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of PUBLIC HEALTH

Lecture 5

Review MLE and inference in logistic regression models
Prediction/classification using logistic regression models

Lecture 4 Review

- We spent all of the time in the 10:30am session working on the confounding analysis.
  ↳ example write-up
- We will start with review of MLE and then delve into inference.

MLE in logistic models

Assume the following model:

$Pr(Y_i = 1)$

- $Y_i \sim Bernoulli(\mu_i)$ for $i = 1, ..., n$ independent observations.
- Define the vector of covariates for subject i as $x_i = (1, x_{1i}, x_{2i}, ..., x_{pi})$.
- Define the vector of association parameters $\beta = (\beta_0, \beta_1, ..., \beta_p)$.
- Assume the logit link such that:

$$log\left(\frac{\mu_i}{1-\mu_i}\right) = x_i'\beta \rightarrow \mu_i = \frac{e^{x_i'\beta}}{1+e^{x_i'\beta}}$$

NOTE: We should really write $\mu_i(x_i, \beta)$ i.e. μ_i is a function of x_i and β. In this handout, I will simplify this to $\mu_i(\beta)$.

MLE in logistic models

We can express the likelihood function as:

$$
\begin{aligned}
L(\beta|y) &= Pr(Y_1 = y_1, Y_2 = y_2, ..., Y_n = y_n|\beta) \\
&= \prod_{i=1}^{n} Pr(Y_i = y_i|\beta) \\
&= \prod_{i=1}^{n} \mu_i(\beta)^{y_i}[1 - \mu_i(\beta)]^{1-y_i}
\end{aligned}
$$

The log-likelihood function is:

$$
log[L(\beta|y)] = \sum_{i=1}^{n} y_i log[\mu_i(\beta)] + (1 - y_i)log[1 - \mu_i(\beta)]
$$

MLE in logistic models

The score equation, $U(\beta)$ is the derivative of the log-likelihood function with respect to β.

$$
\begin{aligned}
U(\beta) &= \frac{\partial log[L(\beta|y)]}{\partial\beta} \\
&= \sum_{i=1}^{n} y_i \frac{\partial log[\mu_i(\beta)]}{\partial\beta} + (1-y_i)\frac{\partial log[1-\mu_i(\beta)]}{\partial\beta} \\
&= \sum_{i=1}^{n} y_i\left(x_i[1-\mu_i(\beta)]\right) + (1-y_i)[-\mu_i(\beta)x_i] \\
&= \sum_{i=1}^{n} x_i\left(y_i - y_i\mu_i(\beta) + (-\mu_i(\beta)) + y_i\mu_i(\beta)\right) \\
&= \sum_{i=1}^{n} x_i(y_i - \mu_i(\beta))
\end{aligned}
$$

Liner model

$\hat{\beta} = (X'X)^{-1}X'y$

$$U(\beta) = X'(Y - \mu(\beta))$$

MLE in logistic models

NOTE: We will also need to know $U'(\beta) = \frac{\partial U(\beta)}{\partial \beta}$

$$\begin{aligned} U'(\beta) &= \frac{\partial U(\beta)}{\partial \beta} \\ &= \frac{\partial}{\partial \beta} X'(Y - \mu(\beta)) \\ &= - X' \frac{\partial \mu_i(\beta)}{\partial \beta} \\ &= \underbrace{- X'VX} \end{aligned}$$

diagonal matrix $\begin{bmatrix} \mu_1(\beta)(1-\mu_1(\beta)) & & 0 \\ & \ddots & \\ 0 & & \mu_n(\beta) \times (1-\mu_n(\beta)) \end{bmatrix}$

where we already showed that:

$$\frac{\partial \mu_i(\beta)}{\partial \beta} = \mu_i(\beta) \frac{\partial log[\mu_i(\beta)]}{\partial \beta} = \mu_i(\beta)(1 - \mu_i(\beta))x_i$$

and $V_{n \times n} = diag(\mu_i(\beta)[1 - \mu_i(\beta)])$.

