Clinical Statistics… A Review of Some Basics

Julie Taub

Goals:

- Sensitivity/Specificity
- PPV/NPV
- Likelihood Ratios

2 x 2 Table

	+Disease +Outcome	**-Disease -Outcome**
+Test +Exposure	True Positive	False Positive
-Test -Exposure	False Negative	True Negative

2 x 2 Table

	+Disease +Outcome	-Disease -Outcome
+Test +Exposure	a	b
-Test -Exposure	c	d

What is the Sensitivity & Specificity ?

Fe Deficiency & Ferritin

Guyatt et al.

		Disease (Fe Deficiency) +	**Disease** (Fe Deficiency) -	
Test (Ferritin)	+ (<45)	**70**	**15**	85
	- (>45)	**15**	**135**	150
		85	150	235

Sensitivity:

- a/a+c = 70/85 = .82
- *Proportion of patients testing positive out of all patients with the disease.*
- *Probability that an individual with the disease will have a positive test.*
- *True Positive Rate*
- *SnNout*

Specificity:

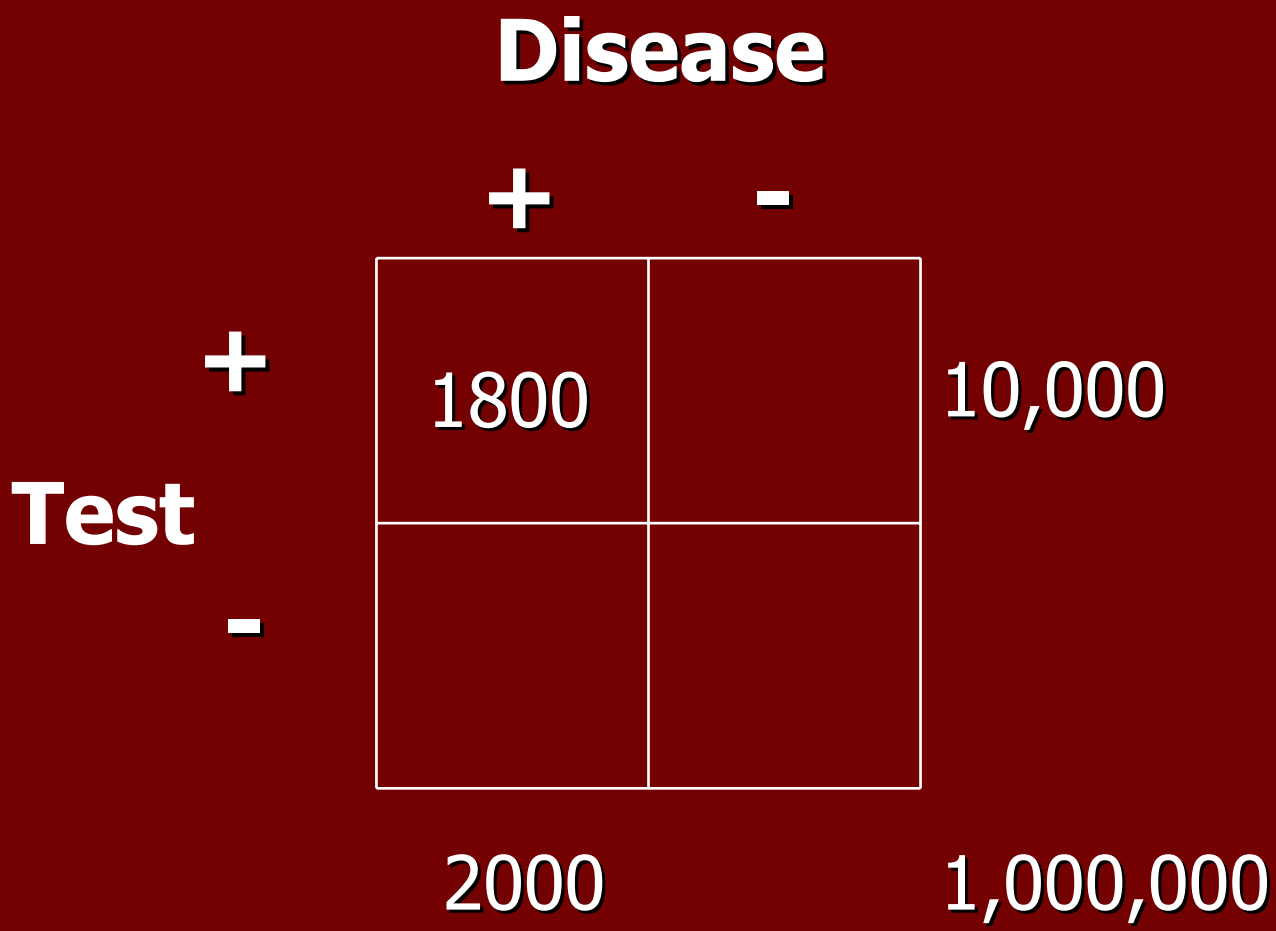
- d/b+d = 135/150 = .9
- *Proportion of patients testing negative out of all patients without the disease.*
- *Probability that an individual without the disease will have a negative test.*
- *True Negative Rate*
- *SpPin*

