

Cel mai bun tip de studiu in functie de tipul intrebarii

Nivel	Tratament	Prognostic	Diagnostic	Etiologie
I	<i>Analiza sistematica a ...</i>			
II	RCT	Cohorta (Inception)	Transversal	Cohorta
III			RCT Cohorta Caz-martor	Caz-martor

EVALUAREA TESTELOR DIAGNOSTICE

Cristian Baicus

www.baicus.com

- **SnNout și SpPin**
- **Probabilitatea posttest depinde de probabilitatea pretest (Bayes)**
- **AUROC mare, Sn și Sp bune**
- **LR**



The NEW ENGLAND JOURNAL of MEDICINE

[HOME](#)[ARTICLES & MULTIMEDIA](#)[ISSUES](#)[SPECIALTIES & TOPICS](#)[FOR AUTHORS](#)[CME](#)

This article is available to subscribers.

[Sign in](#) now if you're a subscriber.

[Free Preview](#) [PRINT](#) [E-MAIL](#) [DOWNLOAD CITATION](#) [PERMISSIONS](#)[MEDICAL INTELLIGENCE](#)[ARCHIVE](#)

Interpretation by Physicians of Cl

Ward Casscells, B.S., Arno Schoenberger, M.D., and Thomas B.
N Engl J Med 1978; 299:999-1001 | November 2, 1978 | DOI: 10.10

JAMA Internal Medicine

Formerly *Archives of Internal Medicine*

[Home](#) [Current Issue](#) [All Issues](#) [Online First](#) [Collections](#) [CME](#) [Multimedia](#)

[June 2014](#) >

[< Previous Article](#)

Full content is available to subscribers

[Subscribe/Learn More](#)

[Next Article](#)

[Research Letter](#) | [June 2014](#)

Medicine's Uncomfortable Relationship With Math Calculating Positive Predictive Value

Arjun K. Manrai, AB^{1,2}; Gaurav Bhatia, MS^{1,3}; Judith Strymish, MD⁴; Isaac S. Kohane, MD, PhD^{1,2}; Sachin H. Jain, MD^{4,5,6}

[\[+\] Author Affiliations](#)

JAMA Intern Med. 2014;174(6):991-993. doi:10.1001/jamainternmed.2014.1059.

Text Size: A A

- 1978: 20 specialisti, 20 rezidenti, 20 studenti anul IV din spitale afiliate Univ Harvard
- 2013: 26 specialisti, 24 rezidenti, 10 studenti, 1 pensionar de la un spital din Boston
- “Daca un test folosit pentru detectarea unei boli a cărei prevalență este 1/1000 are o rată a fals pozitivilor de 5%, care este probabilitatea ca un pacient cu testul pozitiv sa aibă boala, presupunând că nu știm nimic despre semne sau simptome?”

- Din 51 de medici, doar 14 au dat răspunsul corect.

Surse de nesiguranță/variabilitate

- **Instrument de măsură:** imprecizia analitică (același test aplicat aceluiași pacient să dea același rezultat).
- **Variabilitatea subiectului:** intraindividuală (regresia către medie - fluctuații fiziologice)/interindividuală
- **Variabilitatea interpretării examenului:**
Intraindividuală/interindividuală (coeficient de concordanță κ)
- **Validitatea intrinsecă a testului (Sn, Sp, LR).**
- **Prevalența bolii** (probabilitatea pretest).

Variabilitatea interpretării examenului

		Clinician II		
		Retinopatie-	Retinopatie+	
Clinician I	Retinopatie-	46	10	56
	Retinopatie+	12	32	44
		58	42	100

Acord observat= $(46+32)/100 = 78\%$

Variabilitatea interpretarii examenului

- Acordul observat (simplu) = 78%
- Acordul asteptat datorat intamplarii = 51%
- Acordul efectiv excluzand intamplarea = $78\%-51\% = 27\%$
- Acordul potential excluzand intamplarea = $100\%-51\% = 49\%$
- Coef de concordanta (κ) = $27/49 = 0,55$

Kappa	Acord
>0,75	Excelent
0,40-0,75	Intermediar/bun
<0,40	slab

Studiile diagnostice - criterii de validitate

1. A existat o comparatie independenta, “oarba” cu un gold standard?
2. A fost testul diagnostic evaluat la pacienti cu un spectru potrivit de boli?
3. A fost gold standard-ul aplicat indiferent de rezultatul testului diagnostic?

Sackett, Richardson, Rosenberg, Haynes 1997

Studiile diagnostice - criterii de validitate

4. S-a demonstrat ca testul este reproductibil inter/intraobservator?
5. Au fost furnizate intrevalle de incredere pentru Sn, Sp si ceilalți parametri ai testului?

Studiile diagnostice - criterii de validitate

5. Este prezentat *raportul de probabilitate* (likelihood ratio) al testului, sau datele din care acesta sa poata fi calculat?

Jaeschke, Guyatt, Sackett and the Evidence Based Medicine Working Group, JAMA, 1994

		BOALA		TOTAL
		+	-	
TEST DG.	+	RP	FP	
	-	FN	RN	

Evaluarea testelor diagnostice (Sn&Sp)

- Sn
 - proportia celor cu test + printre bolnavi
 - PID
 - $1-Sn = \text{proportia FN}$
 - SnNout

Autoanticorpi la pacienții cu LES

	Prevalenta (Sn) %
ANA	98
<u>Anti-ADN dc</u>	70
<u>Anti-Sm</u>	30

Evaluarea testelor diagnostice (Sn&Sp)

- Sp
 - proportia celor cu test (-) printre sanatosi
 - NIH
 - $1-Sp =$ proportia FP
 - SpPin

Evaluarea testelor diagnostice (valori predictive)

- VPP = probabilitatea ca un pacient cu testul diagnostic pozitiv sa aiba boala
- VPN = probabilitatea ca un pacient cu testul diagnostic negativ sa nu aiba boala
- depind de prevalenta bolii (probabilitatea pre-test) - teorema lui Bayes