Newton-Raphson Method to find “beta”

scalar β

- Step 0: Pick an initial starting value for β, call this $\hat{\beta}^{(k)}$.
- Step 1: Compute the slope of $U(\beta)$ at $\hat{\beta}^{(k)}$, i.e. compute $U'(\hat{\beta}^{(k)})$.
- Step 2: Construct the tangent line, which is a line that passes through the points $(\hat{\beta}^{(k)}, U(\hat{\beta}^{(k)}))$ and $(\hat{\beta}^{(k+1)}, 0)$ and has slope $U'(\hat{\beta}^{(k)})$.
- Step 3: Solve the following for $\hat{\beta}^{(k+1)}$:

$$\begin{aligned}
U'(\hat{\beta}^{(k)}) &= \frac{U(\hat{\beta}^{(k)})-0}{\hat{\beta}^{(k)}-\hat{\beta}^{(k+1)}} \\
[\hat{\beta}^{(k)} - \hat{\beta}^{(k+1)}]U'(\hat{\beta}^{(k)}) &= U(\hat{\beta}^{(k)}) \\
\hat{\beta}^{(k)} - \hat{\beta}^{(k+1)} &= U'(\hat{\beta}^{(k)})^{-1}U(\hat{\beta}^{(k)}) \\
\hat{\beta}^{(k+1)} &= \hat{\beta}^{(k)} - U'(\hat{\beta}^{(k)})^{-1}U(\hat{\beta}^{(k)}) \\
\hat{\beta}^{(k+1)} &= U'(\hat{\beta}^{(k)})^{-1}\left(U'(\hat{\beta}^{(k)})\hat{\beta}^{(k)} - U(\hat{\beta}^{(k)})\right)
\end{aligned}$$

- Step 4: Stop if $|\hat{\beta}^{(k+1)} - \hat{\beta}^{(k)}|$ is small. If not, let $k = k + 1$ and repeat Steps 2 through 4.

Newton-Raphson Method to find "beta"

- In general, when "beta" is a vector:

$U'(\beta) = -X'VX$

$U(\beta) = X'(Y-\mu(\beta))$

$$
\begin{aligned}
\hat{\beta}^{(k+1)} &= U'(\hat{\beta}^{(k)})^{-1}\left(U'(\hat{\beta}^{(k)})\hat{\beta}^{(k)} - U(\hat{\beta}^{(k)})\right) \\
&= -(X'V^{(k)}X)^{-1}\left[-(X'V^{(k)}X)\hat{\beta}^{(k)} - X'(Y-\mu(\hat{\beta}^{(k)}))\right] \\
&= (X'V^{(k)}X)^{-1}\left[X'V^{(k)}\left(X\hat{\beta}^{(k)} + V^{-1(k)}(Y-\mu(\hat{\beta}^{(k)}))\right)\right] \\
\hat{\beta}^{(k+1)} &= \underline{(X'V^{(k)}X)^{-1}(X'V^{(k)}Z^{(k)})}
\end{aligned}
$$

where

$$V^{(k)} = diag(\mu_i(\beta^{(k)})[1-\mu_i(\beta^{(k)})])$$

$$\underline{Z^{(k)}} = X\hat{\beta}^{(k)} + V^{-1(k)}\left(Y - \mu(\hat{\beta}^{(k)})\right) = \text{a surrogate response.}$$

Iteratively Re-weighted Least Squares

IRLS

The general procedure is:

- Step 0: Set an initial value for $\hat{\beta}^{(k)}$, $k = 0$.
- Step 1: Calculate: $V^{(k)}$, $\hat{\mu}(\hat{\beta}^{(k)})$, $Z^{(k)}$.
- Step 2: Update $\hat{\beta}^{(k+1)} = \underbrace{(X'V^{(k)}X)^{-1}(X'V^{(k)}Z^{(k)})}$
- Step 3: Stop if $\sum_{j=1}^{p+1}\left(\hat{\beta}_j^{(k+1)} - \hat{\beta}_j^{(k)}\right)^2 < \epsilon$; if not, let $k = k + 1$ and repeat Steps 2 and 3.

IRLS vs weighted least squares

Compare the IRLS to the weighted least squares solution we derived last term:

$$\hat{\beta}_{WLS} = \left(X'\hat{V}^{-1}X\right)^{-1}\left(X'\hat{V}^{-1}Y\right)$$

These are different! $\hat{V}$ vs. $\hat{V}^{-1}$.