Example:

- Total Population = 1,000,000 people
- Incidence of disease = 1/500 people
- Test sensitivity = 90%
- Frequency of positive tests = 1%

Fill in a 2 x 2 Table &
determine the specificity

Example



Example

		Disease +	Disease -	
Test	+	1800	8200	10,000
	-	200	989,800	990,000
		2000	998,000	1,000,000

Specificity = 99%

The level of ferritin measured in blood is used as a diagnostic test for iron def anemia, the test being (+) if the ferritin is below a critical value. The sensitivity of the diagnostic test:

- *A) is one minus the specificity*
- *B) is a measure of how well the test detects cases of the disease*
- *C) is the proportion of people with the disease who are (+) on the test*
- *D) increases if the critical value is increased*
- *E) measures how well people without the disease are excluded*

Adapted from Bland M. An introduction…

The level of ferritin measured in blood is used as a diagnostic test for iron def anemia, the test being (+) if the ferritin is below a critical value. The sensitivity of the diagnostic test:

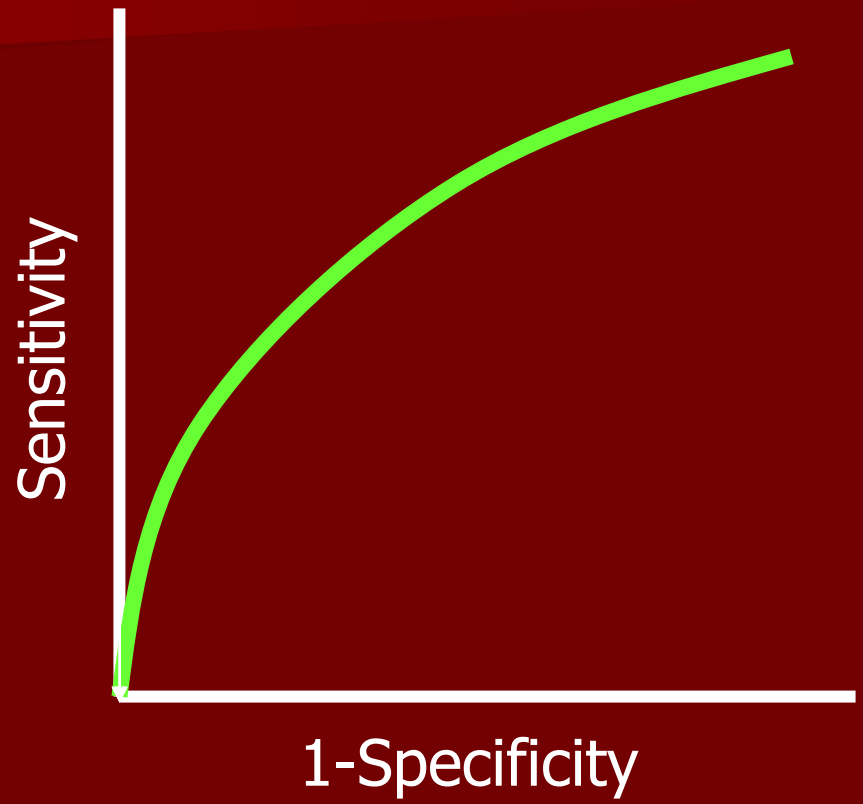
- *A) is one minus the specificity - False*
- ***B) is a measure of how well the test detects cases of the disease - True***
- ***C) is the proportion of people with the disease who are (+) on the test - True***
- ***D) increases if the critical value is increased - True***
- *E) measures how well people without the disease are excluded - False*

