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Diagnostic study

A ALWAYS

S SEEK

K KNOWLEDGE

Objectives

- Phases
- Medical indicators of diagnostic efficacy
  - Se, Sp, PPV, NPV, LR+, LR-, Accuracy
- Interpretations
  - Statistical
  - Clinical
    - Fagan’s nomogram
- ROC curves. Comparison of ROC curve

Research domain

- Description of a new health phenomenon
- Evaluation of a diagnostic procedure
- Evaluation of a therapeutic procedure
- Evaluation of a risk/ protective or prognostic factors

Scenario – test (sign) diagnostic

- Alzheimer's disease - diagnosis is made at autopsy

A new diagnostic procedure – new diagnostic test

! The result is confirmed by
comparison with the autopsy result

New diagnostic test

- Evaluation
  - compare with “Gold standard” diagnostic method of a disease
- Evaluation
  - advantages
  - inconveniences

- analytical study
- observational study

Phase I

- Establish normal values
- Validity
- Reliability

Phase II

- Establish the intrinsic quality of the test
- Case-control study

Phase III

- Establish the extrinsic quality of the test
- Cohort study

Phase IV

- Evaluation of long term cost-benefit
- Cohort studies

Phase I

- Discover the new substance / test / method etc.
- Establish
  - Normal values
    - study made only on healthy patients
  - Validity
    - the measuring instrument actually measures what it was built to measure
  - Reliability
    - intra-observer (or within observer) repeatability
      - the degree to which measurements taken by the same observer are consistent
    - inter-observer (or between observers) repeatability
      - the degree to which measurements taken by different observers are similar.

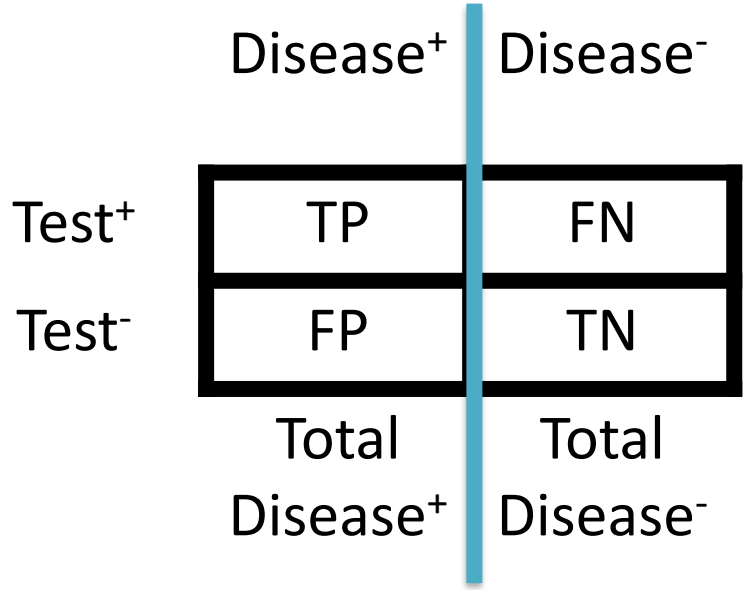
Phase II

- Establish the intrinsic quality of the test
  - Case-control study

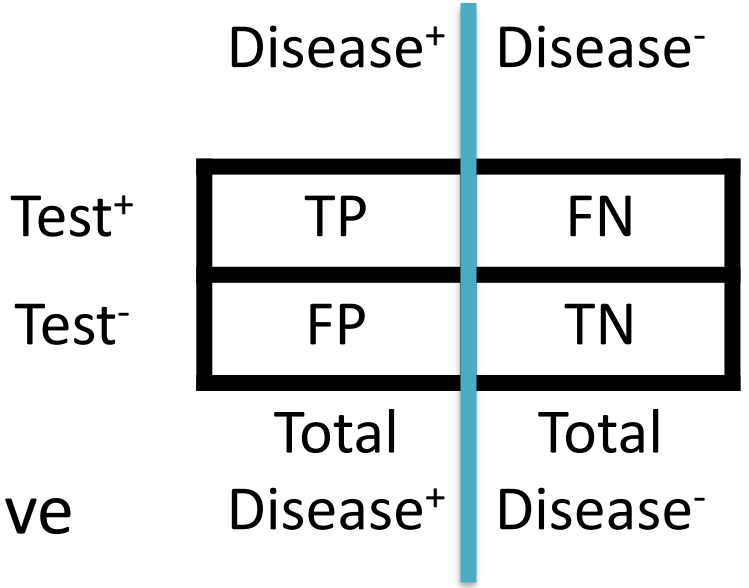
- A study on two groups
  - one with disease
    - Gold standard test positive
  - one without disease
    - Gold standard test positive

	Disease$^+$	Disease$^-$
Test$^+$	TP	FN
Test$^-$	FP	TN
	Total Disease$^+$	Total Disease$^-$

TP – True Positive, FN – Fals negative, FP – False positive, TN – True Negative



- TP – True Positive
  - Gold standard test Positive and New test Positive
- FN – Fals negative
  - Gold standard test Negative and New test Positive
- FP – False positive
  - Gold standard test Positive and New test Negative
- TN – True Negative
  - Gold standard test Negative and New test Negative



- Se – Sensitivity $Se = \frac{TP}{TP + FN}$
  - Probability of a diseased subject to test positive
  - Proportion of subjects who tested positive among the diseased

- Sp – Specificity $Sp = \frac{TN}{TN + FP}$
  - Probability of a non-diseased subject to test negative
  - Proportion of subjects who tested negative among the non-diseased

- High sensitivity → screening test
  - if Se $\approx 100\%$ and subject have negative test
    - near certainly the subject does not have the disease

- High specificity → precision test
  - if Sp $\approx 100\%$ and subject have positive test
    - near certainly the subject has the disease

- Sensitivity and Specificity
  - are used to evaluate the new test
    - how well the test distinguishes between presence or absence of a disease
    - the overall accuracy
  - did not change with the prevalence of the disease
    - ex. prevalence can change from winter to spring in case of the flu
    - ex. prevalence can change from a category of the population to another
      - can be different base on
        - » the age category
        - » gender

- Youden index

$$J = Se + Sp - 1$$

A test with Younden index higher is superior compare to a test with smaller Youden index

(how well the test distinguishes between presence or absence of a disease)

Accuracy

$$Acc = \frac{TP + TN}{TP + FN + FP + TN}$$

	Disease$^+$	Disease$^-$
Test$^+$	TP	FN
Test$^-$	FP	TN
	Total Disease$^+$	Total Disease$^-$

Likelihood ratio

Positive likelihood ratio LR^+ - how many times a positive test result is more likely to appear in a diseased subject than in a non-diseased one

$$LR^+ = \frac{Probability\ of\ a\ positive\ test\ at\ the\ diseased}{Probability\ of\ a\ positive\ test\ to\ a\ non-diseased} = \frac{\boldsymbol{Sensitivity}}{\boldsymbol{1-Specificity}} =$$

$$= \frac{TP/(TP+FN)}{FP/(FP+TN)}$$

Negative likelihood ratio LR^- - how many times a negative test result is more likely to appear in a diseased subject than in a non-diseased one

$$LR^- = \frac{Probability\ of\ a\ negative\ test\ at\ the\ diseased}{Probability\ of\ a\ negative\ test\ to\ a\ non-diseased} = \frac{\boldsymbol{1-Sensitivity}}{\boldsymbol{Specificity}} =$$

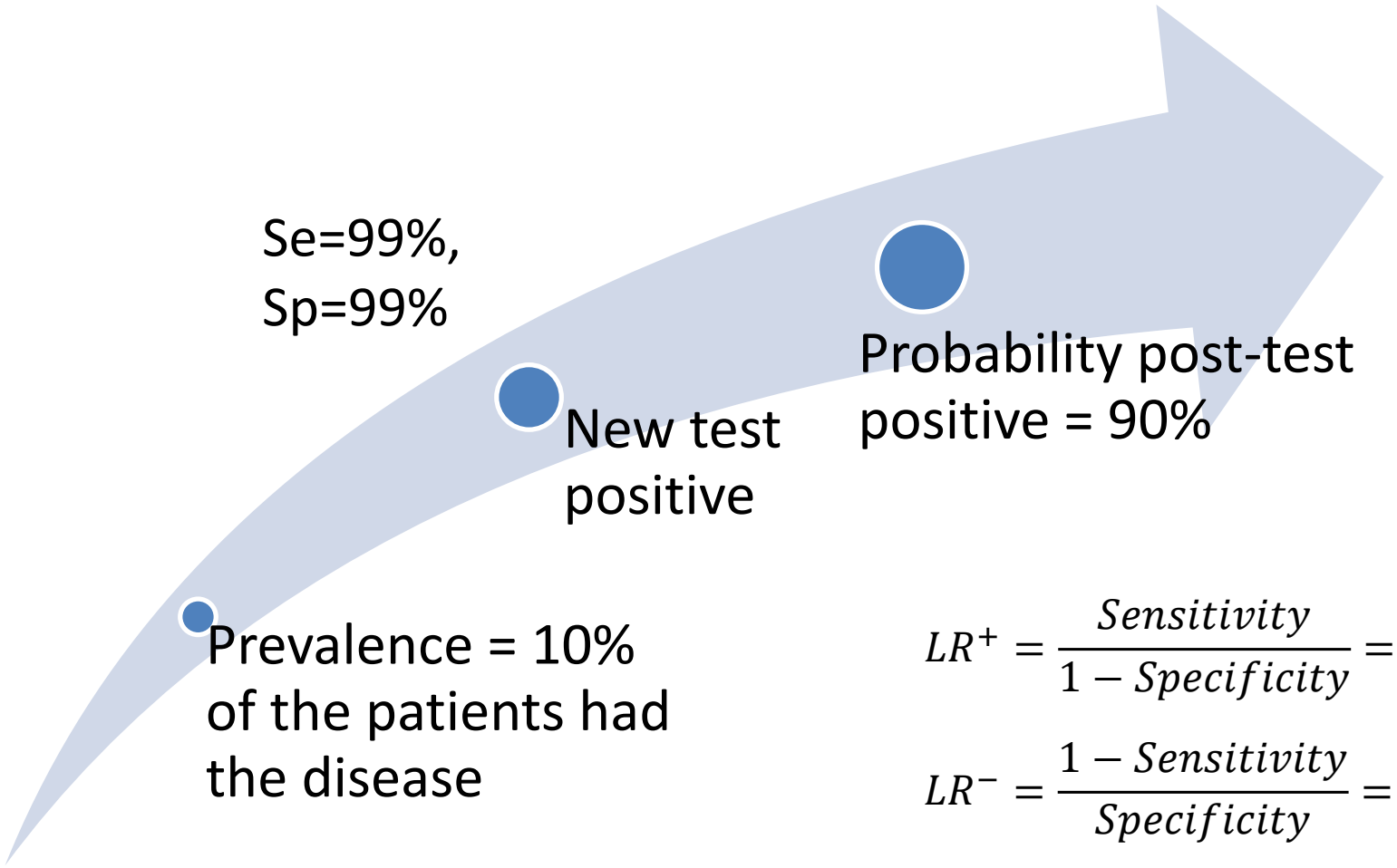
$$= \frac{FN/(TP+FN)}{TN/(FP+TN)}$$

Post-test probability

- $Pre - test\ odds = \frac{Prevalence}{1 - Prevalence}$
- $Post - test\ odds^{+} = LR^{+} * Pre - test\ odds$
- $Post - test\ odds^{-} = LR^{-} * Pre - test\ odds$

- $Post - test\ probability^{+} = \frac{Post\ test\ Odds^{+}}{1 + Post\ test\ Odds^{+}}$
- $Post - test\ probability^{-} = \frac{Post\ test\ Odds^{-}}{1 + Post\ test\ Odds^{-}}$

Probability post-test after positive test



$$LR^{+} = \frac{Sensitivity}{1 - Specificity} = \frac{0.99}{1 - 0.99} = 99$$

$$LR^{-} = \frac{1 - Sensitivity}{Specificity} = \frac{0.01}{0.99} = 0.01$$

Probability post-test after negative test

Prevalence = 10% of the patients had the disease

Se=99%, Sp=99%

New test negative

Post test probability =0.001

$$LR^{+} = \frac{Sensitivity}{1 - Specificity} = \frac{0.99}{1 - 0.99} = 99$$

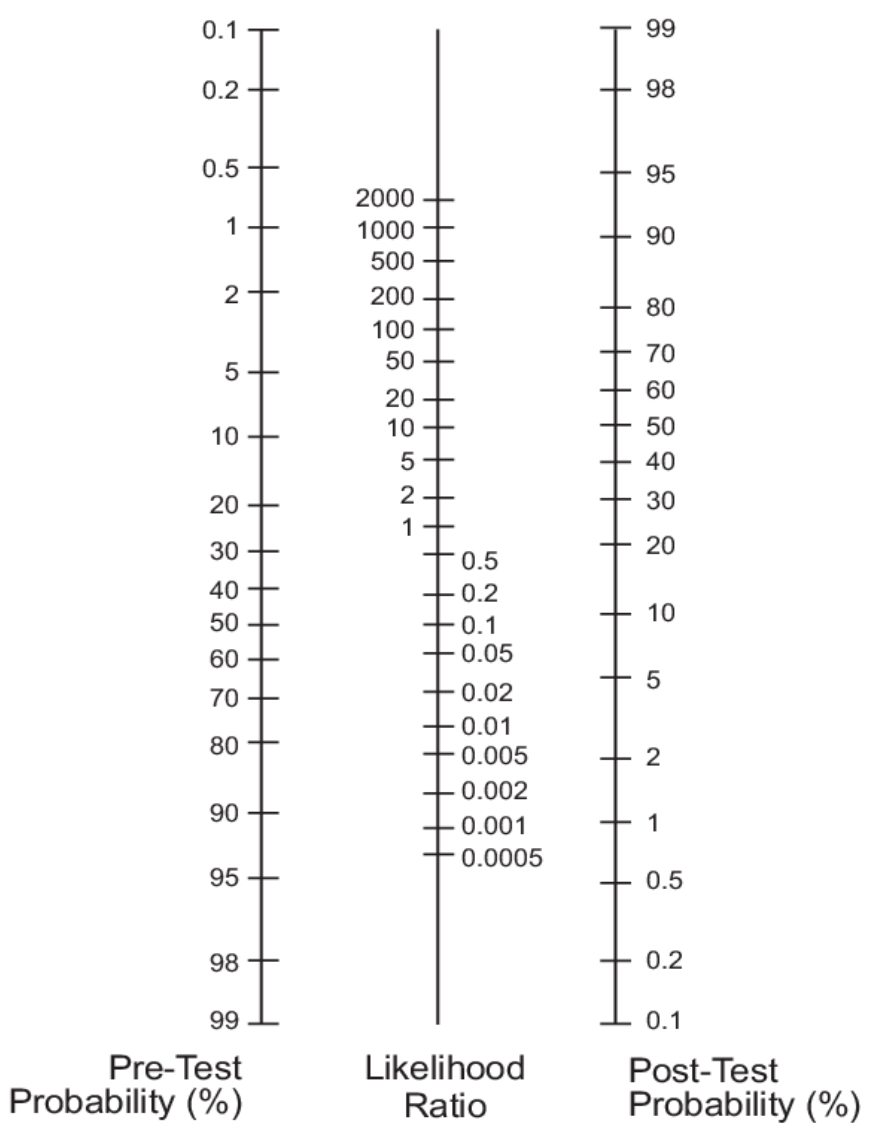
$$LR^{-} = \frac{1 - Sensitivity}{Specificity} = \frac{0.01}{0.99} = 0.01$$