Recall that we derived: $\frac{\partial\mu(\beta))}{\partial\beta} = VX = diag\left[\mu(\beta)(1-\mu(\beta))\right]X$

So that,

$$\begin{aligned}
\hat{\beta}^{(k+1)} &= (X'V^{(k)}X)^{-1}(X'V^{(k)}\boxed{Z^{(k)}}) \\
&= \left(\frac{\partial\hat{\mu}(\beta^{(k)})}{\partial\beta}'\hat{V}^{(k)-1}\frac{\partial\hat{\mu}(\beta^{(k)})}{\partial\beta}\right)^{-1}\left(\frac{\partial\hat{\mu}(\beta^{(k)})}{\partial\beta}'\hat{V}^{(k)-1}Z^{*(k)}\right)
\end{aligned}$$

where $Z^{*(k)} = \frac{\partial\hat{\mu}(\beta^{(k)})}{\partial\beta}\hat{\beta}^{(k)} + \left(Y - \mu(\hat{\beta}^{(k)})\right)$.

Inference in logistic regression models

- Using similar arguments as we did for linear models: $\underbrace{\hat{\beta}_{mle}}_{\text{approx}} \approx N(\beta, [X'VX]^{-1})$

- Inference for a single coefficient:

Test $H_0 : \beta_j = b$ via $Z = \frac{\hat{\beta}_j - b}{\sqrt{[X'VX]^{-1}_{jj}}}$

Confidence intervals can be derived as: $\hat{\beta}_j \pm 1.96\sqrt{[X'VX]^{-1}_{jj}}$

- Inference for a linear combination of coefficients:

Define $d = w'\beta$ where w is a $(p+1) \times 1$ vector of scalars to create the relevant linear combination of β.

Estimate d via $w'\hat{\beta}$ and $se(\hat{d}) = \sqrt{w' [X'VX]^{-1} w}$

Confidence interval for d: $\hat{d} \pm 1.96 se_{\hat{d}}$.

Test $H_0 : d = \delta$ via $Z = \frac{\hat{d} - \delta}{se_{\hat{d}}}$.

Inference in logistic regression models: Nested models

Here we assume we have a model with $\beta = (\beta_0, \beta_1, ..., \beta_p, \beta_{p+1}, ..., \beta_{p+s})$ and define $\beta^+ = (\beta_{p+1}, .., \beta_{p+s})$.

To conduct a Wald test of ~~(H_0~~: all $\beta_{p+j} = 0, for j = 1, ..., s,$

H_0:

$$W = \hat{\beta}^{+'} \left[(X'VX)^{-1}_{(+,+)} \right]^{-1} \hat{\beta}^{+} \approx \sum_{j=1}^{s} Z_j^2 \sim \chi_s^2$$

reject H_0 if $W > \chi^2_{s,1-0.05/2}$.

When the null hypothesis is true and sample size is large enough:

$$\Delta = -2 \left[logLike_N(y, \hat{\beta}_N) - logLike_E(y, \hat{\beta}_E) \right] \sim \chi_s^2$$

Δ represents the "change in deviance" where

$$deviance = -2 \left[logLike_N(y, \hat{\beta}_N) - logLike_E(y, y) \right] \sim \chi_s^2$$

where $logLike_E(y, y)$ is the biggest possible value.

The deviance is a measure of fidelity of the model to the data, like the residual sum of squares for linear regression.

Examples

NMES setup

bigexp = $\begin{cases} 1 & > 1000 \\ 0 & o/w \end{cases}$

```
data1$agec = data1$lastage - 60
data1$agesp1 = ifelse(data1$lastage>65,data1$lastage-65,0)
data1$agesp2 = ifelse(data1$lastage>80,data1$lastage-80,0)

fit0 = glm(bigexp~mscd+agec+agesp1+agesp2,data=data1,family="binomial")
fit1 = glm(bigexp~mscd*(agec+agesp1+agesp2),data=data1,family="binomial")
```

- Write out the model you are fitting in "fit0" and "fit1".

fit0:

$$\text{Logit}\left[\Pr(\text{bigexp}=1 \mid \text{mscd}, \text{age})\right] = {}^{*}\beta_0 + \beta_1 \text{mscd} + \beta_2(\text{age}-60) + \beta_3(\text{age}-65)^+ + \beta_4(\text{age}-80)^+$$

Fit1:

$$\text{Logit}\left[\Pr(\text{bigexp}=1 \mid \text{mscd}, \text{age})\right] = * + \beta_5 \text{mscd}(\text{age}-60) + \beta_6 \text{mscd}(\text{age}-65)^+ + \beta_7 \text{mscd}(\text{age}-80)^+$$

Example: Testing a single coefficient

- Test the null hypothesis that after adjusting for age, there is no relationship between a big expenditure and a MSCD.

