Laboratory Testing

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Laboratory Testing

Accuracy and precision

Reference ranges

Sensitivity and specificity

Predictive value

Pre-analytic and post-analytic considerations

Point of Care Testing

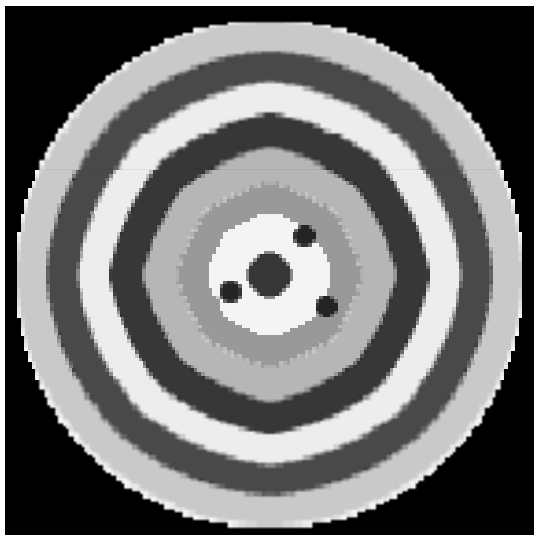
Why test?

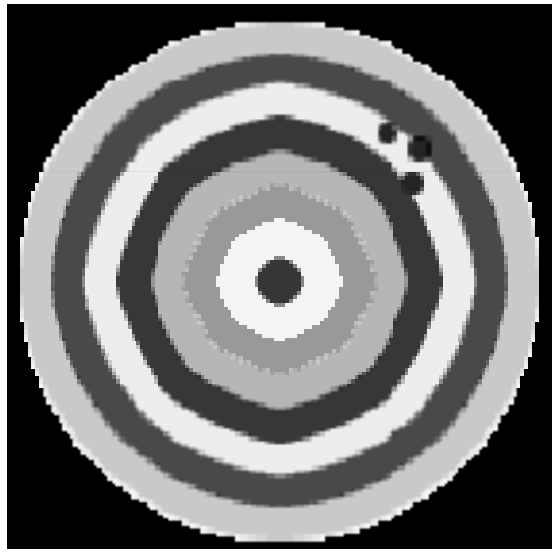
- Clinical impression
- Exclude diagnosis
- Prognostic information
- Guide therapy
- Monitor therapy or disease progression
- Screen for disease

Medical necessity

- Medicare guidelines provide reimbursement for laboratory tests only if the diagnosis supports doing that test.

Accuracy vs Precision





Accuracy vs Precision

- Accuracy
  - How close to the actual value
- Precision
  - Reproducibility
  - Probably more important in clinical medicine!!

Accuracy is telling the truth . . .
Precision is telling the same story over and over again.

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NCEP guidelines for cholesterol measurement

- Accuracy (bias): 3 %
- Precision (cv): 3 %
- Total error: 8.9 %

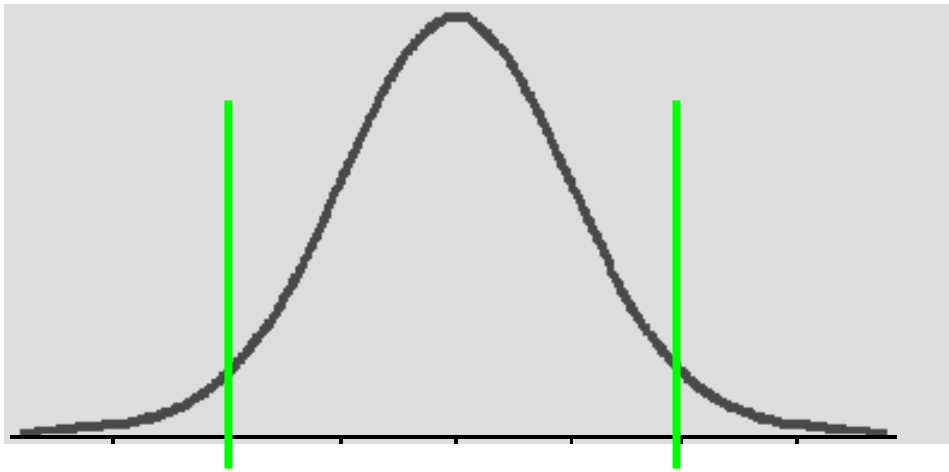
What is normal?

