

Statistics, Probability and Diagnostic Medicine

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Sponsored by the Clinical and Translational Science Institute (CTSI) and the Department of Population Health / Division of Biostatistics



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Outline

- Define measures of diagnostic accuracy
- Statistics for qualitative tests



Observed Data

• Suppose the observed data are organized as shown:

Observed Data

 Suppose the observed data are organized as shown:



Accuracy Measurements

 The ability to identify the presence or absence of the disease/condition

- Sensitivity and specificity

 The ability to predict the presence or absence of the disease/condition

 Positive predictive value (PPV) and negative predictive value (NPV)



Discriminating Accuracy

• Sensitivity: probability of a person with the disease having a positive test result

 $Sensitivity = \frac{TP}{D+}$

 Specificity: probability of a person without the disease having a negative test result

$$Specificity = \frac{TN}{D}$$



Predictive Accuracy

- Positive predictive value (PPV): probability of a person with a positive test result having the disease
- Negative predictive value (NPV): probability of a person with a negative test result being disease-free

NPI

How good is the liver scan at diagnosis of abnormal pathology? (Altman and Bland, 1994)

		Pathology		Row
		Abnormal (+)	Normal (-)	total
Test Results	Abnormal (+)	231	32	
Te Res	Normal (-)	27	54	
Colum	n Total			

How good is the liver scan at diagnosis of abnormal pathology? (Altman and Bland, 1994)



		Pathology		Row	
		Abnormal (+)	Normal (-)	total	
Test Results	Abnormal (+)	231	32	263	
Te Res	Normal (-)	27	54	81	
Col	umn Total	258	86	344	

 $Specificity = \frac{\overline{TN}}{D} = \frac{54}{86} = 0.63$

Interpretation: In this study, 63% of patients with normal pathology has normal scan, i.e., the scan correctly identifies normal pathology 63% of the time.

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		Pathology		Row
		Abnormal (+)	Normal (-)	total

Interpretation: In this study, 88% of patients with abnormal scan has abnormal pathology, i.e., the scan correctly predicts abnormal pathology 88% of the time.

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Disease Prevalence

- *Prevalence*: the probability of a person in a population having the disease. In a randomized study (not case-control), $\frac{D}{Prevalence} = \frac{D}{m}$
- Liver scan example

$$Prevalence = \frac{258}{344} = 0.75$$

• *Prevalence* affects *PPV* and *NPV*



Prevalence

		Disease / Condition		Row
		Present	Absent	total
lest sults	Positive	TP	FP	T+
Tes Resu	Negative	FN	TN	T-
Colum	n Total	D+	D-	Ν

- Sensitivity is calculated using only the group with disease
- Specificity is calculated using only the group without disease

Prevalence

		Disease / Condition		Row
		Present	Absent	total
lest sults	Positive	TP	FP	T+
Tes Resu	Negative	FN	TN	T-
Column Total		D+	D-	Ν

- *PPV* and *NPV* are calculated across the groups with and without disease
- Specific to the performance of a test on the study population

Prevalence

Population A		Pathology		Row
		(+)	(-)	total
st ults	(+)	231	32	263
Test Results	(-)	27	54	81
Column Total		258	86	344

Population B		Pathology		Row
		(+)	(-)	total
st Ilts	(+)	231	1184	1415
Test Results	(-)	27	1998	2025
Column Total		258	3182	3440

Population	А	В
Sensitivity	90%	90%
Specificity	63%	63%
Prevalence	75%	7.5%
PPV	88%	16%
NPV	67%	99%

- Given the same test, the rarer the disease the lower *PPV* and the higher *NPV*.
- High sensitivity required for a high PPV in rare diseases

Likelihood Ratio

- LR: the ratio of the probability of having a test result given the disease to the probability of having the same result without the disease
- Positive LR: reference = 1, high positive LR means test is useful in detecting condition

$$LR = \frac{TP / D +}{FP / D -} = \frac{sensitivity}{1 - specificity}$$



Likelihood Ratio

Receiver-Operating Characteristic (ROC)

- Used for tests with quantitative results
- Compare diagnostic tests
- Choose the optimal cut point to distinguish "abnormal" from "normal"
- For each cut point, calculate the sensitivity and specificity



CT scan example from Hanley and McNeil, 1982

		Disease Status		Row
		Abnormal	Normal	total
	Definitely abnormal (5)	33	2	35
	Probably abnormal (4)	11	11	22
2	Unsure (3)	2	6	8
	Probability normal (2)	2	6	8
	Definitely normal (1)	3	33	36
Сс	olumn total	51	58	109