Adapted from Bland M. An introduction…

What are the axes of an ROC Curve?

ROC = Receiver Operator Characteristic

ROC Curve



ROC Curve

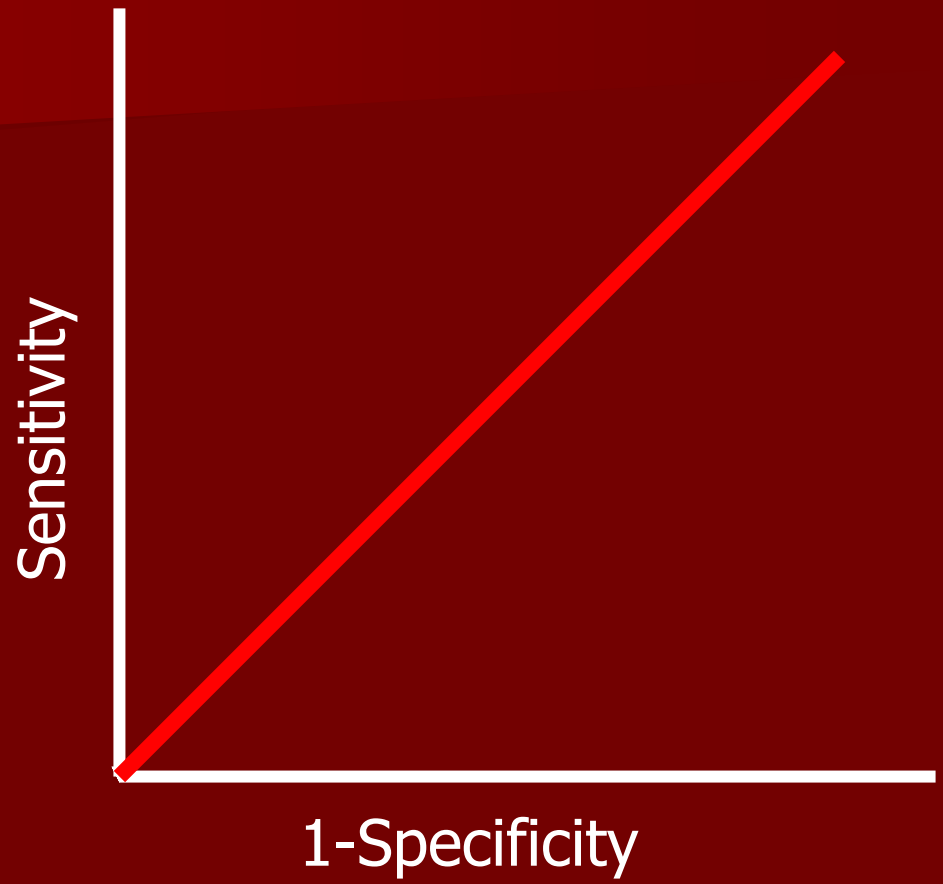
ROC Curve

- Graphical representation of sensitivity & specificity
- The curve is constructed by applying a variety of cutoff values to a population
- Allows a researcher to identify the cut-off value that minimizes both false positives and false negatives *(aka…optimizes sensitivity & specificity)*

For example…

- When screening for a deadly disease such as SARS, you may want to accept more false positives in return for fewer false negatives
- …& thus have a lower specificity in order to have a higher sensitivity.