Normal Distribution

Reference Range

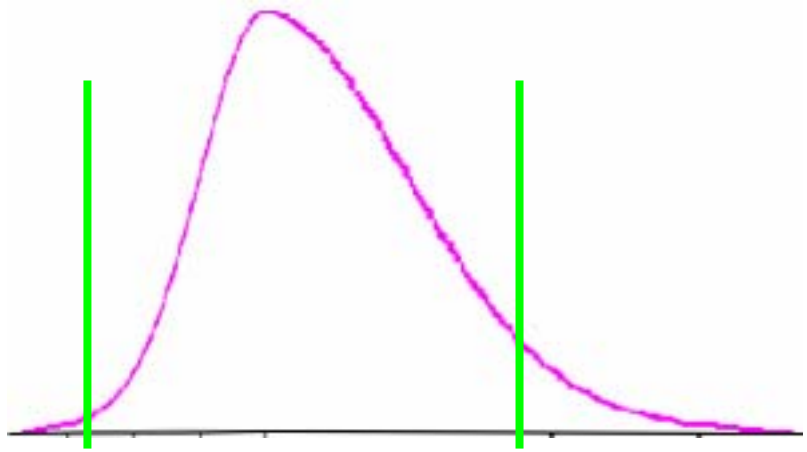
- 95% confidence limits
- Mean +/- 2 SD

Normal Distribution

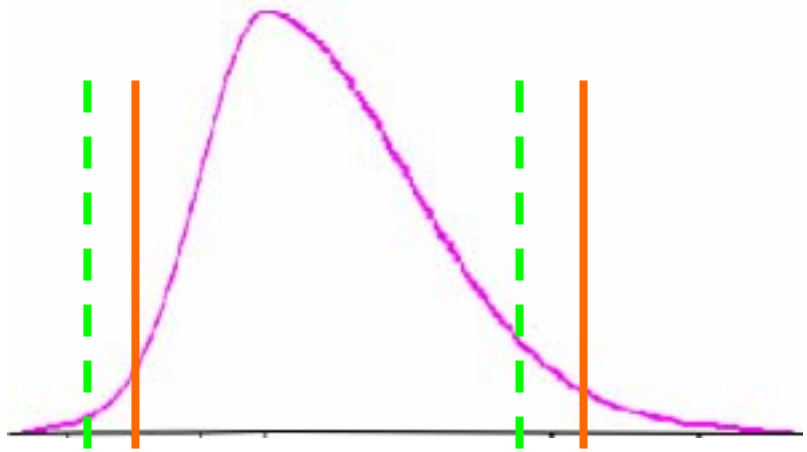


95% confidence limits

Non-parametric distribution



Non-parametric distribution



95% confidence limits

Reference Range

- 95% confidence limits
- Mean +/- 2 SD
- mid 95% of healthy population
- Qualitative: clinical expectation