		BOALA		TOTAL
		+	-	
TEST DG.	+	a	b	a+b
	-	c	d	c+d
		a+c	b+d	a+b+c+d

$$\text{Sensibilitatea} = a/(a+c)$$

$$\text{Specificitatea} = d/(b+d)$$

$$\text{Probabilitatea pretest (prevalența)} = (a+c)/(a+b+c+d)$$

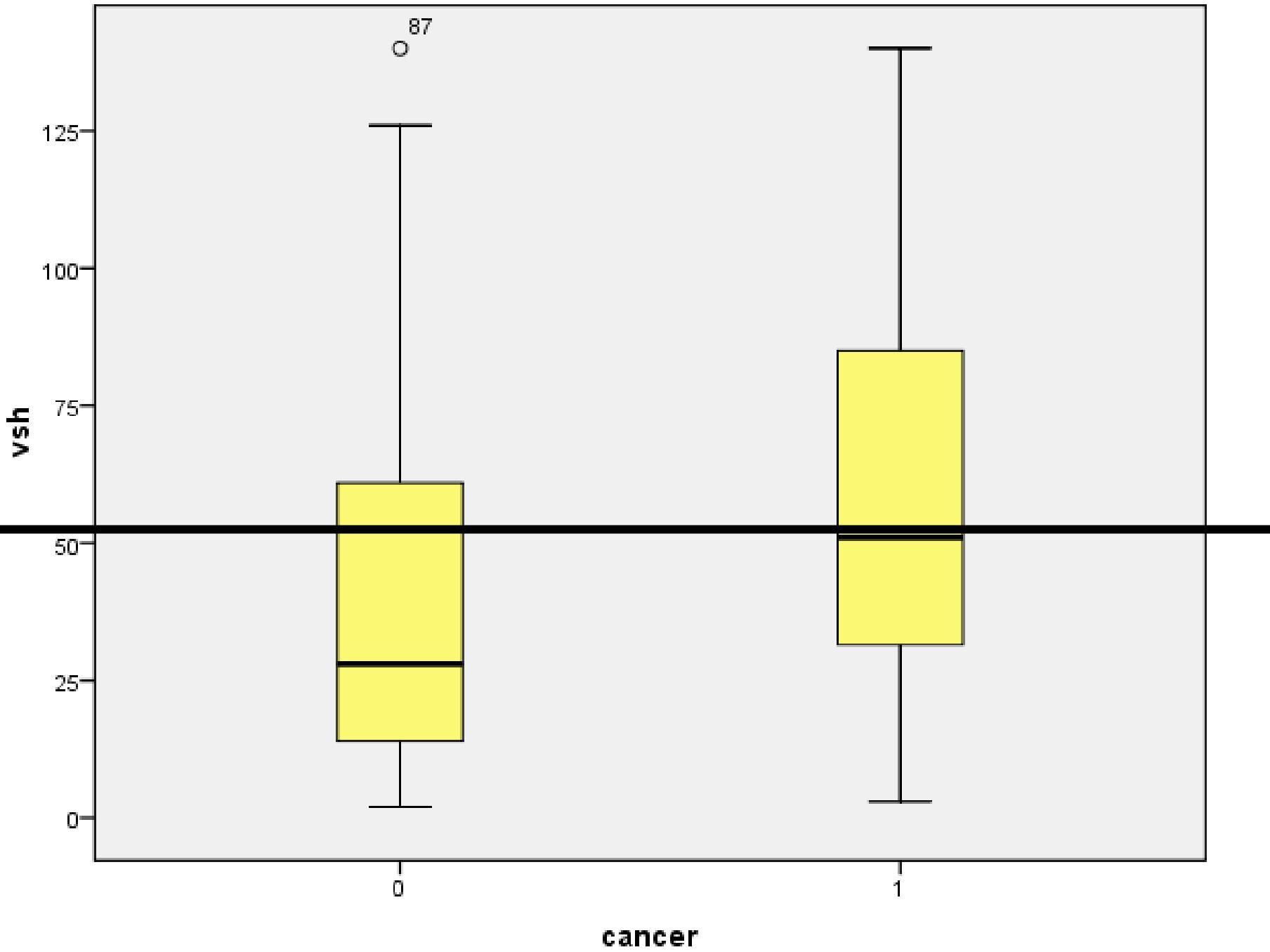
$$\text{Valoare predictivă pozitivă} = a/(a+b)$$

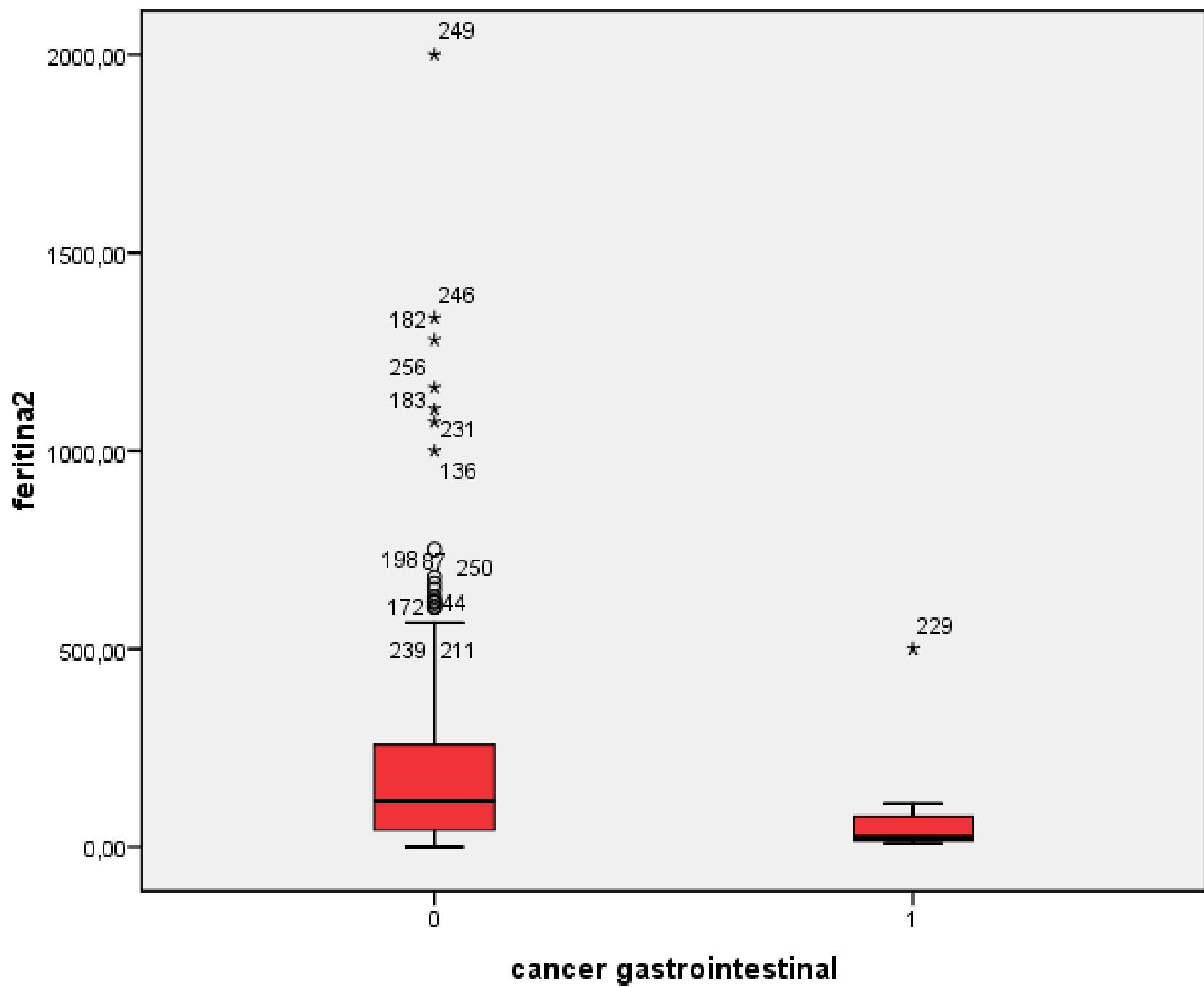
$$\text{Valoare predictivă negativă} = d/(c+d)$$

Teorema lui Bayes

Prev	99	95	90	80	70	60	50	40	30	20	10	5	1	0,5	0,1
VPP	99,9	99,7	99,4	99	98	97	95	93	89	83	68	50	16	9	2
<u>VPN</u>	16	50	68	83	89	93	95	97	98	99	99,4	99,7	99,9	99,9	99,9
p. boala post test neg	84	50	32	17	11	7	5	3	2	1	0,6	0,3	0,1	0,03	0,01

