

Diagnostic and Screening Tests

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Diagnostic and Screening Tests

We use medical tests to diagnose health conditions. Results can have PROFOUND effects on human beings.

Yet--no test is infallible. . .

We may see false positive and false negative results.

Diagnostic and Screening Tests

GOALS

- **Test properties: sensitivity, specificity, predictive value, validity, precision**
- **Fundamentals of screening**
- **Parallel and serial testing**

Diagnostic and Screening Tests

Test properties

		DISEASE		Total
		(+)	(Š)	
TEST	(+)	A (TP)	B (FP)	A+B (all positives)
	(Š)	C (FN)	D (TN)	C+D (all negatives)
Total		A+C (All ill)	B+D (All healthy)	A+B+C+D (Grand Total)

Diagnostic and Screening Tests

Test properties

		DISEASE		Total
		(+)	(š)	
TEST	(+)	A	B	A+B
	(š)	C	D	C+D
Total		A+C	B+D	A+B+C+D

(True) prevalence: Proportion of persons with disease in the population. **Prevalence = $(A+C)/(A+B+C+D)$**

Of 1000 kids, 78 have head lice. Prevalence = 7.8%

Diagnostic and Screening Tests

Test properties

		DISEASE		Total
		(+)	(š)	
TEST	(+)	A (TP)	B (FP)	A+B
	(š)	C (FN)	D (TN)	C+D
Total		A+C	B+D	A+B+C+D

Sensitivity: Likelihood a diseased person will have a positive test **Sensitivity = TP/All disease = $A/(A+C)$**

Of 100 men with prostate cancer, 90 have (+) PSA.
Sensitivity=90%

Diagnostic and Screening Tests

Test properties

		DISEASE		Total
		(+)	(Š)	
TEST	(+)	A (TP)	B (FP)	A+B
	(Š)	C (FN)	D (TN)	C+D
Total		A+C	B+D	A+B+C+D

Specificity: Likelihood a healthy person will have a negative test
Specificity = $TN / \text{All healthy} = D / (B+D)$

Of 100 healthy kids, 3 have a false (+) strep test.
Specificity = 97%

Diagnostic and Screening Tests

There is a yin-yang relationship between sensitivity and specificity. Changing test cut-off values to increase the sensitivity will reduce the specificity, and vice-versa.

Diagnostic and Screening Tests

Example: Diabetes

Diabetes is diagnosed based on a fasting blood sugar ≥ 126 mg/dL. If we raise the cutoff to 180 mg/dL, we make it more difficult have a positive diabetes test, i.e., a diagnosis of DM.

We have made our test **less sensitive** (some true diabetics won't have blood sugar that high) and **more specific** (normal people may get their blood sugar to 126, but are unlikely to get it to 180).

The opposite applies to lowering the cutoff: we become more sensitive but less specific.

Diagnostic and Screening Tests

Sensitivity and specificity give us likelihood of the test result among persons known to be diseased or healthy.

As clinicians, we need to know the opposite: the likelihood of being diseased or healthy among persons with a known test result.

Diagnostic and Screening Tests

Test properties

		DISEASE		Total
		(+)	(š)	
TEST	(+)	A	B	A+B
	(š)	C	D	C+D
Total		A+C	B+D	A+B+C+D

Predictive value of (+): Likelihood that a person with a positive test actually has the disease

$$PV(+)=TP/All\ positives=A/(A+B)$$

Two-thirds of patients with a (+) Exercise Stress Test will have atherosclerosis on angiography $PV(+)=66\%$

Diagnostic and Screening Tests

Test properties

		DISEASE		Total
		(+)	(š)	
TEST	(+)	A	B	A+B
	(š)	C	D	C+D
Total		A+C	B+D	A+B+C+D

Predictive value of (-): Likelihood that a person with a negative test is free of the disease

$$PV(-) = TN / \text{All negatives} = D / (C+D)$$

99 of 100 patients with a (-) syphilis test are free of syphilis
 $PV(-) = 99\%$

Diagnostic and Screening Tests

Consider: What is the likelihood that a person with a positive test will actually have the disease (i.e., what is the PV+) when. . .

Prevalence=20% in a population of 10^4

Sensitivity=90%

Specificity=90%

Diagnostic and Screening Tests

		DISEASE		Total
		(+)	(š)	
TEST	(+)	<i>Sens x 2000</i> 1800	800	2600
	(š)	200	<i>Spec x 8000</i> 7200	7400
Total		2000	8000	10,000

Population: 10,000

Prevalence: 20%

Sensitivity: 90%

Specificity: 90%

$PV(+)=TP/All\ Positives=1800/2600=69.2\%$

Conclude: Only 69.2% of persons with a positive test actually have the disease. (Tests ain't perfect!)

Diagnostic and Screening Tests

Let's see what happens when we make this a rare disease. Test properties stay the same. . .

