EVALUATION OF MEDICAL TESTS AND TREATMENT

PREDICTIVE VALUES

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Prevalence

- The PREDICTIVE VALUE of a test, not its SENSITIVITY or SPECIFICITY, is the clue to its utility.
- The value of a test is dependent upon the population studied.
- The PREVALENCE of a disease is critical to the utility of laboratory tests and the use of medical resources.
- PREVALENCE is the percentage of patients who have the target disorder. (Total cases/ Total population at risk.) This is PRE-TEST PROBABILITY.

Bayes 2x2 table

		Disease	
		+ Present	– Present
Test result	+	a True positive (TP)	b False positive (FP)
	–	c False negative (FN)	d True negative (TN)

Sensitivity = a/(a + c) = TP/(TP + FN)

Specificity = d/(b + d) = TN/(TN + FP)

Positive predictive value = a/(a + b) = (TP/TP + FP)

Negative predictive value = d/(c + d) = TN/(TN + FN)

Diagnostic accuracy = (a + d)/(a + b + c + d) = (TP+ FN)/(TP + FP + TN + FN)

Pre-test (prior) Probability = (a + c)/(a + b + c + d) = (TP + FN)/(TP + FP + TN + FN)

Likelihood ratio for a positive test result (LR+):

= [a/(a + c)]/[b/b(b + d)] = TP rate/FP rate = [TP/(TP + FN)/(FP/TN + FP)] =

= sensitivity/(1 – specificity)

Likelihood ratio for a negative test result (LR–):

= [c/(a + c)]/[d/(b + d)] = FN rate/TN rate = [FN/(TP + FN)]/[TN + FP)] =

= (1 – sensitivity)/specificity

Source: Gardner DG, Shoback D: *Greenspan's Basic and Clinical Endocrinology*, 8th Edition: http://www.accessmedicine.com

Fig. 4-2 Accessed 08/01/2010

Sensitivity

- SENSITIVITY is the percentage of patients WITH the target disorder who have a POSITIVE test result.
- SENSITIVITY is calculated as the number of known patients with disease who have a positive test result, divided by the total number of known patients with disease in the population sampled.
- a/a+c

Specificity

- SPECIFICITY is the percentage of patients WITHOUT the target disorder who have a NEGATIVE test result.
- SPECIFICITY is calculated as the number of known patients without disease who have a negative test result, divided by the total number of known patients without disease in the population sampled.
- d/b+d

Sensitivity and specificity

- A test that is highly SENSITIVE identifies (virtually) all patients WITH disease.
- A test that is highly SPECIFIC identifies (virtually) all patients WITHOUT disease.

Sensitivity and specificity

- A test that is both highly sensitive and highly specific may not be of clinical utility, however, if the prevalence of disease in the population studied is very, very low.
- In such a case, a POSITIVE result does not predict the presence of disease.
- In such a case, a NEGATIVE result is highly predictive of the absence of disease. The number of false positives is high, however; there are few false negatives.

Choice of control groups

		Cushing's Syndrome	
		Present	Absent
1mg overnight dexamethasone suppression	No suppression	151	5
	Suppression	3	461

Sensitivity = 151/(151 + 3) = 98.1%

Specificity = 461/(5 + 461) = 98.9%

A

		Cushing's Syndrome	
		Present	Absent
1mg overnight dexamethasone suppression	No suppression	151	101
	Suppression	3	858

Specificity = 858/(101 + 858) = 89.5%

B

		Cushing's Syndrome	
		Present	Absent
1mg overnight dexamethasone suppression	No suppression	151	96
	Suppression	3	397

Specificity = 397/(96 + 397) = 80.5%

C

Source: Gardner DG, Shoback D: *Greenspan's Basic and Clinical Endocrinology*, 8th Edition: http://www.accessmedicine.com

Diagnosis of Cushing's syndrome with the 1-mg overnight dexamethasone suppression test: test characteristics with normal controls (Panel A); all controls (Panel B); and "obese" and "other" controls (Panel C). These data show how the specificity of the test is affected by the types of control subjects.

(Reproduced with permission from Crapo L: Cushing's syndrome: a review of diagnostic tests. Metabolism 1979;28:955.)

Fig. 4-3 Accessed 08/01/2010

Sensitivity and specificity

- Many screening studies in the US have shown the prevalence of HIV infection (seropositive) to be 0.4%.
- The rapid screening test is 99.6% sensitive and 97.5% specific for this condition.

- Consider the results of HIV screening of ten thousand people selected at random.

HIV

Number of patients	Test positive	Test negative
Infected	0038	0002
Not Infected	0388	9572

Sensitivity and specificity

- SENSITIVITY

  38/40 patients classified correctly.

- SPECIFICITY

  9572/9960 patients classified correctly.

- Ten thousand patients examined.

Predictive value

- The POSITIVE PREDICTIVE VALUE is calculated as a/a+b.
- The NEGATIVE PREDICTIVE VALUE is calculated as d/c+d.

- The FALSE POSITIVE RATE is calculated as b/b+d. These are those patients who do not have the disease but who have tested positive.
- The FALSE NEGATIVE RATE is calculated as c/a+c. These are those patients who have the disease but who have tested negative.

Predictive value

- POSITIVE PREDICTIVE VALUE

  426 patients classified as HIV positive; however, only 38 are infected with HIV.

  Thus, 380 patients are classified incorrectly, the false positives.

- NEGATIVE PREDICTIVE VALUE

  9572/9574 patients classified as HIV negative

  Two patients are classified incorrectly, the false negatives.

  This may be acceptable for screening blood donors as any questionable units will be discarded.

  It is not a good strategy to decide upon quarantine.

When prevalence changes

- If the prevalence of HIV is 1%, then testing will uncover 99/100 infected patients (one will still not be uncovered).
- 99 patients not infected will be categorized inappropriately; 9801 will truly be negative.
- The positive predictive value has risen to 50%; the negative predictive value is 99%.
- INCIDENCE refers to new cases only as those previously identified are no longer considered at risk.
- Differs from PREVALENCE.

When prevalence changes

Number of patients	Test positive	Test negative
Infected	0099	0001
Not Infected	0099	9801

Predictive value

Disease prevalence or pretest probability	0.1%	1%	10%	50%	90%
Positive predictive value	0.89%	8.33%	50.0%	90.0%	98.78%
Negative predictive value	99.99%	99.89%	98.78%	90%	50.0%

Source: Gardner DG, Shoback D: *Greenspan's Basic and Clinical Endocrinology*, 8th Edition: http://www.accessmedicine.com

Positive and negative predictive values as a function of disease prevalence, assuming test sensitivity and specificity of 90% for each.

Fig. 4-7 Accessed 08/01/2010

HIV screening recommendations

- Screen all newborns of HIV positive mothers. (PCR)
- Screen in those populations where prevalence of HIV positive is >1% (sexually transmitted disease clinics, prisons).
- p24 antigen testing is the screen of choice if acute illness suspected. Do not use viral load tests.
- Screen all pregnant women.

HIV screening caveats

- Recent CDC recommendations for universal screening assume the rapid screening antibody test cost is very low (as must be the confirmatory Western Blot)
- AND there is no negative impact from a false positive result
- AND that risk behavior is changed by the result
- AND anti-retroviral therapy completely suppresses HIV in body fluids and thus limits infectivity.
- Those assumptions are not supported by clinical data.