- A total of 67 saliva samples were assessed which were obtained from 36 individuals in the healthy group, 31 individuals in the gingivitis group. From the saliva samples matrix metalloproteinases 8 (MMP-8) was determine. If MMP-8 was high (above normal value) the patient was considered positive else was considered negative. The data collection of this study is

Post-test probability

- Positive
  - **The probability of the disease after a positive test**
- Negative
  - **The probability of the disease after a negative test**
- Depend on
  - the prevalence of the disease
  - on the accuracy of the test

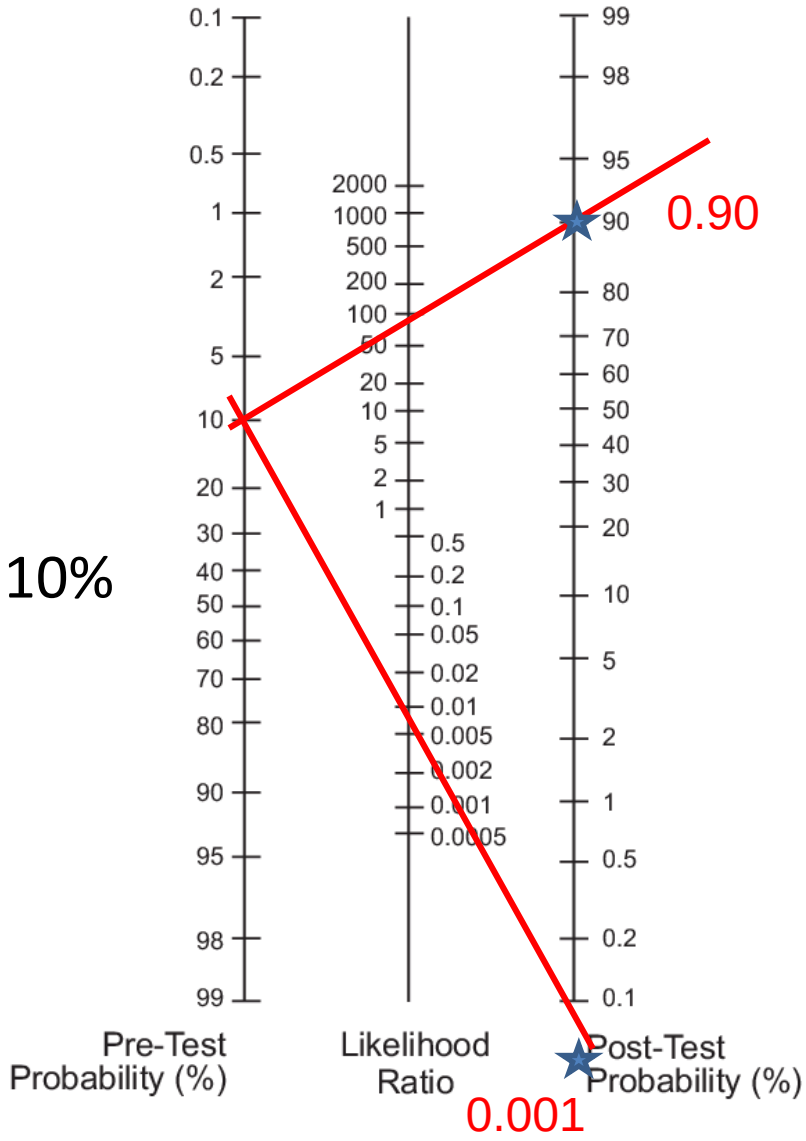
Fagan's nomogram



Prevalence 10%

LR^{+}=99

LR^{-}=0.01



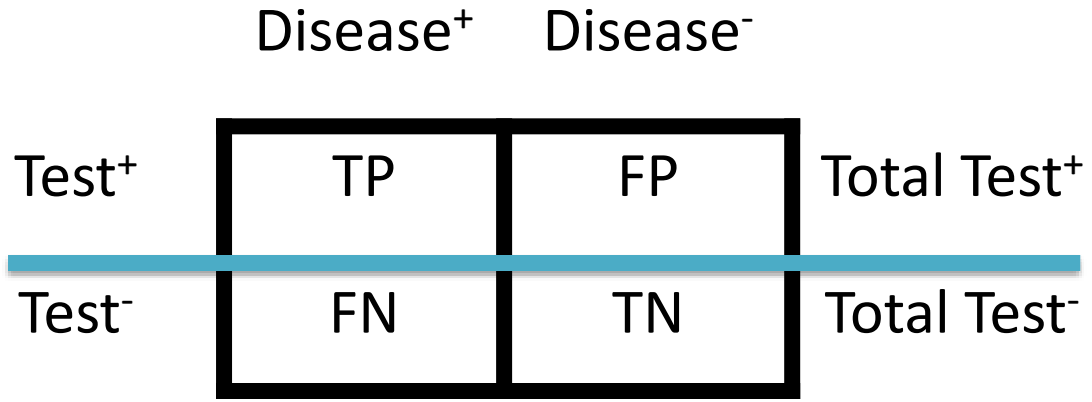
Probability post test positive

Probability post test negative

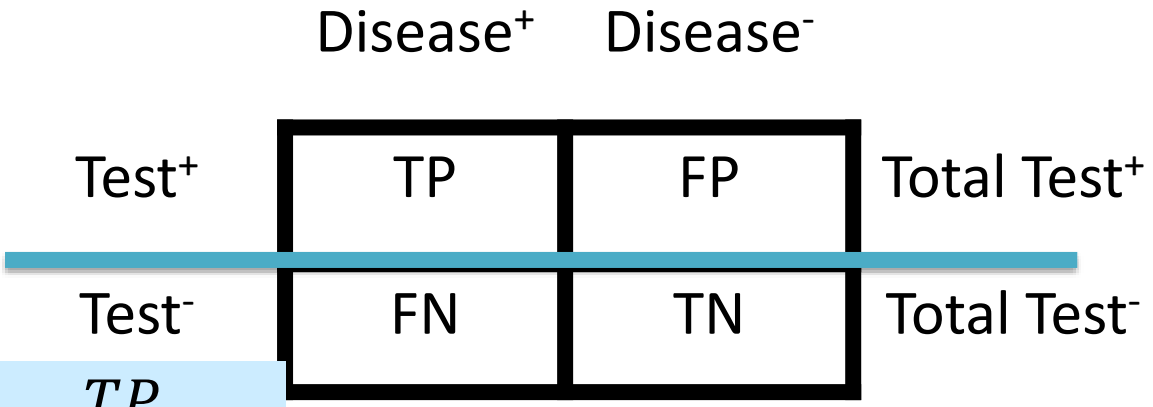
Phase III

- Establish the extrinsic quality of the test
  - cohort study

- A study on two groups
  - one with new test positive
  - one with new test negative



Phase III



- PPV – Positive predictive value $PPV = \frac{TP}{TP + FP}$
  - Probability that a person who receives a positive test result actually has the disease
  - Proportion of subjects who have the disease among the subjects who tested positive
- NPV – Negative predictive value $NPV = \frac{TN}{TN + FN}$
  - Probability that a person who receives a negative test result actually not having the disease
  - Proportion of subjects without the disease among the subjects who tested negative

- PPV and NPV
  - depend on
    - Se, Sp and prevalence
  - if population is different - if the patient from the office of medical doctor is from a group with a different prevalence than the group prevalence from the published study
    - published PPV and NPV cannot be apply in the case of the patient

Application of PPV and NPV

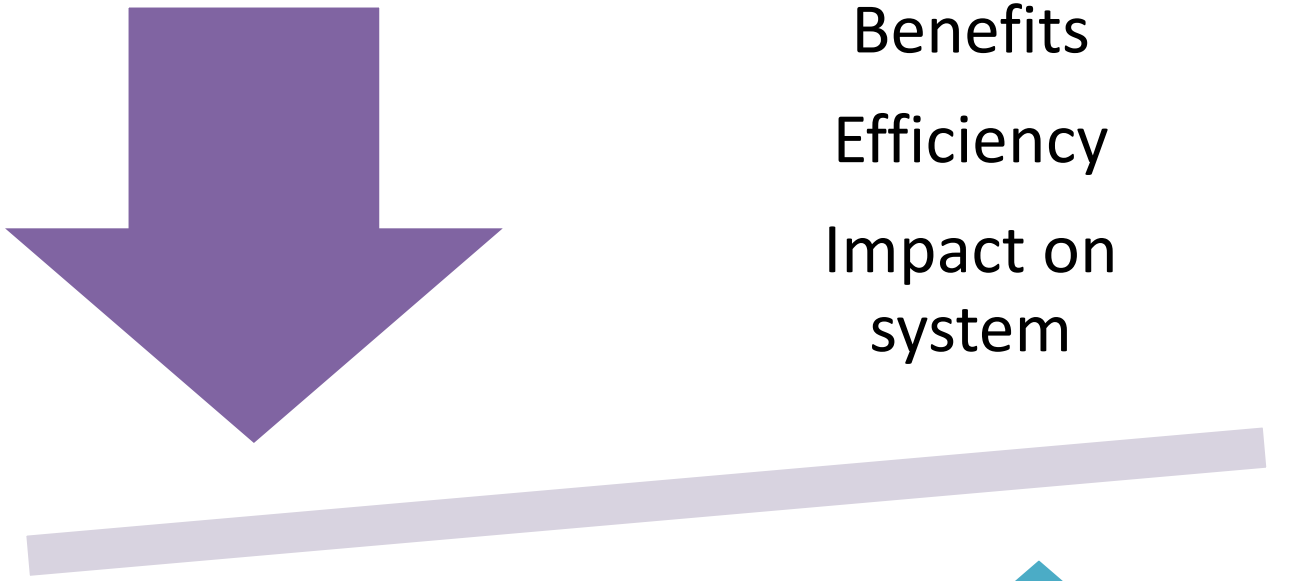
- if the patient from the office of medical doctor is from a group with a different prevalence than the group prevalence from the published study
  - published PPV and NPV cannot be apply in the case of the patient

- PPV and NPV may be computed:

$$PPV = \frac{Se}{Se + (1 - Sp) \times \frac{1 - prevalence}{prevalence}}$$

$$NPV = \frac{Sp}{Sp + (1 - Se) \times \frac{prevalence}{1 - prevalence}}$$

Phase IV - Cohort studies



Benefits

Efficiency

Impact on system

Cost

Side effects

Questions examples

- Does applying the test have an impact on
  - the mortality?
  - the prevention?
  - the medical system?

EXAMPLE

- 20% of the population suffers from depression
- Application of a new diagnostic test
- 1000 randomly selected subjects
- gold standard test for depression Patient Health Questionnaire (PHQ-9)
- new test: questionnaire High-Functioning Depression Test

Case-control study - Phase II

We select 2 groups of subjects
1000 with depression (with positive gold standard)
1000 without depression (with negative gold standard)

Disease / Test	With depression	Without depression	Total
HFDT positive	800	25	-
HFDT negative	200	975	-
Total	1000	1000	-

Case-control study

We select 2 groups of subjects
1000 with depression (with positive gold standard)
1000 without depression (with negative gold standard)

Disease / Test	With depression	Without depression	Total
HFDT positive	800	25	-
HFDT negative	200	975	-
Total	1000	1000	-

Se= 800/1000 =0.8

Sp = 975 / 1000 =0.975

LR^{+}=0,8/(1-0.975)=32

LR^{-}=(1-0.8)/0.975=0.205

prevalence = ~~1000/2000=50%~~ – incorrect

VPP = ~~800/825=0.97~~ – incorrect

VPN = ~~975/1175=0.83~~ – incorrect

J=0.8+0.975-1=0.775

Acc=~~(800+975)/2000=0.888~~ – incorrect

we know the prevalence to be 0.2,

we can calculate:

P(T+)=8/(1+8)=0.89

P(T-)=0.051/(1-0.051)=0.054

PPV =0.89

NPV=0.95

Case-control study

We select 2 groups of subjects
1000 with depression (with positive gold standard)
1000 without depression (with negative gold standard)

Se= 800/1000 =0.8

Sp = 975 / 1000 =0.975

LR^{+}=0,8/(1-0.975)=32

LR^{-}=(1-0.8)/0.975=0.205

In case-control design, the following cannot be calculated:
prevalence
PPV
VPN
Post-test probability after pozitive / negative test
Accuracy

Total	**1000**	**1000**	**-**

PPV =0.89

NPV=0.95

Cohort study – Phase III

We select 2 groups of subjects
1000 with new test positive
1000 with new test negative

Disease / Test	With depression	Without depression	Total
HFDT positive	888	112	1000
HFDT negative	49	951	1000
Total	-	-	-

Cohort study – Phase III

We select 2 groups of subjects
1000 with new test positive
1000 with new test negative

Disease / Test	With depression	Without depression	Total
HFDT positive	888	112	1000
HFDT negative	49	951	1000
Total	-	-	-