Prevalence=0.1% in a population of 10^4

Sensitivity=90%

Specificity=90%

Diagnostic and Screening Tests

		DISEASE		Total
		(+)	(š)	
TEST	(+)	<i>Sens x 10</i> 9	999	1,008
	(š)	1	<i>Spec x 9,990</i> 8,991	8,992
Total		10	9,990	10,000

Population: 10,000

Prevalence: 0.1%

Sensitivity: 90%

Specificity: 90%

$PV(+)=TP/All\ Positives=9/1,008=0.89\%$

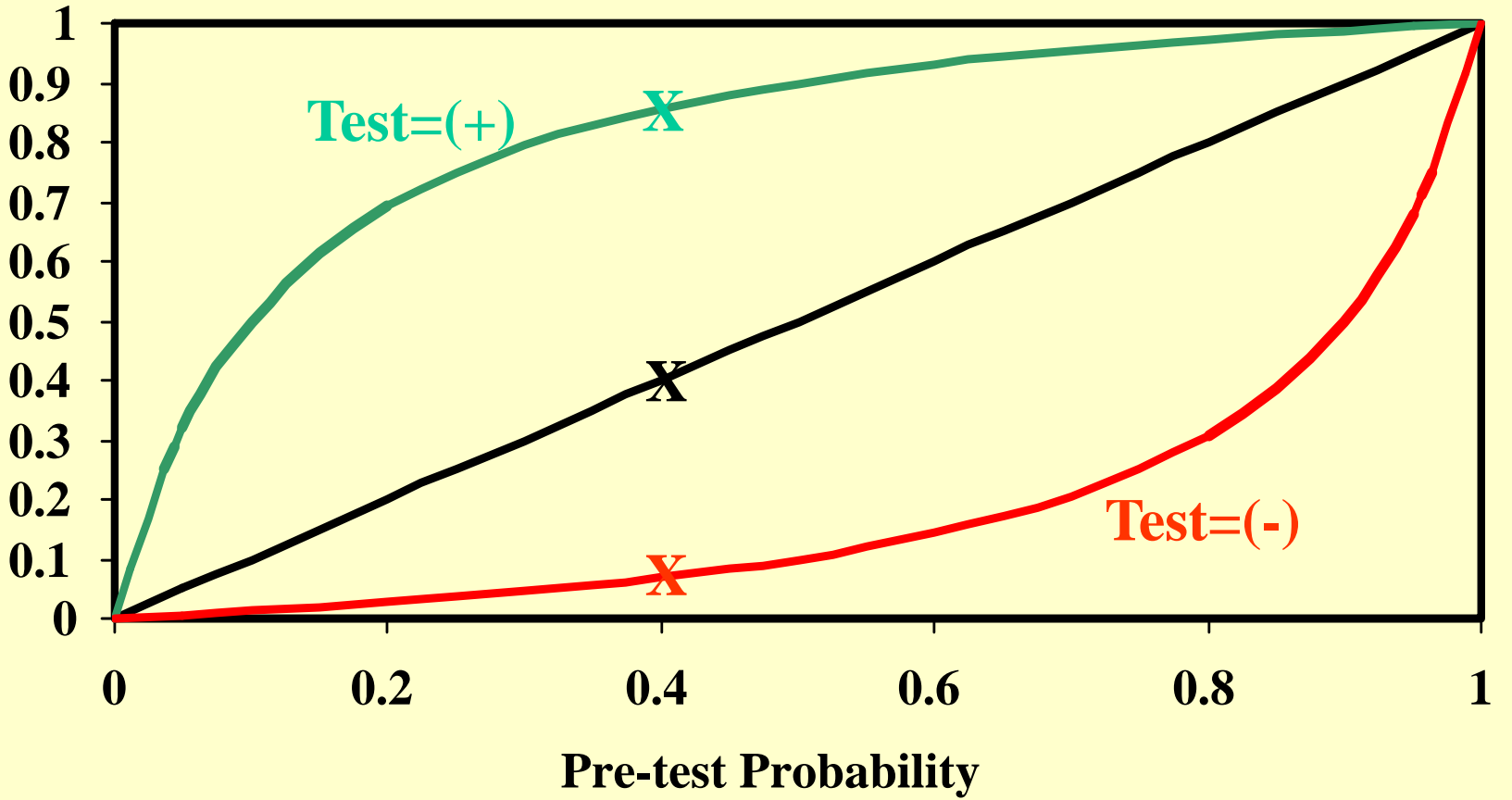
Conclude: Less than 1%(!!) of persons with a positive test actually have the disease.

Diagnostic and Screening Tests

The take-home message: Although a positive test result identifies a group with increased prevalence of the disease, the prevalence may still be very low when you are starting with a rare disease.

Implication: Don't do cardiac stress tests on marathon runners! Any positive is likely to be a false positive.

Tests should be limited to situations in which there is some intermediate probability of disease, where the result will affect your approach. (See following slide.)



Diagnostic and Screening Tests

Two other test attributes:

Validity = Accuracy: The likelihood that a test result will be correct, *on average*.

Precision = repeatability = reliability: The likelihood that repeated measures on the same sample or subject will yield the same result.

Ideal tests have high validity and high precision.

Diagnostic and Screening Tests

Consider validity and precision for five repeated measurements where the true value is 120

Results of five measurements	Validity	Precision
120, 120, 119, 121, 120	High (average is 120)	High (results all very close together)
120, 100, 140, 90, 150	High (average is still 120!)	Low (results all over the place)
100, 100, 99, 101, 100	Low (average is way off at 100)	High (results all very close together)
100, 80, 120, 70, 130	Low (average is way off at 100)	Low (results all over the place)

Diagnostic and Screening Tests

Sometimes we use tests in combination:

Series testing: The second test is given only to those positive on the first. To be positive for the combination, one must be positive on both the first AND second test.

This saves money, lowers sensitivity, and raises specificity.

Example: HIV is first tested with a sensitive (but not specific) serological test. This catches all positives, but includes many false positives. The Western blot is done only on positives. It is very specific and identifies the false positives.

Diagnostic and Screening Tests

Sometimes we use tests in combination:

Parallel testing: Both tests are given to everyone.

To be positive for the combination, a positive for either one of the tests will suffice.

This raises sensitivity and lowers specificity.

Example: Ischemic heart disease is diagnosed on the basis of a positive exercise tolerance test OR a positive exercise ECHO scan. (Many other tests are also available.) A positive result from either of these establishes the diagnosis.

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