Test panels

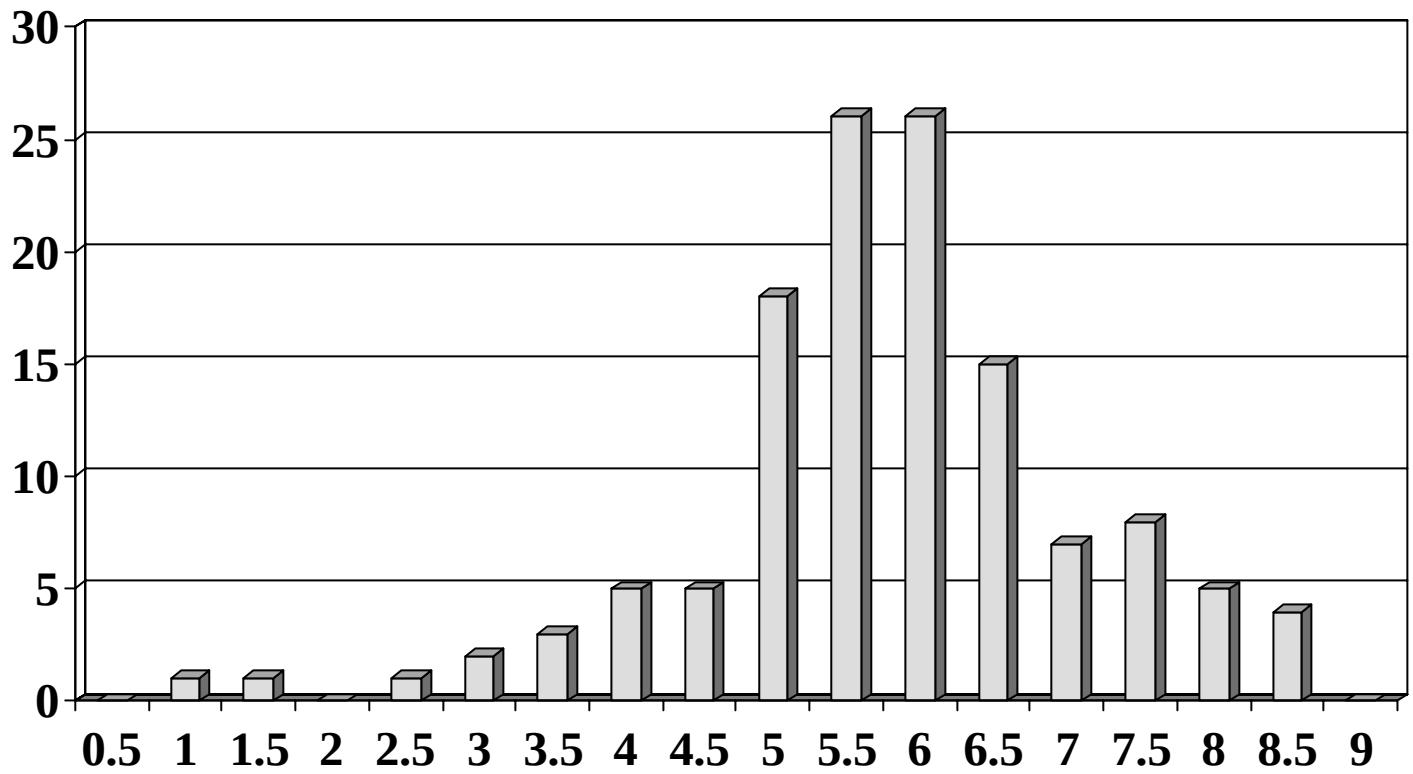
- If you run 12 tests on a healthy person, what's the chance that they'll all be within the reference range?

Test panels

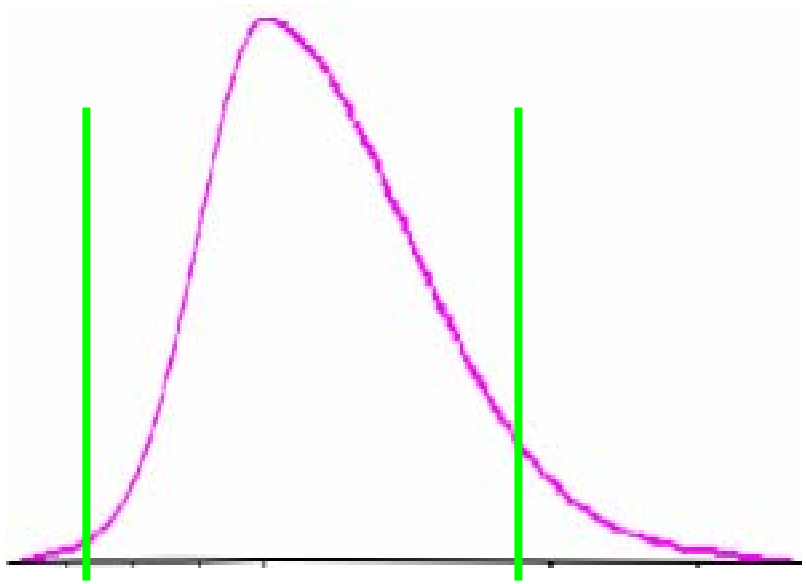
Tests	All in ref range	At least 1 out
1	0.95	5 %
2	$0.95^2 = 0.90$	10%
3		
12		
20		