PPV=888/1000=0.89

NPV = 951 / 1000 = 0.95

~~Se= 888/937 =0.95~~ – incorrect

~~Sp = 951 / 1063 =0.90~~ – incorrect

~~LR^+=0.948/(1-0.895)=9.02~~ – incorrect

~~LR^-=(1-0.948)/0.895=0.058~~ – incorrect

– incorrect

~~prevalenta=937/2000=0,47~~ – incorrect

~~$P(T^+)$=[0.47/(1-0,47)]*9.02/{1+ [0.47/(1-0.47)]*9.02} =0.89~~ – incorrect

~~$P(T^-)$=[0.47/(10.47)]*0.058/{1+[0.47/(1-0,47)]*0.058} =0.048~~ – incorrect

~~J=0.948+0.895-1=0.843~~ – incorrect

~~Ac=(888+951)/2000=0.920~~ – incorrect

Cohort study – Phase III

We select 2 groups of subjects
1000 with new test positive
1000 with new test negative

VPP=888/1000=0.89

VPN = 951 / 1000 = 0.95

~~Se= 888/937 =0.95~~ – incorrect

In cohort design, the following cannot be calculated:
prevalence
Se
Sp
LR+
LR-
Post-test probability after pozitive / negative test
J
ACC

Representative sample

We select 1 group of subjects
1000 subjects

Disease / Test	With depression	Without depression	Total
HFDT positive	160	20	180
HFDT negative	40	780	820
Total	200	800	1000

Representative sample

We select 1 group of subjects
1000 subjects

Prevalenta=200/1000=0.2

Disease / Test	With depression	Without depression	Total
HFDT positive	160	20	180
HFDT negative	40	780	820
Total	200	800	1000

PPV=160/180=0.888

NPV = 780 / 820 = 0.951

Se= 160/200 =0.8

Sp = 780 / 800 =0.975

LR^{+}=0,8/(1-0.975)=32

LR^{-}=(1-0.8)/0.975=0,205

$P(T^{+})=P(T^{+})$=8/(1+8)=0.89

$P(T^{-})$=0.051/(1-0.051)=0.054

J=0.8+0.975-1=0.775

Acc=(160+780)/1000=0.94

Repr

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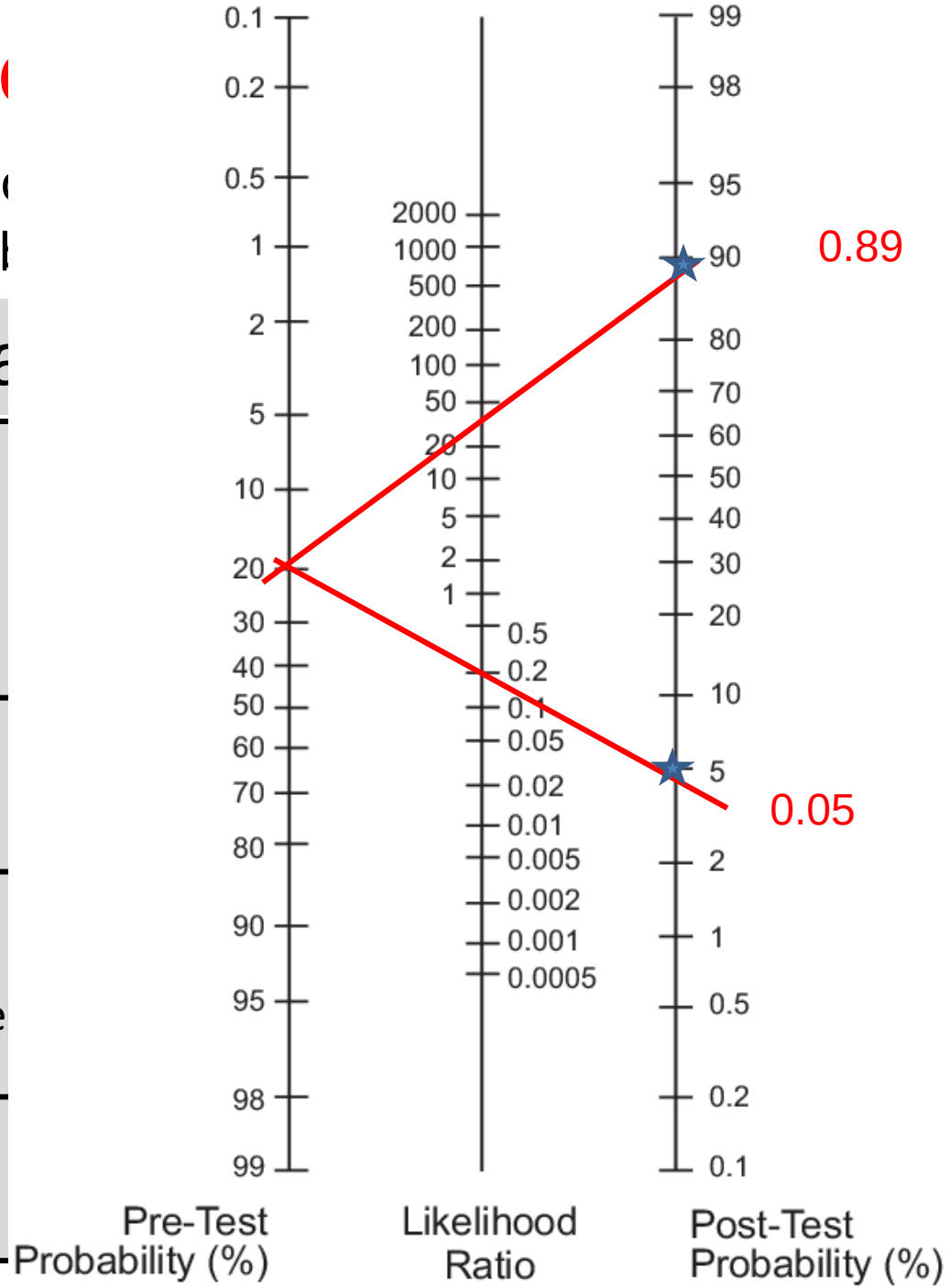
Preva	
Disease / Test	
HFDT positive	
HFDT negative	
Total	



PPV=160/180=0.888

NPV = 780 / 820 = 0.951

Se= 160/200 =0.8

Sp = 780 / 800 =0.975

LR^{+}=0,8/(1-0.975)=32

LR^{-}=(1-0.8)/0.975=0,205

$P(T^{+})=P(T^{+})=8/(1+8)=0.89$

$P(T^{-})=0.051/(1-0.051)=0.054$

J=0.8+0.975-1=0.775

Acc=(160+780)/1000=0.94

Diagnostic study - characteristics

- two medical doctors
  - one evaluate the gold standard test
  - one evaluate the new test
- The tests results interpretation
  - should be performed without previous knowing about the results of the other test or of the gold test - blind

Clinical interpretation

≥ 95% desirable value for clinical use

90% - 95% good for clinical use, if desirable test are not available

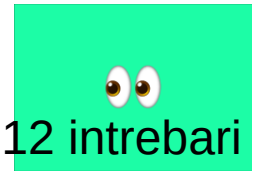
80% - 90% acceptable for clinical use, if better tests are not available

60% - 80% little clinical value

50% - 60% no clinical value (like tossing a coin)

Exemplu

https://app.wooclap.com/HANPLU?from=event-page



Afecţiunea / Testul	Cu depresie	Fără depresie	Total
Scor chestionar pozitiv	160 (a)	20 (b)	180
Scor chestionar negativ	40 (c)	780 (d)	820
Total	200	800	1000

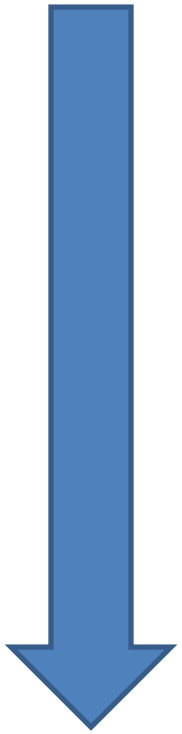
Prevalenta=(a+c)/n=?

Influence of prevalence on predictive value

Scenario

- a rapid test for Covid-19
- Se=0.67
- Sp=0.71

- we apply the test



- the test come positive:
- what is its truth value?
- (how many of those who test positive have Covid-19?)

- we are conducting a study
- representative sample collection
- different times of the year
- summer – we do not have Covid-19 – prevalence 15%
- winter – we have a wave of Covid-19 epidemic – prevalence 30%

Prevalence = 0.15

On the prospect

Se=0.67 Sp=0.71

For 100 subjects

	(B^+)	(B^-)	Total
T^+	10	25	35
T^-	5	60	65
Total	15	85	100

Prevalence = 0.15

Se=10/15=0.67 Sp=60/85=0.71

	(B^+)	(B^-)	Total
T^+	10	25	35
T^-	5	60	65
Total	15	85	100

VPP=10/35=0.29

VPN=60/65=0.92

Prevalence = 0.15

Se=10/15=0.67 Sp=60/85=0.71

We simulated the data with a prevalence of 0.3 and the same Se and Sp

Covid-19 in winter in full epidemics

	(B^+)	(B^-)	Total
T^+	20	20	40
T^-	10	50	60
Total	30	70	100

Prevalence = 0.30

Se=10/15=0.67 Sp=60/85=0.71

Covid-19 in winter in full epidemics

	(B^+)	(B^-)	Total
T^+	20	20	40
T^-	10	50	60
Total	30	70	100

VPP=20/40=0.50

VPN=50/60=0.83

Prevalence = 0.30

Se=10/15=0.67

Sp=60/85=0.71

Covid-19 in summer - no epidemics

	(B^+)	(B^-)	Total
T^+	10	25	35
T^-	5	60	65
Total	15	85	100

VPP=10/35=0,29

VPN=60/65=0,92

Prevalența = 0,15

Covid-19 in winter in full epidemics

	(B^+)	(B^-)	Total
T^+	20	20	40
T^-	10	50	60
Total	30	70	100

VPP=20/40=0,50

VPN=50/60=0,83

Prevalența = 0,30

Se=10/15=0,67 Sp=60/85=0,71

Efectul prevalentei asupra valorii predictive

Se=10/15=0,67 Sp=60/85=0,71

	(B^+)	(B^-)	Total
Total	30	70	100

Covid-19 vara – nu este epidemie

Prevalența = 0,15

VPP=10/35=0,29

VPN=60/65=0,92

Prevalența = 0,30

VPP=20/40=0,50

VPN=50/60=0,83

Crește prevalența:

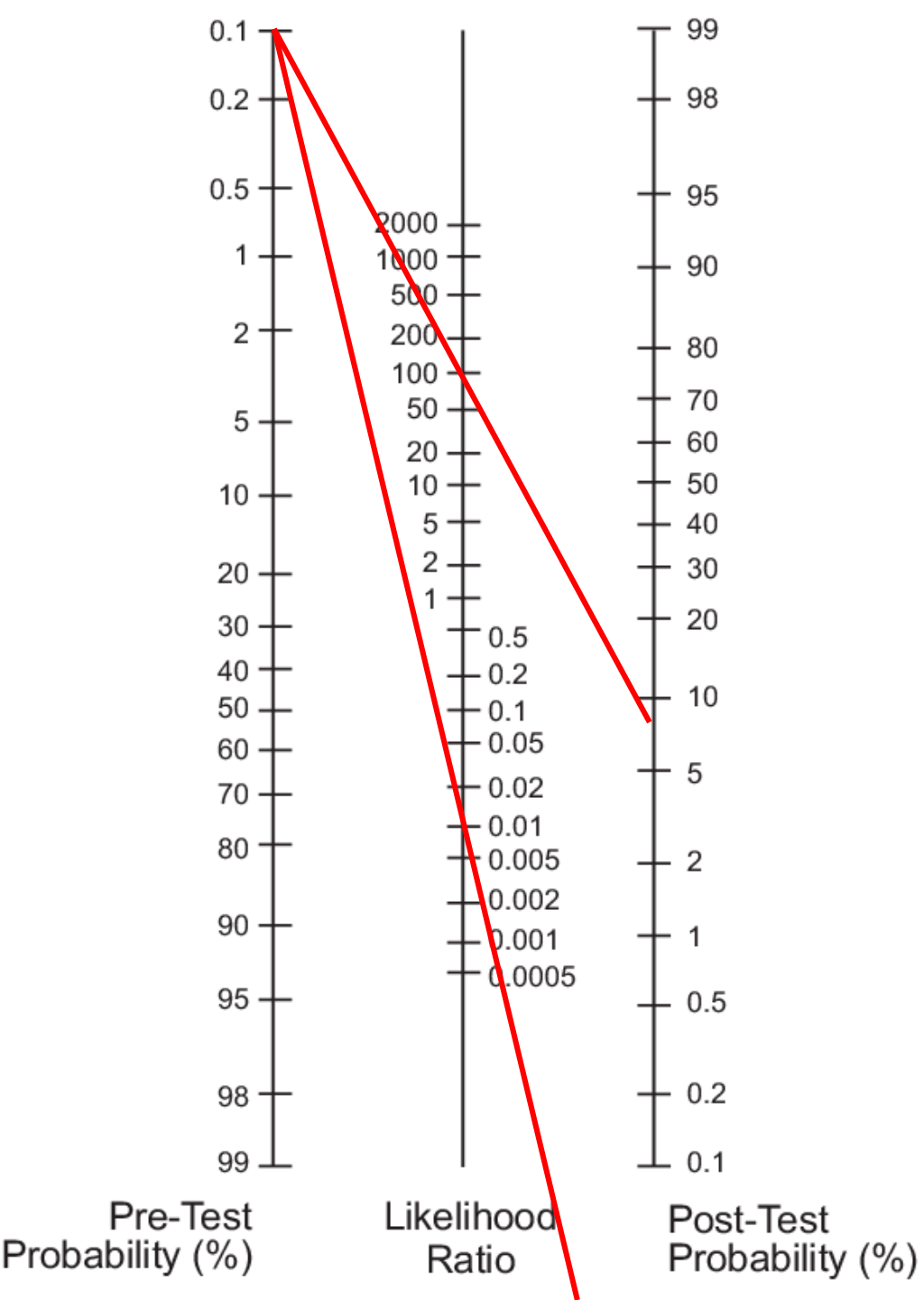
- probabilitatea ca un test pozitiv să fie corect e mai mare – crește VPP
- probabilitatea ca un test negativ să fie corect e mai mică – scade VPN

rare disease example HIV Test

Prevalence=100/100,000=0.001

	With HIV (B^+)	Without HIV (B^-)	Total
Test (T^+)	99	1	100
Test (T^-)	1	90.899	90.900
Total	100	90.900	100.000

