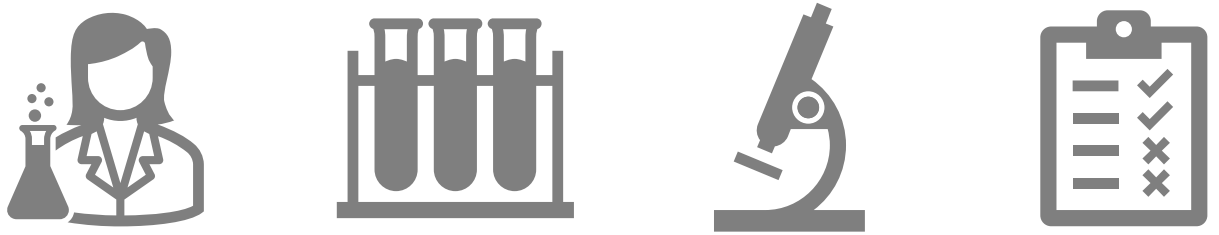
Screening Tests



Clinical Oncology

Curriculum 2021

Clinical Oncology
The Royal College of Radiologists

Medical statistics module

3.6 Screening tests	▪ Calculate and interpret the meaning of sensitivity, specificity, positive and negative predictive values and accuracy

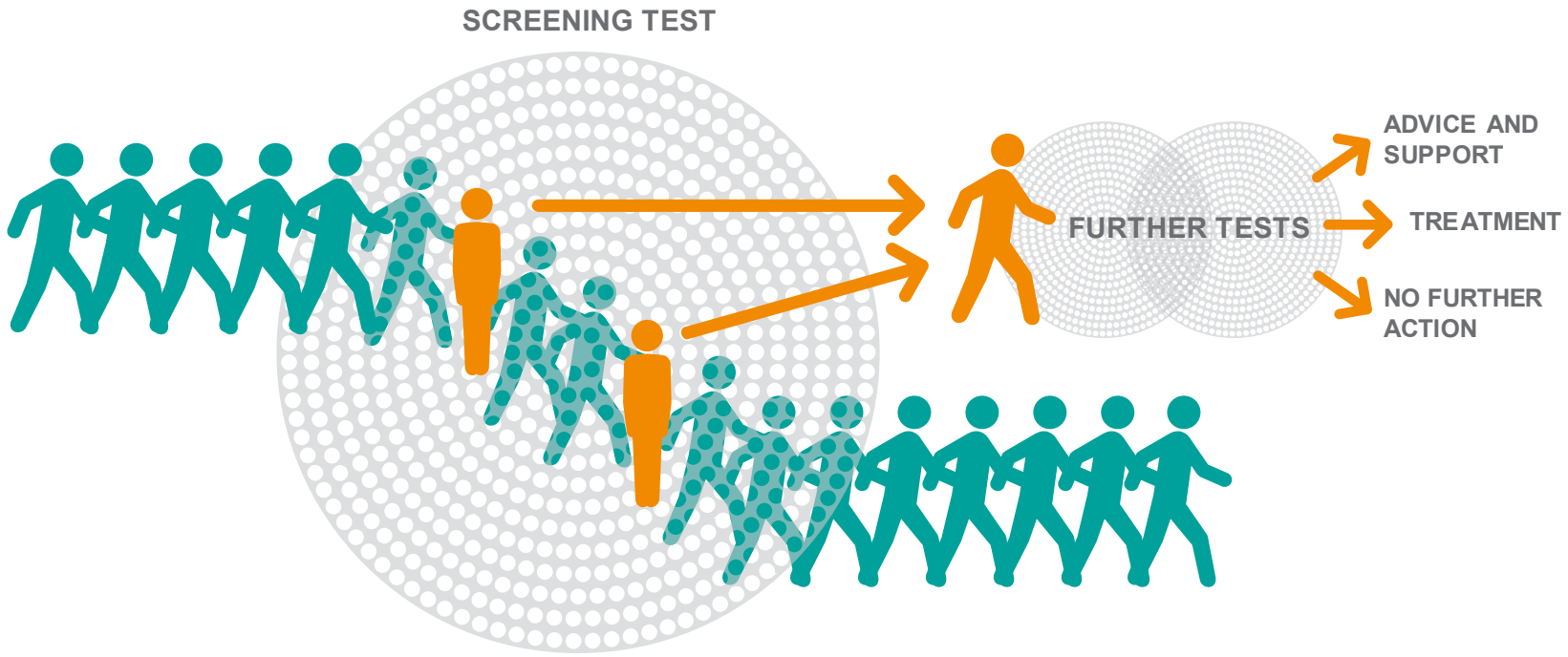
Screening test

- A simple test to ascertain which individuals in an apparently healthy population are **likely** to have the disease of interest