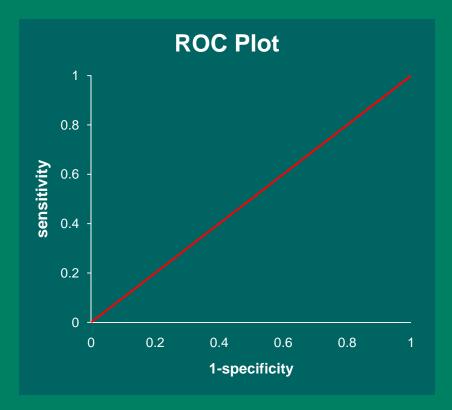
sensitivity	specificity	1- <i>specificity</i>
0.65	0.97	0.03
0.86	0.78	0.22
0.90	0.67	0.33
0.94	0.57	0.43

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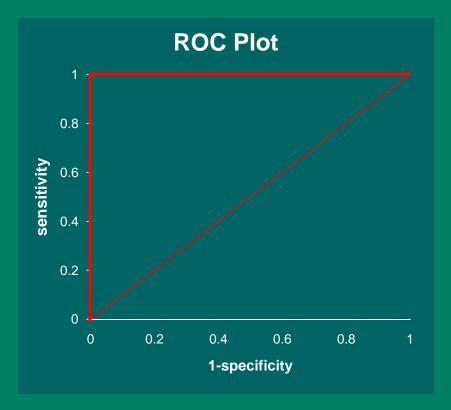
Receiver-Operating Characteristic (ROC)

• Reference line - useless test





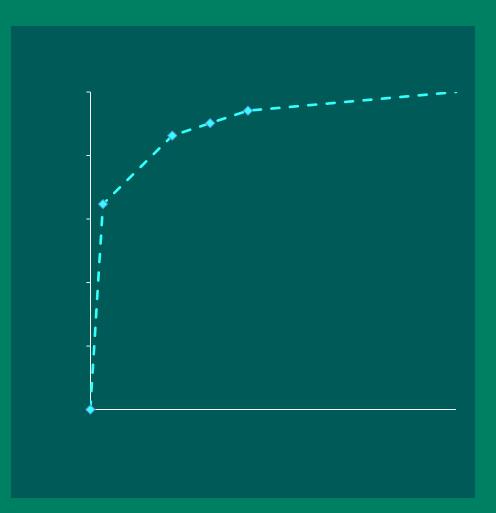
• Test with perfect discrimination



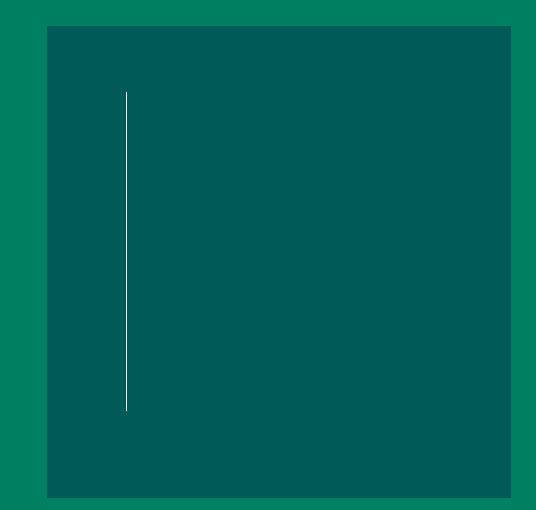




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- Area under the ROC curve gives the global assessment of performance of the test.
- It is the probability of a random person with the disease has a higher (more positive) value than a random person without the disease.
- For an uninformative test, the area under the ROC curve = 50%.

 Having determined a good test, pick the best cut point

• Consider:

- Cost of false diagnose
- Prevalence of disease

Summary

- Sensitivity and specificity are properties of diagnostic tests
- *PPV* and *NPV* are predictive measures and affected by *prevalence*
- *LR* used to adjust post-test probability
- Use ROC curves and AUCs to compare performance of multiple tests
- Optimal cut point based on ROC curve depends on costs of false diagnoses and disease prevalence

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Resources

- The Clinical and Translation Science Institute (CTSI) supports education, collaboration, and research in clinical and translational science: <u>www.ctsi.mcw.edu</u>
- The Biostatistics Consulting Service provides comprehensive statistical support <u>http://www.mcw.edu/biostatsconsult.htm</u>



Free drop-in consulting

- MCW/Froedtert/CHW:
 - Monday, Wednesday, Friday 1 3 PM @ Froedtert Pavilion, Room #L777A (TRU Offices)
 - Tuesday, Thursday 1 3 PM @ Health Research Center, H2400
- VA: 1st and 3rd Monday, 8:30-11:30 am
 - VA Medical Center, Building 111-B-5423
- Marquette: 2nd and 4th Monday, 8:30-11:30 am
 - Olin Engineering Building, Room 338D



- The best cut point can be chosen by minimizing the expected costs.
- It is affected by:
 - Cost of false diagnoses
 - Prevalence of disease