Uric Acid

reference range



88 year old female



Chest pain at rest; not relieved by nitroglycerine

CK

Ref range: 25-150

Patient: 73 → 142

CK-MB

Ref range: 0 – 6.3

Patient: 1.7 → 5.2

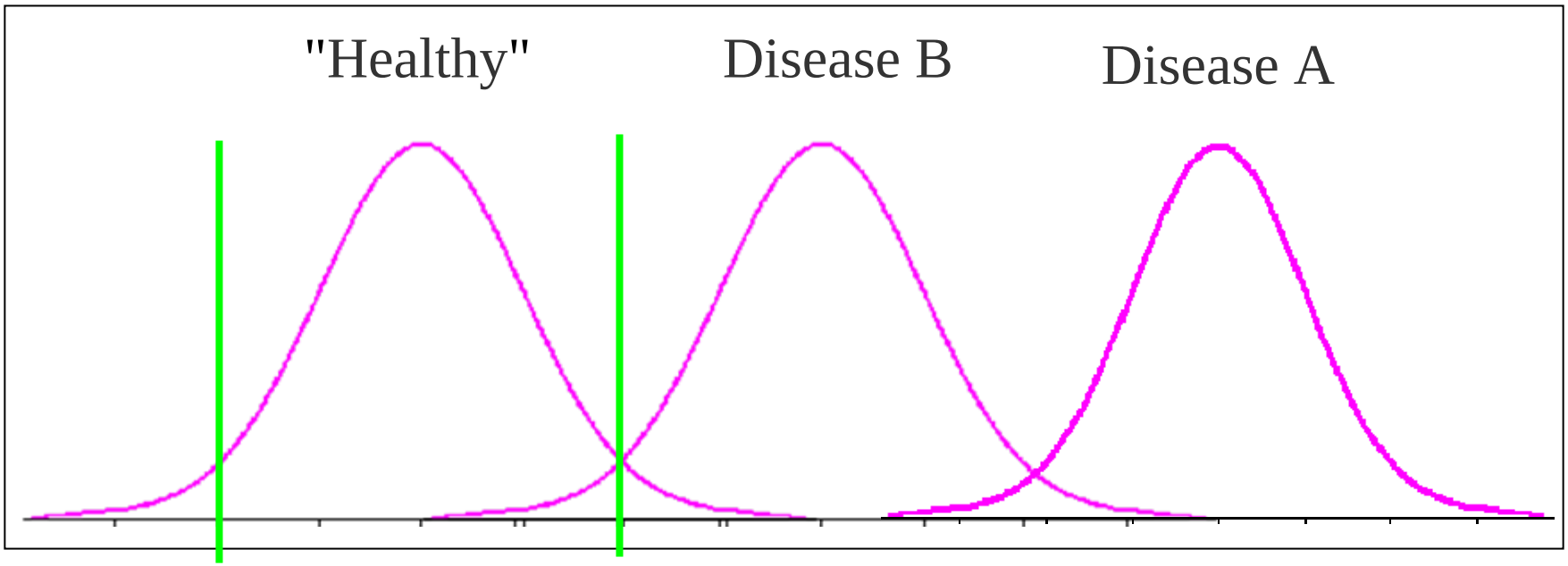
cTnI

Ref range: 0 – 0.5

Patient: 0.02 → 0.34

Reference ranges are for reference. They are not absolute.

Where should the cutoff be?



Sensitivity

- How well can we detect disease
- How many people (what percent) with disease will have a positive test
- TP / (Those with disease)
- TP / (TP + FN)

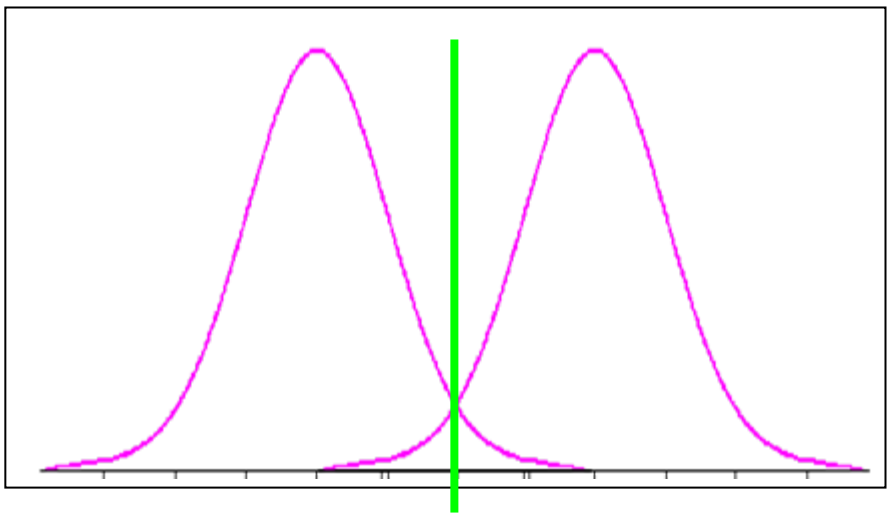
Specificity

- Is the test positive specific for the disease
- Is it positive only if disease is present

- How many people (what percent) without disease have a negative test?

