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Patients and Populations
Medical Decision-Making: Diagnostic Reasoning I and II

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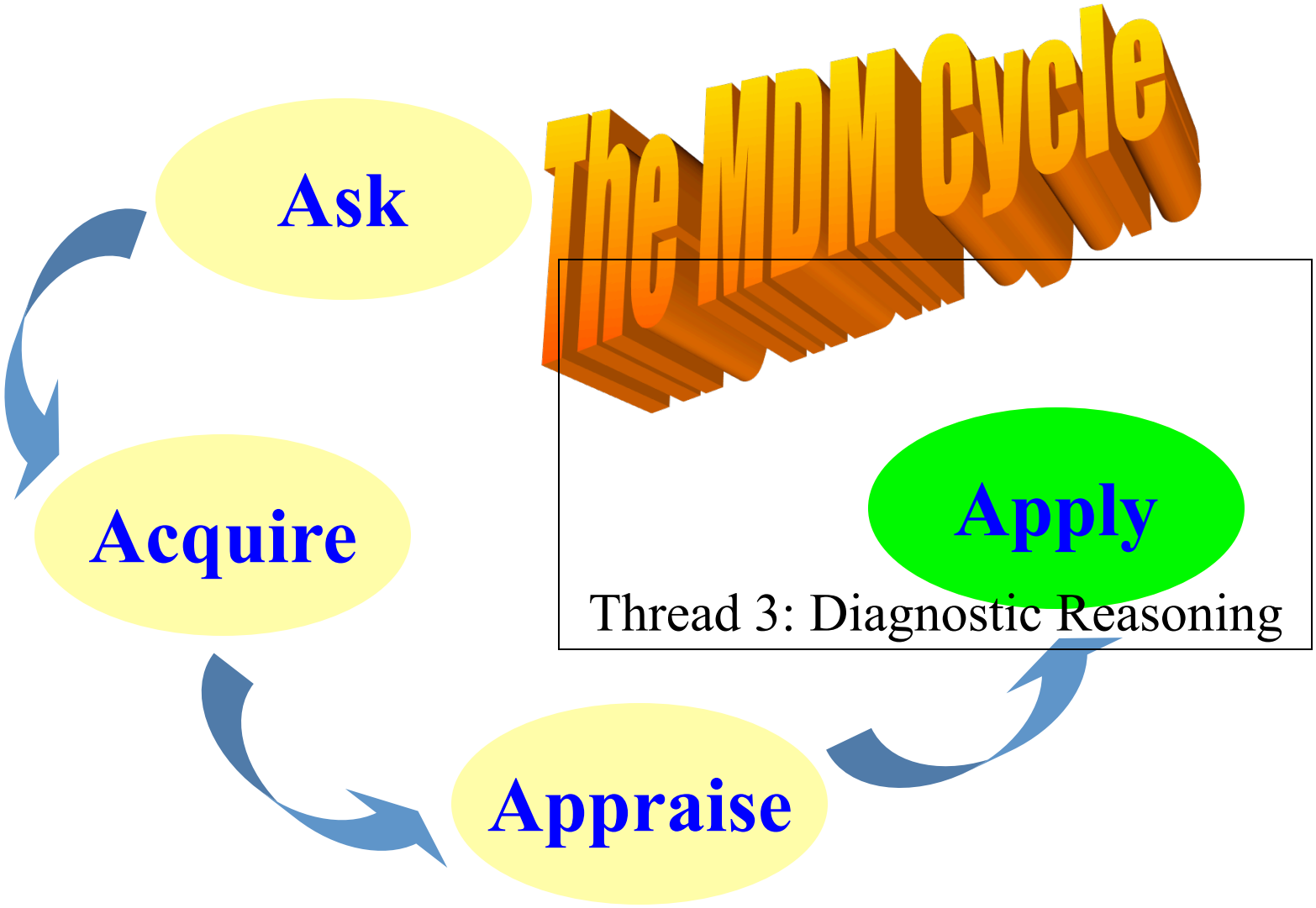

The MDM Cycle
Ask
Acquire
Apply
Appraise
Thread 3: Diagnostic Reasoning

Learning Objectives

By the end of this lecture, you will…

- demonstrate diagnostic question formulation
- define and calculate sensitivity, specificity, and predictive values for diagnostic tests
- explain how risk factors drive prior probabilities, and how this concept relates to prevalence
- modify probabilities from test results through 2x2 table calculations, Bayesian reasoning, and Likelihood Ratios

Case: Diagnostic Reasoning

- The case: A 60 year old man without heart disease presents with sudden onset of shortness of breath.
- Description of the problem: Yesterday, after flying in from California the day before, the patient awoke at 3AM with sudden shortness of breath. His breathing is not worsened while lying down.

Diagnostic Reasoning: Your Intake

- Q: “What other symptoms were you feeling at the time?”
- A: He has had no chest pain, no leg pain, no swelling. He just returned yesterday from a long plane ride. He has no history of this problem before. He takes an aspirin every day. He smokes a pack of cigarettes a day.

Diagnostic Reasoning: First Steps

The *differential diagnosis*

<u>Basic Tasks:</u>

- Assign likelihoods to each possibility
  - E.g. P(X) = probability that "X" is the cause of the patient's symptoms
- Place the possibilities in descending order of likelihood
- State why (rationale)

My list

My *differential diagnosis*

- Pulmonary embolism
- Congestive heart failure
- Emphysema exacerbation
- Asthma exacerbation

Probabilities

(1) PE	P(PE) = 40%
(2) CHF	P(CHF) = 30%
(3) Emphysema	P(emphysema) = 20%
(4) Asthma	P(asthma) = 10%

- What is the probability that the shortness of breath is due to either PE or CHF?

Prior Probabilities

- Based on many factors:
  - Clinician experience
  - Patient demographics
  - Characteristics of the patient presentations (history and physical exam)
  - Previous testing
  - Basic science knowledge
- Quite variable but can be standardized
  - Clinical Prediction Rules
  - http://medcalc3000.com/PulmonaryEmbRiskPisa.htm

More information

- Family history: he has had a DVT in the past (age 40)
- Physical Exam:
  - His blood oxygen saturation is normal on room air
  - His respiratory rate is 16, but his pulse rate is 105 beats per minute
  - Examination of his lungs reveals some crackles and wheezes, but no pleural rub or evidence of consolidation.
  - Swollen right leg, with firm vein below the knee
- CXR: normal
- EKG: sinus tachycardia

http://medcalc3000.com/PulmonaryEmbRiskPisa.htm

Diagnostic Reasoning: Testing

- If a Test existed that could "rule in" PE as the diagnosis with 100% certainty:

  then P(PE | Test+) = 100%

- Two questions:
  - What is this test called?
  - Does P(CHF | Test+) = 0%?

Diagnostic Testing

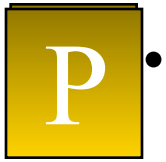
- Facilitates the modification of probabilities.
- Can include any/all of the following:
  - Further history taking
  - Physical Examination maneuver
  - Simple testing (laboratory analysis, radiographs)
  - Complex technology (stress testing, angiography, CT/MRI, nuclear scans) $$$

PICO: The Anatomy of a Diagnostic Foreground Question

- Patient: define the clinical condition or **disease** clearly.

- Intervention: define the diagnostic **test** clearly

- Comparison group: define the accepted **gold standard** diagnostic test to compare the results against.