Probabilitatea posttest pentru un test diagnostic cu Sn si Sp = 95%





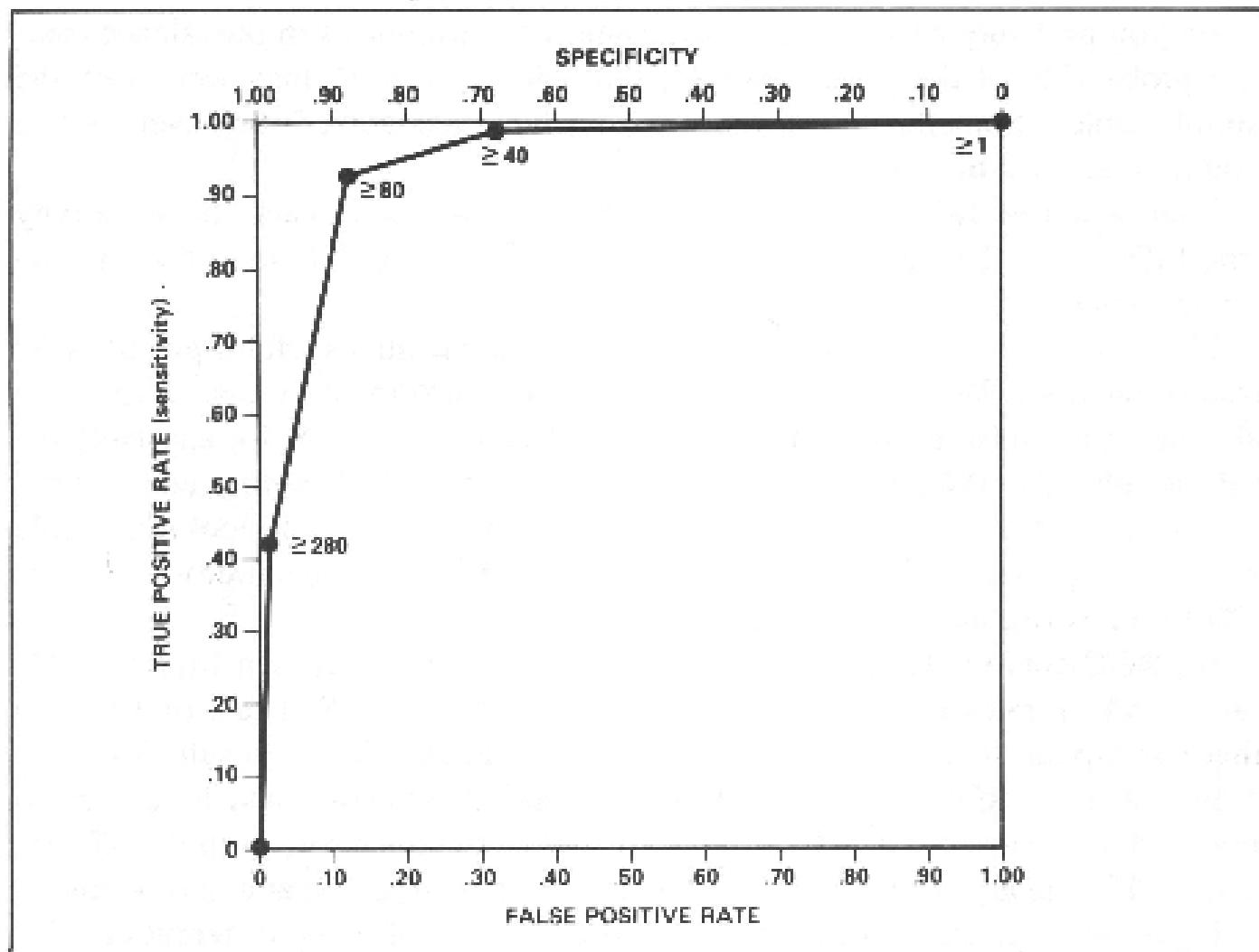
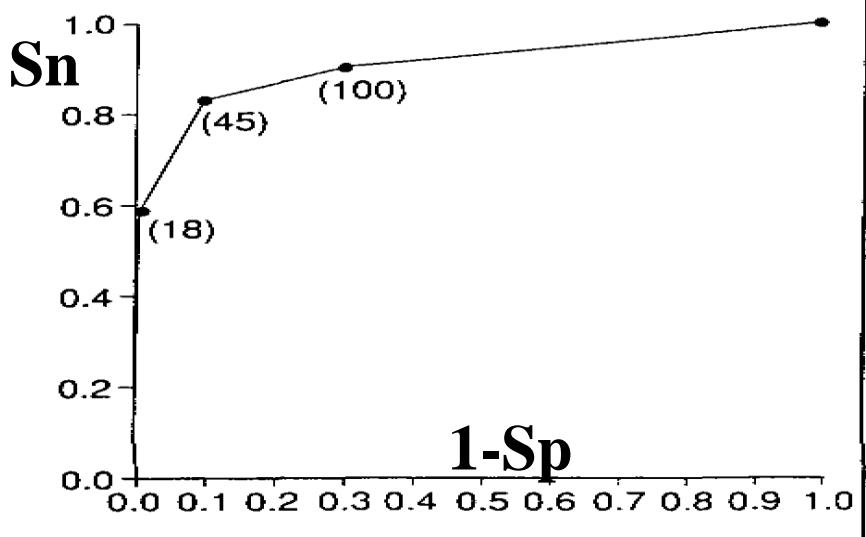
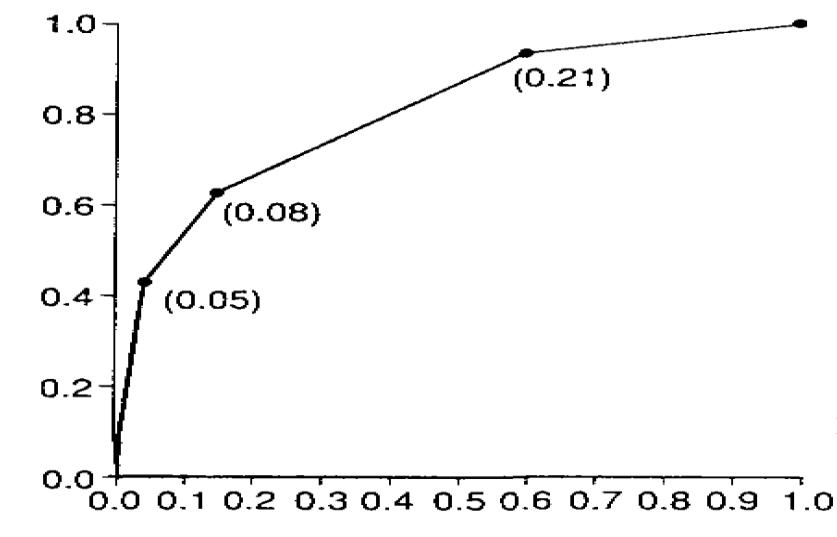


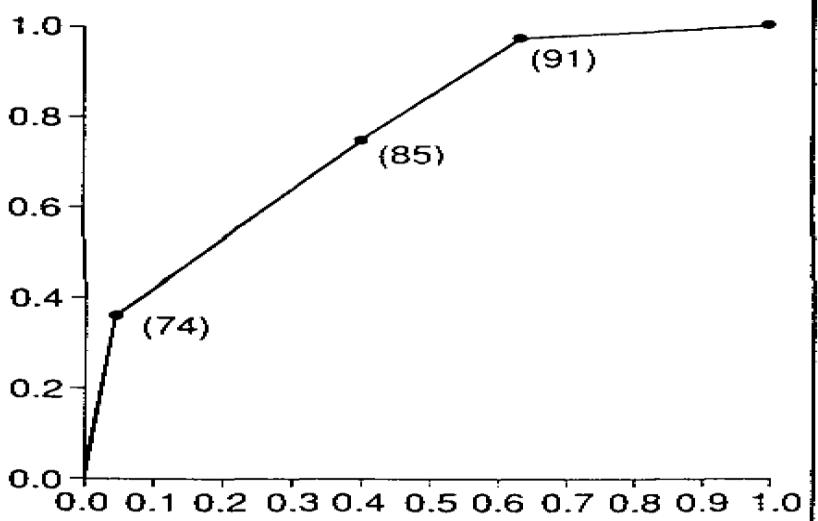
Figure 4-11. An ROC curve for CK values in myocardial infarction.



