() and rbind() functions) such that each row represents two variables for each person in the dataset: the score on the CMMS and whether or not a person has dementia. Apply the Epi package in R to plot the ROC curve and obtain the AUC (you can refer to the R code in Lecture 9).

```
###Part E - Plot ROC curve and obtain AUC

## First, expand the dataframe above separtely for those w/ and w/o dementia
# For those with dementia:
dem_expand <- data.frame(score=rep(cmms$score, cmms$d))
r_dem1 <- rep(1, length(dem_expand))

# Merge the two columns for those with dementia
dem_r <- cbind(dem_expand, r_dem1)

# For those without dementia:
nodem_expand <- data.frame(score=rep(cmms$score, cmms$nd))
r_dem1 <- rep(0, length(nodem_expand))

# Merge the two columns for those without dementia
dem_nr <- cbind(nodem_expand, r_dem1)

# Now merge/bind the rows of the two data frames together into one data frame
cmms_exp <- rbind(dem_r, dem_nr)

# Now obtain the ROC plot with AUC using the Epi package function - Lecture 9
library(Epi)
ROC(form = r_dem1 ~ score, data = cmms_exp, plot = "ROC", main = "ROC for CMM
S Score"  )
```



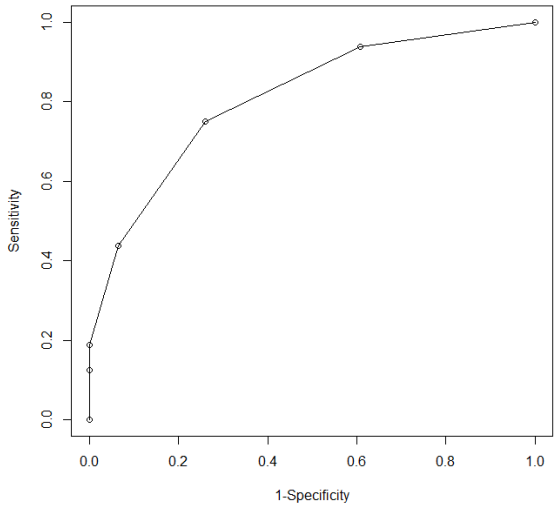
Our AUC is 0.809. Yes, there is fairly good discrimination. In 80% of possible pairs of persons with and without dementia the CMMS is lower in the person with dementia.

F) Extra Credit: Plot the ROC curve using your answers in B. Use programming statements to implement the trapezoidal rule to obtain the AUC. How similar is it to the AUC from part E?

Commented [AK4]: 1 extra credit point

```
###Part F: extra credit-plot ROC curve based on answers from part B and imple
ment the trapezoidal rule to obtain AUC

plot(1 - roc["specificity", ], roc["sensitivity", ], type = "o", xlab='1-Spec
ificity', ylab='Sensitivity')

##Create function for trapezoidal rule calculation
auc_trap_calculation <- function(index){

        x1 <- 1 - roc["specificity", index]
        y1 <- roc["sensitivity", index]

        x2 <- 1 - roc["specificity", index + 1]
        y2 <- roc["sensitivity", index + 1]

        abs( (y1 + y2) * (x2 - x1) /2 )
}

sum( sapply(1:(ncol(roc) - 1), auc_trap_calculation) )
[1] 0.8091033
```

The AUC using the trapezoidal rule in this case is nearly the same as AUC in part E (AUC=0.809 for both with rounding).



G) For a cutoff of ≤20, what would the positive and negative predictive values (PPV, NPV) of the CMMS be in a Chinese population with dementia prevalence of 10%? Of 40%? Comment on the difference in the sets of predictive values for the two prevalence values.

Commented [AK5]: 25 points

```
###Part G: calculuate PPV and NPV for given prevalence values based on a cuto
ff of <=20
Se <- as.numeric( roc['sensitivity', which(roc['cutoff',]==20)] )
Sp <- as.numeric( roc['specificity', which(roc['cutoff',]==20)] )

##10% prevalence
p <- 0.10
PPV_10 <- Se*p/(Se*p + (1-Sp)*(1-p))
PPV_10
  0.2421053

NPV_10 <- Sp*(1-p)/((1-Se)*p + Sp*(1-p))
NPV_10
  0.9637795

##40% prevalence
p <- 0.40
PPV_40 <- Se*p/(Se*p + (1-Sp)*(1-p))
PPV_40
  0.6571429

NPV_40 <- Sp*(1-p)/((1-Se)*p + Sp*(1-p))
NPV_40
  0.816
```

At 10% prevalence, we have PPV=24.2% and NPV=96.4%. At 40% prevalence we have PPV=65.7% and NPV=81.6%. In general, PPV will tend to be high when prevalence is high and NPV will be high when prevalence is low, which we see by comparing our two prevalence values.

