User Guide for Diagnostic Test

- **The Results**
  - **Are likelihood ratios for the test results presented (or calculatable)?**
- **Will it help with my patients?**
  - **Will the reproducibility of the test result and its interpretation be satisfactory in my setting?**
  - **Are the results applicable to my patients?**
  - **Will the results change my management?**
  - **Will patients be better off as a result of the test?**

Several equivalent methods

- 2x2 table method
- Decision tree method
- Bayes's theorem
- The likelihood ratio (odds form)
- Each method produces the same result

General Method

- Start with a current probability (=prior probability, = prevalence) of having the disease P(D+)
- Obtain the result of a test T
- Revise our estimate of probability to take T into account: P(D+|T)

2x2 tables

- Sens = TP/ (TP+FN)
- Spec = TN/(TN+FP)
- FP rate = 1-Spec
- FN rate = 1-Sens
- Prevalence = (TP+FN)/(TP+FN+FP+TN)
- PPV = TP/(TP+FP)
- NPV = TN/(FN+TN)

	TP	FP
	FN	TN

PPV and NPV from prevalence, sens, spec

- ECG for Dx of acute MI: Sens=0.8, Spec=0.95
- Prevalence: 0.5
- Work backwards from prev & sens to fill in first column
- Use (1-prev) & spec to fill in second column
- Now use rows to calculate PPV and NPV
- PPV = 400 / 425 = 0.94
- NPV = 475 / 575 = 0.83

	MI+	MI-	Total
EKG+	400	25	425
EKG-	100	475	575
Total	500	500	1000

Bayes's Theorem

- **Relationship of odds to probability:**
  - **Odds = p/(1-p)**
  - **Prob = odds / (1+odds)**

1 **2**

p = 2/3
O = 2/1 = 2

Bayes's Theorem

	D+	D-
T+		
T-		

What are the odds that *this patient* has the disease?

Prior Odds

This will typically depend on the prevalence

$$\frac{P(D+)}{P(D-)}$$

Example: MI

Prevalence = 0.5

Prior odds ratio = 0.5 / 0.5 = 1

Bayes's Theorem

	D+	D-
T+		
T-		

We would like to know the odds that an individual *with a positive test* actually has the disease.

Prior odds

$$\frac{P(D+|T+)}{P(D-|T+)} \qquad \frac{P(D+)}{P(D-)}$$

This is based on the probability of having the disease or not, considering only those who would test positive.

This is called the *posterior odds.*
It is also called the *predictive odds with a positive test.*

Bayes's Theorem

The posterior odds depends on how accurate the test is

$$\frac{P(D+|T+)}{P(D-|T+)} = \boxed{\frac{P(T+|D+)}{P(T+|D-)}} \times \frac{P(D+)}{P(D-)}$$

$$\frac{\text{sensitivity}}{(1\text{-specificity})}$$

likelihood ratio

How do we combine the prior odds with the likelihood ratio to obtain the posterior odds?

Bayes's Theorem

$$\frac{P(D+|T+)}{P(D-|T+)} = \frac{P(T+|D+)}{P(T+|D-)} \times \frac{P(D+)}{P(D-)}$$

posterior odds	**=**	**likelihood ratio**	**X**	**prior odds**
updated info	**=**	**info from test**	**X**	**original info**

Updating information

Bayes's Theorem

	CA +	CA -	Totals
DRE +	62	127	189
DRE -	10	101	111
Totals	72	228	300

Post-test Odds		Likelihood Ratio		Pre-test Odds
$\frac{62}{127}$	=	$\frac{0.86}{(1-0.44)}$	x	$\frac{72}{228}$
$\frac{1}{2.0}$	=	1.54	x	$\frac{1}{3.2}$

Example: Diagnosis of acute MI

(Johnson HA, JAMA, 1991; 265: 2229-2231)

- **ECG: sens=0.80, spec = 0.95**
- **Creatine kinase (CK): sens=.95, spec=0.97**
- **Hx, PE suggest 50-50 chance of MI**
  - **This gives P(D+)**
  - **Based on judgment, presentation, sex, etc**
- **Prior odds of MI = 1**
- **LR for positive ECG = .80/.05 16.**
- **Thus, pos ECG $\rightarrow$ odds = 16:1 in favor of MI (posterior probability = 16/(1+16) 0.94)**

The next day

- **Prior odds of MI = 16 (at this point).**
- **We get the CK tests back**
- **CK is positive:**
- **LR for + CK 32, thus**
- **Posterior odds = 16 $\times$ 32 500**
- **Posterior probability 0.998**