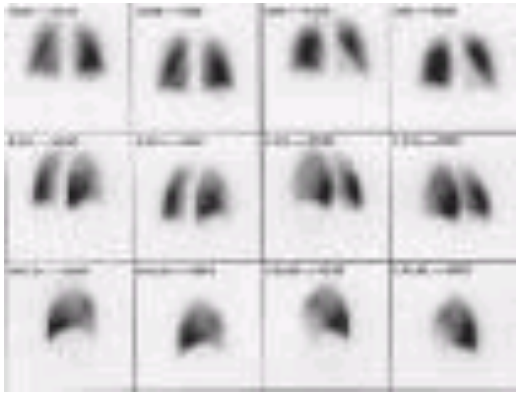


- Outcomes of interest: the outcomes of interest are the properties of the test itself (e.g., **performance** and others we'll discuss).

Practice PICO

Case: A 60 year old man without heart disease presents with sudden onset of shortness of breath. Considering *PE*.

Diagnostic Test to consider: *Ventilation / Perfusion Scanning*



Test: V/Q + means that there is a HIGH probability of a PE (mismatch between ventilation and perfusion)

V/Q – the probability is NOT high.

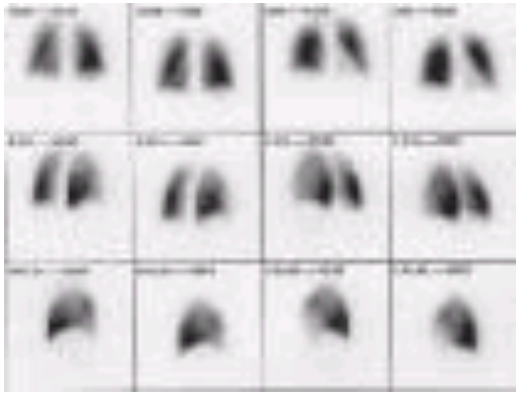
Practice PICO

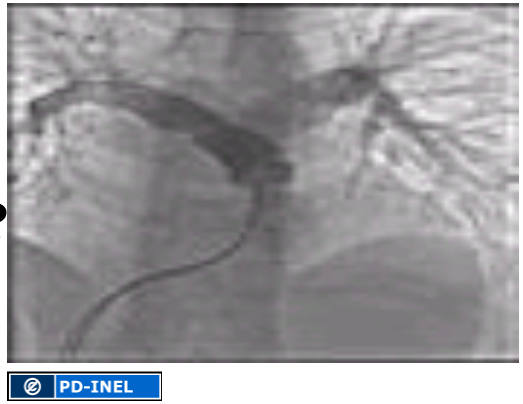
Case: A 60 year old man without heart disease presents with sudden onset of shortness of breath. Considering *PE*. P

Diagnostic Test to consider: *Ventilation / Perfusion Scanning* I

Gold standard: *Pulmonary angiography* C

Need: *Diagnostic performance* O





Can the test be used?

Step 1 - Accuracy and Precision

- Accuracy - The result of the test corresponds consistently with the true result.
  - The test yields the correct value
- Precision - The measure of the test's reproducibility when repeated on the same sample.
  - The test yields the same value

Accuracy vs. Precision

High Accuracy
High Precision

Proceed to Step 2

High Precision
Low Accuracy

Calibrate Equipment

High Accuracy
Low Precision

Start Over

Can the test be used?

Step 2 - Diagnostic Performance

1. A well-defined group of people being evaluated for a condition undergo:
   - an experimental test, and
   - the gold standard test.

2. Comparison is made between the result of the new test and that of the gold standard.

Diagnostic Performance: *Statistical* Significance

- Statistical significance: strength of the association between…
  - Diagnostic study results (for the diagnosis of a particular disease)
  - Gold standard results (for the diagnosis of the same disease, in the same population)

- Strength = degree of correlation

Diagnostic Performance: *Clinical* Significance

- Clinical significance: how likely is the diagnostic test going to affect patient care?
  - Magnitude of the association between test results and the accepted gold standard
  - Other literature (including those of the gold standard)
  - Cost of the test, reproducibility of test
  - Disease characteristics (will the test result affect management of the disease?)

What are the results - Diagnosis

Diagnostic performance is an association between test result and diagnosis of a condition (as assessed by the gold standard)

BONUS
What type of variable is disease state?

	Disease +	**Disease -**
Test +	**A** TP	**B** FP
Test -	**C** FN	**D** TN

Which test characteristics?

- There are prevalence-dependent and prevalence-independent measures in diagnostic tests.
- Prevalence-independent: sensitivity and specificity.
- Prevalence-dependent: positive and negative predictive values.

Test Characteristics: SeNsitivity

Sensitivity:

- The probability that the test will be positive when the disease is present.

  P (Test + | Disease +)

- Of all the people WITH the disease, the percentage that will test positive.
- A seNsitive test is one that will detect most of the patients who have the disease (low false-Negative rate).

Test Characteristics: SPecificity

Specificity:

- The probability that the test will be negative when the disease is absent.

  P (Test - | Disease -)

- Of all the people WITHOUT the disease, the percentage that will test negative.
- A sPecific test is one that will rarely be positive in patients who don't have the disease (low false-Positive rate).

Test Characteristics: Predictive Values

- Positive predictive value: the probability that a patient has a disease, given a positive result on a test.

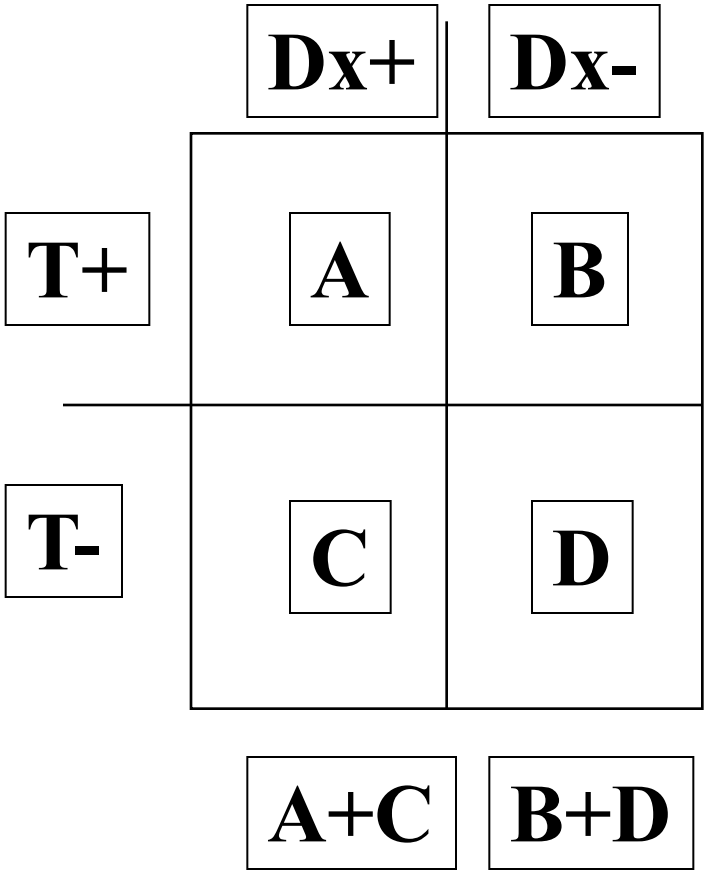
  P (Disease + | Test +)

- Negative predictive value: the probability that a patient does not have a disease, given a negative result on a test.

  P (Disease - | Test -)

Diagnostic Test Characteristics

- Sens = A/(A+C)
- Spec = D/(B+D)
- PPV = A/(A+B)
- NPV = D/(C+D)



To reflect upon...

Why?