H) Extra Credit: In contrast to the PPV and NPV, likelihood ratios (LR+ and LR-) are measures of a test's clinical utility that do not depend on prevalence. (Note: A rule of thumb is "LR+ ≥ 5" helps "rule in" disease, whereas LR- ≤ 0.2 helps "rule out" disease.)

i. Calculate the LR+ and LR- for each of the cut-offs in Part B. Summarize what you observe. Is there a single cutoff that makes the CMMS a good test for both ruling in and ruling out dementia?

Commented [AK6]: 1 extra credit point

```
###Part H: Extra credit
##H.i-calculuate LR+ and LR- values

LR_POS <- roc["sensitivity", ] / (1 - roc["specificity", ])
LR_POS
[1]      NaN      Inf      Inf 6.708333 2.875000 1.540179 1.000000
LR_NEG <- (1 - roc["sensitivity", ]) / roc["specificity", ]
LR_NEG
[1] 1.0000000 0.8750000 0.8125000 0.6017442 0.3382353 0.1597222       NaN

LR <- rbind(roc, LR_POS, LR_NEG) #append LR values to roc
LR
            [,1]  [,2]    [,3]        [,4]        [,5]        [,6] [,7]
cutoff         0 5.000 10.0000 15.0000000 20.0000000 25.0000000   30
sensitivity    0 0.125  0.1875  0.4375000  0.7500000  0.9375000    1
specificity    1 1.000  1.0000  0.9347826  0.7391304  0.3913043    0
LR_POS       NaN   Inf     Inf  6.7083333  2.8750000  1.5401786    1
LR_NEG         1 0.875  0.8125  0.6017442  0.3382353  0.1597222  NaN
```

No cutoff is good for both ruling in and ruling out dementia. 15 is a good cutoff for ruling in, LR+= 6.7, and 25 is a good cutoff for ruling out, LR- = 0.16.

ii. Assuming prior odds of dementia of 0.3, obtain the posterior odds of dementia and the posterior odds of no dementia for the various combinations of LR+ and LR-. Summarize what you observe.

Commented [AK7]: 2 extra credit points

```
##H.ii-posterior odds
Pr_Odds_Dem <- 0.3
Pr_Odds_Dem
[1] 0.3
Pr_Odds_NoDem <- 1/Pr_Odds_Dem
Pr_Odds_NoDem
[1] 3.333333

Post_Odds_Dem <- Pr_Odds_Dem*LR_POS
Post_Odds_NoDem <- Pr_Odds_NoDem*(1/LR_NEG)

Posterior <- rbind(LR, Pr_Odds_Dem, Post_Odds_Dem, Pr_Odds_NoDem, Post_Odds_NoDem)
Posterior
                    [,1]     [,2]      [,3]       [,4]       [,5]       [,6]       [,7]
cutoff          0.000000 5.000000 10.000000 15.0000000 20.0000000 25.0000000 30.000000
sensitivity     0.000000 0.125000  0.187500  0.4375000  0.7500000  0.9375000  1.000000
specificity     1.000000 1.000000  1.000000  0.9347826  0.7391304  0.3913043  0.000000
LR_POS               NaN      Inf       Inf  6.7083333  2.8750000  1.5401786  1.000000
LR_NEG          1.000000 0.875000  0.812500  0.6017442  0.3382353  0.1597222       NaN
Pr_Odds_Dem     0.300000 0.300000  0.300000  0.3000000  0.3000000  0.3000000  0.300000
Post_Odds_Dem        NaN      Inf       Inf  2.0125000  0.8625000  0.4620536  0.300000
Pr_Odds_NoDem   3.333333 3.333333  3.333333  3.3333333  3.3333333  3.3333333  3.333333
Post_Odds_NoDem 3.333333 3.809524  4.102564  5.5394525  9.8550725 20.8695652       NaN
```

The posterior odds of dementia are maximized at the cutoff of 15 and the posterior odds of no dementia are maximized at the cutoff of 25.