- Screening is sensible if a treatment is available for pre-symptomatic stages and it's more effective than when given at a later stage

- A diagnostic test may be used to:
  - To confirm the diagnosis in screening test positive individuals
  - For staging (for treatment planning)
  - For monitoring the progress/ recurrence over time

Screening → Diagnosis



Examples

Disease	Screening test	Confirmatory test	Age group	Frequency
Breast cancer	Mammography	Further imaging, clinical examination, biopsy	50-70	3 yearly
Cervical cancer	HPV testing	Colposcopy	25-64	5 yearly
Bowel cancer	Faecal immunochemical testing (FIT)	Colonoscopy	50-74	2 yearly
Diabetic retinopathy	Digital image of retina	Hospital eye service/ treatment service review	Age 12+ with type 1 or 2 diabetes	1 yearly

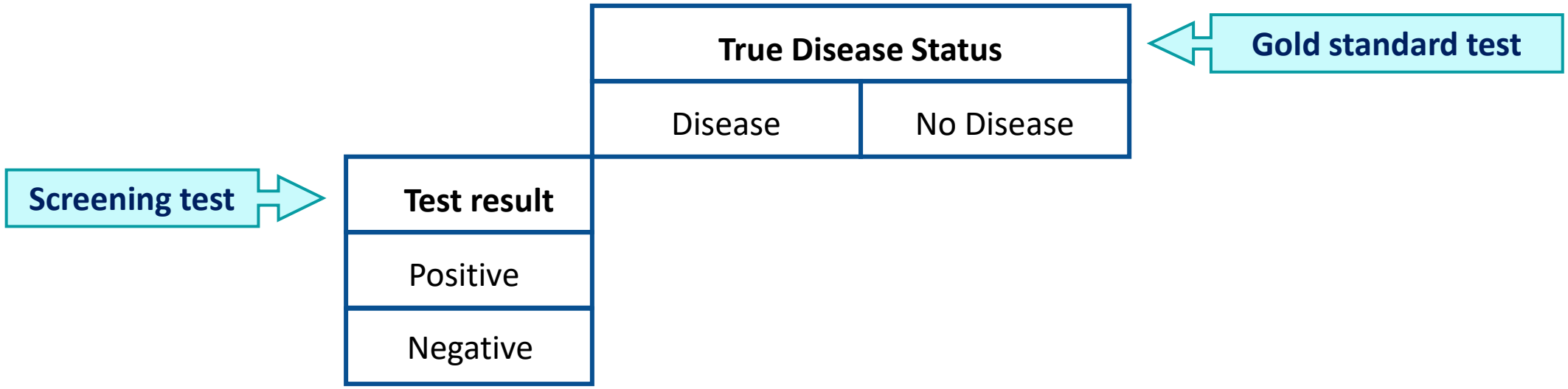
Screening tests vs. Diagnostic tests

	Screening Tests	Diagnostic tests
Purpose	• To detect potential disease indicators	• To establish the presence or absence of a disease
Target population	• Large number of asymptomatic, but potentially at-risk individuals	• Asymptomatic individuals with a positive screening test • Symptomatic individuals to establish the diagnosis
Test method	• Simple, usually non-invasive, and acceptable to patients and staff	• Maybe invasive, but justifiable as necessary to establish diagnosis
Positive result threshold	• Generally chosen towards high sensitivity (true positives) not to miss potential disease	• Chosen towards high specificity (low false positives). • More weight given to accuracy and precision than patient acceptability
Positive result	• Essentially indicates suspicion of disease (often used in combination with other risk factors) that warrants confirmation	• Results provide a definitive diagnosis
Cost	• Cheap, benefits should outweigh the costs as a large number of people will need to be screened to identify a small number of potential cases	• Higher costs associated with diagnostic test may be justified to establish diagnosis

Evaluation of screening tests

- Measures for assessing the effectiveness of the test:
  - Sensitivity
  - Specificity
  - Positive predictive value
  - Negative predictive value

- To evaluate a potential screening test →
  - Apply the test to a group of individuals whose **true disease status** is known



		True Disease Status		
		Disease	No Disease	Total
Test result	Positive	true positive (a)	false positive (b)	a+b
	Negative	false negative (c)	true negative (d)	c+d
	Total	a+c	b+d	N=a+b+c+d

Sensitivity is the proportion of individuals ***with the disease*** who are correctly identified by the test.