Sensitivity and Specificity

Prevalence-Independent characteristics

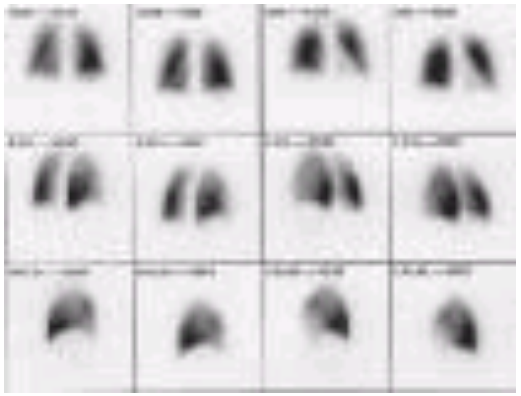
Positive and Negative Predictive Values

Prevalence-Dependent characteristics

Let's try it out

Case: To determine the diagnostic performance of V/Q scans for detecting pulmonary embolism, a study was conducted where 300 patients underwent both a V/Q and pulmonary angiogram. 150 patients were found to have a PE by PA gram. Of those, 75 patients had a V/Q + result (high probability). Of the 150 patients without a PE, 125 had a V/Q – result.

V/Q scan



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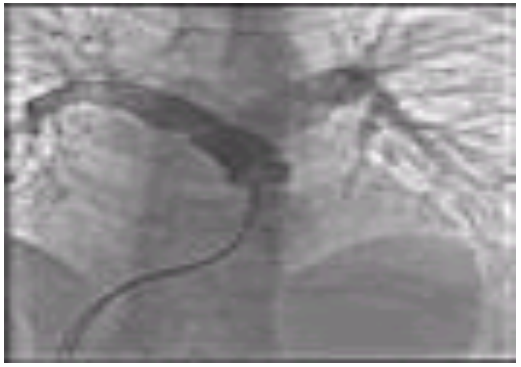
Pulmonary Angiogram



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Let's try it out

Case: To determine the diagnostic performance of V/Q scans for detecting pulmonary embolism, a study was conducted where 300 patients underwent both a V/Q and pulmonary angiogram. 150 patients were found to have a PE by PA gram. Of those, 75 patients had a V/Q + result (high probability). Of the 150 patients without a PE, 125 had a V/Q – result.

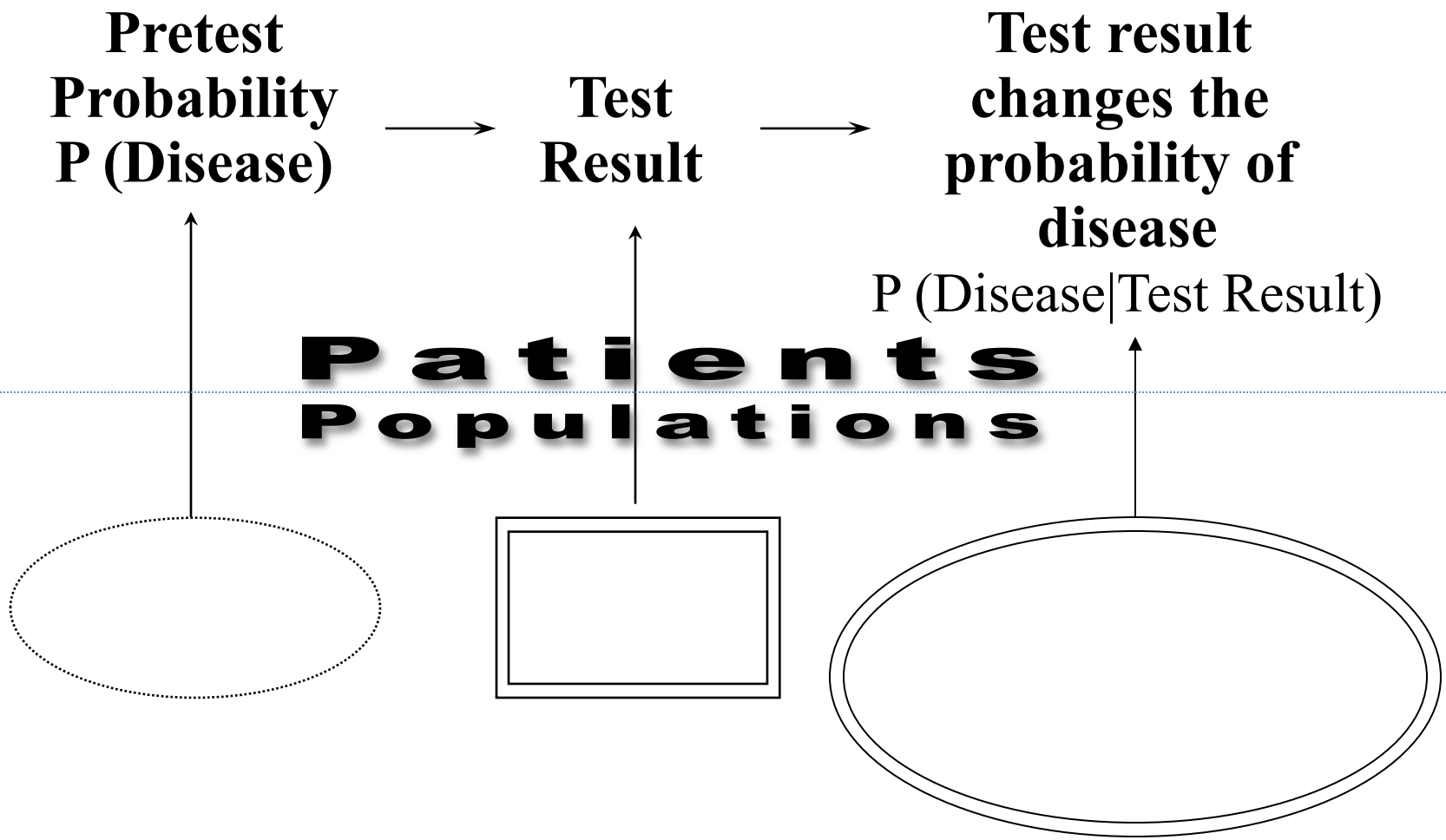
	PE+	PE-
VQ +	75	25
VQ -	75	125
	150	150

Let's try it out

	PE+	PE-
VQ +	75	25
VQ -	75	125
	150	150

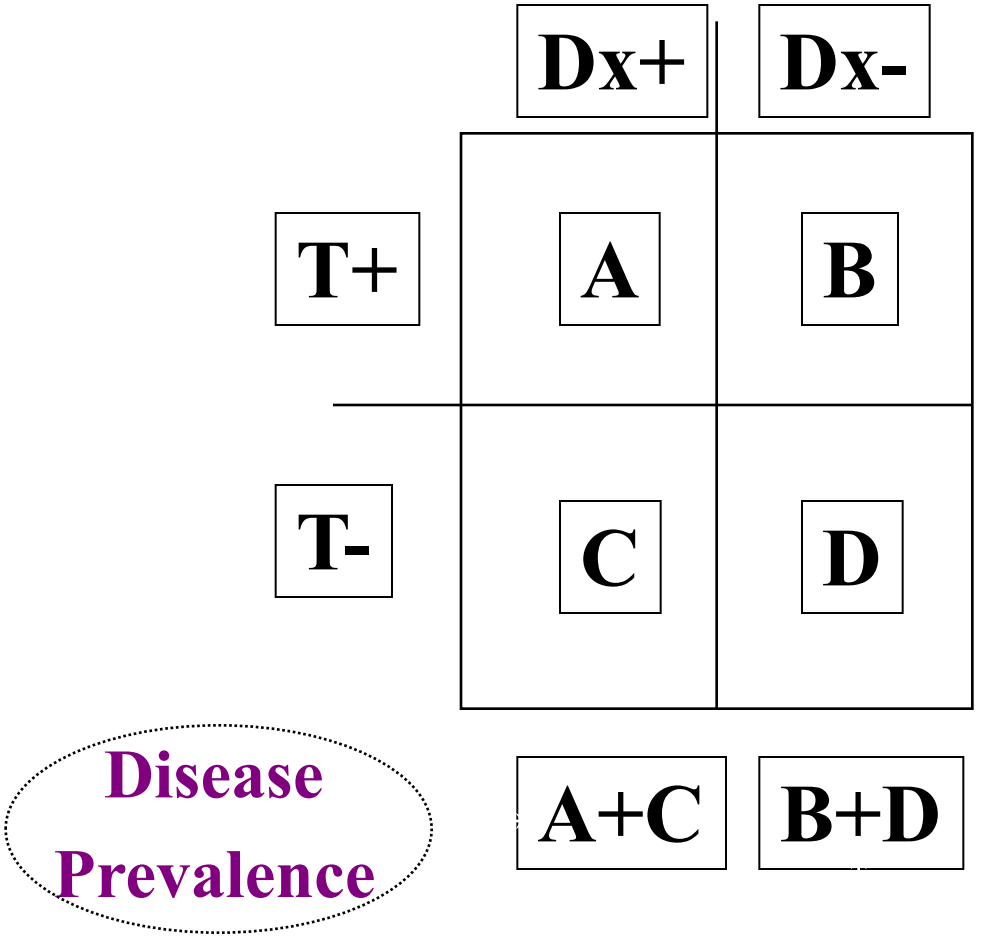
- Sens = 75/(75+75)
  = 50%
- Spec = 125/(125+25)
  = 83%
- PPV = 75/(75+25)
  = 75%
- NPV = 125/(125+75)
  = 63%