Example: ECG and CK negative

- Prior odds = 1
- LR for negative ECG = .95/.20 = 4.75
- Posterior odds of no MI = 4.75
- Posterior prob of no MI = 4.75/5.75 = 0.826. [Posterior probability of MI is still 0.174—worth finding out about the CK]
- LR for negative CK = .97/.05 19. Thus, posterior odds becomes 90, for a probability of 0.989 of not having had an MI

Costs of increasing diagnostic certainty

- Johnson's framework: compare P(D+|T+) to P(D+), that is
- Consider the amount by which a positive result could change your assessment
- The posterior probability depends on both the test characteristics and prevalence
- Ordering a test = buying diagnostic information.
- If Dx is essentially certain, the relative cost of even very inexpensive tests is unwarranted

Logistic regression…

- **…fits the logit (log odds)as a linear function of the predictor variables**
- **logit =** $\alpha + \beta_1 X_1 + \beta_2 X_2 + \beta_3 X_3$
- **The response variable (Y) is a 0-1 outcome**
- **One needs special computer programs to do logistic regression**
  - **GLIM and Stata are examples**

GI Bleeding in Critical Care Patients

(Cook, et al. N EJM 1994; 330: 377-381)

- **Is respiratory failure a risk factor for significant GI bleed?**
- **Example uses Stata**

```
. blogit Bleed N RespFail

Logit Estimates                                   Number of obs =   2252
                                                  chi2(1)       =  56.97
                                                  Prob > chi2   = 0.0000
Log Likelihood = -143.63437                       Pseudo R2     = 0.1655
------------------------------------------------------------------------------
_outcome |      Coef.   Std. Err.       z     P>|z|    [95% Conf. Interval]
---------+--------------------------------------------------------------------
RespFail |   3.238835   .6073632      5.333   0.000    2.048425    4.429245
   _cons |   -6.27539   .5778899    -10.859   0.000   -7.408033   -5.142746
------------------------------------------------------------------------------

. blogit, or
------------------------------------------------------------------------------
_outcome | Odds Ratio   Std. Err.       z     P>|z|    [95% Conf. Interval]
---------+--------------------------------------------------------------------
RespFail |     25.504   15.49019      5.333   0.000    7.755678     83.8681
------------------------------------------------------------------------------
```

Multiple risk factors

- **Some patients have multiple risk factors.**
- **What is the (additional) effect of respiratory failure after taking all other possible risk factors into account?**
- **This is given in the “multiple regression” column of the table: odds that are 15.6 larger.**

```
. blogit Bleed N RespFail Coag, or

Logit Estimates                                   Number of obs =   2252
                                                  chi2(2)       =  72.11
                                                  Prob > chi2   = 0.0000
Log Likelihood = -136.06203                       Pseudo R2     = 0.2095

------------------------------------------------------------------------------
_outcome | Odds Ratio   Std. Err.       z     P>|z|     [95% Conf. Interval]
---------+--------------------------------------------------------------------
RespFail |   15.65489   9.76461      4.410   0.000     4.610205    53.15939
    Coag |   4.299613   1.701604     3.685   0.000     1.979521    9.338964
------------------------------------------------------------------------------
```

These are essentially the "Multiple regression" odds ratios in Table 4.

A worksheet

• Baseline odds of GI Bleed			0.001426*
• Respiratory failure	1	x 15.6=	x 15.6
• Coagulapathy	-	x 4.3 =	
• Product = Odds of GI Bleed			0.02224

Odds = 1 : 45

*** Baseline odds = 1 : 700**

A worksheet

• Baseline odds of GI Bleed			0.001426
• Respiratory failure	-	x 15.6=	
• Coagulapathy	1	x 4.3 =	x 4.3
• Product = Odds of GI Bleed			0.00613

Odds = 1 : 163

A worksheet

• Baseline odds of GI Bleed		0.001426
• Respiratory failure	1 x 15.6=	x 15.6
• Coagulapathy	1 x 4.3 =	x 4.3
• Product = Odds of GI Bleed		0.09562

Odds = 1 : 10

How to use?

• Neither Respiratory Failure nor Coagulopathy	0.0014	B= 2 / 1403	1:702
• Respiratory Failure Only	0.0223	B x 15.65	1:45
• Coagulopathy Only	0.0061	B x 4.3	1:163
• Both Respiratory Failure and Coagulopathy	0.0959	B x 15.65 x 4.3	1:10