		True Disease Status		
		Disease	No Disease	Total
Test result	Positive	a (true positive)	b (false positive)	a + b
	Negative	c (false negative)	d (true negative)	c + d
	Total	a + c	b + d	N=a+b+c+d

$$\boldsymbol{Sensitivity = \frac{a}{a + c}}$$

Specificity is the proportion of individuals ***without the disease*** who are correctly identified by the test.

		True Disease Status		
		Disease	No Disease	Total
Test result	Positive	a (true positive)	b (false positive)	a + b
	Negative	c (false negative)	d (true negative)	c + d
	Total	a+c	b + d	N=a+b+c+d

$$\boldsymbol{Specificity = \frac{d}{b + d}}$$

- Sensitivity and specificity quantify the diagnostic ability of the test.

Sensitivity	Specificity
Sensitivity refers to a test's ability to correctly identify those who truly have the condition being investigated.	Specificity refers to a test's ability to correctly identify individuals who do not have the condition being investigated
Identifies true positives	Identifies true negatives
Minimises false negatives	Minimises false positives
Ability to **rule out** the disease (If the test is negative)	Ability to **rule in** the disease (If the test is positive)

Positive predictive value is the proportion of individuals with ***a positive test*** result ***who have the disease***

		True Disease Status		
		Disease	No Disease	Total
Test result	Positive	a (true positive)	b (false positive)	a + b
	Negative	c (false negative)	d (true negative)	c + d
	Total	a+c	b + d	N=a+b+c+d

$$PPV = \frac{a}{a+b}$$

Negative predictive value is the proportion of individuals with a ***negative test*** result ***who do not have the disease***

		True Disease Status		
		Disease	No Disease	Total
Test result	Positive	a (true positive)	b (false positive)	a + b
	Negative	c (false negative)	d (true negative)	c + d
	Total	a+c	c + d	N=a+b+c+d

$$NPV = \frac{d}{c + d}$$

Summary

- **Sensitivity –** proportion of individuals **with** the disease who are correctly identified by the test

$$\frac{a}{(a+c)}$$

- **Specificity –** proportion of individuals **without** the disease who are correctly identified by the test

$$\frac{d}{(b+d)}$$

- **Positive predictive value –** proportion of individuals with a positive test results who have the disease

$$\frac{a}{(a+b)}$$

- **Negative predictive value –** proportion of individuals with a negative test results who do not have the disease

$$\frac{d}{(c+d)}$$

- The predictive values indicate how likely an individual has or does not have the disease, given the test result.
- Predictive values are dependent on the **prevalence** of the disease in the population.

Prevalence is the proportion of the population who have the disease.

		True Disease Status		
		Disease	No Disease	Total
Test result	Positive	a (true positive)	b (false positive)	a + b
	Negative	c (false negative)	d (true negative)	c + d
	Total	a + c	c + d	N=a+b+c+d

$$\boldsymbol{Prevalence} = \frac{\boldsymbol{a + c}}{\boldsymbol{N}}$$

Likelihood ratio

The **likelihood ratio** (LR) for a positive test result is the ratio of the probability of a positive result if the patient has the disease (sensitivity) to the probability of a positive result if the patient does not have the disease (1-specificity).

$$likelihood\ ratio = \frac{sensitivity}{1 - specificity}$$

prob(+ve | disease)

prob(+ve | no disease)

For example, a LR of 4 indicates that a positive result is four times as likely to occur in an individual with the disease compared to one without it.

The **likelihood ratio** (LR) for a negative test result:

$$likelihood\ ratio = \frac{specificity}{1 - sensitivity}$$

prob(-ve | no disease)

prob(-ve | disease)

A LR of 4 for a negative result indicates that a negative result is four times as likely to occur in an individual without the disease compared to one without it.