$\rightarrow$ Fit0 $\quad H_0: \beta_1 = 0 \quad H_A: \beta_1 \neq 0$

```r
summary(fit0)$coefficients
```

```
##                 Estimate  Std. Error    z value      Pr(>|z|)
## (Intercept) -0.716235408 0.030036992 -23.8451109 1.138097e-125
## mscd         1.603178804 0.068286173  23.4773561 6.949175e-122
## agec         0.028079056 0.002891139   9.7121075  2.677428e-22
## agesp1      -0.005830743 0.007465457  -0.7810296  4.347851e-01
## agesp2      -0.002128496 0.019276490  -0.1104193  9.120769e-01
```

$$z = \frac{\hat{\beta}_1 - 0}{se(\hat{\beta}_1)} = \frac{1.60 - 0}{.068} \approx 23.48$$

Example: Linear combination of coefficients

- Using Model1, estimate the log odds ratio of a big expenditure comparing persons with and without a MSCD whom are 70 years old.

$= \beta_0 + \beta_1 \text{mscd} + \beta_2 (\text{age}-60) + \beta_3 (\text{age}-65)^+ + \beta_4 (\text{age}-80)^+ + \beta_5 \text{mscd} (\text{age}-60) + \beta_6 \text{mscd} \times (\text{age}-65)^+ + \beta_7 \text{mscd} (\text{age}-80)^+$

- What is the appropriate linear combination of β?

$\beta_1 + 10\beta_5 + 5\beta_6$

package biostat3

```
## Confirm using lincom command
lincom(fit1,c("mscd+10*mscd:agec+5*mscd:agesp1"))
```

```
##                              Estimate    2.5 %  97.5 %    Chisq   Pr(>Chisq)
## mscd+10*mscd:agec+5*mscd:agesp1 1.513507 1.351594 1.67542 335.6613 5.620428e-75
```

Example: Linear combination of coefficients

β_1 β_5 β_6

```
## In Model 1: Compute the OR for big expenditure vs. mscd for 70 year olds
w = c(0,1,0,0,0,10,5,0)
var.cov = summary(fit1)$cov.scaled
beta = fit1$coefficients
# estimate
t(w) %*% beta
```

$Var(\hat{\beta})$

$\rightarrow \hat{\beta}$

```
##              [,1]
## [1,] 1.513507
```

```
# standard error
t(w) %*% var.cov %*% w
```

```
##                [,1]
## [1,] 0.006824451
```

```
# test statistic
t(w) %*% beta / sqrt(t(w) %*% var.cov %*% w)
```

```
##              [,1]
## [1,] 18.32106
```

```
# Square test statistic ~ chi-square 1
(t(w) %*% beta / sqrt(t(w) %*% var.cov %*% w))^2
```

```
##              [,1]
## [1,] 335.6613
```

Example: Nested models

- Model0 is nested within Model1.

- What null and alternative hypothesis are you testing if you compare Model1 and Model 0?

$H_0: \beta_5 = 0, \beta_6 = 0, \beta_7 = 0$ H_A: at least one is non-zero

Does the logodds ratio for a big exp comparing those with and without a mscd differ by age?