Modification of Probability



Test Characteristics and Prevalence

- Sens = A/(A+C)
- Spec = D/(B+D)
- PPV = A/(A+B)
- NPV = D/(C+D)



Prevalence

	PE+	PE-
VQ +	75	25
VQ -	75	125
	150	150

- Sens = 50%
- Spec = 83%
- PPV = 75%
- NPV = 63%
- Prevalence = ? **50%**

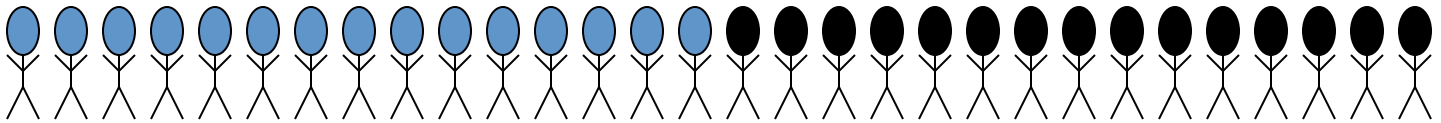
Populations and Patients

Population view

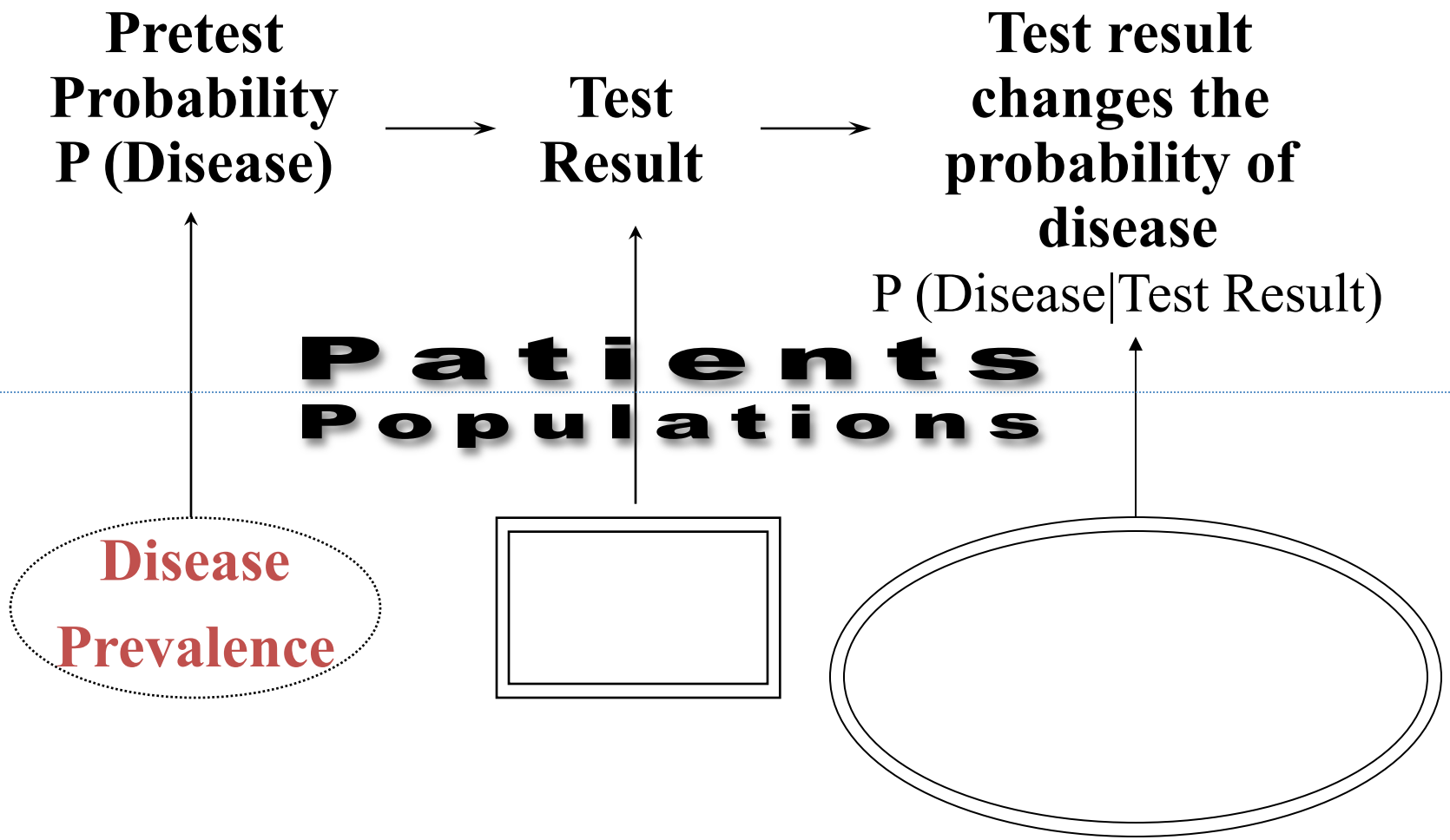
- Prevalence reflects the number of people with the disease at a given moment

Patient view

- Same concept implies how likely an individual patient has the disease
- P (Disease)