What does the following ROC Curve imply?



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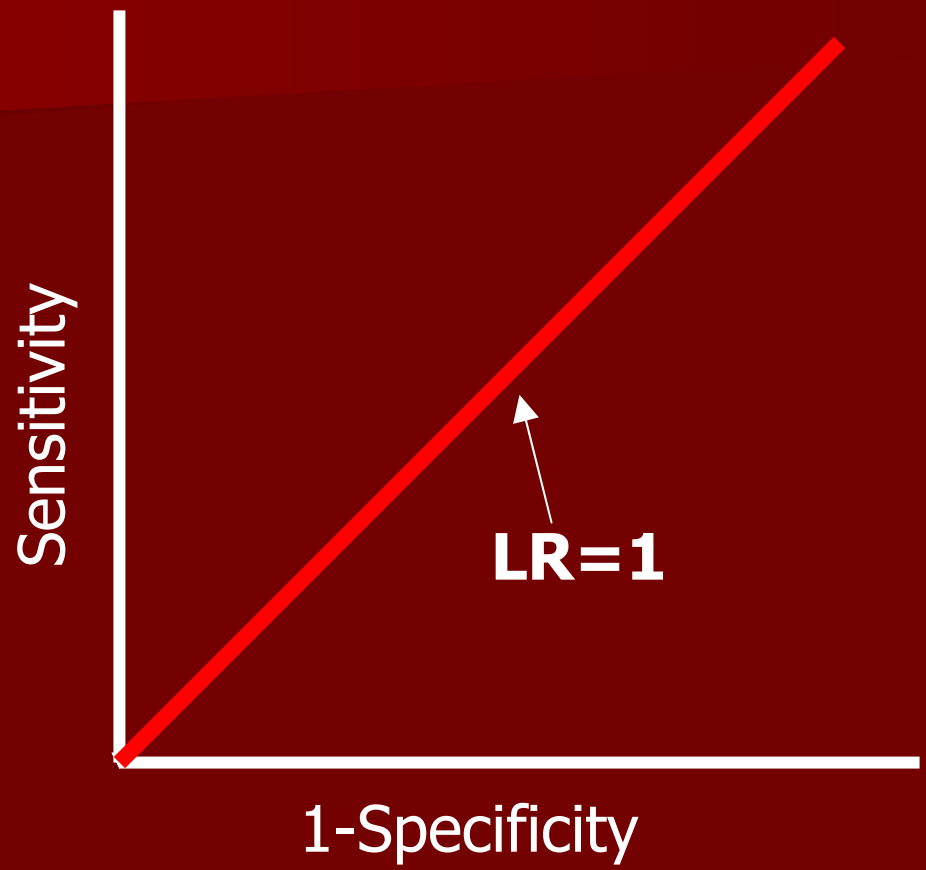