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 MAY 27, 2004 VOL. 350 NO. 22

Prevalence of Prostate Cancer among Men with a Prostate-Specific Antigen Level ≤4.0 ng per Milliliter

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ABSTRACT

BACKGROUND

The optimal upper limit of the normal range for prostate-specific antigen (PSA) is unknown. We investigated the prevalence of prostate cancer among men in the Prostate Cancer Prevention Trial who had a PSA level of 4.0 ng per milliliter or less.

METHODS

Of 18,882 men enrolled in the prevention trial, 9459 were randomly assigned to receive placebo and had an annual measurement of PSA and a digital rectal examination.

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Table 2. Relationship of the Prostate-Specific Antigen (PSA) Level to the Prevalence of Prostate Cancer and High-Grade Disease.*

PSA Level	No. of Men (N=2950)	Men with Prostate Cancer (N=449)	Men with High-Grade Prostate Cancer (N=67)	Sensitivity	Specificity
		no. of men (%)	*no./total no. (%)*		
≤0.5 ng/ml	486	32 (6.6)	4/32 (12.5)	1.0	0.0
0.6–1.0 ng/ml	791	80 (10.1)	8/80 (10.0)	0.93	0.02
1.1–2.0 ng/ml	998	170 (17.0)	20/170 (11.8)	0.75	0.33
2.1–3.0 ng/ml	482	115 (23.9)	22/115 (19.1)	0.37	0.73
3.1–4.0 ng/ml	193	52 (26.9)	13/52 (25.0)	0.12	0.92

True Disease Status	
Prostate Ca.	No prostate ca.
449	2501

PSA Test result	
Positive ≥2.1	Negative <2.1
675	2275

Sensitivity is the proportion of individuals ***with the disease*** who are correctly identified by the test.

		True Disease Status		
		Prostate Ca.	No Prostate Ca.	Total
Test result	Positive	167	508	675
	Negative	282	1993	2275
	Total	449	2501	N=2950

$$sensitivity = \frac{167}{449} = 0.37$$

Specificity is the proportion of individuals ***without the disease*** who are correctly identified by the test.

		True Disease Status		
		Prostate Ca.	No Prostate Ca.	Total
Test result	Positive	167	508	675
	Negative	282	1993	2275
	Total	449	2501	N=2950

$$sensitivity = \frac{167}{449} = 0.37$$

$$\boldsymbol{specificity = \frac{1993}{2501} = 0.80}$$

Positive predictive value is proportion of individuals with ***a positive test*** result ***who have the disease***

		True Disease Status		
		Prostate Ca.	No Prostate Ca.	Total
Test result	Positive	167	508	675
	Negative	282	1993	2275
	Total	449	2501	N=2950

$$sensitivity = \frac{167}{449} = 0.37$$

$$specificity = \frac{1993}{2501} = 0.80$$

$$\boldsymbol{PPV = \frac{167}{675} = 0.25}$$

Negative predictive value is proportion of individuals with a ***negative test*** result ***who do not have the disease***

		True Disease Status		
		Prostate Ca.	No Prostate Ca.	Total
Test result	Positive	167	508	675
	Negative	282	1993	2275
	Total	449	2501	N=2950

$$sensitivity = \frac{167}{449} = 0.37$$

$$specificity = \frac{1993}{2501} = 0.80$$

$$PPV = \frac{167}{675} = 0.25$$

$$\boldsymbol{NPV = \frac{1993}{2275} = 0.88}$$

$$sensitivity = \frac{167}{449} = 0.37;\ specificity = \frac{1993}{2501} = 0.80;$$

$$likelihood\ ratio\ for\ positive\ result = \frac{0.37}{1 - 0.80} = 1.85$$

$$likelihood\ ratio\ for\ negative\ result = \frac{0.80}{1 - 0.37} = 1.26$$

If the test is positive, the patient is 1.85 times as likely to have prostate cancer as not have it.