Modification of Probability



An Important Question and Assumption

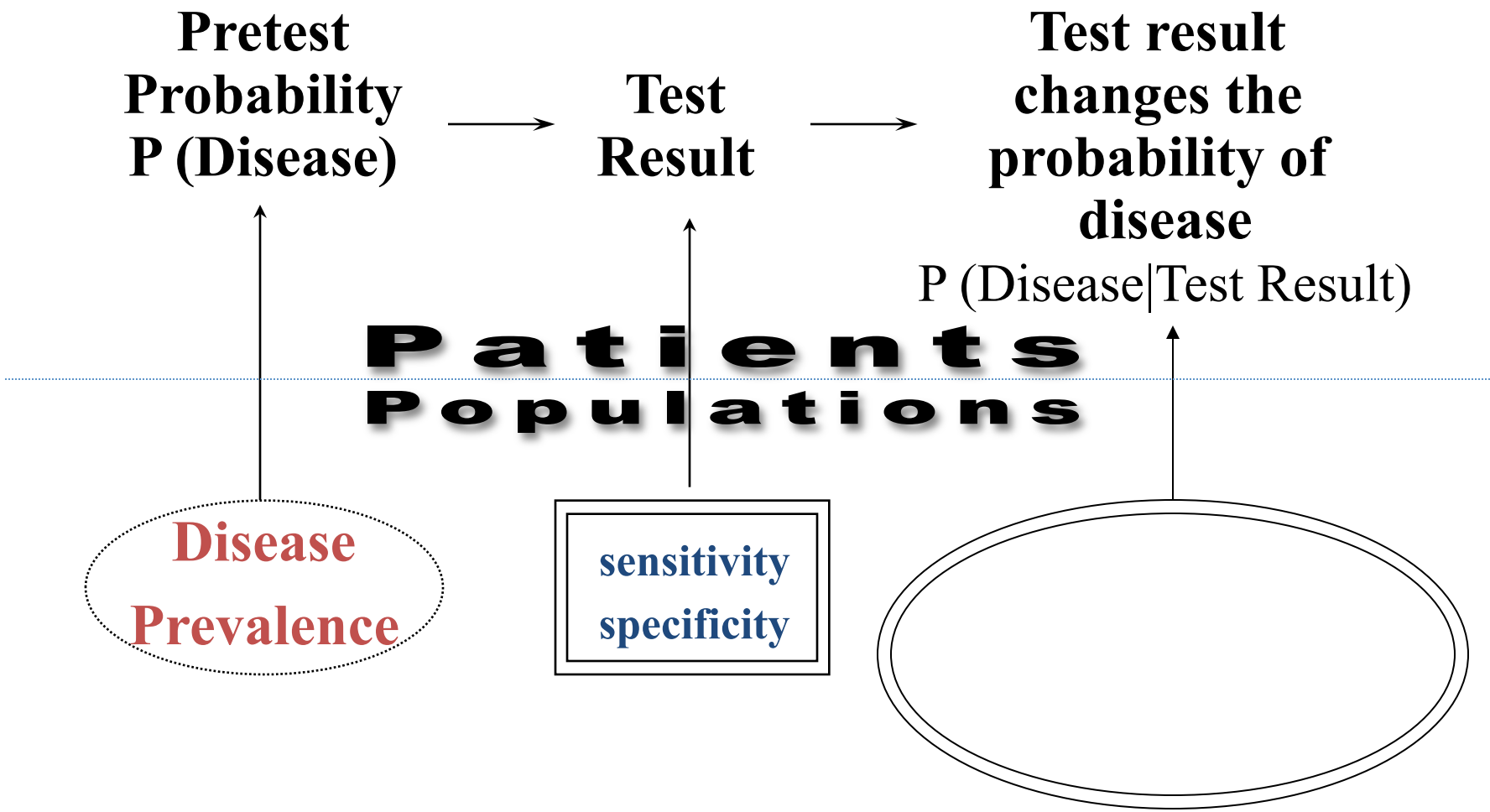
Question: Are certain test characteristics fixed?

Answer: Generally, yes.

Sensitivity and specificity are constants, regardless of the prevalence of the disease in the studied population (prevalence-INdependent)*

*Exceptions and caveats to this assumption are real, but are beyond the scope of this course

Modification of Probability



Importance of Pre-Test Probability

- V/Q + Sens = 50%, Spec = 83%

	Post-TP	
Pre-TP/Prev	**PPV**	**NPV**
50%	**75%**	**63%**

	D+	D-
T+	75	25
T-	75	125

How do our predictive values relate to our probability after the test result is obtained (our post-test probabilities)?

Importance of Pre-Test Probability

- V/Q + Sens = 50%, Spec = 83%

	Post-TP	
Pre-TP/Prev	**PPV**	**NPV**
50%	**75%**	**63%**

	D+	D-
T+	75	25
T-	75	125

- If our Pre-test Probability was 50%, and we obtain a V/Q + scan on this patient, what is our Post-test probability?