- PPV=99/100=**0.99**
- NPV = 90899 / 90900 = **0.99**
- Se= 99/100 =**0.99**
- Sp = 99980 / 99989 =**0.99**
- LR^+=0.99/0.01=99.99
- LR^-=0.01/0.99=0.01
- $P(T^+)$=[0.001/(1-0.001)]*99.99/{1+[0.001/(1-0.001)]*99.99}=0.09/(1+0.09)=**0.083**
- $P(T^-)$= [0.001/(1-0.001)]*0.01/{1+[0.001/(1-0.001)]*0.01} =0.00001/(1-0.00001)=**0.000001**
- Ac=(99+90899)/100000=0.91



Prevalence=100/100,000=0.001

PPV=99/100=**0.99**

NPV = 90899 / 90900 = **0.99**

Se= 99/100 =**0.99**

Sp = 99980 / 99989 =**0.99**

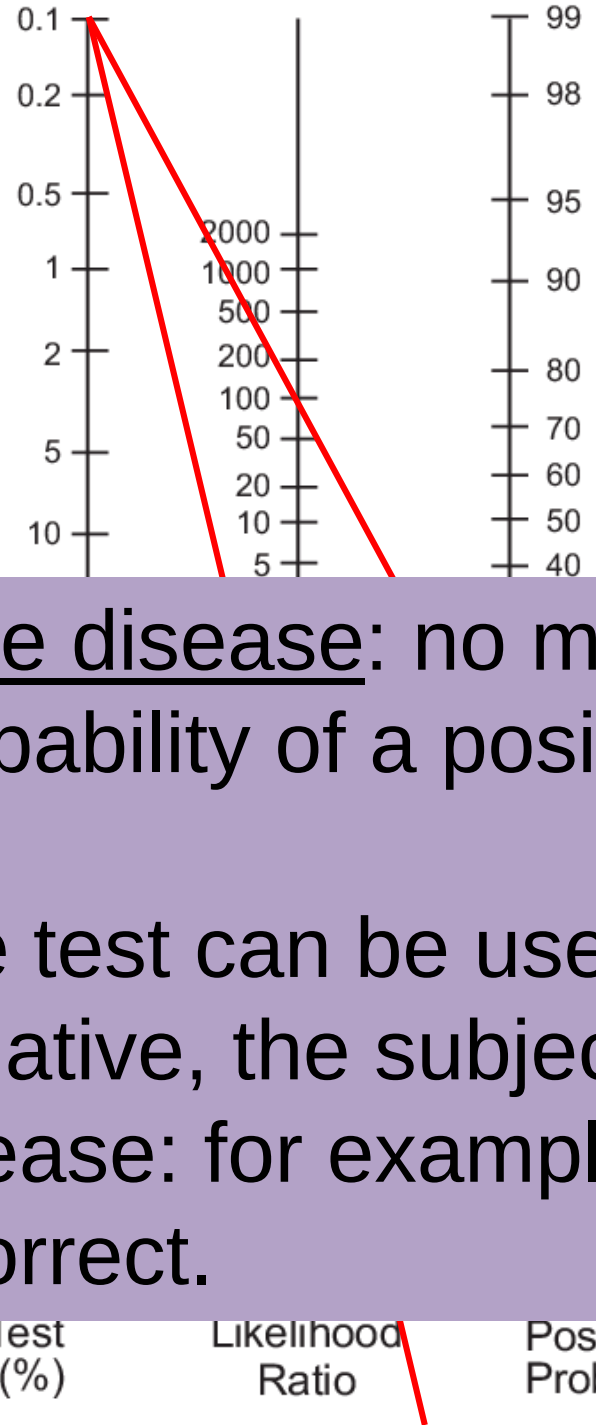
LR^{+}=0.99/0.01=99.99

LR^{-}=0.01/0.99=0.01

$P(T^{+})$=[0.001/(1-0.001)]*99.99/{1+[0.001/(1-0.001)]*99.99}=0.09/(1+0.09)=**0.083**

$P(T^{-})$= [0.001/(1-0.001)]*0.01/{1+[0.001/(1-0.001)]*0.01} =0.00001/(1-0.00001)=**0.000001**

Ac=(99+90899)/100000=0.91



Prevalence=100/100,000=0.001

PPV=99/100=**0.99**

NPV = 90899 / 90900 = **0.99**

Se= 99/100 =**0.99**

Sp = 99080 / 99089 =**0.99**

Ac=(99+90899)/100000=0.91

<u>Rare disease</u>: no matter how sensitive the test is, the probability of a positive post-test is very small.
but
The test can be used as a screening test: if it comes out negative, the subject almost certainly does not have the disease: for example, 1 case in 90,900 negative cases is incorrect.

Scenario

- 110 diabetic patients
- standard neuropathy test nerve conduction velocity (NCV)
  - positive versus negative
- new test – categorical variable
  - MNSI - Michigan Neuropathy Screening Instrument - examination score
    - from 1 to 10 points
    - a high score indicates neuropathy

	With neuropathy	Without neuropathy	Total
Test score = 0	1	15	16
Test score = 1	3	5	8
Test score = 2	4	4	8
Test score = 3	3	4	7
Test score = 4	4	2	6
Test score = 5	4	3	7
Test score = 6	5	2	7
Test score = 7	13	2	15
Test score = 8	18	1	19
Test score = 9	10	1	11
Test score = 10	5	1	6
Total	70	40	110

It is the new test a high-performant test?

- Se?
- Sp?
- PPV?
- NPV?
- 11 scores
- How to use the diagnostic test?

Cut-off value

- a value to discriminate the diseased subjects from non-diseased
- Optimum cut-off value
  - a value that gives maximum of correct classified subjects in positive and negative

  ↔! minimum false positive + false negative

  ↔ maximum accuracy

How to find the best cut-off value for the test?

- scores from 0 to 10
- we will calculate for each
  - Se and Sp

Algoritm

- score 1
  - those with a score below 1 are considered negative
  - those with a score above or equal to 1 are considered positive
  - what % of those with neuropathy are correctly diagnosed?
    - calculate Se
  - what % of those without neuropathy are correctly diagnosed?
    - calculate Sp

	With neuropathy	Without neuropathy	Total
Test score = 0	1	15	16
Test score = 1	3	5	8
Test score = 2	4	4	8
Test score = 3	3	4	7
Test score = 4	4	2	6
Test score = 5	4	3	7
Test score = 6	5	2	7
Test score = 7	13	2	15
Test score = 8	18	1	19
Test score = 9	10	1	11
Test score = 10	5	1	6
Total	70	40	110

Algoritm

- score 1
  - Se=69/70=0.99
  - Sp=15/40=0.38

Disease / Test	With neuropathy	Without neuropathy	Total
Score ≥1= pozitive	69	25	94
Score <1= negative	1	15	16
Total	70	40	110

Algoritm

- score 2
  - those with a score below 2 are considered negative
  - those with a score above or equal to 2 are considered positive
  - what % of those with neuropathy are correctly diagnosed?
    - calculate Se
  - what % of those without neuropathy are correctly diagnosed?
    - calculate Sp

	With neuropathy	Without neuropathy	Total
Test score = 0	1	15	16
Test score = 1	3	5	8
Test score = 2	4	4	8
Test score = 3	3	4	7
Test score = 4	4	2	6
Test score = 5	4	3	7
Test score = 6	5	2	7
Test score = 7	13	2	15
Test score = 8	18	1	19
Test score = 9	10	1	11
Test score = 10	5	1	6
Total	70	40	110

Algoritm

- score 2
  - Se=66/70=0.94
  - Sp=17/40=0.43

Disease / Test	With neuropathy	Without neuropathy	Total
Score ≥2= pozitive	66	23	99
Score <2= negative	4	17	21
Total	70	40	110

Algoritm

- score 3
  - those with a score below 3 are considered negative
  - those with a score above or equal to 3 are considered positive
  - Se=62/70=0.89
  - Sp=21/40=0.53

Disease / Test	With neuropathy	Without neuropathy	Total
Score ≥3= pozitive	62	19	2981
Score <3= negative	8	21	29
Total	70	40	110

Algoritm

- score 4
  - those with a score below 4 are considered negative
  - those with a score above or equal to 5 are considered positive
  - Se=59/70=0.84
  - Sp=25/40=0.63

Disease / Test	With neuropathy	Without neuropathy	Total
Score ≥4= pozitive	59	15	74
Score <4= negative	11	25	36
Total	70	40	110

Algoritm

- score 5
  - those with a score below 5 are considered negative
  - those with a score above or equal to 5 are considered positive
  - Se=55/70=0.79
  - Sp=33/40=0.75

Disease / Test	With neuropathy	Without neuropathy	Total
Score ≥5= pozitive	55	10	65
Score <5= negative	15	30	45
Total	70	40	110

Algoritm

- score 6
  - those with a score below 6 are considered negative
  - those with a score above or equal to 6 are considered positive
  - Se=51/70=0.73
  - Sp=33/40=0.83

Disease / Test	With neuropathy	Without neuropathy	Total
Score ≥6= pozitive	51	7	58
Score <6= negative	19	33	52
Total	70	40	110

Algoritm

- score 7
  - those with a score below 7 are considered negative
  - those with a score above or equal to 7 are considered positive
  - Se=46/70=0.66
  - Sp=35/40=0.88

Disease / Test	With neuropathy	Without neuropathy	Total
Score ≥7= pozitive	46	5	51
Score <7= negative	24	35	59
Total	70	40	110

Algoritm

- score 8
  - those with a score below 8 are considered negative
  - those with a score above or equal to 8 are considered positive
  - Se=33/70=0.47
  - Sp=37/40=0.93

Disease / Test	With neuropathy	Without neuropathy	Total
Score ≥8= pozitive	33	3	36
Score <8= negative	37	37	74
Total	70	40	110

Algoritm

- score 9
  - those with a score below 9 are considered negative
  - those with a score above or equal to 9 are considered positive
  - Se=15/70=0.21
  - Sp=38/40=0.95

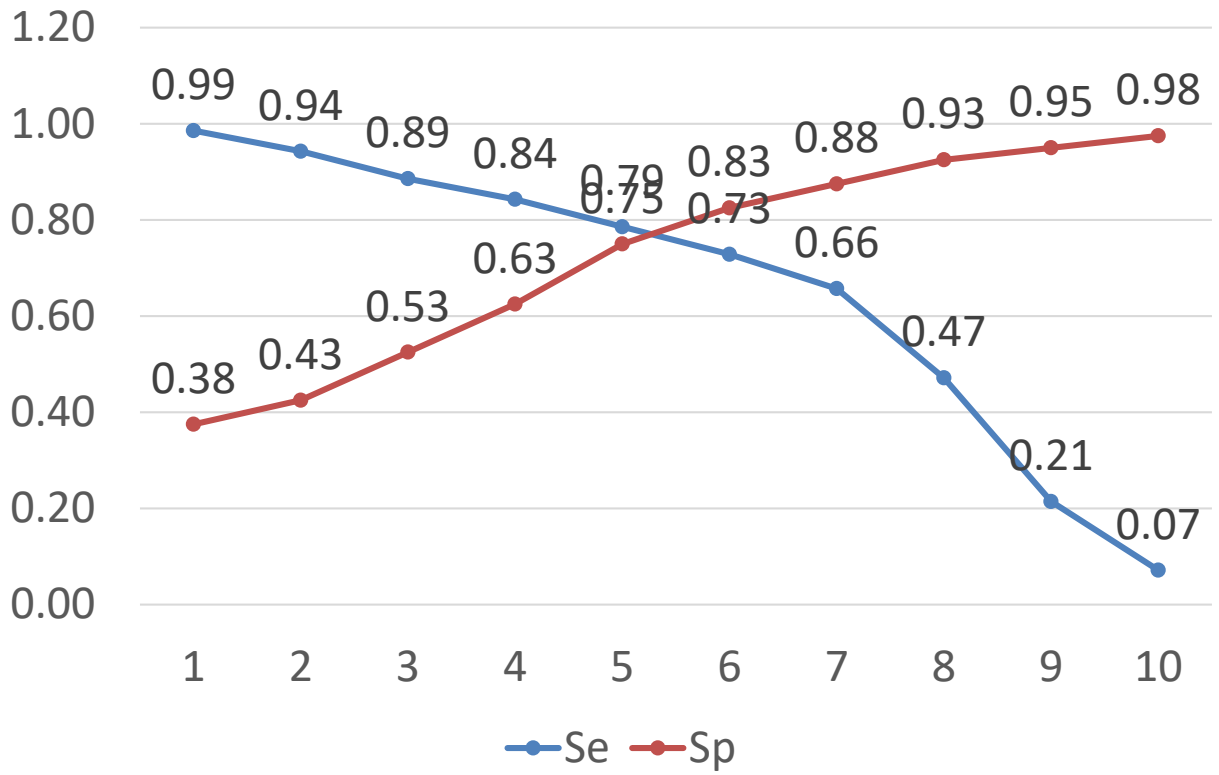
Disease / Test	With neuropathy	Without neuropathy	Total
Score ≥9= pozitive	15	2	17
Score <9= negative	55	38	93
Total	70	40	110

Algoritm

- score 10
  - those with a score below 10 are considered negative
  - those with a score above or equal to 10 are considered positive
  - Se=15/70=0.07
  - Sp=38/40=0.98

Disease / Test	With neuropathy	Without neuropathy	Total
Score ≥10= pozitive	5	1	6
Score <10= negative	65	39	104
Total	70	40	110

	Se	Sp
Score 1	0.99	0.38
Score 2	0.94	0.43
Score 3	0.89	0.53
Score 4	0.84	0.63
Score 5	0.79	0.75
Score 6	0.73	0.83
Score 7	0.66	0.88
Score 8	0.47	0.93
Score 9	0.21	0.95
Score 10	0.07	0.98