- Wald test

```r
## Nested model: Wald test for interaction
index = 6:8
# Compute the wald test
w = t(fit1$coeff[index]) %*% solve(var.cov[index,index]) %*% fit1$coeff[index]
w
```

```
##              [,1]
## [1,] 14.53997
```

$\sim \chi^2_3$

```r
pchisq(w,lower.tail=FALSE,df=3)
```

```
##                [,1]
## [1,] 0.002255128
```

Example: Nested models

- Likelihood ratio test

```r
## Nested model: likelihood ratio test
lrtest(fit1,fit0)
```

```
## Likelihood ratio test
##
## Model 1: bigexp ~ mscd * (agec + agesp1 + agesp2)
## Model 2: bigexp ~ mscd + agec + agesp1 + agesp2
##   #Df  LogLik Df  Chisq Pr(>Chisq)
## 1   8 -7126.9
## 2   5 -7134.5 -3 15.185   0.001665 **
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

Logistic regression models as classifiers!

- Models for binary responses can be used to classify individuals
  - Logistic regression models
  - Classification and regression trees
  - Random forests

- May be interested in identifying
  - Persons at high risk for a big expenditure
  - Persons from a community clinic who are infected with HIV
  - Patients at high risk for requiring post acute care placement

- Diagnosis of disease or screening for procedures is classification!

Notation and definitions

- Data: $(Y_1, X_1), ..., (Y_n, X_n)$ where X_i is a $(p+1) \times 1$ vector of exposures/predictors.
- Model: $logit[Pr(Y_i = 1|X_i)] = X_i^{'}\beta$
- Fit the Model: $\hat{\beta} \to \hat{\mu}_i = \frac{exp(X_i^{'}\hat{\beta})}{1+exp(X_i^{'}\hat{\beta})}$ $= \hat{Pr}(Y_i = 1)$

- Define a classification rule: $d_i(\hat{\mu}_i, c) = \begin{cases} 1 \text{ if } \hat{\mu}_i > c \\ 0 \text{ if } \hat{\mu}_i \leq c \end{cases}$