Importance of Pre-Test Probability

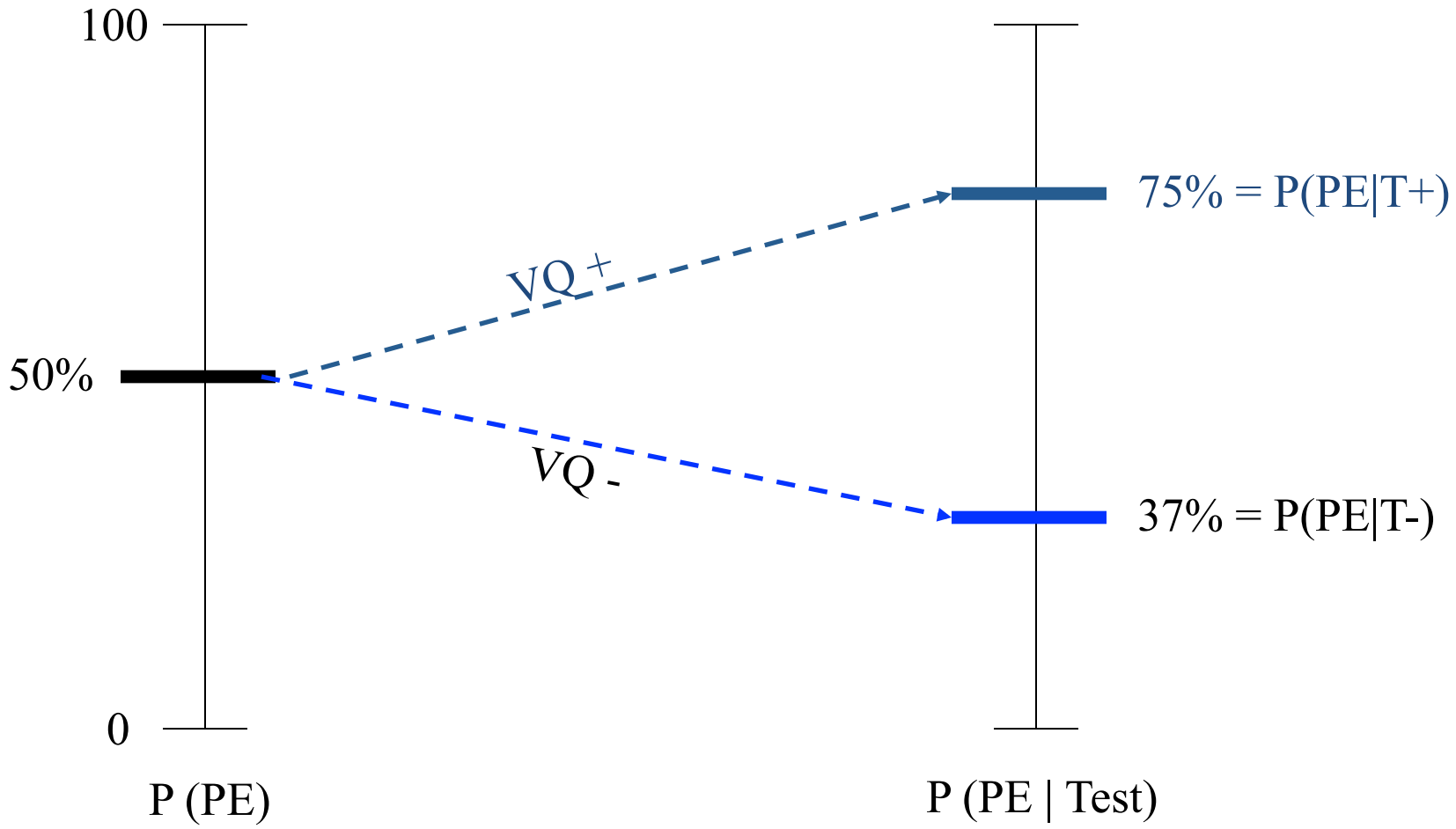
- V/Q + Sens = 50%, Spec = 83%

	Post-TP	
Pre-TP/Prev	**PPV**	**NPV**
50%	**75%**	**63%**

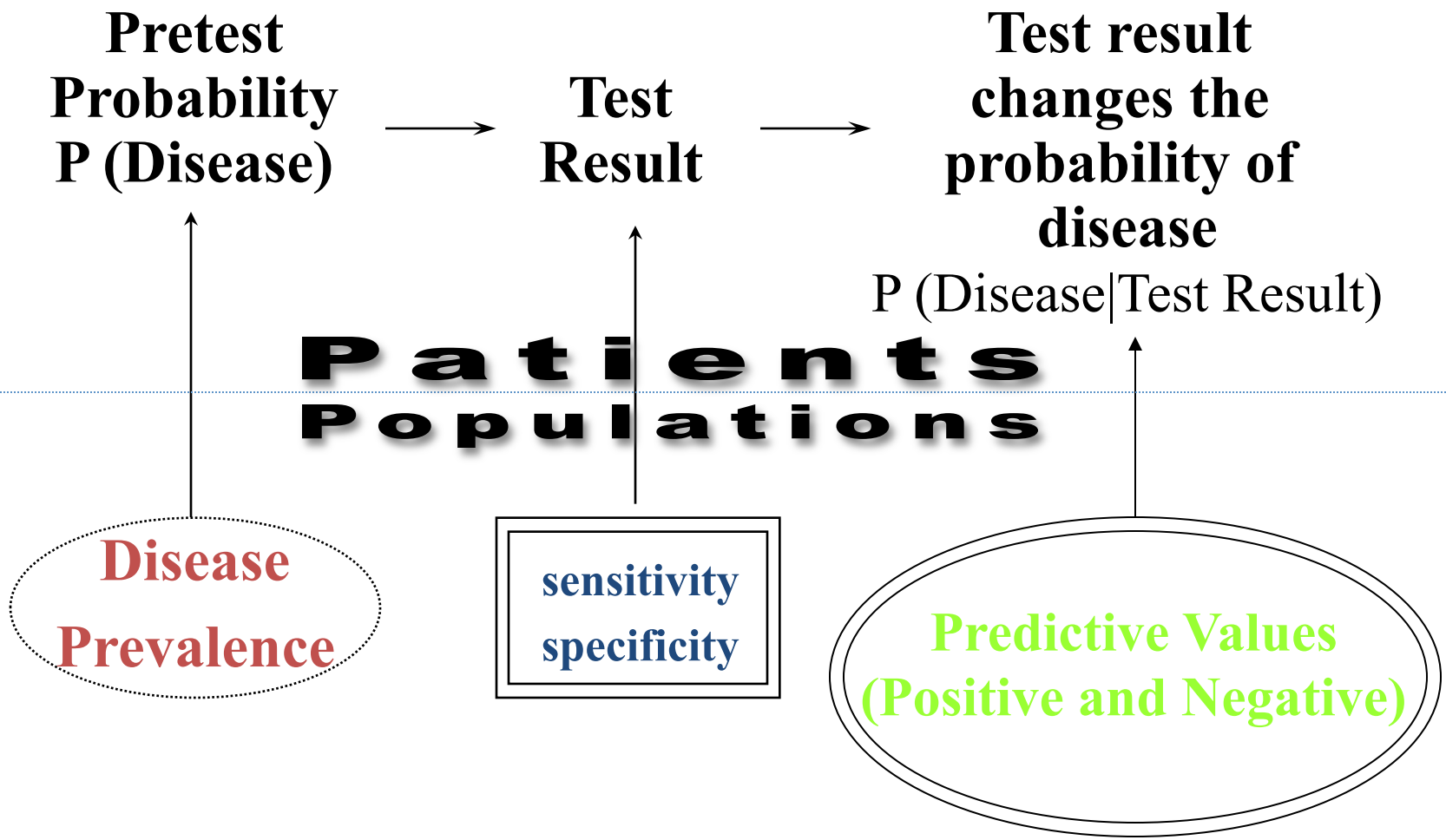
	D+	D-
T+	75	25
T-	75	125

- If our Pre-test Probability was 50%, and we obtain a V/Q – scan on this patient, what is our Post-test probability?

What did we just do?



Modification of Probability



Fundamental Assumptions

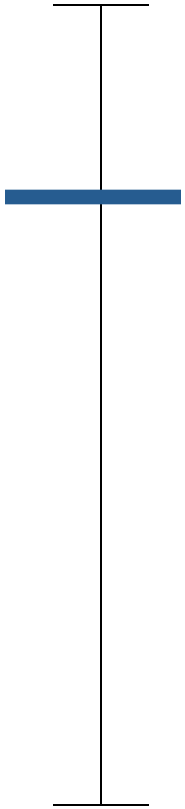
Sensitivity and specificity are constants, regardless of the prevalence of the disease in the studied population (prevalence-INdependent)*

Positive and Negative Predictive Values are dependent on the prevalence of the disease in the studied population (prevalence-DEpendent)

*with exceptions

Now, what do we do?

*clickers



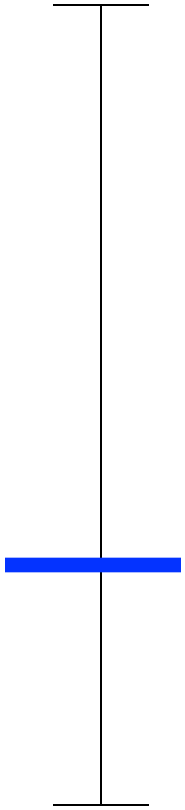
Q1: Choices:

a) Treat as if patient has PE
b) Decide to get another test
c) Decide that patient does not have a PE

What factors do you consider when making the next decision?

Now, what do we do?

*clickers



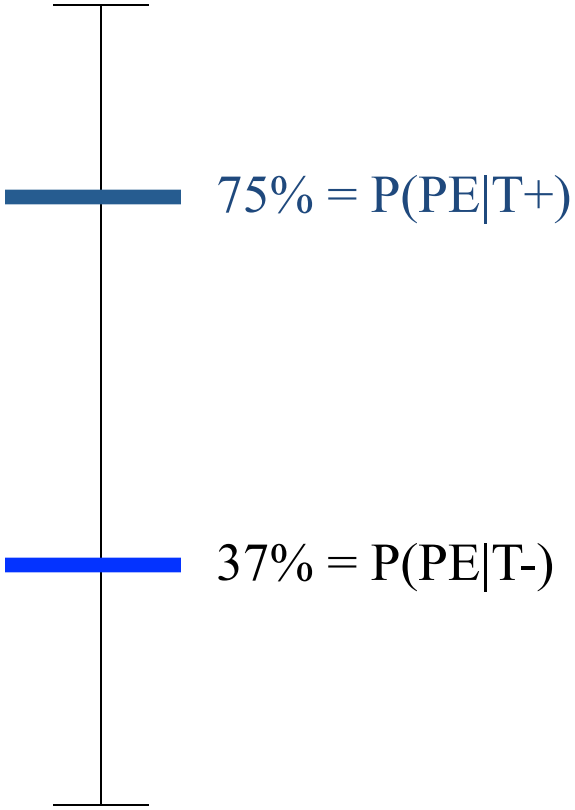
Q2: Choices:

a) Treat as if patient has PE
b) Decide to get another test
c) Decide that patient does not have a PE

37% = P(PE|T-)

What factors do you consider when making the next decision?

Now, what do we do?



Choices:
- Treat as if patient has PE
- Decide to get another test
- Decide that patient does not have a PE

Choices:
- Treat as if patient has PE
- Decide to get another test
- Decide that patient does not have a PE

What factors do you consider when making the next decision?

What if we change our pretest probability?