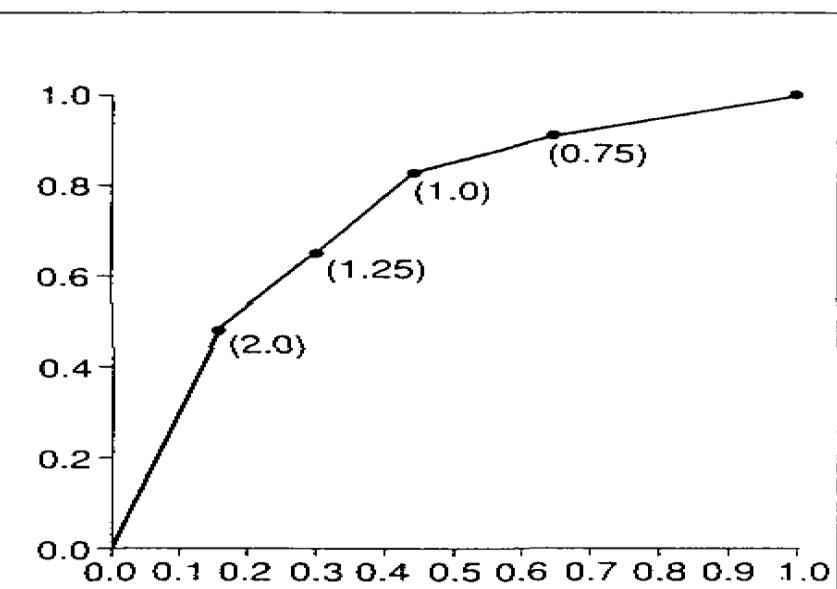
Curba ROC pt. feritina serica



saturatia transferinei

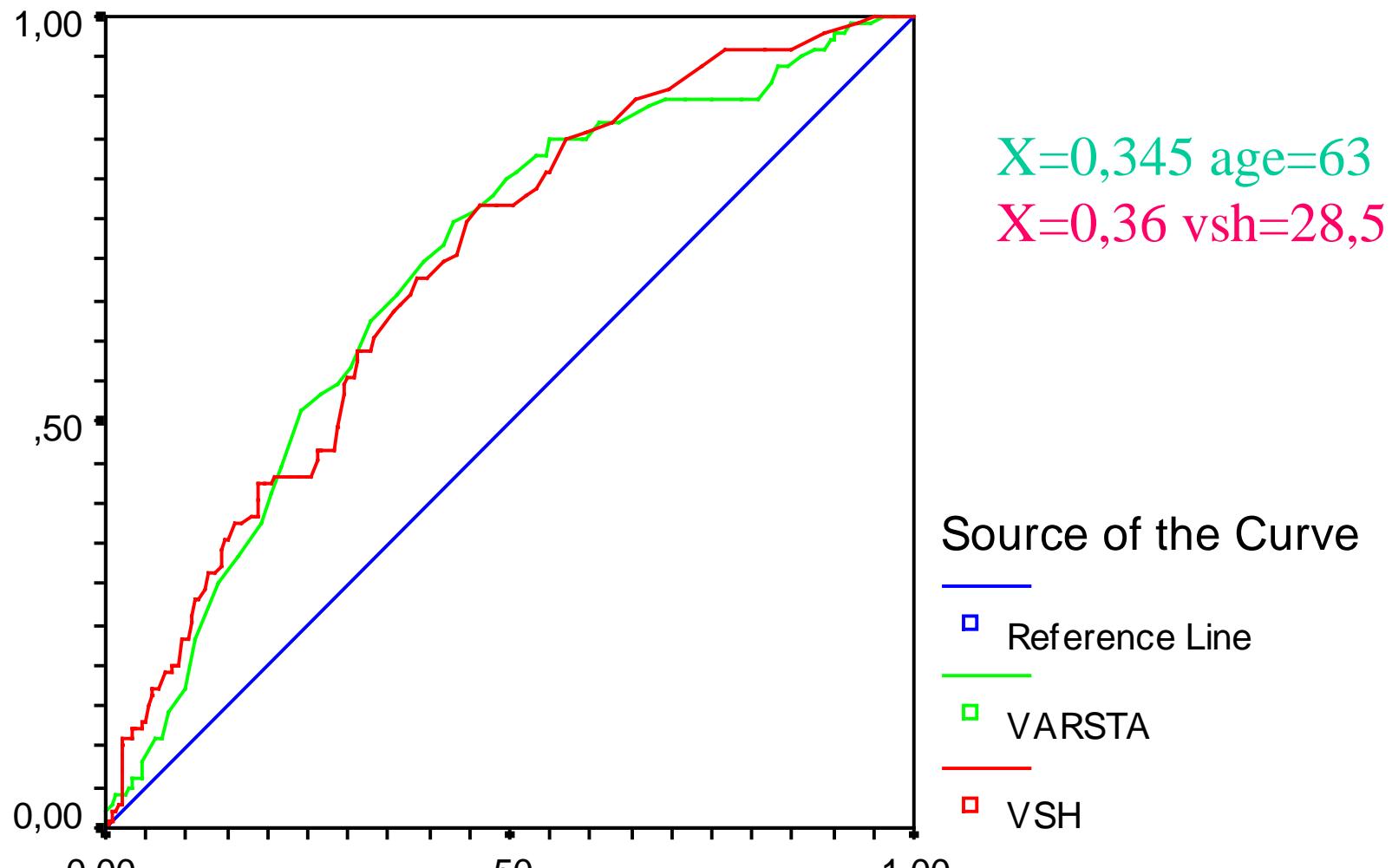


Curba ROC pt. VEM



Curba ROC pt. protoporfirina

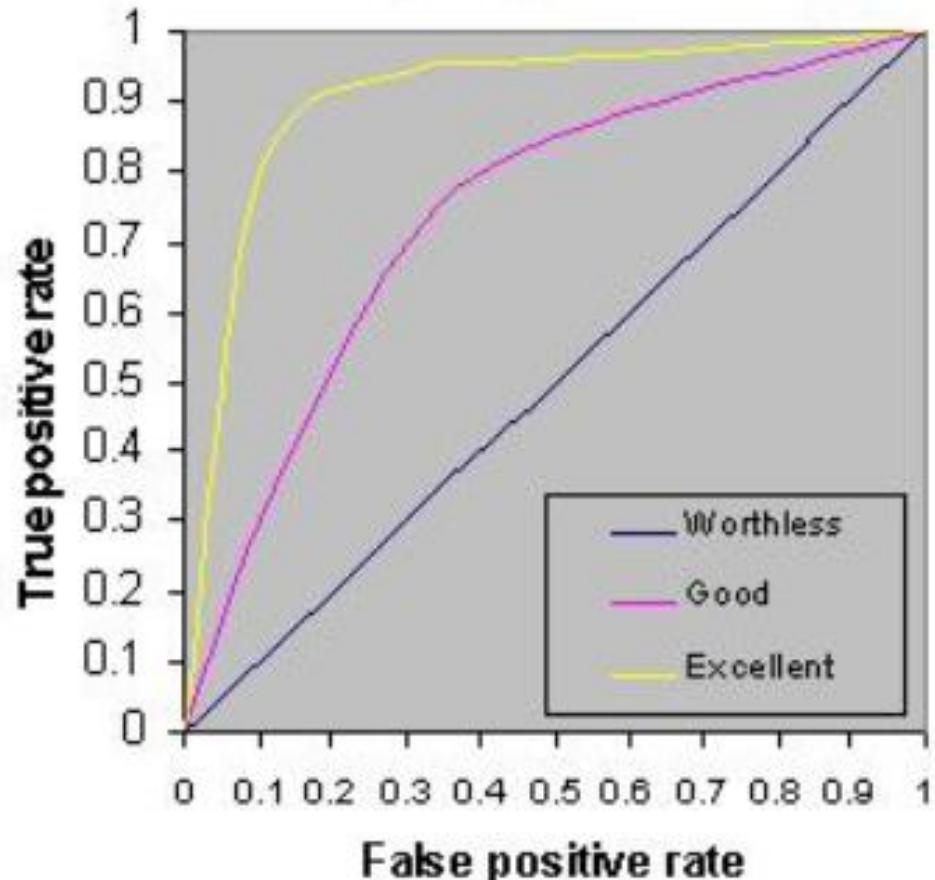
ROC Curve



1 - Specificity

Diagonal segments are produced by ties.

Comparing ROC Curves



0.9-1.0	Excelent
0.8-0.9	Bun
0.7-0.8	Corect
0.6-0.7	Slab
0.5-0.6	Inutil

Evaluarea testelor diagnostice (Likelihood ratio)

- LR+
 - probabilitatea test + bolnav
$$\frac{\text{probabilitatea test} + \text{bolnav}}{\text{probabilitatea test} + \text{sanatos}}$$
 - Sn/(1-Sp)
 - LR-
 - probabilitatea test - sanatos
$$\frac{\text{probabilitatea test} - \text{sanatos}}{\text{probabilitatea test} - \text{bolnav}}$$
 - Sp/(1-Sn)

LR - proprietati:

- Fiind, calculate, ca si Sn si Sp pe verticala, nu se modifica odata cu prevalenta (probabilitatea pretest) bolii tinta.
- Pot fi calculate pe mai multe nivele ale semnului, simptomului sau testului de laborator, si numai pe doua (+/-); acest lucru le face mai stabile decat Sn si Sp la modificarile prevalentei.
