Laboratory Medicine: Basic QC Concepts

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Laboratory Error, "Normal Ranges," & Predictive Values

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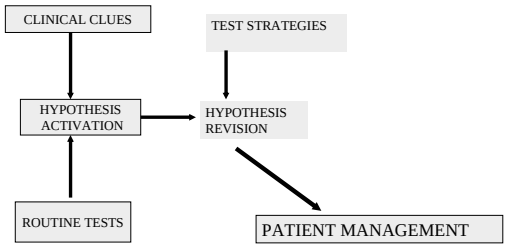
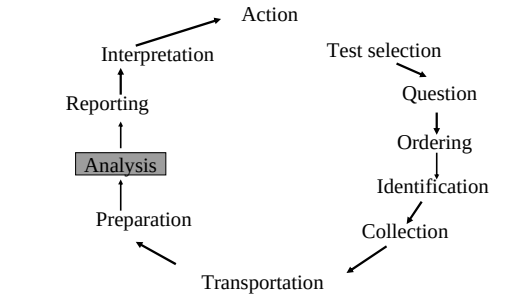
Laboratory Diagnosis

- laboratory error
  - preanalytical
  - analytical: accuracy & precision
- "normal" or "reference" values
- sensitivity, specificity & prevalence
- predictive value
- pretest & posttest probabilities
- thresholds & test strategy



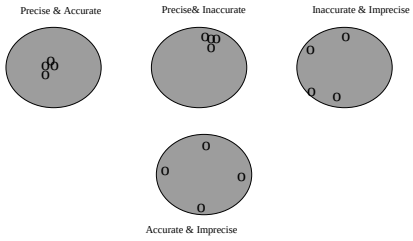


Laboratory Error: Preanalytical

- patient preparation
  - diet, activity
- specimen collection
  - wrong name, wrong tube, wrong time
    wrong technique
- specimen transport & storage
  - delays, wrong temperature

Accuracy & Precision

- Accuracy: "closeness to truth"
  - maintained routinely by calibrators
  - checked by inter-laboratory surveys
- Precision: " reproducibility"
  - estimated by Standard Deviation (SD)
    or Coefficient of Variation (CV)
  - monitored by quality control sera

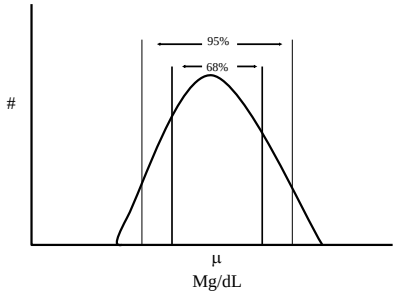


Importance of Quality Control to the Physician

- QUESTION:
  when is the difference between two successive test results within the limits of analytical imprecision?
- ANSWER:
  when the results differ by more than 3 x SD of the laboratory method

"Normal" or "Reference"

- "reference"is the appropriate word
  - central 95 percent of the range of values in an apparently healthy population
- "normal" could mean:
  - free of neurosis, usual, ideal, free of disease, or including the central 95 percent of a "normal" or gaussian distribution



Relationship of "Expected Abnormal Results" to Number of Measured Constituents

Number of Measured Constituents	Expected % of one or more "abnormal" Results
1	5
2	10
4	19
6	26
10	40
15	54
20	64

Probability of abnormal result: $1 - 0.95^n$: n equals test number

CLINICAL VALUE

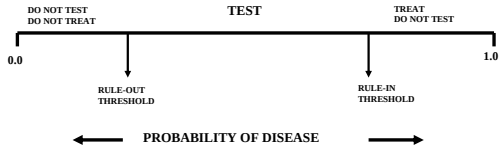
DIAGNOSTIC VALUE

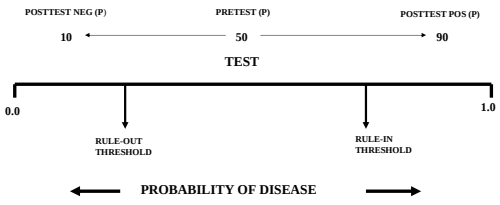
TECHNICAL RELIABILITY

POST-TEST PROBABILITIES

POST-TEST PROBABILITY, GIVEN A POSITIVE TEST RESULT = PV+

POST-TEST PROBABILITY, GIVEN A NEGATIVE TEST RESULT = 100 – PV-





Sensitivity & Specificity

- SENSITIVITY
  - the percentage of diseased individuals with abnormal test results
- SPECIFICITY
  - the percentage of healthy individuals with normal results

False Negatives & False Positives

- FALSE NEGATIVE RATE
  - 100 minus SENSITIVITY
- FALSE POSITIVE ATE
  - 100 minus SPECIFICITY

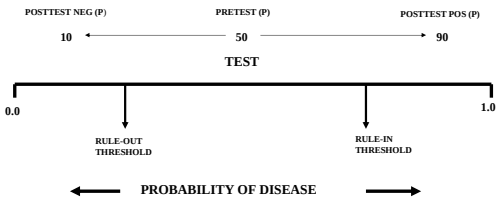
Predictive Values

- POSITIVE PREDICTIVE VALUE (PV+)
  - the percentage of true positive test results among all positive test results
- NEGATIVE PREDICTIVE VALUE (PV-)
  - the percentage of true negative test results among all negative test results