Choosing the optimum cut-off value

	Se	Sp	J=Se+Sp-1
Score 1	0.99	0.38	0.36
Score 2	0.94	0.43	0.37
Score 3	0.89	0.53	0.41
Score 4	0.84	0.63	0.47
Score 5	0.79	0.75	0.54
Score 6	**0.73**	**0.83**	**0.55**
Score 7	0.66	0.88	0.53
Score 8	0.47	0.93	0.40
Score 9	0.21	0.95	0.16
Score 10	0.07	0.98	0.05

! optimum = maximum of accuracy, maximum of correct classified subjects with and without disease

Maximum J

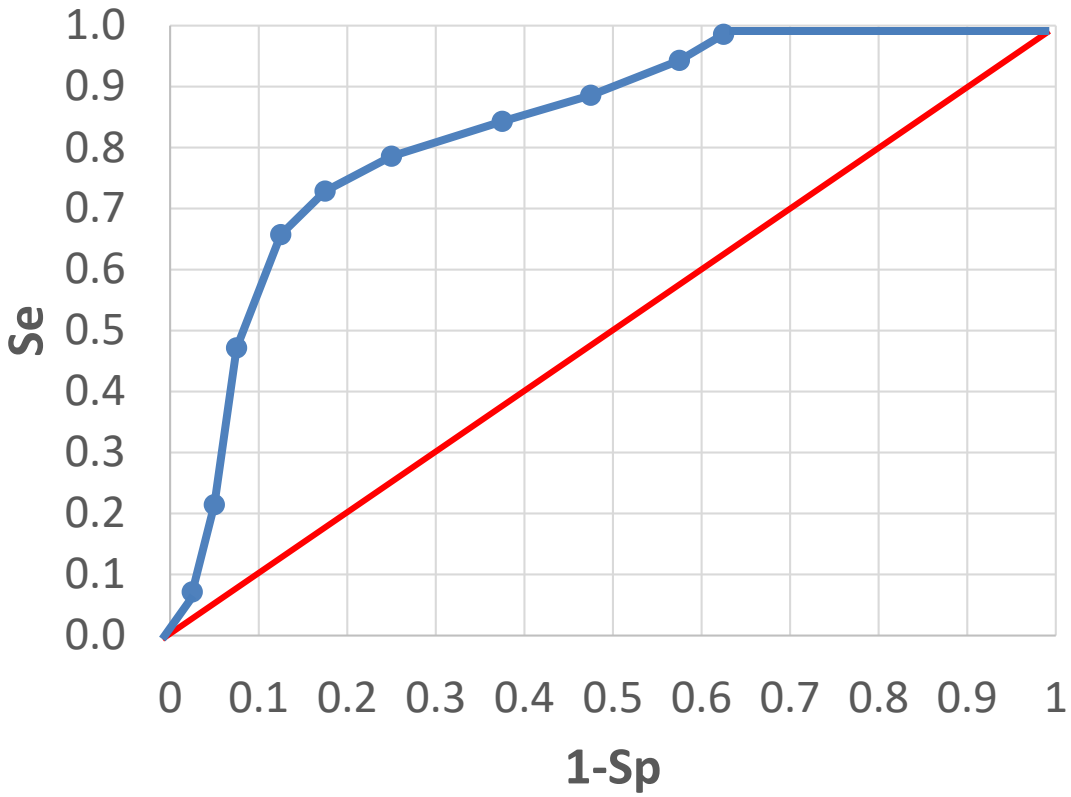
- those with a score below 6 are considered negative
- those with a score above or equal to 6 are considered positive

the best cut-off is 6

– easy to appreciate the cut-off value

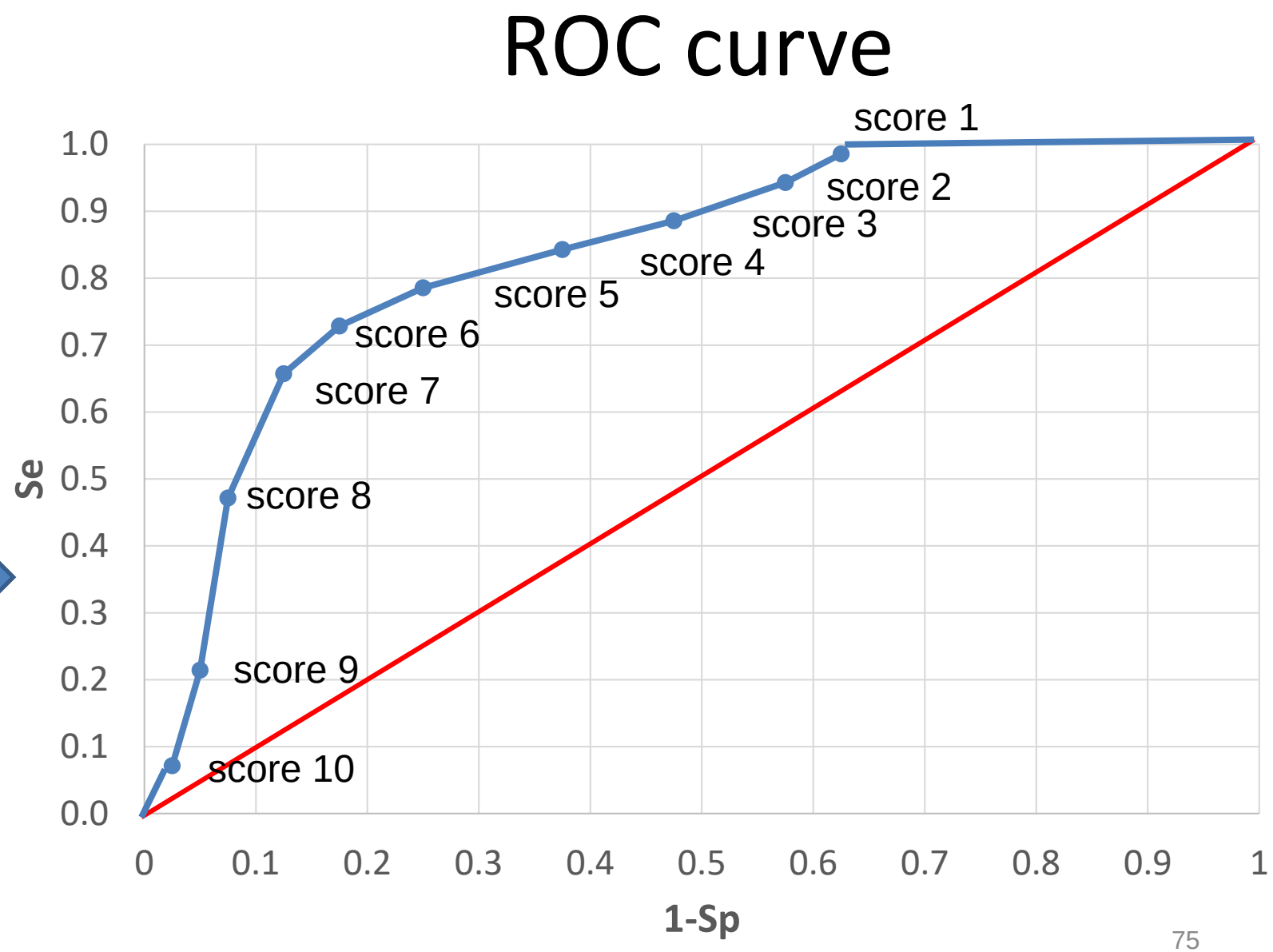
	Se	Sp	1-Sp	J=Se+Sp-1
Score 1	0.99	0.38	0.63	0.36
Score 2	0.94	0.43	0.58	0.37
Score 3	0.89	0.53	0.48	0.41
Score 4	0.84	0.63	0.38	0.47
Score 5	0.79	0.75	0.25	0.54
Score 6	0.73	0.83	0.18	0.55
Score 7	0.66	0.88	0.13	0.53
Score 8	0.47	0.93	0.08	0.40
Score 9	0.21	0.95	0.05	0.16
Score 10	0.07	0.98	0.03	0.05

ROC curve

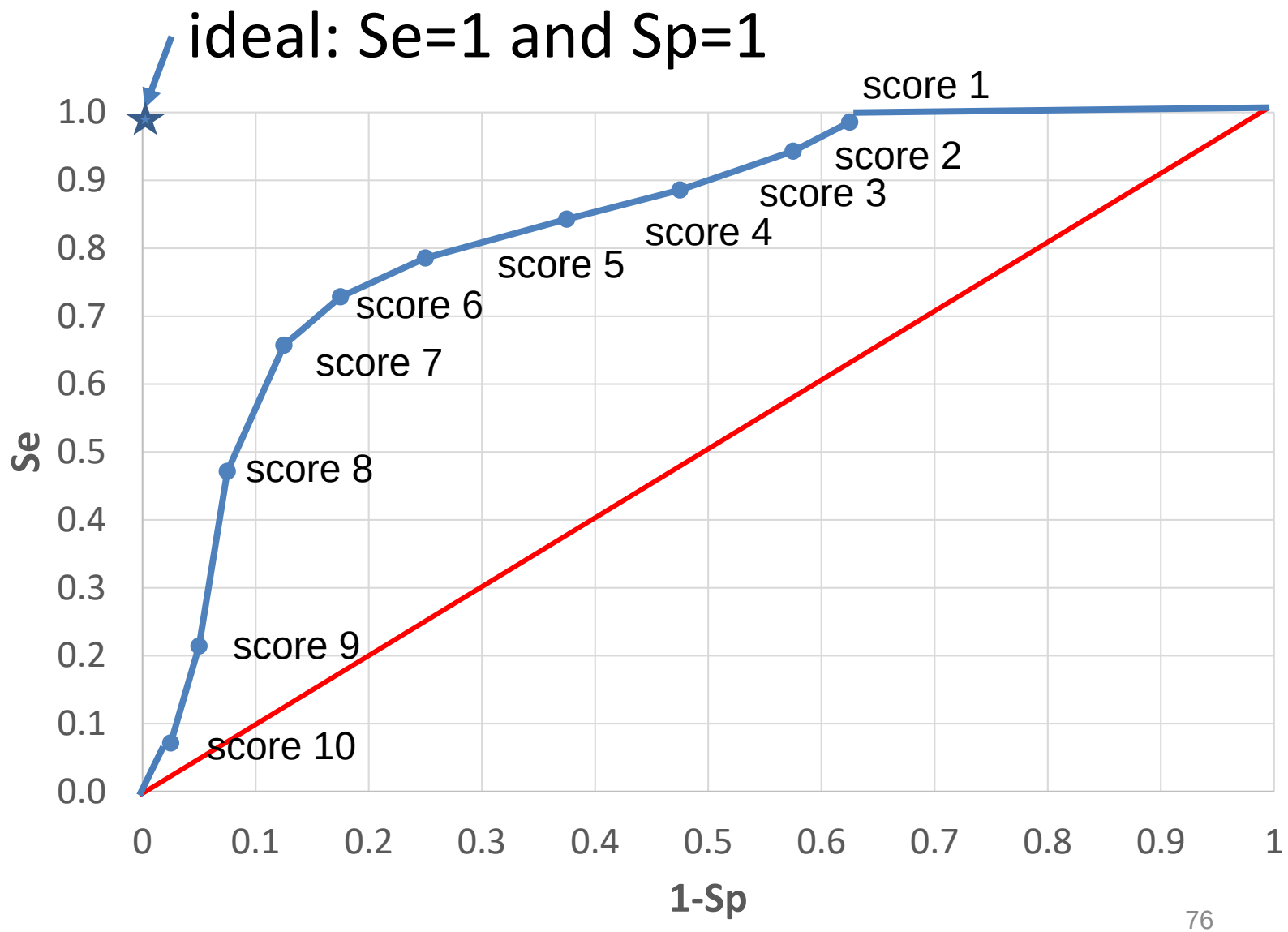


– easy to appreciate the cut-off value

	Se	1-Sp
Score 1	0.99	0.63
Score 2	0.94	0.58
Score 3	0.89	0.48
Score 4	0.84	0.38
Score 5	0.79	0.25
Score 6	0.73	0.18
Score 7	0.66	0.13
Score 8	0.47	0.08
Score 9	0.21	0.05
Score 10	0.07	0.03

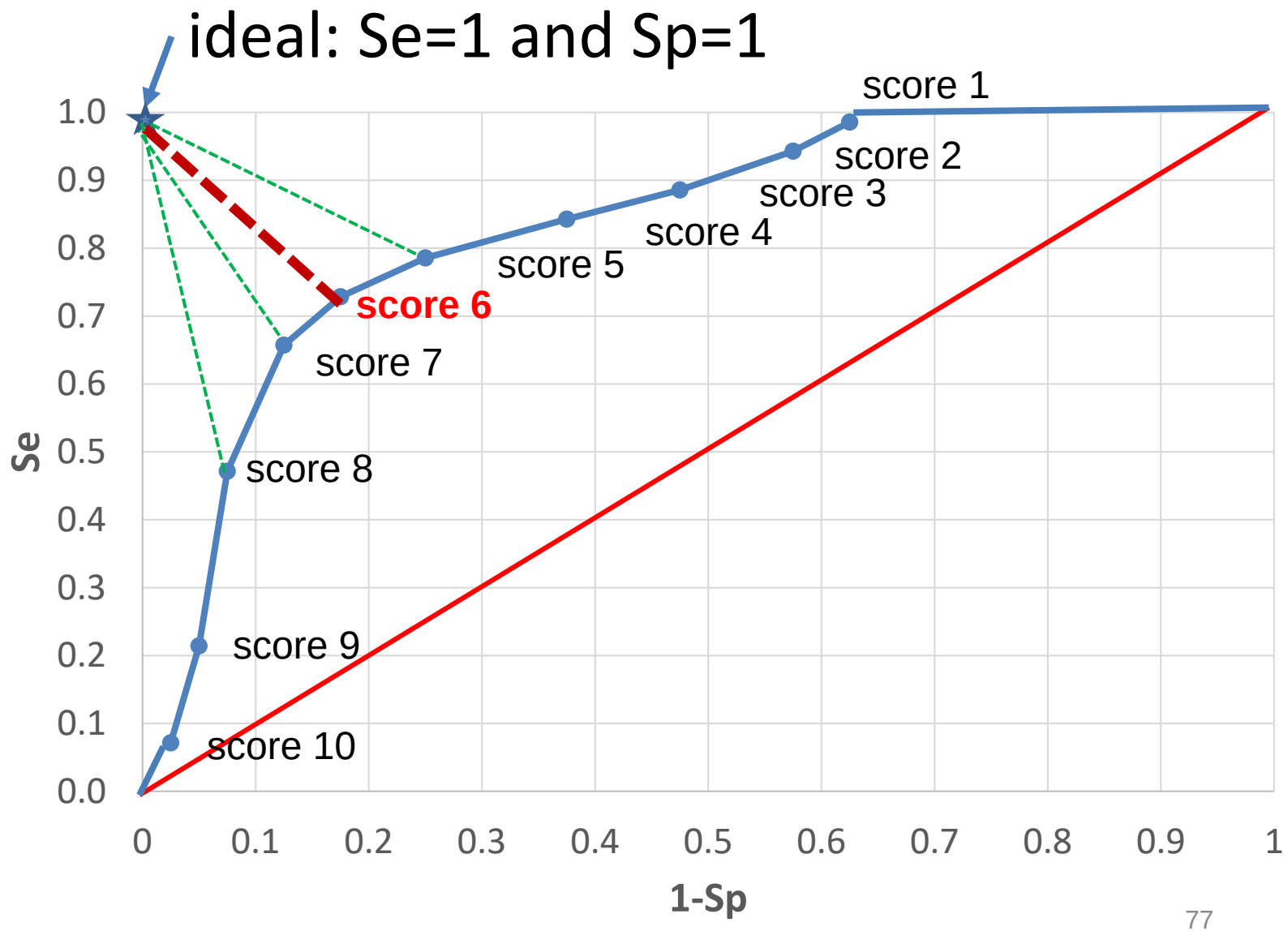


– the score nearest to the ideal point is the optimum cut-off



ROC curve

– the score nearest to the ideal point is the optimum cut-off



ROC curve

Our interest

- to diagnose
  - as many patients with neuropathy as possible
    - a score with high Se
      - FP to approach 0
- to exclude
  - as many patients without neuropathy as possible
    - a score with high Sp
      - FN to approach 0
- Conclusion: both those with and those without neuropathy
  - a score with high Sp and Se
    - FP and FN to approach 0