- Stiind probabilitatea pretest (prevalenta), se ajunge usor la probabilitatea posttest.
- Se poate calcula usor probabilitatea posttest dupa o secventa de teste diagnostice.

Likelihood Ratios

- Dimensionless numbers
- Definition:

The percentage of diseased patients with a given test result divided by the percentage of well people with the same test result.



Positive likelihood ratio

$$\frac{\text{TPR}}{\text{FPR}} \text{ or } \frac{\text{sensitivity}}{1 - \text{specificity}}$$



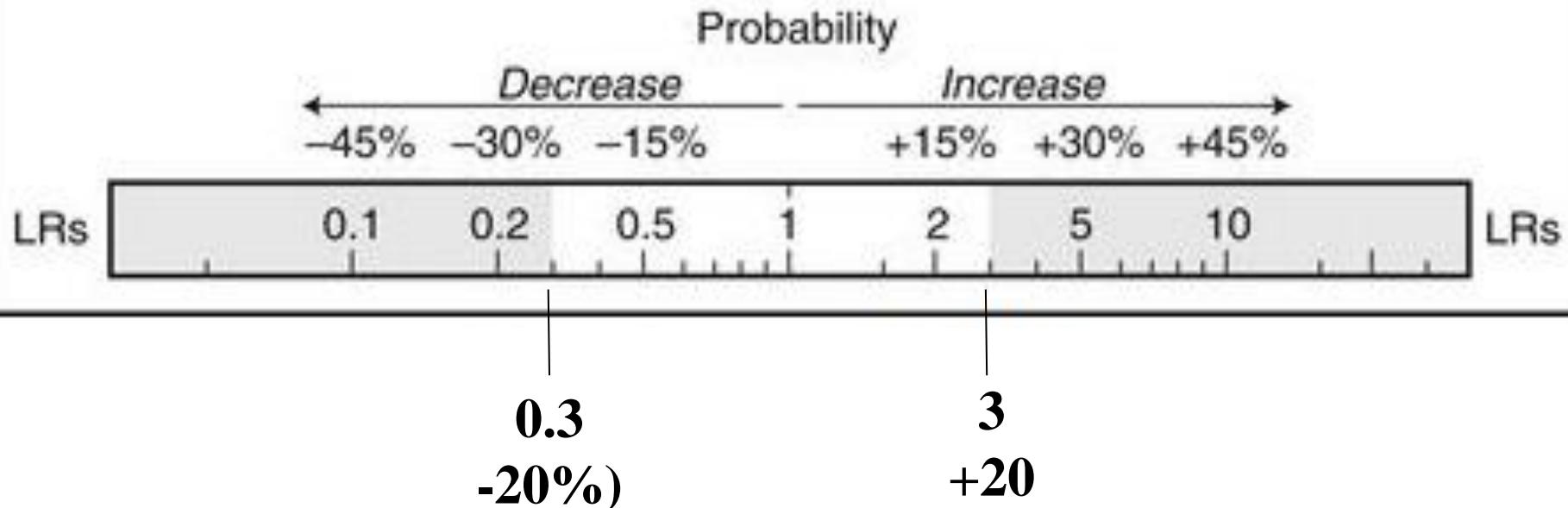
Negative likelihood ratio

$$\frac{\text{FNR}}{\text{TNR}} \text{ or } \frac{1 - \text{sensitivity}}{\text{specificity}}$$

Evaluarea testelor diagnostice (Likelihood ratio)

- **LR >10 sau < 0.1** genereaza modificari mari, deseori decisive de la probabilitatea pre- la post-test;
- **LR de 5-10 si 0.1-0.2** genereaza modificari moderate ale probabilitatii;
- **LR de 2-5 si 0.5-0.2** genereaza modificari mici (dar uneori importante) ale probabilitatii;
- **LR de 1-2 and 0.5-1** modifica probabilitatea intr-un grad f. mic (si rareori important).

