Understanding diagnostic tests

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Goals

- Understand sensitivity and specificity
  - inform why they are in general problematic
- Discuss likelihood ratios
- Inform pretest and posttest probabilities of disease
- Understand testing and treatment thresholds
- Go through case examples
  - convince you that understanding diagnostic properties is essential to good clinical practice

Diagnostic Tests: Definitions

Gold Standard

	Disease present	Disease absent
Test positive (+ve)	(a) True positive (TP)	(b) False positive (FP)
Test negative (-ve)	(c) False negative (FN)	(d) True Negative (TN)

Sensitivity: proportion of people with disease who have +ve test

$$\text{Sensitivity} = \frac{TP}{TP+FN} = \frac{a}{a+c}$$

SNOUT-Sensitive test, Negative result rule OUT disease

Specificity: proportion of people free of disease who have -ve test

$$\text{Specificity} = \frac{TN}{TN+FP} = \frac{d}{d+b}$$

SPIN-Specific test, Positive result rules IN disease

	Disease present	Disease absent
Test positive (+ve)	(a) True positive (TP)	(b) False positive (FP)
Test negative (-ve)	(c) False negative (FN)	(d) True Negative (TN)

Post-test probability of disease given a positive result = $\frac{TP}{TP+FP} = \frac{a}{a+b}$.

Post-test probability of disease given a negative result = $\frac{FN}{FN+TN} = \frac{c}{c+d}$.

Likelihood ratios

Positive likelihood ratio (+ve LR) = LR for +ve test
- defined as likelihood of +ve test among individuals with disease, relative to likelihood of +ve test among those without disease

Negative likelihood ratio (-ve LR) = LR for –ve test
- defined as likelihood of -ve test among individuals with disease, compared to probability of -ve test among those without disease

	Cystoscopy (Reference Test)	
NMP 22 Result	Bladder Cancer	No Bladder Cancer
Positive	44	179
Negative	35	1073
Total	79	1252
Likelihood ratio for positive test result = (44/79)/(179/1252) = 3.90		
Likelihood ratio for negative test result = (35/79)/(1073/1252)] = 0.52		

Coronary Artery Disease (CAD)

- This example will deal with exercise stress testing (EST) in diagnosis of CAD
- Before testing we need to make some cut off points for post-test probability of disease given a +ve or –ve test
  - such that we will except as being truly positive, negative, or still indeterminate
  - What we are talking about is referred to as testing and treatment thresholds

Testing and treatment thresholds

- Reason for this decision is that we are not using gold standard test which tell us disease present or absent with certainty
- We are using another test which is not 100% accurate therefore you will never be 100% confident that disease is present or absent after test
- However, accurate tests can sometimes get you very close to 100% confident of your diagnosis
- With this in mind lets set some cut off points so that after the test we can tell patient
    a. They have CAD and need treatment with drug X
    b. They do not have CAD and can rest assured
    c. They still remain in an uncertain category, where more testing is needed

Case

35y/o male presents to your office with

- 3 month hx of substernal chest pain, predictably brought on with exertion
- lasts 45 minutes before resolving with rest

What is his pretest probability of CAD?

CAD % probability of ≥ 75% coronary stenosis

Symptoms:

1. Substernal location
2. Brought on by exertion
3. Relieved in <ten minutes by rest or nitroglycerin

	Ages:	30-39	40-49	50-59	60-69
Asymptomatic (0 symptoms)	MEN WOMEN	2% .3%	6% 1%	10% 3%	12% 8%
(1 symptom)	MEN WOMEN	5% 1%	14% 3%	22% 8%	28% 19%
(2 symptoms)	MEN WOMEN	22% 4%	46% 13%	59% 32%	67% 54%
Typical angina (all 3 Sx)	MEN WOMEN	70% 26%	87% 55%	92% 79%	94% 91%

EST

Next, you decide to do an EST and he gets 1.7 mm of ST depression

What is the specificity?

98%

What is the sensitivity?

9%

What do you tell him?

1. He has CAD and needs drug X
2. He does not have CAD and can rest assured
3. He is in an uncertain category and needs further testing

Post-test probability of CAD

- To determine his post-test probability of disease start by setting up 2X2 table
  - with knowledge that his pretest likelihood of disease was 21.8%
    - this value corresponds to # of people with disease

CAD

	Present 218	Absent 782
EST + ve	TP	FP
EST – ve	FN	TN

Sensitivity (9%) = $\frac{TP}{TP+FN}$ $\frac{}{(218)}$ Therefore, TP=19 and FN=218-19=199

Specificity (98%) = $\frac{TN}{TN+FP}$ $\frac{}{(782)}$ Therefore, TN=766 and FP=782-766=16

Now table looks like

	Present 218	Absent 782
EST+ve	TP (19)	FP (16)
EST-ve	FN (199)	TN (766)

Post-test probability of disease given this positive results $= \frac{TP}{TP+FP} = \frac{19}{19+16} = 54\%$

Case

45 y/o female with history of epigastric pain

undergoes endoscopy and this reveals 2 cm duodenal ulcer

biopsy taken for clo test, comes back -ve

What is her pretest probability of H. pylori?

What is the sensitivity of clo test?

What is the specificity of clo test?

What would you tell her?