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AREA under the ROC curve

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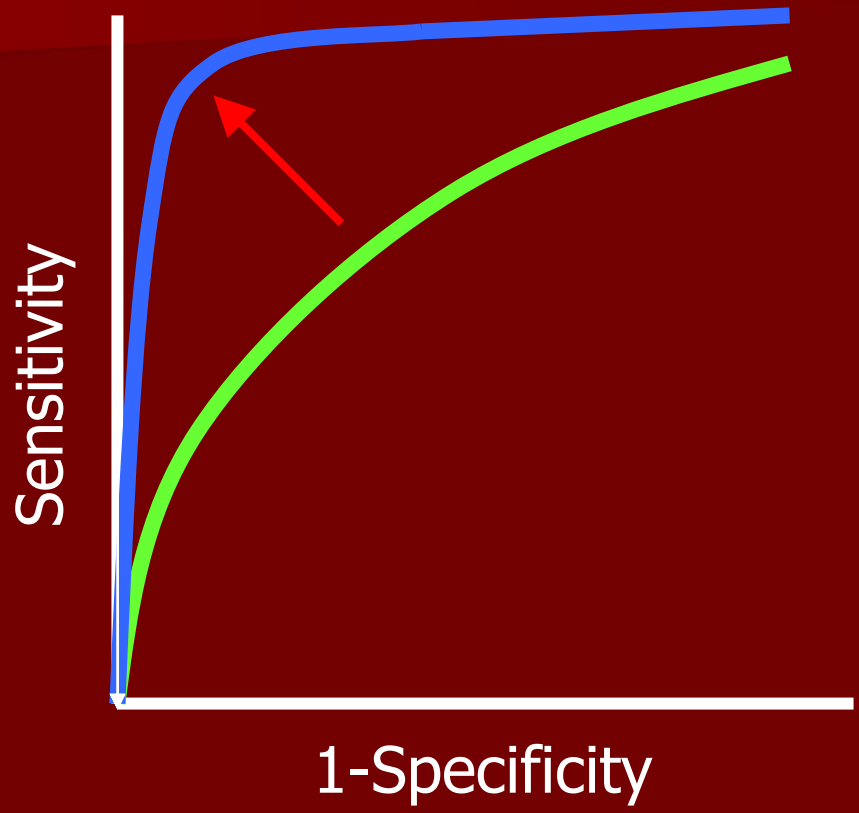
Area under the ROC Curve = 1

X (1-specificity)= 0

y (sensitivity)= 1

ROC Curve



A perfect test would have 100% Specificity and 100% Sensitivity.

It would be graphed at a right angle in the upper left corner.

What is the PPV & NPV ?

Fe Deficiency & Ferritin

Guyatt et al.

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Test (Ferritin)	+ (<45)	**70**	**15**	85
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		85	150	235

Positive Predictive Value:

- a/a+b = 70/85 = .82
- *Proportion of patients with the disease out of all patients testing positive.*
- *Probability that an individual with a positive test will have the disease (Given a positive test, what is the probability of having the disease)*

Negative Predictive Value:

- d/c+d = 135/150 = .9
- *Proportion of patients without the disease out of all patients testing negative.*
- *Probability that an individual with a negative test will not have the disease (Given a negative test, what is the probability of not having the disease)*

Which of the following are affected by prevalence:

- A. Sensitivity/Specificity
- B. PPV/NPV
- C. Likelihood Ratios

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- A. Sensitivity/Specificity
- **B. PPV/NPV**
- C. Likelihood Ratios

If a disease has a low prevalence, are the PPV & NPV increased or decreased ?

If a disease has a low prevalence…

a. the PPV is decreased
b. the NPV is increased

Most screening tests involve diseases that have a low prevalence, so the number of false positives increase (& the number of false negatives decrease).

- When a disease is rare
  - Many positive tests will be false (+)
- When a disease is common
  - Many negative tests will be false (-)