LRs = Diagnostic Weights



$$2 = +15\%$$

$$5 = +30\%$$

$$10 = +45\%$$

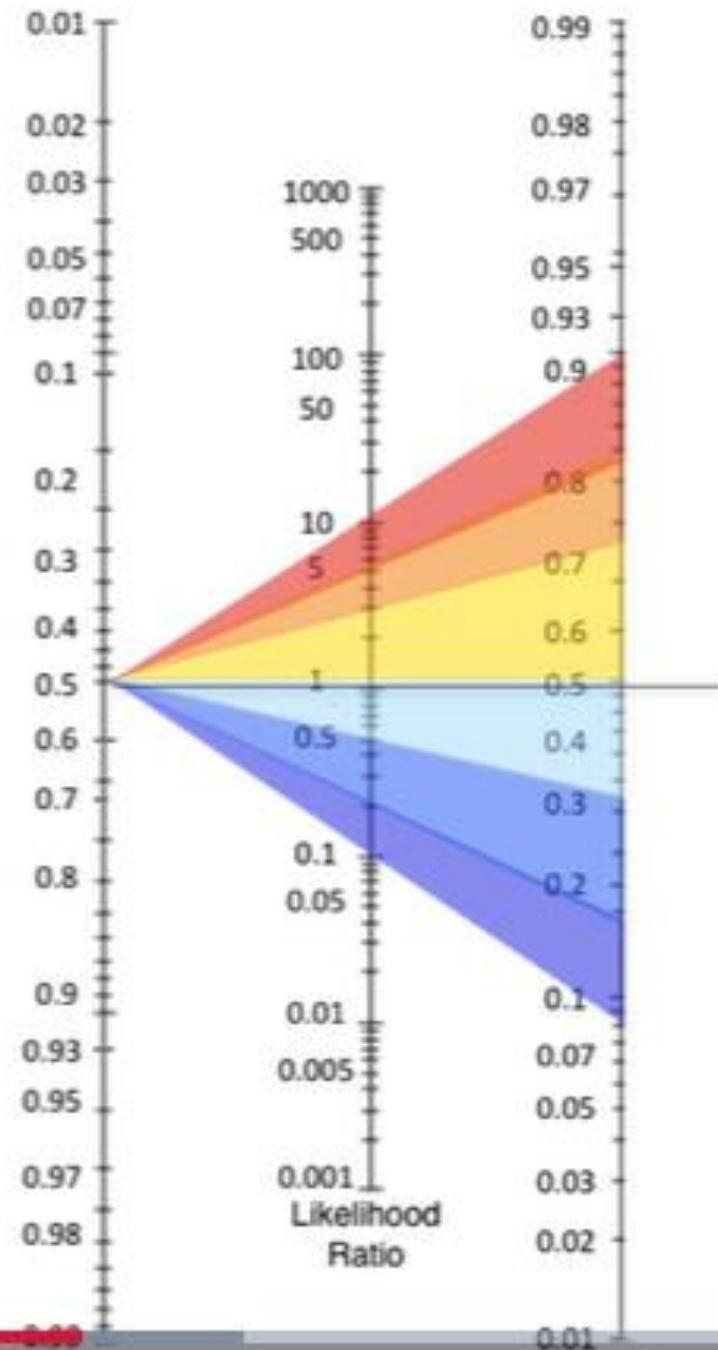
$$0.5 = -15\%$$

$$0.2 = -30\%$$

$$0.1 = -45\%$$

(valori assoluti)

Anchoring and adjusting heuristic

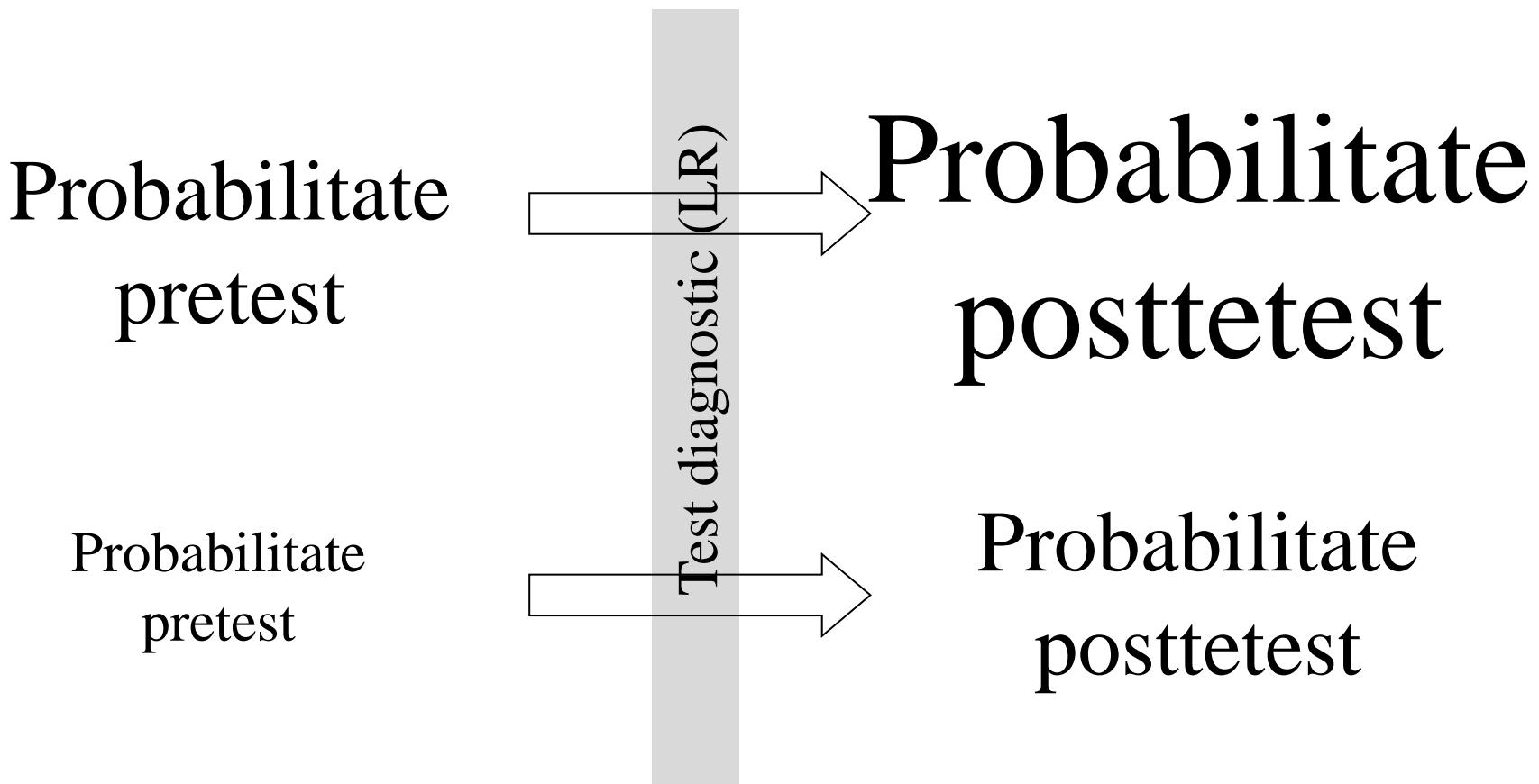


Ex: subdenivelare ST la ECG effort:

Subdenivelare (mm)	LR
> 2,5	39
2-2,49	11
1,5-1,99	4,2
1-1,49	1
0,05-0,99	0,92

Teorema lui Bayes

Probabilitatea **posttest** ~ Probabilitatea **pretest**
~ LR



p pretest = 24%

LR

1. Varsta = 53 ani 0,67

2. VSH = 70 2,23

3. Hb = 9 g % 2,83

Odds pretest = $p/(1-p) = 0,315$

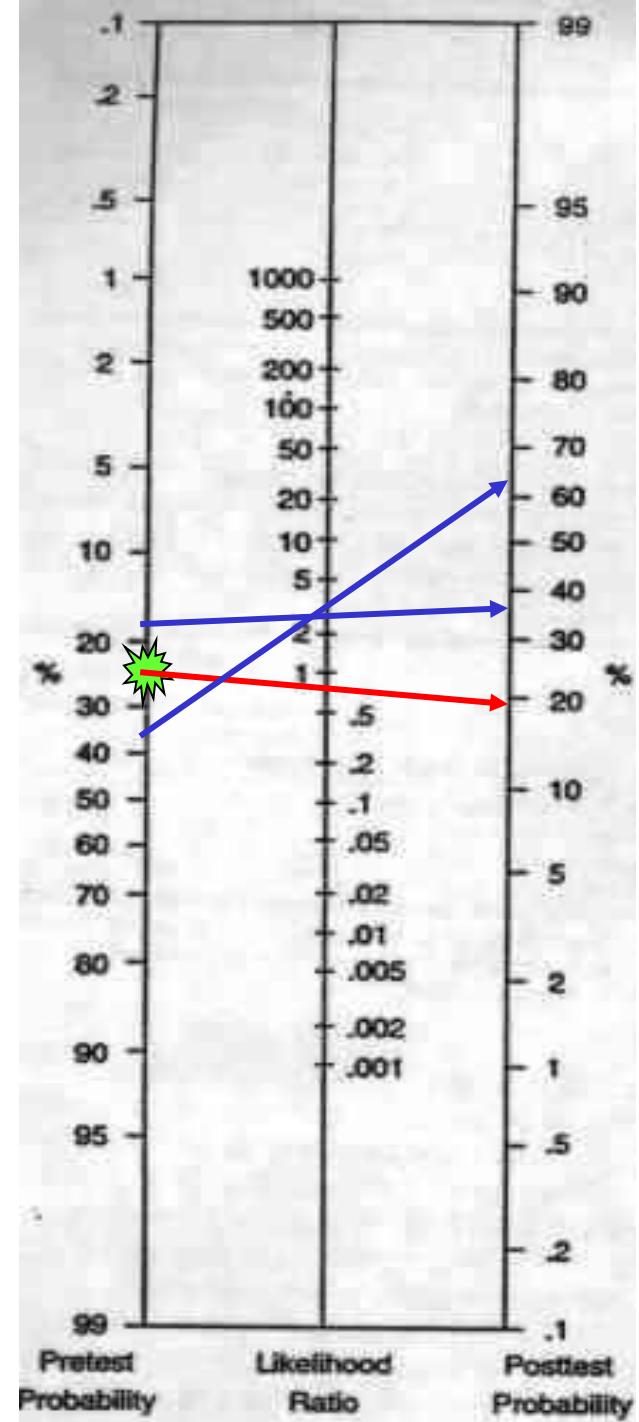
$$0,315 \times 0,67 = 0,21$$

$$0,21 \times 2,23 = 0,47$$

$$0,47 \times 2,83 = 1,33 = \text{odds posttest}$$

Probabilitatea = odds/(1+odds) =
 $1,33/2,33 = 0,57$

Probabilitatea posttest = 57%



Baterii de teste

- Aplicate in paralel - cresc S_n
 - + cand macar unul dintre ele este pozitiv
 - - cand toate sunt negative
- Aplicate in serie - cresc S_p
 - + cand toate sunt pozitive
 - - cand macar unul este negativ

Tabelul XVIII.3. Anemia, VSH și scăderea ponderală ca teste diagnostice în cancer (simplificat din¹) (sunt date intervalele de încredere 95%). Se vede cum aplicarea în paralel crește sensibilitatea, iar cea în serie specificitatea.

TEST	Sensibilitate	Specificitate
ANEMIE	37 (CI=36-39)	92 (CI=91-93)
VSH	52 (CI=51-54)	89 (CI=88-90)
SLĂBIT	46 (CI=45-48)	94 (CI=93-94)
Testele în paralel	87 (CI=86-88)	79 (CI=78-81)
Testele în serie	9 (CI=9-10)	99,6 (CI=99-100)

1. Baicus C, Tanasescu C, Ionescu R. Has this patient a cancer? The assessment of weight loss, anemia and erythrocyte sedimentation rate as diagnostic tests in cancer. A retrospective study based in a secondary care university hospital in Romania. *Rom J Intern Med.* 1999; 37:261-7.

Test	Sn (%)	Sp (%)
Anti-CCP	56	90
IgM RF	73	82
IgM RF & anti-CCP	48	96

- Curba ROC și rapoarte de probabilitate (*Revista Romana de Medicina Internă*)
[\(http://www.srmi.ro/doc/R6-2007.pdf\)](http://www.srmi.ro/doc/R6-2007.pdf)
- Criteriile CONSORT de raportare a studiilor clinice randomizate
- Criteriile STARD de raportare a studiilor diagnostice:
 1. Patrick M. Bossuyt, Johannes B. Reitsma, David E. Bruns, Constantine A. Gatsonis, Paul P. G. David Moher, Drummond Rennie, and Henrica C.W. de Vet, for the STARD Group*. Towards Consistency in Reporting of Diagnostic Accuracy: The STARD Initiative.
 2. Patrick M. Bossuyt, Johannes B. Reitsma, David E. Bruns, Constantine A. Gatsonis, Paul P. G. David Moher, Drummond Rennie, Henrica C.W. de Vet, and Jeroen G. Lijmer. The STARD Statement for Reporting Diagnostic Accuracy Studies: Explanation and Elaboration
- Criteriile STROBE de raportare a studiilor observaționale
 1. Erik von Elm, MD; Douglas G. Altman, DSc; Matthias Egger, MD; Stuart J. Pocock, PhD; Peter Gøtzsche, MD; and R. Brian Egger, PhD, for the STROBE Initiative. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement: Guidelines for Reporting Observational Studies.
 2. Jan P. Vandenbroucke, MD; Erik von Elm, MD; Douglas G. Altman, DSc; Peter C. Gøtzsche, MD; Richard P. Hulley, PhD; James J. Schlesselman, PhD; and Matthias Egger, MD, for the STROBE initiative. Strengthening the Reporting of Observational Studies in Epidemiology (STROBE): Explanation and Elaboration

Surse secundare de informație medicală:

Gratuite:

- Evidence-based Medicine (Sinopsisuri)



equator network

[En Español](#)[Login](#)

Search:

Enhancing the QUAlity and Transparency Of health Research

[Home](#)[About](#)[Resource](#)[Courses](#)[Research](#)[Contact](#)[News](#)[Forum](#)

www.equator-network.org



Too often, good research evidence is undermined by poor quality reporting.

The EQUATOR Network is an international initiative that seeks to improve reliability and value of medical research literature by promoting transparent and accurate reporting of research studies.

[RESEARCH REPORTING](#)**Authors**[Information for authors of research reports](#)**Editors**[Resources for journal editors and peer reviewers](#)**Latest news** [more news](#)

International register for systematic reviews

PROSPERO, the first online international register for registering systematic reviews has been launched in the UK

Highlights

EQUATOR Spanish website

New site launched on 16 July 2010 in collaboration with the Pan American Health Organization (PAHO). Find out [more](#) and visit the [site](#)

Promote good reporting

Print and display EQUATOR leaflets

EQUATOR Newsletter

Developers[Resources for developers](#)

Single step inference

Randomised trial

Target population

New test or strategy:
Triage
Replacement
Add-on

Old test or strategy

Test positive	Test negative
True and false positives	True and false negatives

Test positive	Test negative
True and false positives	True and false negatives

Management

Outcomes important to patients

Management

Outcomes important to patients

Accuracy study

Target population

New test or strategy:
Triage
Replacement
Add-on

Reference test

New test positive
True and false positives

New test negative
True and false negatives

Judgments about outcomes with new test

Judgments about outcomes with reference test

Two step inference

Example

Randomised control trials (RCTs) explored a diagnostic strategy guided by the use of B type natriuretic peptide (BNP)—designed to aid diagnosis of heart failure—compared with no use of BNP in patients presenting to the emergency department with acute dyspnoea.^{8,9} As it turned out, the group randomised to receive BNP spent a shorter time in the hospital at lower cost, with no increased mortality or morbidity.