- TN / (those without disease)
- TN / (TN + FP)

	Positive Test	Negative Test	
Disease	True Positive	False Negative	
No Disease	False Positive	True Negative	

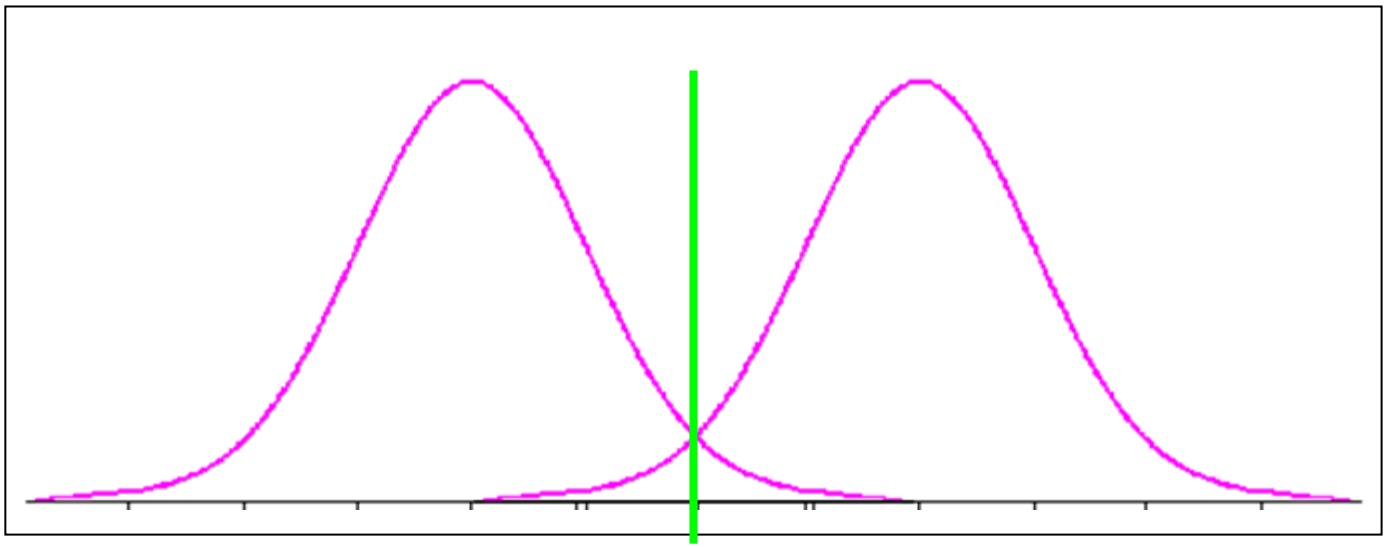


	Pos	Neg	
D	95	5	100
no D	5	95	100

Sensitivity: 95%

Specificity: 95%

Where should the cutoff be?