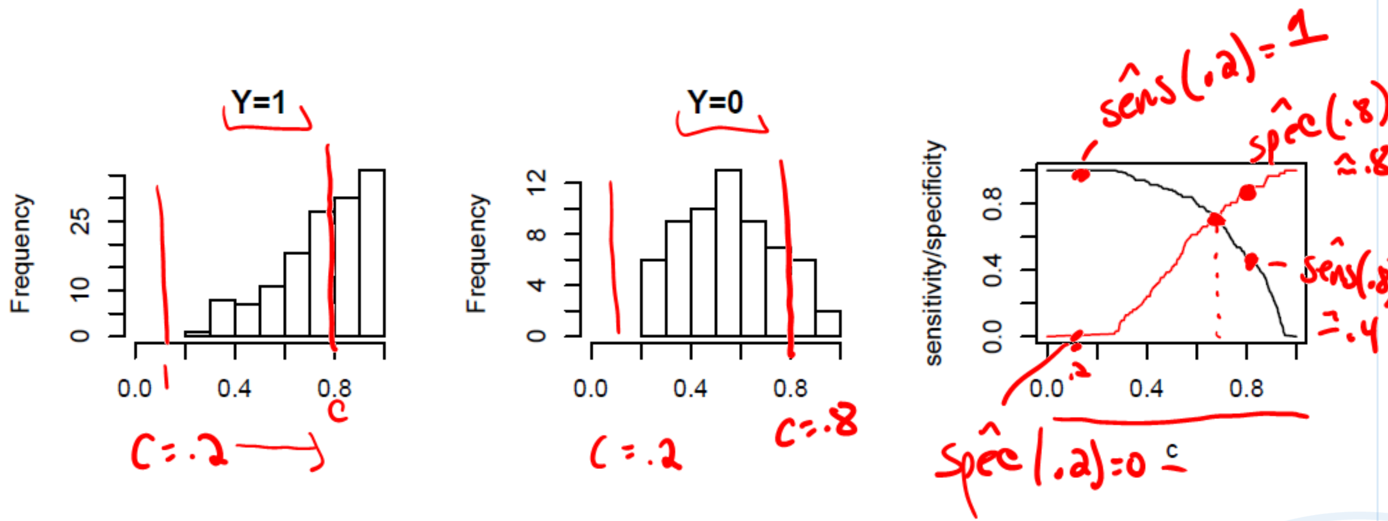
- Define sensitivity and specificity based on the classification rule:

$\hat{sens}(c) = Pr(d_i(\hat{\mu}_i, c) = 1 \mid Y_i = 1) = Pr(\hat{\mu}_i > c \mid Y_i = 1)$

$\hat{spec}(c) = Pr(d_i(\hat{\mu}_i, c) = 0 \mid Y_i = 0) = Pr(\hat{\mu}_i \leq c \mid Y_i = 0)$

Defining and evaluating the classifier

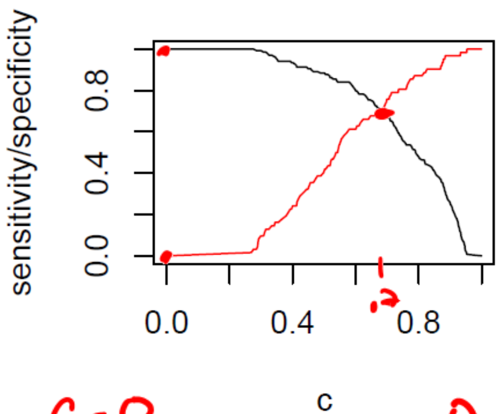
- Set c so we can maximize both sensitivity and specificity
  - Plot sens and spec as a function of c

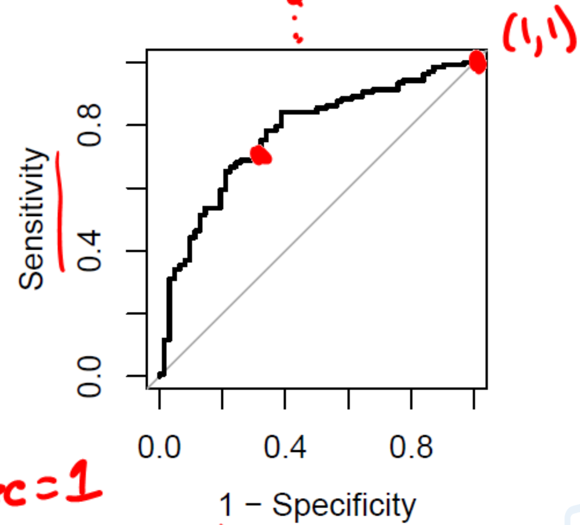


Defining and evaluating the classifier

- Evaluate the entire model upon which the classifier is based
  - Receiver Operating Characteristic (ROC) curve
  - Plot sens vs. 1-spec for each c

c	sens(c)	1-spec(c)
0		
.1		
.2		
⋮		



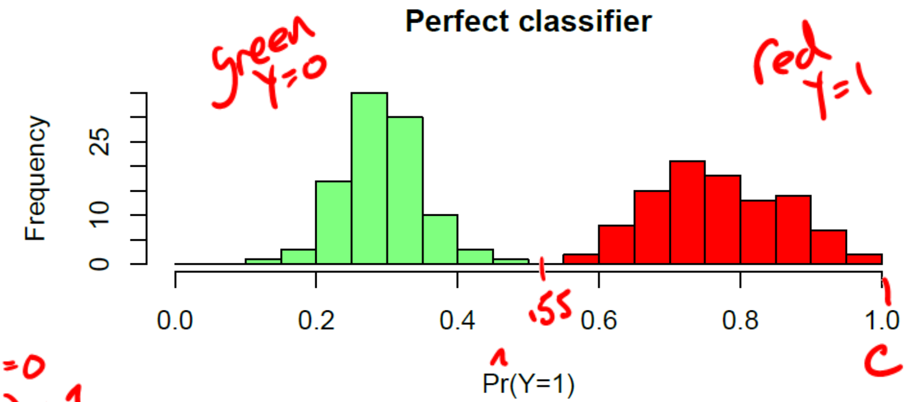


C = 0 sens = 1, spec = 0, 1-spec = 1

C = .7 sens = .7 spec = .7, 1-spec = .3

Example: Perfect classifier

- Plot sens vs. 1-spec for each c



- When c = 1:

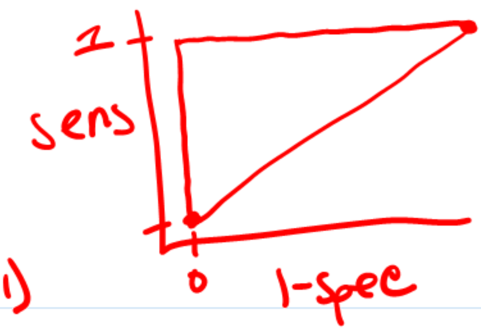
$Sens = Pr(\hat{\mu}_i > 1 \mid Y=1) = 0$

$Spec = Pr(\hat{\mu}_i \le 1 \mid Y=0) = 1$

- When 0.55 < c < 1:

$spec = 1$

$sens = Pr(\hat{\mu}_i > c \mid Y=1) \in (0,1)$



- When 0 < c < 0.55:

$Sens = Pr(\hat{\mu}_i > c \mid Y=1) = 1$

$spec = Pr(\hat{\mu}_i \le c \mid Y=0) \in (0,1)$

Example: No discrimination

- When c = 1:

$$\widehat{sens}(1) = Pr(\hat{\mu}_i > 1 \mid Y_i = 1) = 0$$
$$\widehat{spec}(1) = Pr(\hat{\mu}_i \le 1 \mid Y_i = 0) = 1$$

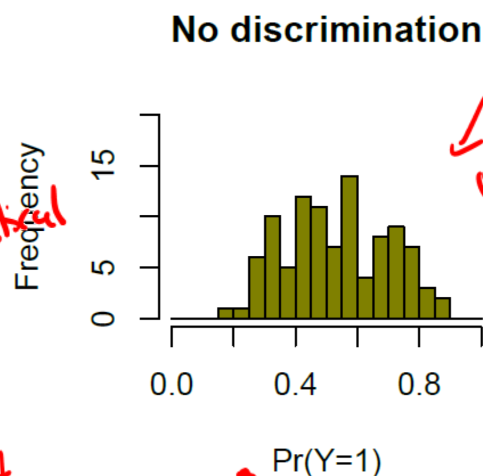
- When 0 < c < 1:

$$\widehat{sens}(c) = Pr(\hat{\mu}_i > c \mid Y_i = 1)$$
$$1-\widehat{spec}(c) = Pr(\hat{\mu}_i > c \mid Y_i = 0)$$