- In essence, we are simultaneously changing the prevalence:
  - Original pre-TP = P(PE) = 50% HIGH RISK
  - New pre-TP = P(PE) = 25% MED RISK
- Assuming that sensitivity and specificity are fixed…then we must recalculate our predictive values to determine our new post-test probabilities.

Importance of Pre-Test Probability

- V/Q + Sens = 50%, Spec = 83%

	Pre-TP/Prev	Post-TP PPV	Post-TP NPV
hi risk	50%	75%	63%
med risk	25%	50%	83%
		38/(38+38)	187/(187+37)

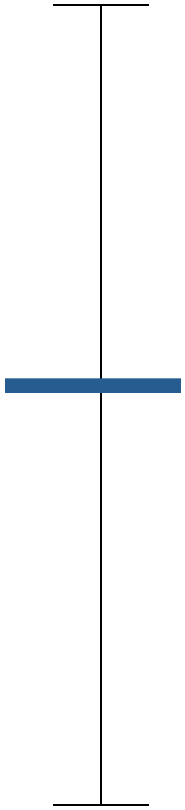
	D+	D-
T+	75	25
T-	75	125

	D+	D-
T+	38	38
T-	37	187

Our Pre-test Probability was 25%, we obtain a V/Q – scan on this patient, our Post-test probability is now…

Decision time

*clickers



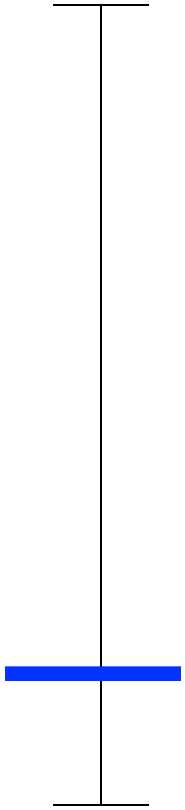
Q3: Choices:

a) Treat as if patient has PE
b) Decide to get another test
c) Decide that patient does not have a PE

50% = P(PE|T+)

Decision time

*clickers

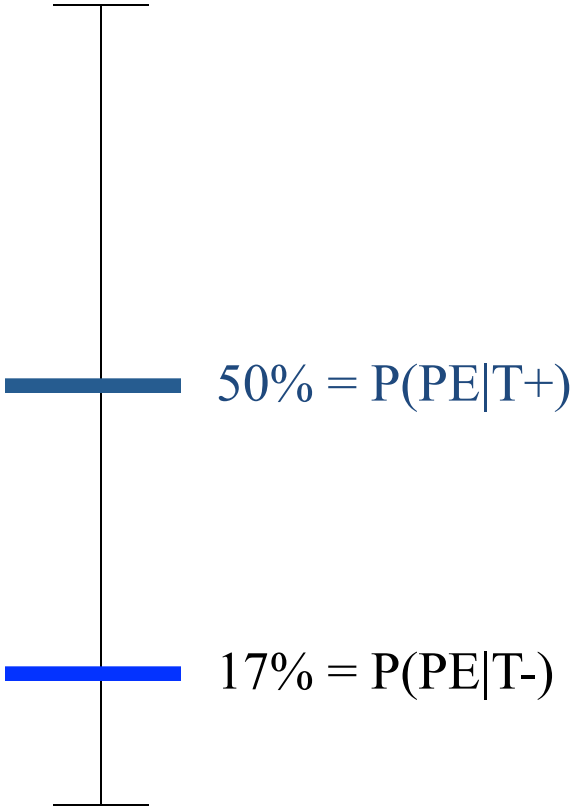


17% = P(PE|T-)

Q4: Choices:

a) Treat as if patient has PE
b) Decide to get another test
c) Decide that patient does not have a PE

Decision time



Choices:
- Treat as if patient has PE
- Decide to get another test
- Decide that patient does not have a PE

Choices:
- Treat as if patient has PE
- Decide to get another test
- Decide that patient does not have a PE

Let's change it again…

- Again, we are changing the prevalence:
  - Young woman, no risk factors, some dyspnea, no history, normal exam
  - If we consult our clinical prediction rule:
    - New pre-TP = P(PE) = 5%: LOW RISK

Importance of Pre-Test Probability

- V/Q + Sens = 50%, Spec = 83%

	Pre-TP/Prev	Pred Val PPV	Pred Val NPV
hi risk	50%	75%	63%
lo risk	5%	15%	97%
		8/(8+47)	238/(238+7)

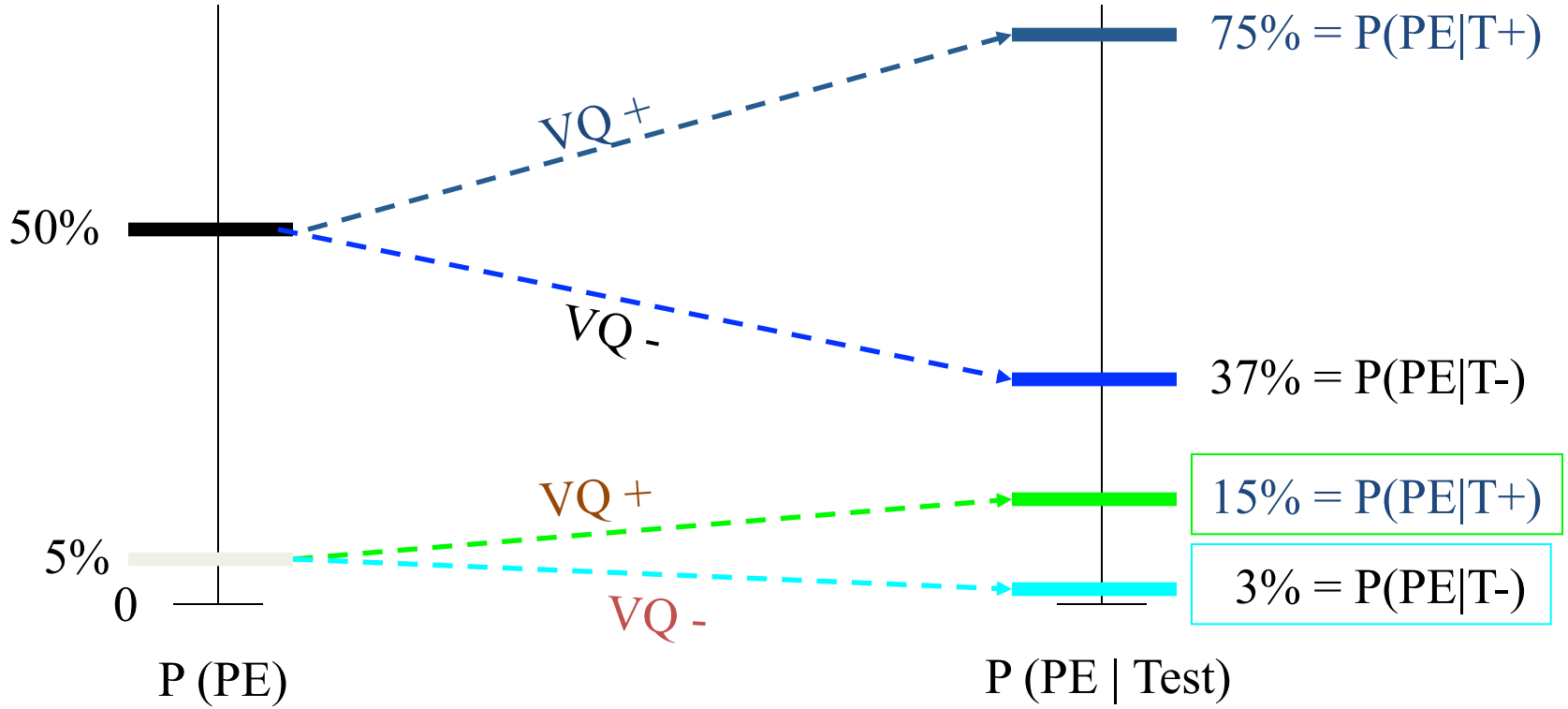
	D+	D-
T+	75	25
T-	75	125

	D+	D-
T+	8	47
T-	7	238

What did we just do?