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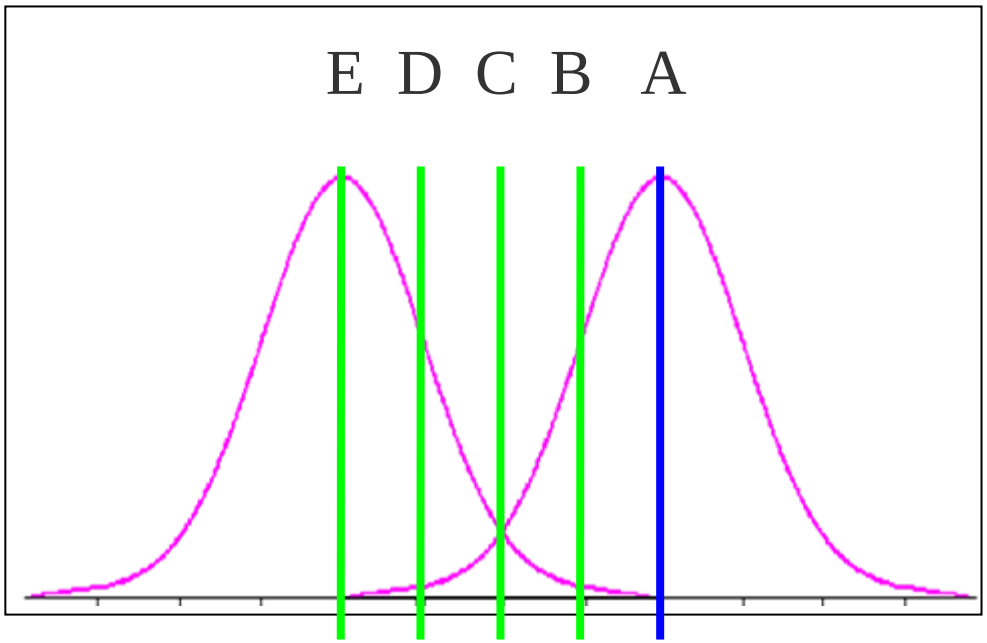
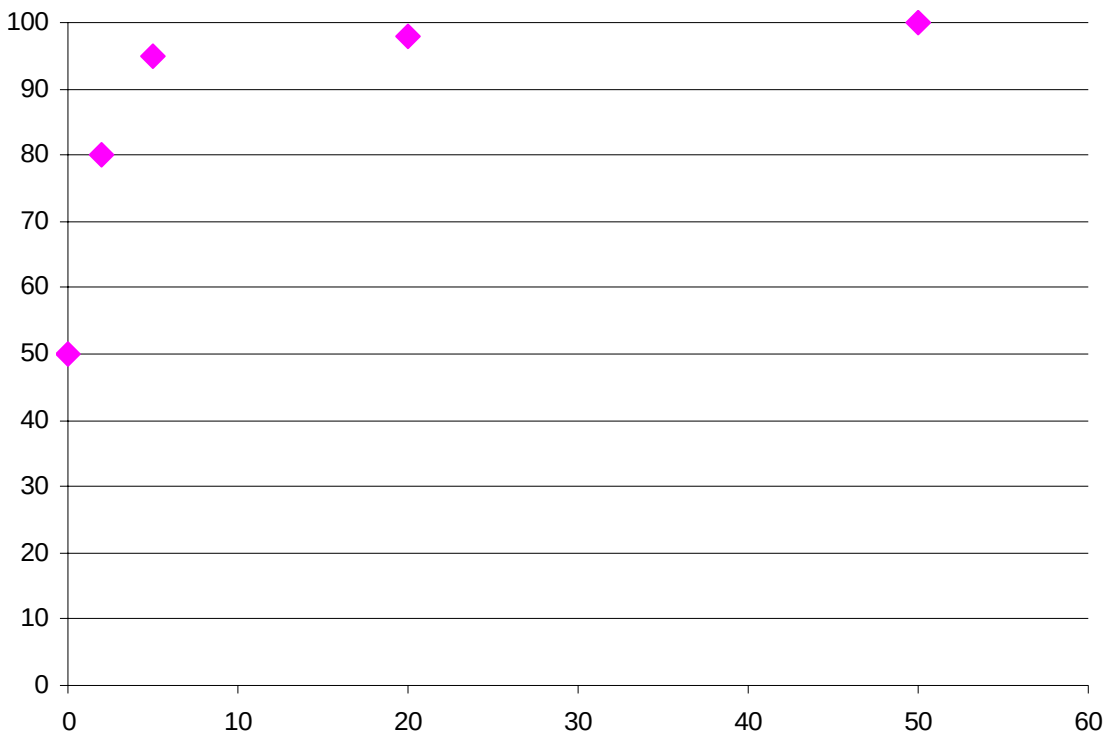