identical $\in (0,1)$

- When c = 0:

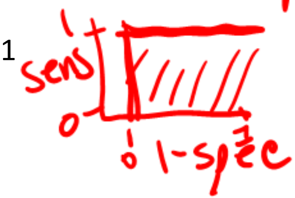
$$\widehat{sens}(0) = Pr(\hat{\mu}_i > 0 \mid Y_i = 1) = 1$$
$$1-\widehat{spec}(0) = Pr(\hat{\mu}_i > 0 \mid Y_i = 0) = 1$$



complete overlap of Y=1 / Y=0

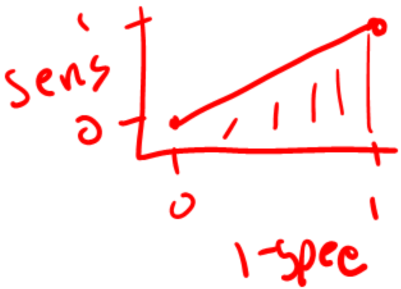
Area under the ROC curve (AUC)

- The area under the ROC curve represents a measure of discrimination between cases and controls
- Probability that a randomly selected case (Y = 1) has a higher predicted probability than a randomly selected control (Y = 0).
  - You can prove this for fun!
- Perfect discrimination: AUC = 1
- No discrimination: AUC = 0.5



AUC = 1

$$\Pr\left(\hat{\mu}_i(Y_i=1) > \hat{\mu}_i(Y_i=0)\right)$$



AUC = .5

Minimize optimism

- To minimize optimism for your classifier/prediction, you should generate the ROC curve and compute the AUC based on a cross-validation procedure.

- Fit logistic model using subsets 2,3,4
- get $\hat{\mu}_i$ for subset 1

repeat to obtain $\hat{\mu}_i$ for subset

subset	Training data
2	1,3,4
3	1,2,4
4	1,2,3

$\hat{\mu}_{i,cv} \Rightarrow$ ROC $\Rightarrow$ AUC

CI's for AUC

↳ bootstrap procedure

Where to next?

- So far, we have considered using a logistic regression model to define a classifier.
- This approach requires that we build the regression model, i.e. we know the key predictors, including functional form for continuous variables and important interactions, etc.
- Instead of building a logistic regression model for developing a classifier, we will consider a classification and regression tree.
  - Removes the need for us to specify the model.

* random forests