Example

Consistent evidence from well designed studies shows fewer false negative results with non-contrast helical computed tomography (CT) than with intravenous pyelography (IVP) in the diagnosis of suspected acute urolithiasis.¹⁰ However, the stones in the ureter that CT detects but IVP “misses” are smaller, and hence are likely to pass more easily. As RCTs evaluating the outcomes in patients treated for smaller stones are not available, the extent to which reduction in cases that are missed (false negatives) and follow-up of incidental findings unrelated to renal calculi with CT have important health benefits remains uncertain¹¹

- “Daca un test folosit pentru detectarea unei boli a cărei prevalență este $1/1000$ are o rată a fals pozitivilor de 5%, care este probabilitatea ca un pacient cu testul pozitiv sa aibă boala, presupunând că nu știm nimic despre semne sau simptome?”
- Prevalența=probabilitatea pretest= $1/1000$
- Rata fals pozitivi=5% \rightarrow Sp=95%

2%

		BOALA		TOTAL
		+	-	
TEST DG.	+	a	b(50)	a+b
	-	c	d(949)	c+d
	1	999	1000	

$$\text{Sensibilitatea} = a/(a+c)$$

$$\text{Specificitatea} = d/(b+d) = d/999 = 0.95 \rightarrow d = 949$$

$$\text{Probabilitatea pretest (prevalența)} = (a+c)/(a+b+c+d)$$

$$\text{Valoare predictivă pozitivă} = a/(a+b)$$

$$\text{Valoare predictivă negativă} = d/(c+d)$$

work | Search Re... Centre for Evidence-Based

ktclearinghouse.ca/cebm/toolbox/statscalc

Clicknet Email - Tele... UpToDate Inc. Essential Evidence Pl... DynaMed | Evidence... PubMed home Cochrane Reviews Archie - The Cochrane...

LR Tables
NNT Tables
Stats Calculator
OR to NNT Converter
Palm OS CQLogbook
Contact

cannot be guaranteed.

This calculator is also available in a [Palm OS version](#) and a [Pocket PC version](#).

CEBM Statistics Calculator

Diagnostic Test ▾

Disease	No Disease
Test Pos.	1.5 A
Test Neg.	0.5 C 949.5 D
LR+	LR-

Option 1: Enter values into the first table on the right.

Option 2: Enter the LR values only.

Results

	Estimate	95% CI
Sensitivity	0.75	[0.198 to 0.973]
Specificity	0.95	[0.934 to 0.961]
PPV	0.029	[0.007 to 0.116]
NPV	0.999	[0.995 to 1]
LR+	14.851	[6.385 to 34.542]
LR-	0.263	[0.024 to 2.904]

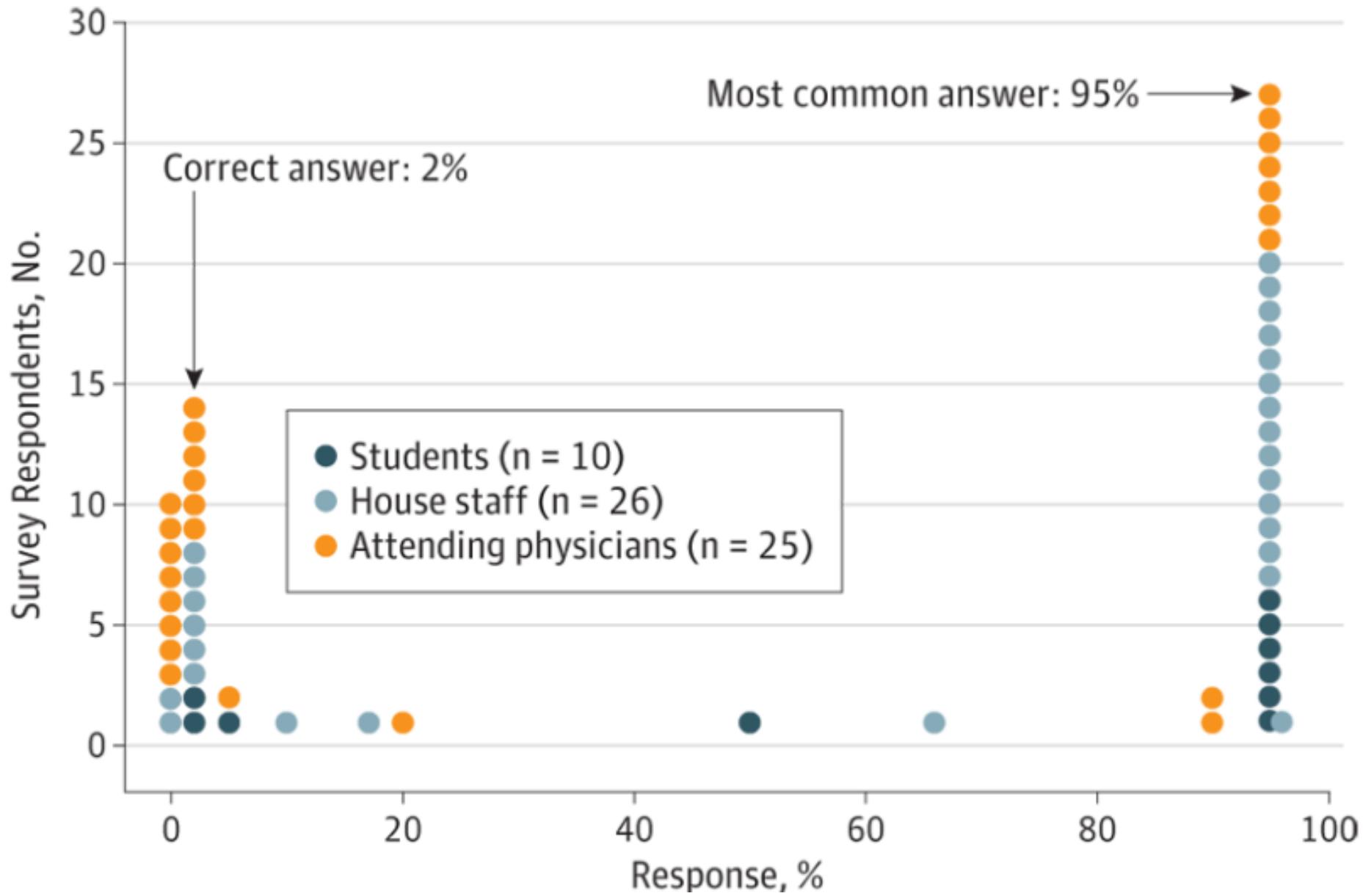
The graph plots PostTest Probability on the y-axis (0.0 to 1.0) against PreTest Probability on the x-axis (0.0 to 1.0). Two sigmoidal curves are shown: a blue curve for 'positive (+)' and a red curve for 'negative (-)'. Both curves pass through the point (0.5, 0.5).

PostTest Probability

positive (+) — negative (-) —

?

- “Dacă un test folosit pentru detectarea unei boli a cărei prevalență este 1/1000 are o rată a fals pozitivilor de 5%, care este probabilitatea ca un pacient cu testul pozitiv să aibă boala, presupunând că nu știm nimic despre semne sau simptome?”
- Prevalență=probabilitatea pretest=1/1000
- $LR = 15$
- Cota pretest= $p/(1-p) = 0,001/0,999 = 0,001$
- Cota posttest=cota pretest x LR = $0,001 \times 15 = 0,015$
- Prob posttest =
 $cota/(1+cota) = 0,015/(1+0,015) = 0,015 = 1,5\%$



- **SnNout și SpPin**
- **Probabilitatea posttest depinde de probabilitatea pretest (Bayes)**
- **AUROC mare, Sn și Sp bune**
- **LR**