if FP and FN equally important

- optimal threshold:
- maximum Youden index= Se+Sp-1

if FP (high Se) more important than FN

- optimal threshold:
- maximum Se

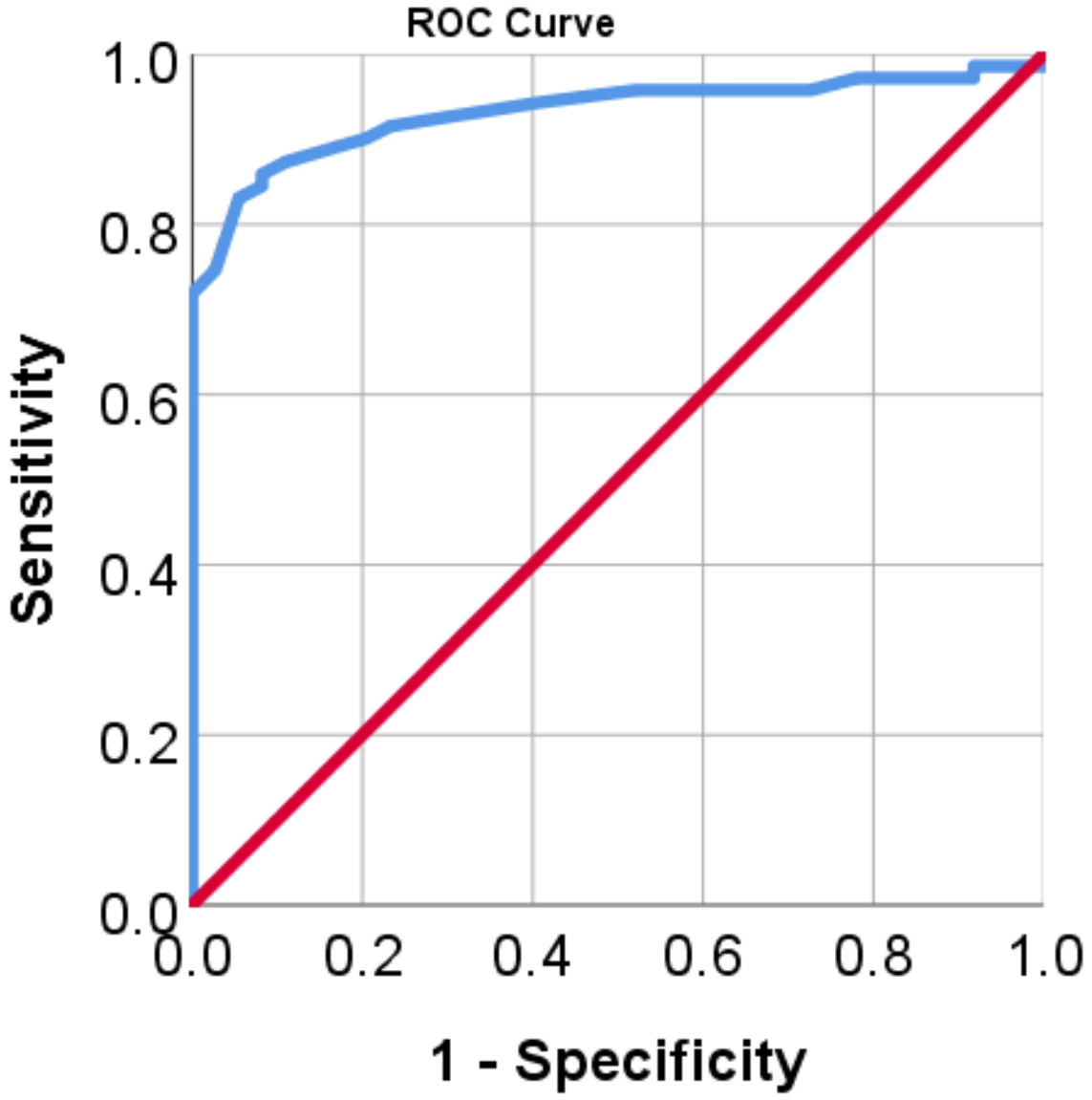
if FN (high Sp) more important than FP

- optimal threshold:
- maximum Sp

ROC Curve

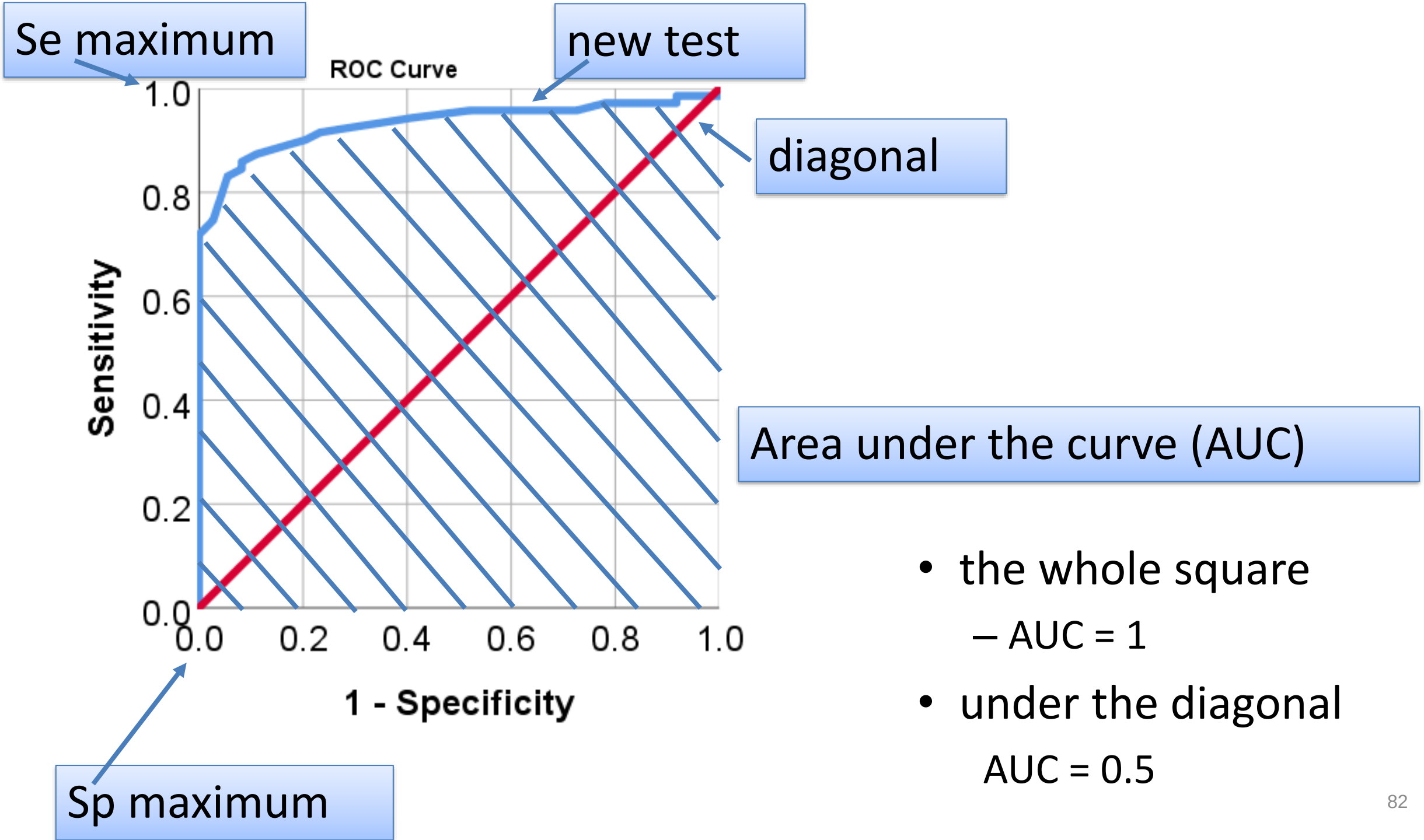
- Receiver Operating Characteristic Curve

- historical
- World War II (1950 England):
- identifying enemy aircraft on radar in the presence of extraneous signals (e.g. geese)
  - True Positives and True Negatives – good results
  - False Positives – wasting resources on geese
  - False Negatives – buildings and lives lost due to bombing