	+Dz	-Dz
+Test	900	300
-Test	100	2700

Dz Prevalence = 25%

Sensitivity = 90%
Specificity = 90%

PPV = 75%
NPV = 96%

+LR = 9
-LR = .11

	+Dz	-Dz
+Test	3240	40
-Test	360	360

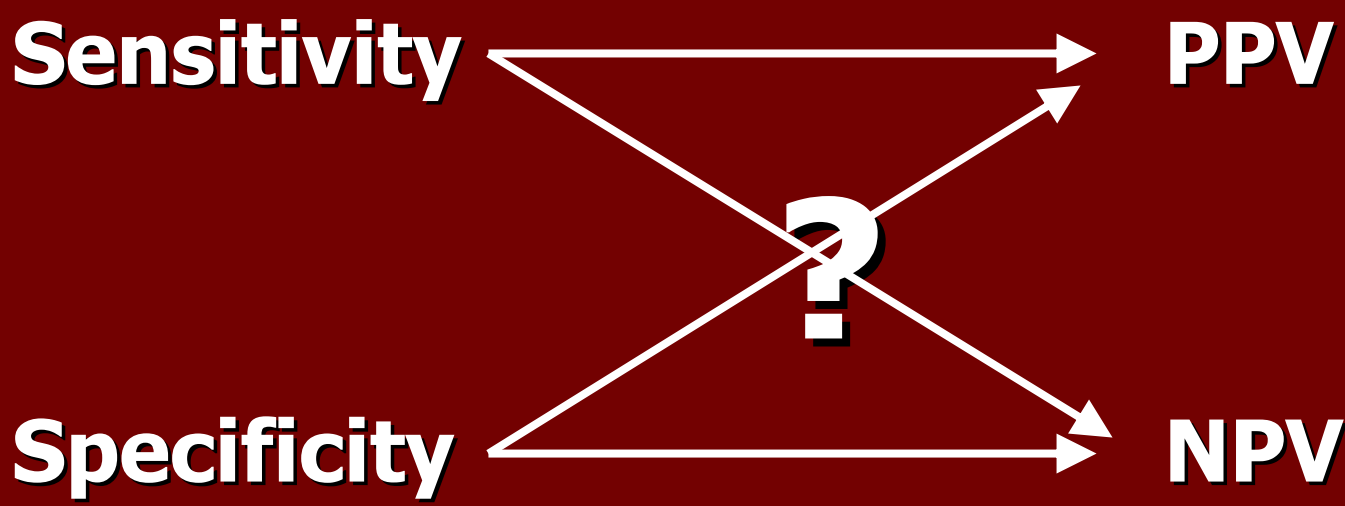
Dz Prevalence = 90%

Sensitivity = 90%
Specificity = 90%

PPV = 99%
NPV = 50%

+LR = 9
-LR = .11

Which are closely related:



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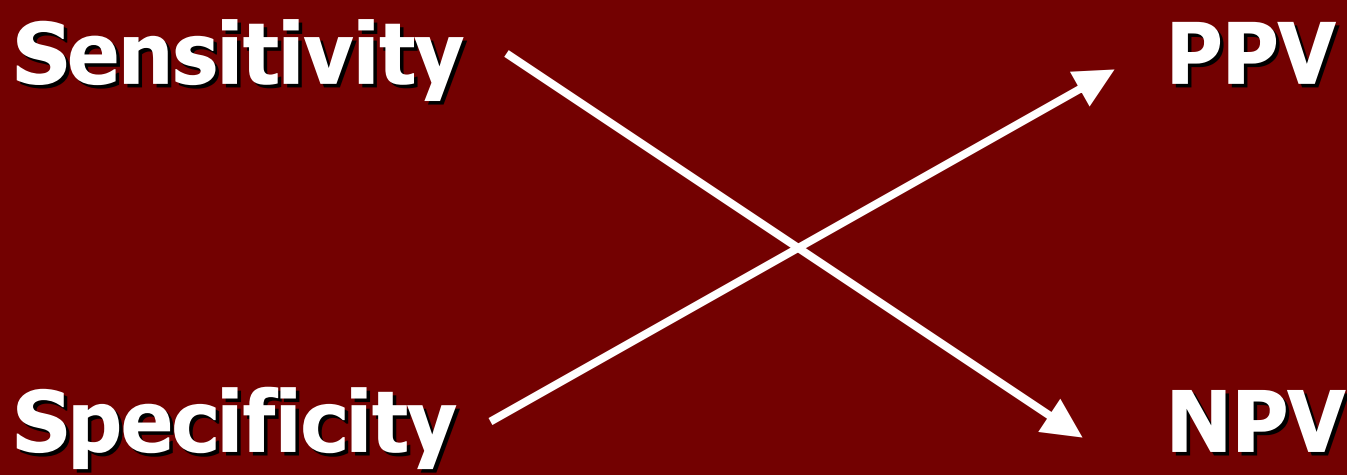

- Increased Sensitivity
  - Increased NPV
- Increased Specificity
  - Increased PPV

What are the Positive & Negative Likelihood Ratios ?

Fe Deficiency & Ferritin

Guyatt et al.