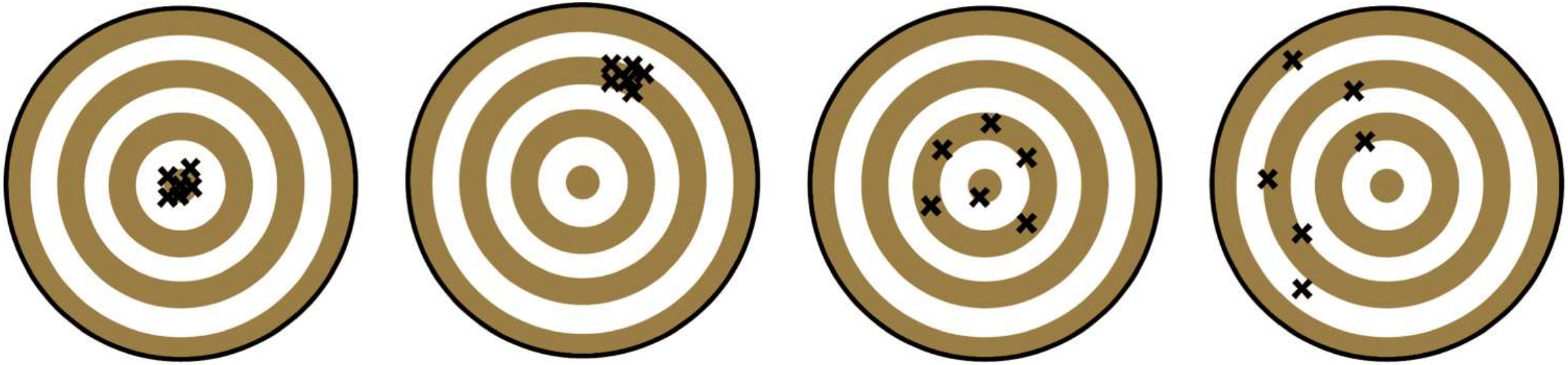
If the test is negative, the patient is 1.26 times as likely to not have prostate cancer as have it.

Accuracy and Precision

- **Accuracy -** Closeness of a test result/ measurement to true value
- **Precision -** Closeness of repeat test results/ measurements to each other

	Mnemonic	What it is	Things to remember
Accuracy	Accuracy = Validity	• The closeness of test results to the true values • The absence of systematic error in a test	• Systematic error ↓ accuracy in a test
Precision	Precision = Reliability Reproducibility	• The consistency and reproducibility of a test • The absence of random variation in a test	• Random error ↓ precision in a test • ↑ precision →↓ standard deviation • ↑ precision →↑ statistical power (1-β)

Accuracy and Precision



High accuracy
High precision

Low accuracy
High precision

High accuracy
Low precision

Low accuracy
Low precision


QUIZ TIME

Q1. Which scenario describes a test that is Accurate but not Precise?

A. Readings: 9.8, 9.9, 9.7 (True value: 9.81)

B. Readings: 10.5, 10.6, 10.7 (True value: 10.0)

C. Readings: 9.0, 10.0, 11.0 (True value: 10.0)

D. Readings: 9.9, 10.1, 10.0 (True value: 10.0)

Q2. Which type of error primarily affects the accuracy of measurements?

A. Random error

B. Systematic error

C. Human error

D. Instrumental error

Q3. A simple routine test for the presence of HIV was carried out on 300 high risk subjects (intravenous drug users). A more accurate 'gold standard' test was also carried out on the subjects to assess the accuracy of the routine test. The following results were obtained:

		HIV by 'gold standard'		
		Yes	No	Total
Routine test	+ve	92	10	102
	-ve	2	196	198
	Total	94	206	300

Select all of the following statements which you believe to be true.

A. The sensitivity of the test is 90.2%
B. The specificity of the test is 97.9%
C. The estimated prevalence of HIV in the relevant population is 0.31
D. The positive predictive value of the test is 97.9%.
E. The negative predictive value of the test is 99.0%.

Q4. Properties of a diagnostic test

A. The sensitivity of a diagnostic test is the proportion of individuals without the disease who are correctly identified by the test.

B. The positive predictive value of a diagnostic test is the proportion of individuals with the disease who are correctly identified by the test.

C. The negative predictive value of a diagnostic test will not change if the prevalence of the condition increases.

D. For a condition which is easily treatable, we should like the diagnostic test to have a high sensitivity.

E. The likelihood ratio for a positive diagnostic test result is the ratio of the chance of a positive result if the patient has the disease to the chance of a positive result if he/she does not have the disease.

References

- Previous year's course materials by Philip McLoone
- Introduction to Medical Statistics - The Beatson West of Scotland Cancer Centre
- Medical Statistics at a Glance – Petrie & Sabin 3rd Ed 2009 (Wiley-Blackwell)
- Medical Statistics at a Glance – WORKBOOK (Quiz)