Observation

As prevalence (pre-test probability) decreases,
positive tests are more likely to be false-positives



Fundamentally...

Question: If you get a **V/Q +** scan for the diagnosis of pulmonary embolism, is it more likely to represent a false positive test if the patient presented with…

(a) many clinical features of PE (shortness of breath, chest pain, long plane ride), or

(b) no clinical features of PE (no shortness of breath, no chest pain, no leg swelling, no long plane ride)?

Alternative Vocabulary - Rates

- True Positive Rate = sensitivity
- False Positive Rate = 1-specificity

- False Negative Rate = 1-sensitivity
- True Negative Rate = specificity

Combining Rates - Methods

- Likelihood Ratios
- ROC Curves

Combining Rates - Method 1
Likelihood Ratios (LR)

- Concept - LRs depict the relationship between true and false rates
  - TPR/FPR = LR for a positive test result
  - FNR/TNR = LR for a negative test result

$$LR = \frac{TPR}{FPR} = \frac{sens}{1\text{-}spec}$$

Typically >1, excellent >10

$$LR = \frac{FNR}{TNR} = \frac{1\text{-}sens}{spec}$$

Typically <1, excellent <0.1

Application
Likelihood Ratios (LR)

Key Concept: LRs can be combined with pre-test odds to get post-test odds

Remember our scenario:

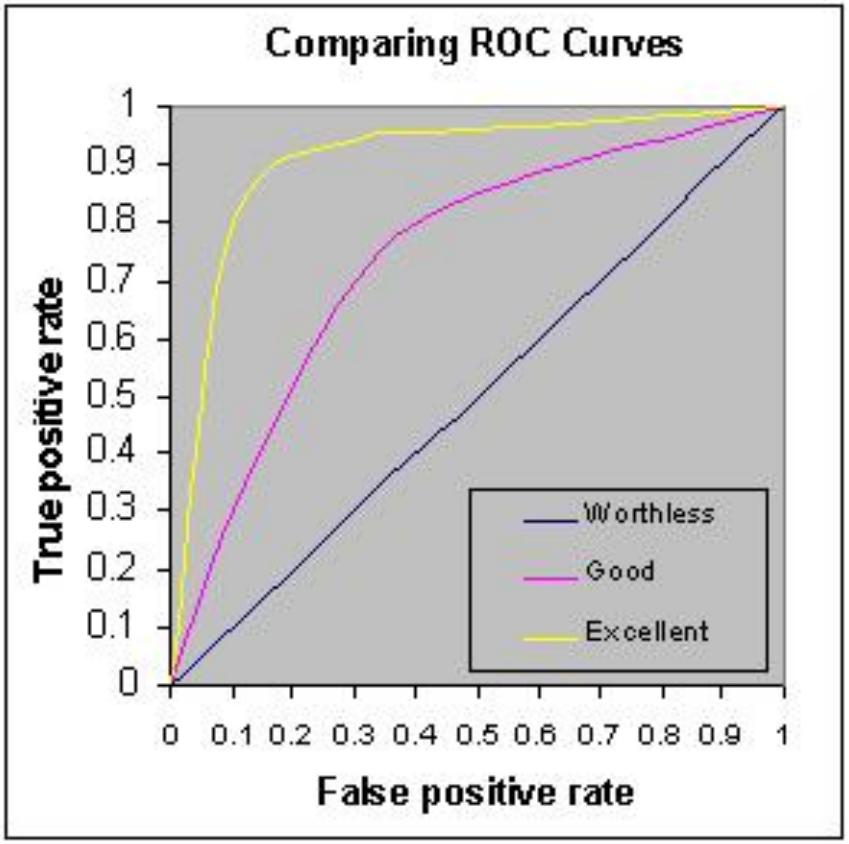
High risk pt - 50% (PreTP)

$$\text{LR (VQ hi)} = \frac{0.50}{1-0.83} = 2.94$$

Pre TP	* →	Pre TO	x	LR	=	Post TO	* →	Post TP
50%		1.0		2.94		2.94		75%

*converting odds to probability and vice and versa - many references online

Combining Rates - Method 2
ROC Curves



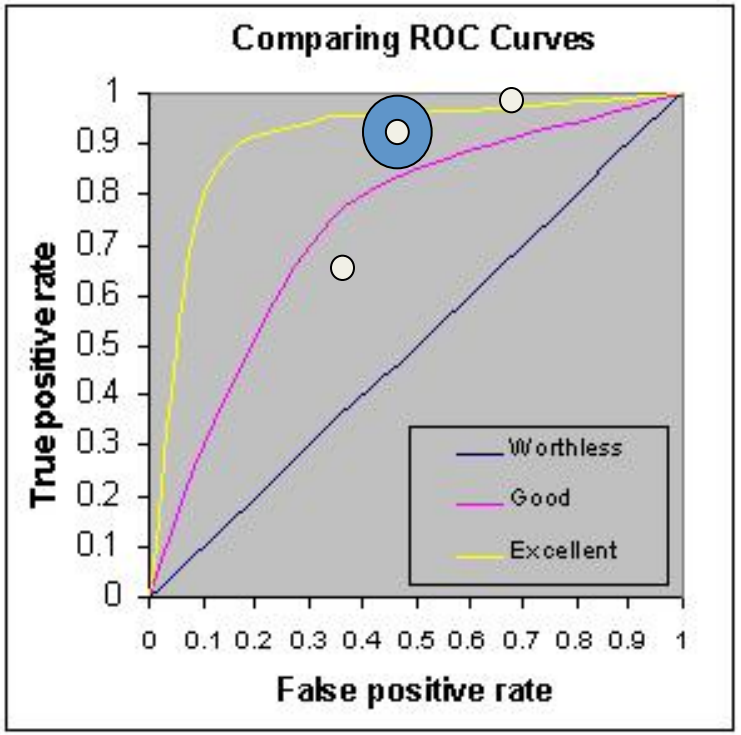
Visual depiction of LR

- Tests with continuous values only
- Sensitivity-specificity tradeoff at different cutoffs
- TPR plotted against FPR

Application
ROC Curves

ROC Curves

- Area under the curve determines overall utility of the test
- Inflection point reflects optimal threshold
- More in Small Group Exercise
  - Assignment 3



Take Home Points

- Research studies of diagnostic tests give you test characteristics, not predictive values.
- Relationships between sensitivity and specificity can be captured in ROC curves (for tests with thresholds) and Likelihood Ratios (LRs)
- Appropriate use of tests stem from large differences between pre-test and post-test probabilities, resulting from LRs that strongly deviate from 1.
- If your pre-test probability is very low (<10%) or very high (>90%), it is rare that a single test can help.

The Odyssey: Conclusion

Initial Possibilities

#1: Trunk latch defect (recall pending)

#2: Ajar sensing defect on side door

#3: Side door not closing properly

→

The Answer

#2: Ajar sensing defect on side door

Initial Diagnostic Reasoning

The Odyssey Reloaded

The Mechanic	The Clinician
• Failure to entertain all possibilities • Failure to pay attention to all symptoms • Failure to inform customer • Failure to perform diagnostic tests	• Entertain all important possibilities • Elicit and pay attention to description of all symptoms • Inform and involve patients • Perform effective diagnostic tests

The MDM Cycle

Ask

Acquire

Appraise

Additional Source Information

for more information see: http://open.umich.edu/wiki/AttributionPolicy

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