		Disease (Fe Deficiency) +	**Disease** (Fe Deficiency) -	
Test (Ferritin)	+ (<45)	**70**	**15**	85
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		85	150	235

Positive Likelihood Ratio:

- a/a+c ÷ b/b+d = 70/85 ÷ 15/150 = .82/.1 = 8.2
- sensitivity ÷ (1-specificity)
- *The odds (likelihood) of having the disease if the test result is positive.*

Negative Likelihood Ratio:

- c/a+c ÷ d/b+d = 15/85 ÷ 135/150 = .18/.9 = 0.2
- (1-sensitivity) ÷ specificity
- *The odds (likelihood) of having the disease if the test result is negative.*

Which of the following Likelihood Ratios describe a perfect test?

- A) +LR=1 & -LR=0
- B) +LR=Infinity & -LR=0
- C) +LR=100 & -LR=0
- D) +LR=0 & -LR=0
- E) +LR=0 & -LR=Infinity

A perfect test has a…

- Positive LR = Infinity

  (the greater the +LR, the better the test)

- Negative LR = Zero

  (the lower the –LR, the better the test)

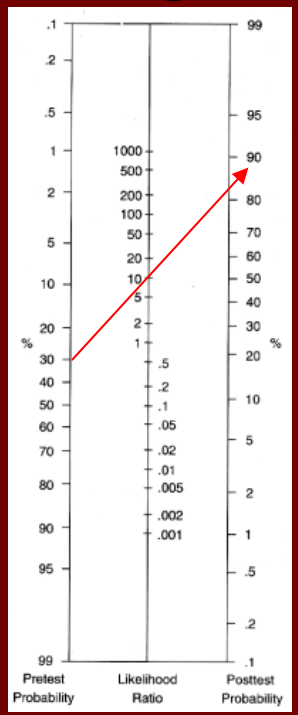
Likelihood ratios measure…

The ability of a test to change the pre-test probability into the post-test probability of a disease being present.

What are the 2 ways to calculate the post-test probability of disease if you know the likelihood ratio and the pre-test probability ?

2 Ways to get the post-test probability:

1. Using the Fagan Likelihood Ratio nomogram



2. Calculate

Pretest Odds = prevalence/(1-prevalence)

Post-test Odds = pretest odds X LR

Post-test probability = post-test odds / (post-test odds +1)

Probability & Odds

- Odds = Ratio of probability of occurrence to non-occurrence of an event
- Odds = probability/ 1-probability

Likelihood Ratio & Probability:

Likelihood Ratio	Approx change in Probability
0.1	- 45 % (reduction in probability of disease)
0.2	- 30 %
0.5	- 15 %
1	0
2	15 % (increase in probability of disease)
5	30 %
10	45 %

Likelihood ratios

> ____ & < ____

are considered significant for changing disease likelihood.

Likelihood ratios
>10 & <0.1
are considered
significant for changing
disease likelihood.

When the pre-test probability of a disease is **30% - 70%**…

- LR > 10 may rule in the disease
- LR < 0.1 may rule out the disease

"During a routine physical examination, a healthy 65-year-old man is found to have a loud, harsh, systolic murmur heard maximally in the second intercostal space that is also heard at the apex and radiates to the carotids. The cardiac examination is otherwise normal, with normal carotid upstrokes. The patient has no history of chest pain or tightness, shortness of breath, dizziness, syncope, or other cardiac symptoms. He has no history of cardiac disease and has never had an echocardiogram. You consult a textbook and learn that the positive likelihood ratio for such a murmur is 1.8 in predicting severe aortic stenosis."

Epstein PE, et al.

Based upon the previous, what do you tell the patient?

- A) He likely has an innocent flow murmur that warrants no further evaluation.
- B) He likely has severe narrowing of his aortic valve.
- C) He has a narrowing of his aortic valve with a 40% chance that it is severe.
- D) He may have a narrowing of his aortic valve but the chance that it is severe is low.

Epstein PE, et al.

D) He may have a narrowing of his aortic valve but the chance that it is severe is low.

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