1. She needs Tx for H. pylori
2. She does not need Tx for H. pylori
3. She needs further investigations

Post-test probability of H.pylori

To determine her post-test probability of H. pylori start by setting up a 2X2 table

with knowledge that her pretest likelihood was 95%

this value would therefore correspond to the # of people with disease

H. PYLORI

	Present 950	Absent 50
Clo test +ve	TP	FP
Clo test –ve	FN	TN

Sensitivity (95%) = $\frac{TP}{TP+FN}$ Therefore, TP = 902 and FN = 950-902=48

(950)

Specificity (98%) = $\frac{TN}{TN+FP}$ Therefore, TN = 49 and FP = 50-49=1

(50)

Now table looks like

	Present 950	Absent 50
Clo test +ve	TP (902)	FP (1)
Clo test –ve	FN (48)	TN (49)

Post-test probability of disease given this positive results $= \frac{FN}{FN+TN} = \frac{48}{48+49} = 49\%$

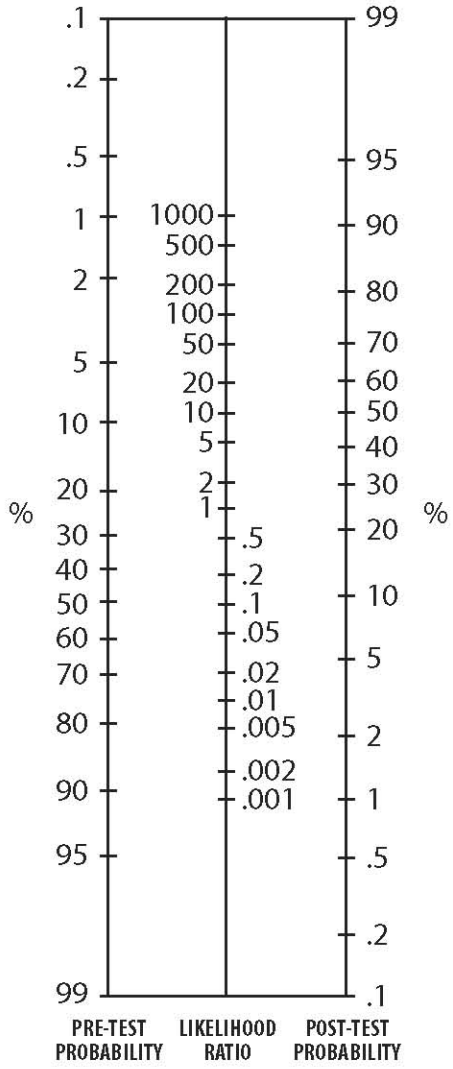
Now use likelihood ratios

For question 1 the finding of 1.7 mm of ST Depression has LR=4.2

Start off by finding pretest probability of disease on left-hand column

Then place a ruler through LR in center column and read off post-test likelihood in right hand column

NOMOGRAM* FOR INTERPRETING DIAGNOSTIC TEST RESULTS



EXAMPLE: For patient described on the other side of this card the pre-test probability was 50%. Anchor a straight edge at 50% on the pre-test side of the nomogram. For the patient who answers yes to two questions the likelihood ratio is 7 (see over). Direct the straight edge through the central column at 7. The post-test probability can then be read off as 87.5%.

* Adapted from FAGAN TJ: Nomogram for Bayes's Theorem (c), N Engl J Med 1975: 293: 257

Summary

- In clinical decision making
  - sensitivity and specificity have substantial limitations
  - likelihood ratios are practical
- Pretest probability is important to inform post-test probability
- Understand testing and treatment thresholds can facilitate consistency in clinical care
- Understanding diagnostic properties is essential to good clinical practice

Searching for studies evaluating diagnostic tests

- OVID click on “limits” and find “clinical queries”
  - then click on “diagnosis (sensitivity)” or “diagnosis (specificity)” depending on your goal
- PubMed on left hand side of page find PubMed Services
  - click on “clinical queries” and then click on “search by clinical study category”
    - next under category click on “diagnosis”
      - and then under scope click “specific search” or “sensitive search” depending on your goal

Resources for evaluating diagnostic tests

- Empirical evidence of design-related bias in studies of diagnostic tests
  - JAMA September 1999;282:1061-1066
- MOST IMPORTANT RESOURCE FOR YOU TO BUY
  - Diagnostic Strategies for Common Medical Problems. Editor: Robert J. Panzer

Likelihood ratios

1. Pulmonary embolism: V/Q scanning

High probability:	18.3
Intermediate probability:	1.2
Low probability:	0.36
Normal/near normal	0.10

2. DVT:

IPG	Duplex U/S
-L.R. = 0.05	-L.R. = 0.07
+L.R. = 19	+L.R. = 47

3. Exudative pleural effusion:

LDH ratio > 0.6	Protein ratio > 0.5
-L.R. = 0.14	-L.R. = 0.10
+L.R. = 43	+L.R. = 45

For ≥ 75% coronary artery stenosis

Taking a history	+ typical angina		115
	+ atypical angina		15
Exercise ECG	+ nonslopping ST seg.		
	+ depression (mm)	≥ 2.5	40
		2 - 2.49	11
		1.5 - 1.99	4
		1.0 - 1.49	2
		.5 - 0.99	1
		< 0.5	0.2

	Disease present	Disease absent
Test positive (+ve)	(a) True positive (TP)	(b) False positive (FP)
Test negative (-ve)	(c) False negative (FN)	(d) True Negative (TN)

- Positive predictive (+PV) value: proportion of people with +ve tests who have disease

$$+PV = \frac{TP}{TP+FP} = \frac{a}{a+b}$$

+PV = post-test probability of disease given +ve result

- Negative predictive (-PV) value: proportion of people with -ve test who are free of disease.

$$-PV = \frac{TN}{FN+TN} = \frac{d}{c+d}$$

100-(-PV)= post-test probability of disease given -ve test