TEST RESULT	DISEASE PRESENT	DISEASE ABSENT	
POSITIVE	TP	FP	POSTTEST PROBABILITY GIVEN A POSITIVE RESULT : TP/TP+FP
NEGATIVE	FN	TN	POSTTEST PROBABILITY GIVEN A NEGATIVE RESULT: FN/TN+FN
TOTALS	TP + FN	TN + FP	
	SENSITIVITY TP/TP+FN	SPECIFICITY TN/FP+TN	

POSTTEST PROBABILITY OF DISEASE WHEN PRETEST PROBABILITY IS 50%

TEST RESULT	DISEASE PRESENT	DISEASE ABSENT	
POSITIVE	90	10	POSTTEST PROBABILITY GIVEN A POSITIVE RESULT : 90/100 (90%)
NEGATIVE	10	90	POSTTEST PROBABILITY GIVEN A NEGATIVE RESULT: 10/100 (10%)
TOTALS	100	100	
	SENSITIVITY 90%	SPECIFICITY 90%	



POSTTEST PROBABILITY OF DISEASE WHEN PRETEST PROBABILITY IS 90%

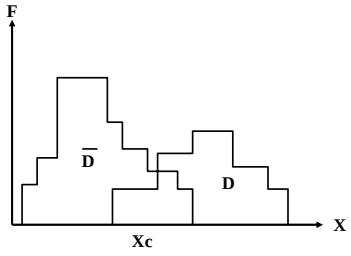
TEST RESULT	DISEASE PRESENT	DISEASE ABSENT	
POSITIVE	810	10	POSTTEST PROBABILITY GIVEN A POSITIVE RESULT : 810/820 (99%)
NEGATIVE	90	90	POSTTEST PROBABILITY GIVEN A NEGATIVE RESULT: 90/180 (50%)
TOTALS	900	100	
	SENSITIVITY 90%	SPECIFICITY 90%	

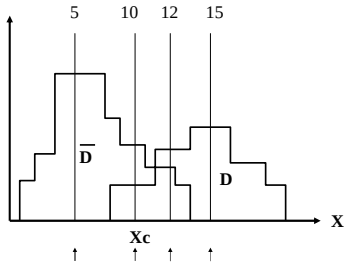
POSTTEST PROBABILITY OF DISEASE WHEN PRETEST PROBABILITY IS 10%

TEST RESULT	DISEASE PRESENT	DISEASE ABSENT	
POSITIVE	90	90	POSTTEST PROBABILITY GIVEN A POSITIVE RESULT : 90/180 (50%)
NEGATIVE	10	810	POSTTEST PROBABILITY GIVEN A NEGATIVE RESULT: 10/820 (1%)
TOTALS	100	900	
	SENSITIVITY 90%	SPECIFICITY 90%	

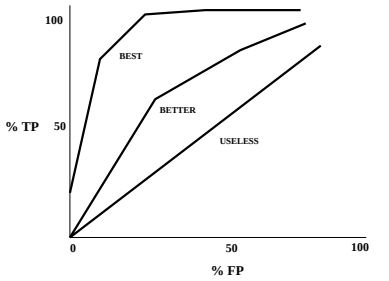
Effects of Prevalence

- DECREASING PREVALENCE
  - decreases (PV+) & increases (PV-)
- INCREASING PREVALENCE
  - increases (PV+) & decreases (PV-)





RECEIVER-OPERATOR CHARACTERISTIC (ROC) CURVES



- DETERMINANTS OF SENSITIVITY
  - choice of cutoff or reference limit
  - severity of disease in patients chosen to determine sensitivity
  - increased by multiple testing in parallel
- DETERMINANTS OF SPECIFICITY
  - choice of cutoff or reference limit
  - type of nondiseased persons chosen to determine specificity
  - increased by multiple testing in series

WHICH TEST TO ORDER?

↓

WHAT IS THE PRETEST PROBABILITY OF THE PROBLEM?

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WHAT ARE THE "RULE IN" & "RULE OUT" THRESHOLDS

TO RULE IN	TO RULE OUT
↓	↓
KEY IS: SPECIFICITY	KEY IS: SENSITIVITY
↓	
POSTTEST PROBABILITY (+) SHOULD BE HIGHER THAN "RULE IN" THRESHOLD	POSTEST PROBABILITY (-) SHOULD BE LOWER THAN THE "RULE OUT" THRESHOLD

POSTTEST PROBABILITY OF CHD WHEN PRETEST PROBABILITY IS 10%

TEST RESULT	DISEASE PRESENT	DISEASE ABSENT	
POSITIVE	86	207	POSTTEST PROBABILITY GIVEN A POSITIVE RESULT : 86/293 (29%)
NEGATIVE	14	693	POSTTEST PROBABILITY GIVEN A NEGATIVE RESULT: 14/707 (2%)
TOTALS	100	900	
	SENSITIVITY 86%	SPECIFICITY 77%	

POSTTEST PROBABILITY OF CHD WHEN PRETEST PROBABILITY IS 90%

TEST RESULT	DISEASE PRESENT	DISEASE ABSENT	
POSITIVE	774	23	POSTTEST PROBABILITY GIVEN A POSITIVE RESULT : 774/797 (97%)
NEGATIVE	126	77	POSTTEST PROBABILITY GIVEN A NEGATIVE RESULT: 126/203 (62%)
TOTALS	900	100	
	SENSITIVITY 86%	SPECIFICITY 77%