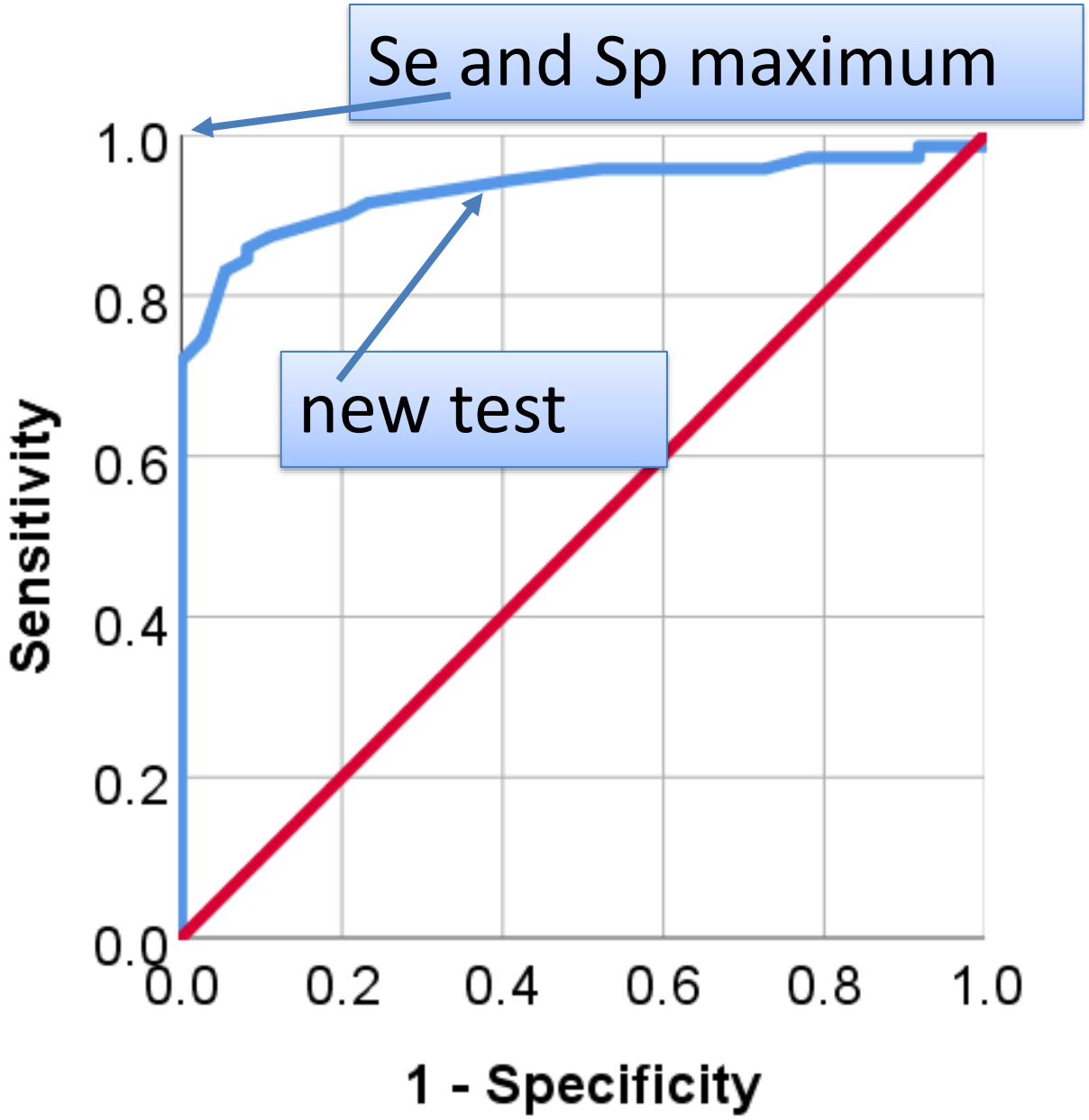
ROC curve

- diagonal = random diagnostic
  - ex. toss a coin

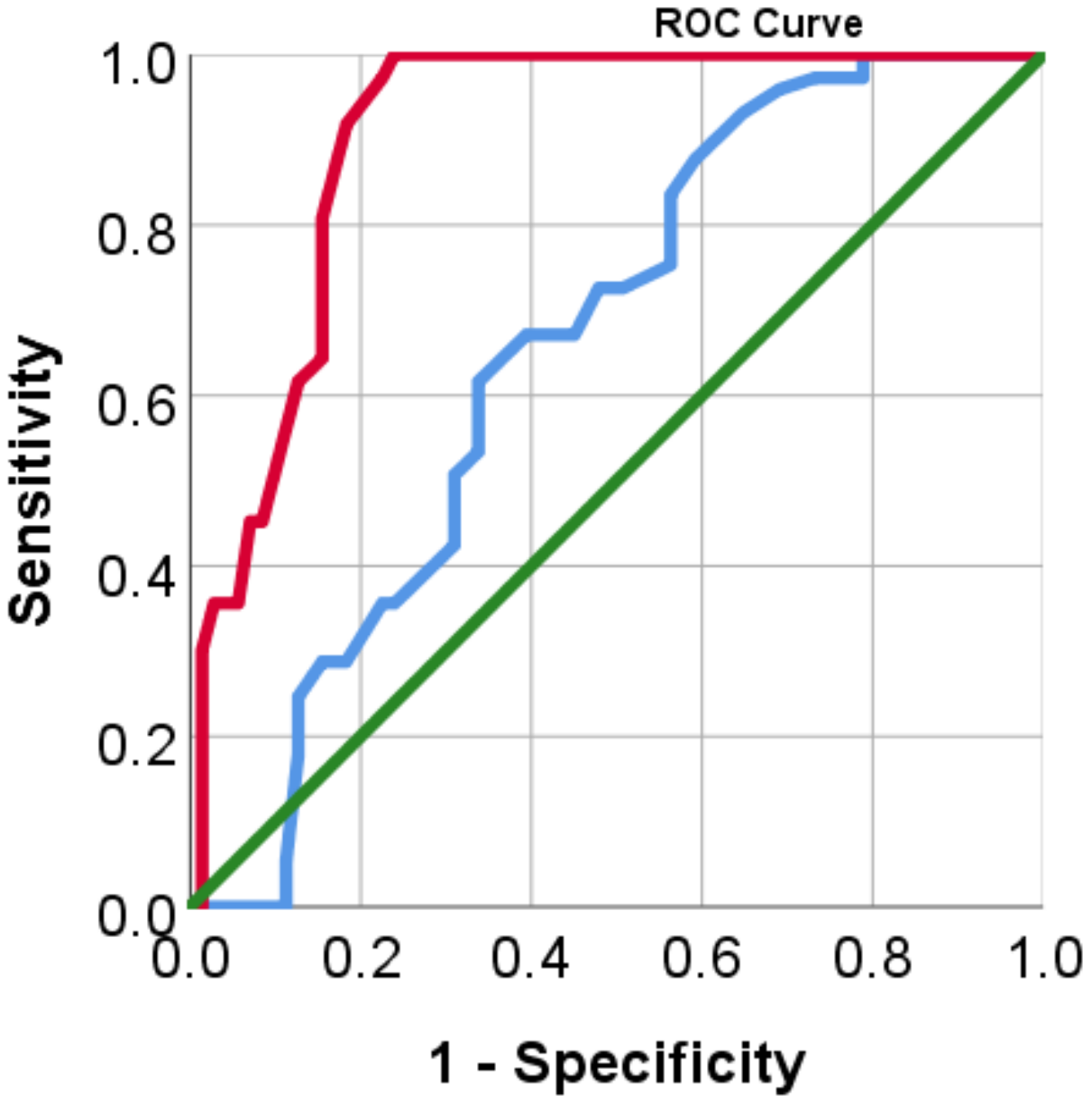


- the whole square
  - AUC = 1
- under the diagonal

  AUC = 0.5



- !!! the bigger the AUC, the better the test



MDI test have high accuracy than GDS

AUC for MDI better than AUC for GDS

BMC Oral Health. 2016 Jun 2;16(1):64. doi: 10.1186/s12903-016-0216-x.

A new screening method for periodontitis: an alternative to the community periodontal index

Yoshiaki Nomura [1], Ayako Okada [1], Erika Kakuta [1], Takahide Gunji [2], Seiji Kajiura [3], Nobuhiro Hanada [4]

Affiliations + expand

PMID: 27388493 PMCID: PMC4937556 DOI: 10.1186/s12903-016-0216-x

Abstract

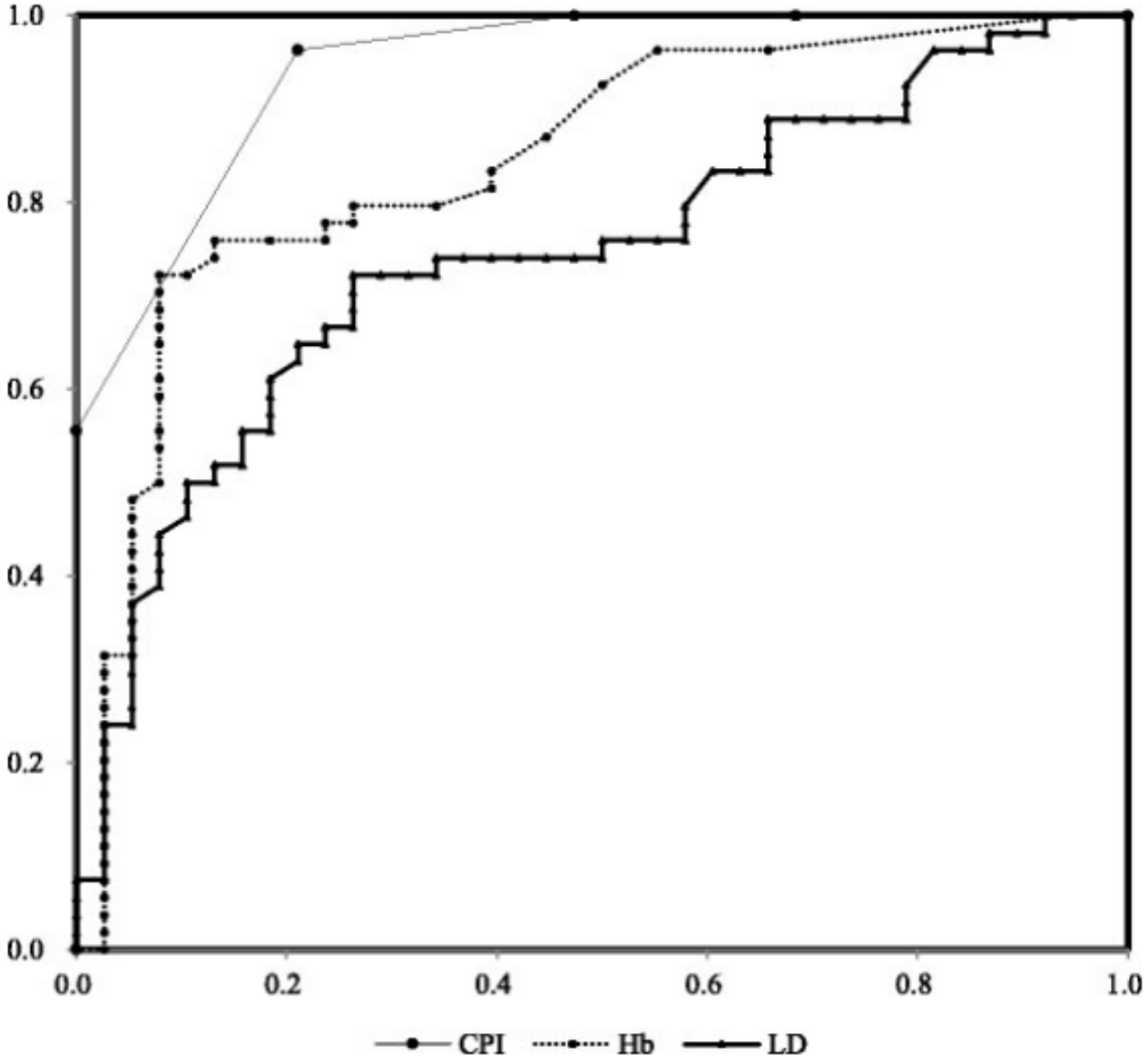
Background: Periodontal screening plays an important role in the prevention of periodontal disease and promotes an improvement in oral health-related quality of life. The World Health Organization's Community Periodontal Index should be carried out by well-trained dentists. However, the Community Periodontal Index is an invasive technique, and if used for periodontal screening, increases the cost of evaluation. In order to overcome these issues, we developed saliva tests for periodontal screening. The purpose of this study was to calculate the sensitivity and specificity of our method for measuring hemoglobin and lactate dehydrogenase levels in saliva.

Methods: Inclusion criteria were adults aged over 20 years with at least 20 teeth remaining. The study population comprised 38 men and 54 women with a mean age of 50.03 years. Oral examinations were carried out by dentists, and the number of remaining teeth, presence or absence of calculus, bleeding on probing and pocket depth were recorded. In this study, periodontitis was defined according to the criteria of the Center for Disease Control and Prevention in partnership with the American Academy of Periodontology. In order to examine hemoglobin and lactate dehydrogenase levels in saliva, participants were instructed to chew on a standard-sized tasteless and odorless gum base for 5 min, during which time, stimulated whole saliva was continuously collected.

Results: The sensitivity and specificity for hemoglobin levels were 0.759 and 0.763, respectively, and 0.722 and 0.711, respectively, for lactate dehydrogenase levels. Combining these two tests, when samples tested positive for both hemoglobin and lactate dehydrogenase, the positive predictive value was 91.7 %.

Conclusion: Measuring hemoglobin and lactate dehydrogenase levels in saliva is a less invasive method than the Community Periodontal Index. Therefore, our saliva tests may be a viable alternative to the Community Periodontal Index for periodontal screening.

- 92 patients
- 3 test for periodontitis
- gold standard: CDC criteria



Figure

Caption

Receiver operator characteristics (ROC) curves for periodontitis based on the Community Periodontal Index (CPI) and salivary hemoglobin (Hb), and lactate dehydrogenase (LD) levels. The area under the ROC curve (AUC) was higher for the CPI than for the saliva tests (CPI, 0.954; Hb, 0.846; LD, 0.737)

Nomura Y, Okada A, Kakuta E, Gunji T, Kajiura S, Hanada N. A new screening method for periodontitis: an alternative to the community periodontal index. BMC Oral Health. 2016 Jun 2;16(1):64.

Table 3 Community Periodontal Index (CPI) values and hemoglobin (Hb) and lactate dehydrogenase (LD) levels at screening

	Cutoff	*P*	Sensitivity	Specificity	Positive predictive value	Negative predictive value	Crude hit rate	Yorden's index	AUC-ROC
CPI	3	<0.001	0.964	0.789	0.869	0.938	0.892	0.753	0.954
Hb (μg/mL)	1.25	<0.001	0.764	0.763	0.824	0.690	0.763	0.527	0.846
LD (IU/L)	298	<0.001	0.709	0.711	0.780	0.628	0.710	0.420	0.737

Sensitivities, specificities, positive and negative predictive values, Youden's index and areas under the receiver operator characteristics curve (AUC-ROC) for periodontitis were calculated. *P* values were calculated using Fisher's exact test
Hb hemoglobin, *LD* lactate dehydrogenase, *CPI* Community Periodontal Index

Nomura Y, Okada A, Kakuta E, Gunji T, Kajiura S, Hanada N. A new screening method for periodontitis: an alternative to the community periodontal index. BMC Oral Health. 2016 Jun 2;16(1):64.

Area under the ROC curve

Interpretation according to the traditional academic point system:

AUC between

0.90 – 1 = excellent test,

0.80–0.90 = good,

0.70–0.80 = fair,

0.60–0.70 = poor,

0.50–0.60 = failure

Area under the ROC curve

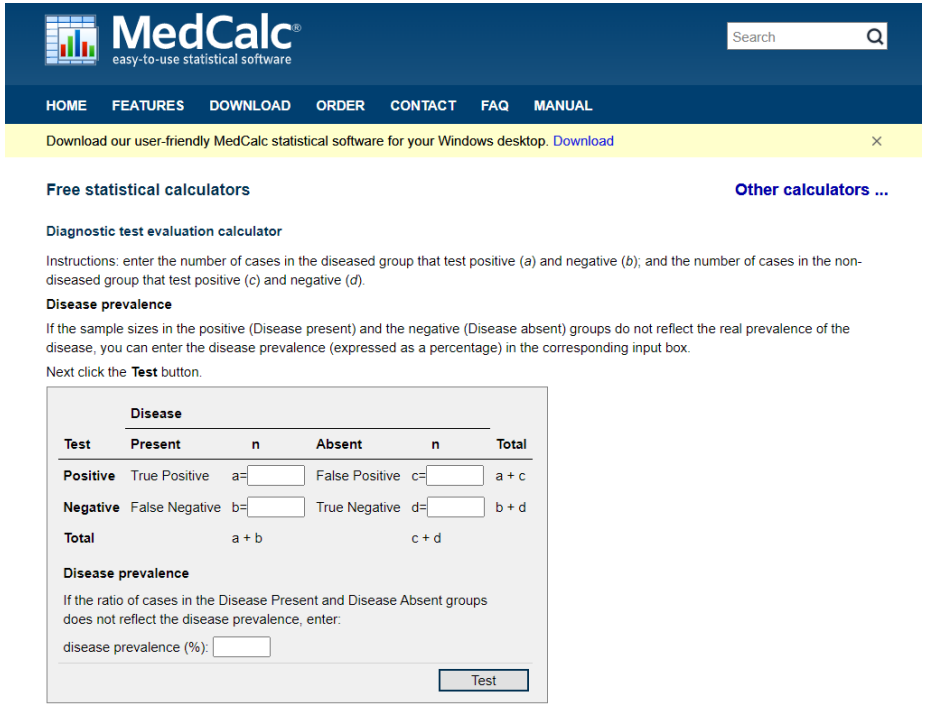
- compare with the area under the diagonal = 0.5
- H0 (null hypothesis): AUC is not statistically significantly different from 0.5

- $p<0.05$ – AUC is significantly different from 0.5
  - It can be said that the diagnostic test has statistically significantly better discriminatory power than the random test

- $p\geq0.05$ – AUC does not differ significantly from 0.5
  - It can be said that we fail to demonstrate that the diagnostic test have statistically significantly better discriminatory power than the random test

Soft online - MedCalc

- https://www.medcalc.org/calc/diagnostic_test.php



Soft online – Alan Schwartz

- http://araw.mede.uic.edu/cgi-bin/testcalc.pl

Diagnostic Test Calculator

This calculator can determine diagnostic test characteristics (sensitivity, specificity, likelihood ratios) and/or determine the post-test probability of disease given given the pre-test probability and test characteristics. Given sample sizes, confidence intervals are also computed.