	Sensitivity	Specificity
A	50%	100%
B		
C		
D		
E		

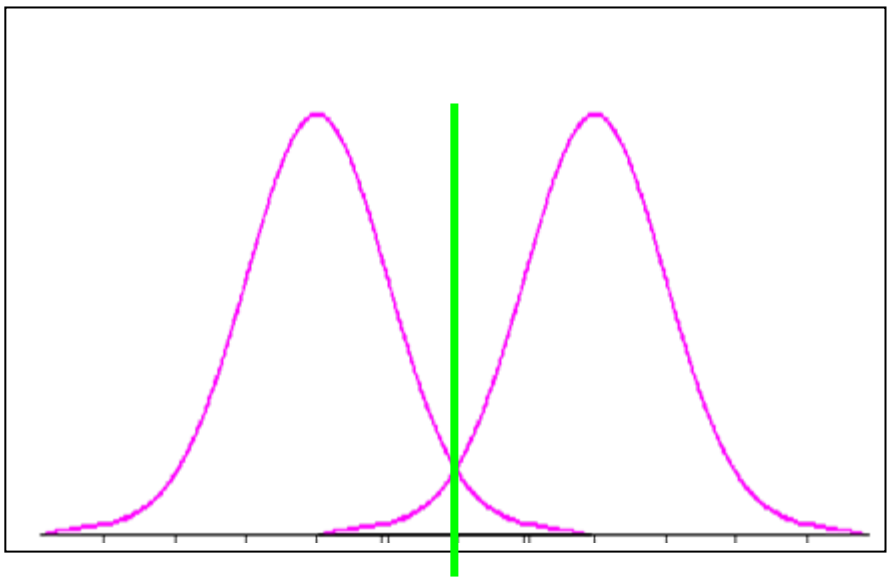
ROC curve

Sensitivity (TP)



1-Specificity (FP)

Predictive Value



	Pos	Neg	
D			100
no D			100

Sensitivity: 95%

Specificity: 95%

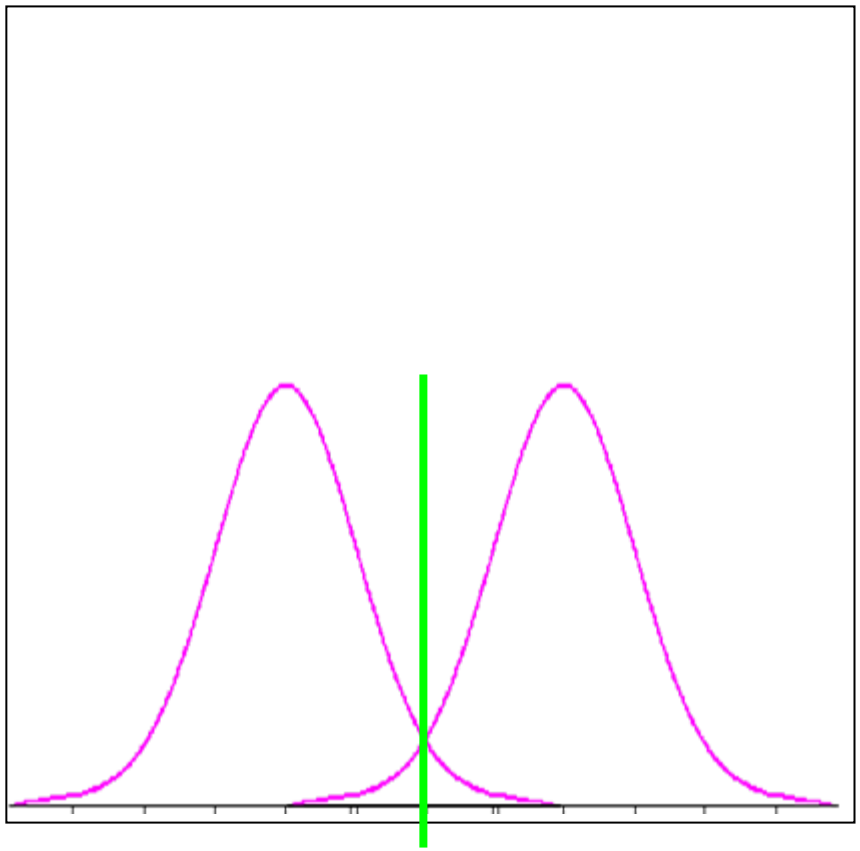
Predictive Value

What's the chance that the result is clinically correct?