Fill out one of the sections below on the left, and then click on the 'Compute' button. Sections you don't fill out will be computed for you, and the nomogram on the right will display the probability that a patient has the disease after a positive or negative test.

Numbers of patients with and without the disease who test positive and negative:

	Disease present	Disease absent	Total
Test positive			
Test negative			
Total			

Compute

or
disease prevalence, test sensitivity, and test specificity (and, optionally, sample size):

Prevalence (e.g. 0.10):	
Sensitivity (e.g. 0.80):	
Specificity (e.g. 0.80):	
Total sample size:	

Compute

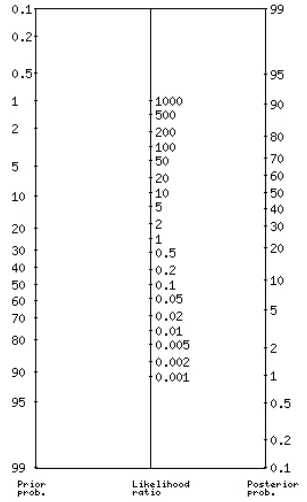
or
disease prevalence, positive likelihood ratio, and negative likelihood ratio (and, optionally, sample size):

Prevalence (e.g. 0.10):	
+LR (e.g. 4):	
-LR (e.g. 0.01):	
Total sample size:	

Compute

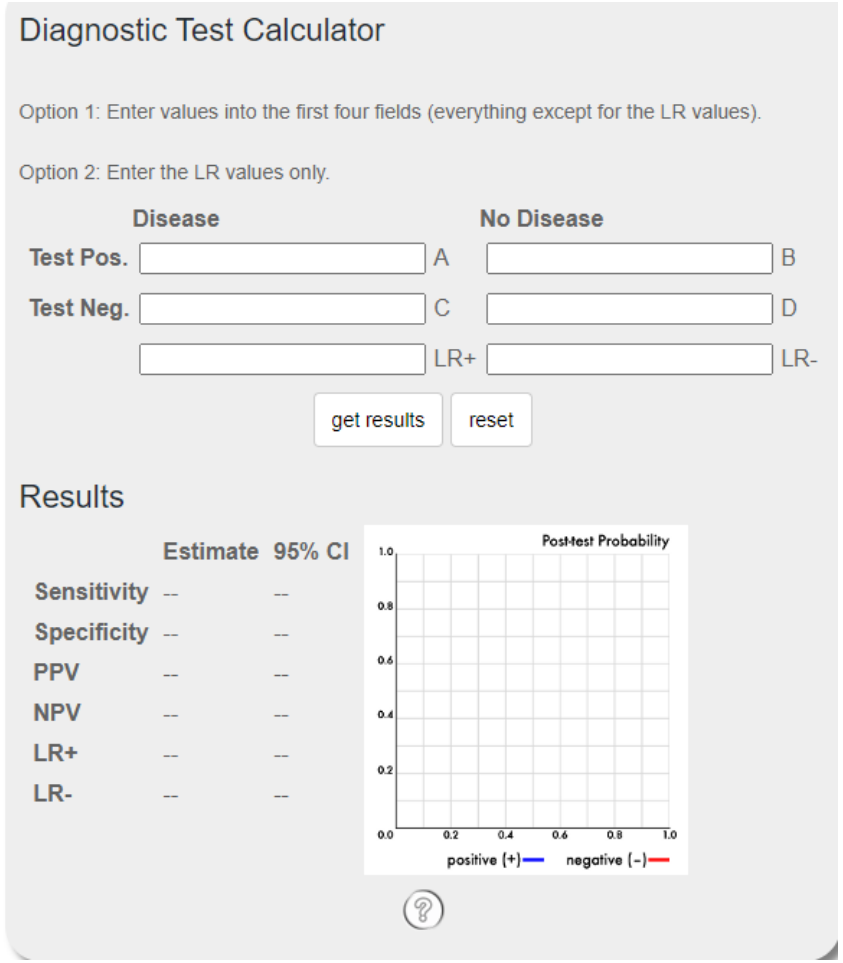
Optional information:

Your local prevalence (e.g. 0.10):	
Probability of disease at or above which you would be **comfortable** treating with no further testing (e.g. 0.8)	
Probability of disease at or below which you would be **comfortable** managing with no futher treatment or testing (e.g. 0.25)	



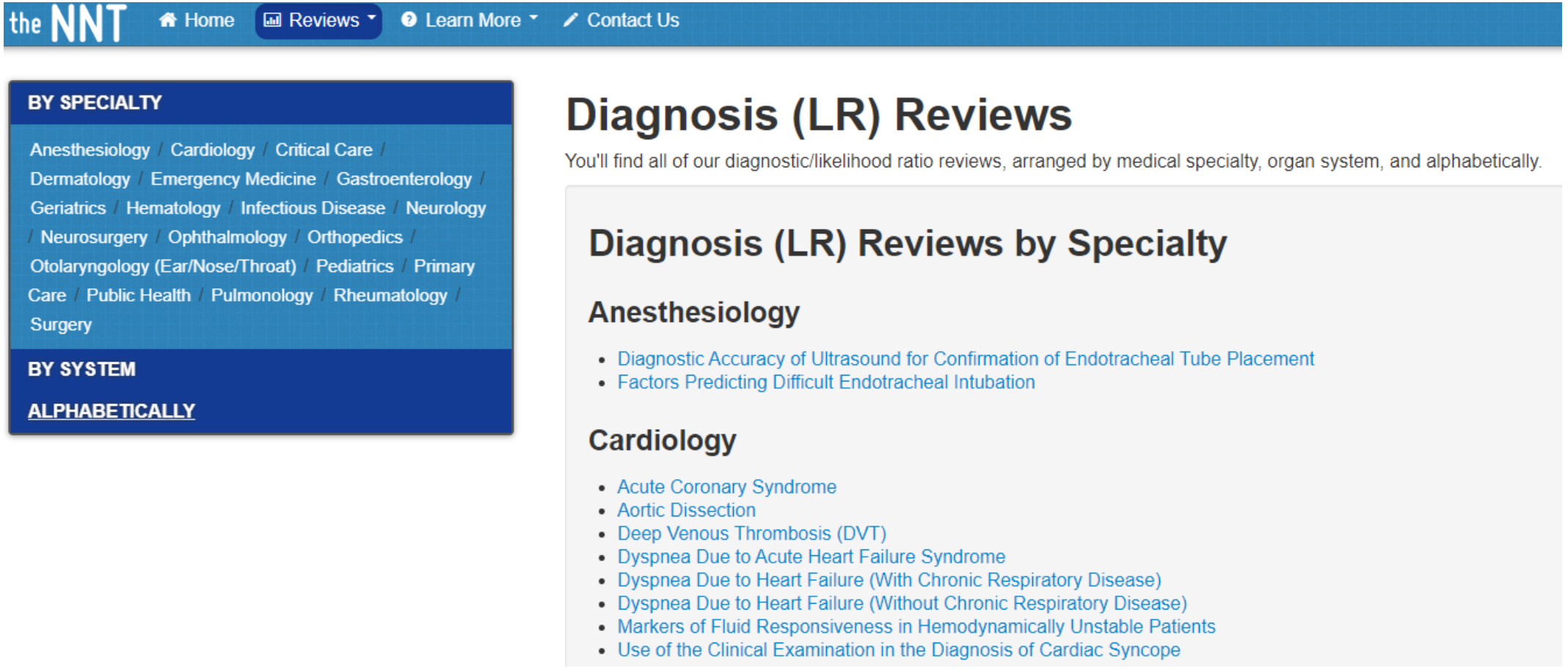
Soft online - Evidence-Based Medicine Toolbox

- https://ebm-tools.knowledgetranslation.net/calculator/diagnostic/



Reviews for diagnostic test

- https://www.thennt.com/home-lr/



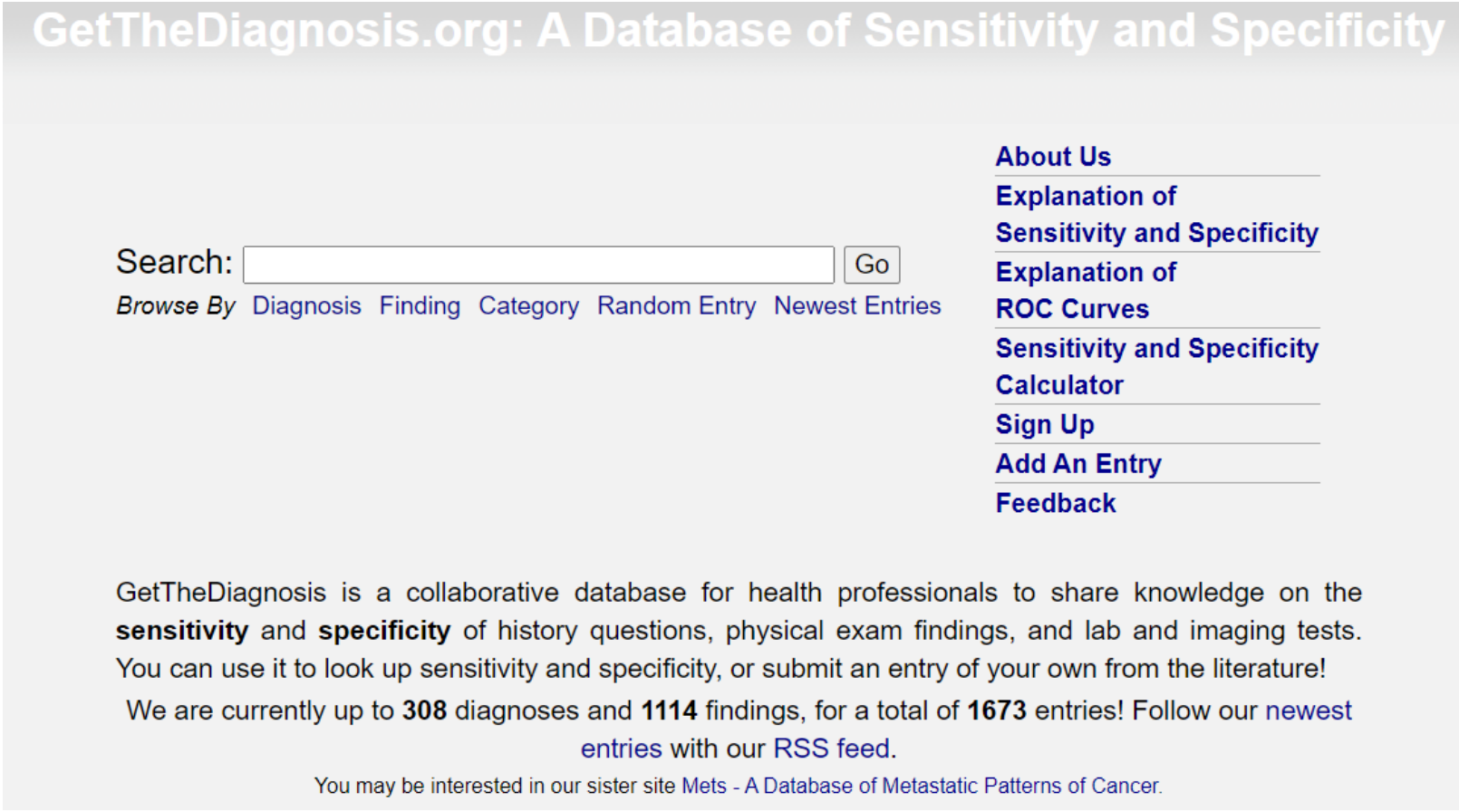
Positive Findings (Patient Has This)

Symptoms	Increased Disease Probability (Positive Likelihood Ratio)
Strep exposure in the past 2 weeks	1.9× (1.3-2.8)
Myalgias	1.4× (1.1-1.7)
No cough	1.1-1.7
History of sore throat	1.0-1.1
Reported fever	0.97-2.6
Headache	0.81-2.6
Nausea	0.76-3.1
Duration <3d	0.72-3.5

Signs on Physical Exam	Increased Disease Probability (Positive Likelihood Ratio)
Tonsillar exudates	3.4× (1.8-6.0)
Pharyngeal exudates	2.1× (1.4-3.1)

Knowledge about diagnostic tests

- http://getthediagnosis.org/



Knowledge about diagnostic tests

Acute Streptococcal Pharyngitis: Sensitivity and Specificity

Introduction: None written.

[Edit Diagnosis] [Merge dx] [Add prevalence]

Tags: Infection *Tag this Diagnosis.*

Differential Diagnoses include: Kawasaki Disease, Viral Pharyngitis

The sensitivity and specificity of findings for Acute Streptococcal Pharyngitis are listed below. See the left navigation bar to change the display.

Sensitive and Specific Findings

Finding	*Sensitivity*	*Specificity*	*Comments, Study*
Throat Culture	100%	100%	**Study:** JAMA. 2004 Apr 7;291(13):1587-95. PMID: 15069046
Modified Centor Criteria	85%	92%	=>2 criteria: • history of objective fever (>38C) • exudative pharyngitis • lack of cough • tender cervical LAD • +1 for <=15 years old, -1 for >45 years old **Differential Diagnosis:** Viral Pharyngitis **Study:** CMAJ. 2000 Oct 3;163(7):811-5. PMID: 11033707 rather similar results also in JAMA. 2004 Apr 7;291(13):1587-95. PMID: 15069046
Rapid Streptococcal Antigen Test *Duplicate*	91.1%	89%	**Study:** no study specified.

Specific Findings

Finding	*Sensitivity*	*Specificity*	*Comments, Study*
Rapid Streptococcal Antigen Test *Duplicate*	83%	99%	**Study:** JAMA. 2004 Apr 7;291(13):1587-95. PMID: 15069046

Thank you!


WARNING: Patient will be charged extra for annoying the doctor with any self-diagnosis gotten off the Internet.
K.LEMIEUX 1-3
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