PV (+) = TP / (all positives)

PV (+) = TP / (TP + FP)

Predictive Value

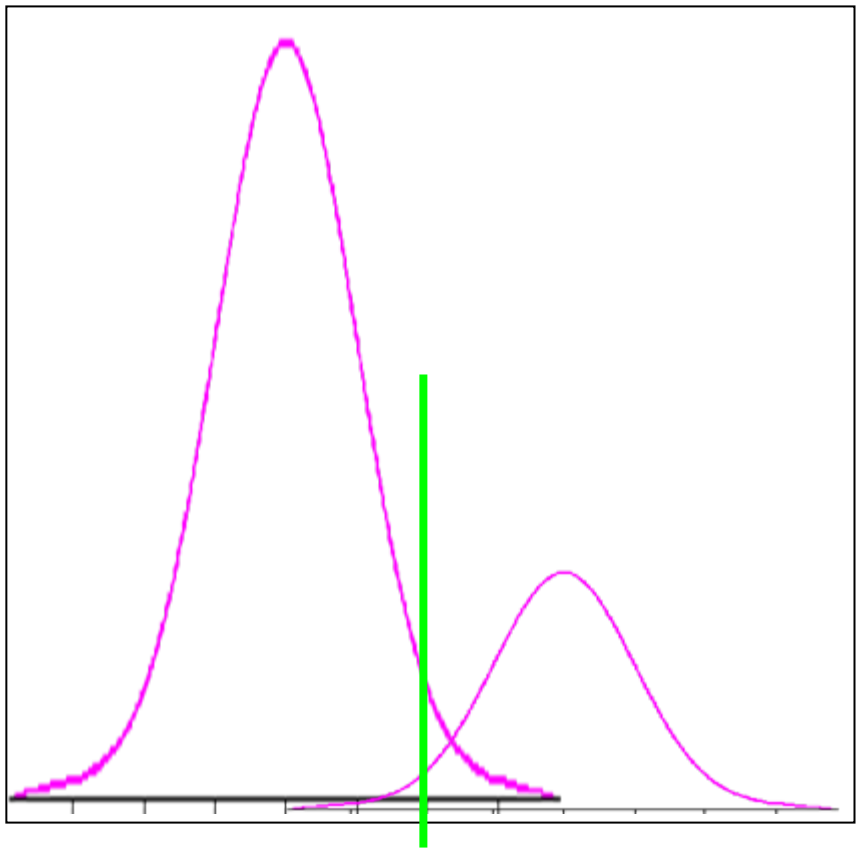


	Pos	Neg	
D	95	5	100
no D	5	95	100
	100	100	

PV (+): 95%

PV (-): 95%

Predictive Value



	Pos	Neg	
D			50
no D			200

PV (+):

PV (-):

Predictive Value

- The prevalence or likelihood of disease (pre-test probability) alters the predictive value

Predictive Value of HIV testing

- Sensitivity = 99.6%
- Specificity = 99.9%

- Prevalence:
  - Blood donors: 1/10,000
  - Military recruits: 1/1,000
  - High risk NJ populations: 2.6%

Predictive Value of HIV testing

Population (per 10,000)	True Positives	False Positives	PV (+)
At risk population			
Recruits			
Blood Doors			

Predictive Value

- As the probability of disease increases, the predictive value of a positive result increases.

- Lab tests are better at supporting or confirming a clinical diagnosis than they are at screening for disease.

Predictive Value

- D-dimer testing can be used to exclude pulmonary embolus, but only in patients with a low or moderate pre-test probability.

Pre-analytic variables

- Patient:
  - Time of day
  - Clinical setting/patient condition
  - Age
- Sample:
  - IV fluid dilution/contamination
  - Technique (hemolysis)
  - Specimen (tube) type
  - Fill volume (anticoagulant; dilution)
  - Labeling

Pre-analytic variables

- Sample (continued):

Pre-analytic variables

- Handling (transport, processing, storage):
  - temperature
  - time
- Analytic:
  - Precision; accuracy
- Reporting:
  - Transcription
  - Calculations
  - Timeliness (Critical values)

POCT

- Near-patient testing
- Same quality requirements (to assure accuracy/precision)
- Comparability to other methods
- Federal and state regulations
  - State licensure
  - Federal CLIA
  - Hospital JCAHO
  - Office COLA

Summary

- Test performance
  - Reference ranges are for reference, not absolute
  - Sensitivity and Specificity depend on comparison group
- Test interpretation
  - Predictive value varies with pre-test probability
  - Test panels provide low yield, and many false positives
- Pre-analytic variables
  - IV fluids can skew results
  - Specimen identification is essential. **Label at the bedside.**
- POCT regulation