Statistics in Evidence Based Medicine II

Lecture 3: Summary Statistics for Diagnostic Tests

Rizwana Rehman, PhD
Regional Statistician
Southeast Epilepsy Centers of Excellence
Durham VA Medical Center, Durham NC
Rizwana.Rehman@va.gov
(919)286-0411 ext: 5024

Audio Information: Dial 1-855-767-1051
Conference ID 61304911

Epilepsy Centers of Excellence
SOUTHEAST

Text Books

- **Main: Statistics at Square One 12th edition (2010)**

  M J Campbell & T D V Swinscow

  http://www.phsource.us/PH/EPI/Biostats/

- **Secondary: Basic and Clinical Biostatistics (2004)**

  Beth Dawson, Robert G. Trapp

  http://www.accessmedicine.com/resourceTOC.aspx?resourceID=62

- For more information, program materials, and to complete evaluation for CME credit visit

  www.epilepsy.va.gov/Statistics

Audio Information: Dial 1-855-767-1051
Conference ID 61304911

Overview

- Vocabulary
  - Prevalence
  - Sensitivity and Specificity
  - Positive predictive value
  - Likelihood ratios
- Comparison
- Reading an article about a diagnostic test
- Reporting the results for publication

Evaluation of a Diagnostic Test

- A gold standard is needed to evaluate the performance of a test.
- Gold standard or reference standard is a definite tool that identifies if a person has a particular condition.
- Why not use gold standard all the time?
  - Expensive
  - Difficult to administer

Binary Outcomes

		Gold Standard		
		Positive	Negative	
Diagnostic test	Positive	a	b	
	Negative	c	d	
	Total	**a+c**	**b+d**	**n=a+b+c+d**

a=number of true positives, d=number of true negatives.
c= number of false negatives, b=number of false positives

Example of Binary Outcomes

		Diagnosis of Generalized Anxiety Disorder (GAD) by Mental Health Professionals		
		Positive	Negative	
GAD 2	≥3(+ve)	63	152	215
	<3(-ve)	10	740	750
	Total	73	892	965

Statistics At Square One 11th edition

Prevalence of a Disease

Prevalence is the proportion of people diagnosed by the gold standard.

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

$$\text{Prevalence}=73/965=0.076=7.6\%$$

		Diagnosis by Mental Health Professional		
		Positive	Negative	
GAD 2	≥3(+ve)	63	152	215
	<3(-ve)	10	740	750
	Total	73	892	965

Sensitivity of the Diagnostic Test

Given a person has the disease, sensitivity is the proportion of people who have a positive diagnostic test.

Sensitivity=a/(a+c)

Sensitivity=63/73=0.86=86%

		Diagnosis by Mental Health Professional		
		Positive	Negative	
GAD 2	≥3(+ve)	63	152	215
	<3(-ve)	10	740	750
	Total	73	892	965

Specificity of a Diagnostic Test

Given a person does not have the disease, specificity is the proportion of people who have a negative diagnostic test.

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

$$\text{Specificity} = 740/892 = 0.83 = 83\%$$

		Diagnosis by Mental Health Professional		
		Positive	Negative	
GAD 2	≥3(+ve)	63	152	215
	<3(-ve)	10	740	750
	Total	73	892	965

Useful Mnemonic

- SeNsitivity=1-proportion of false negatives (*n* in each sides)
- SPecificity=1-proportion of false positives (*p* in each side)

Things to Remember

- For a test with high sensitivity, a negative result rules out the disease.

  mnemonic=SnNout

- For a test with high specificity, a positive result rules in the disease.

  mnemonic=SpPin

Positive Predictive Value

Proportion of truly positive cases among the positive cases detected by the test.

"If I have a positive test, what are the chances I have the disease?"

Positive Predictive Value=*PPV*=a/(a+b)

PPV=63/215=0.29=29%

		Diagnosis by Mental Health Professional		
		Positive	Negative	
GAD 2	≥3(+ve)	63	152	215
	<3(-ve)	10	740	750
	Total	73	892	965

Negative Predictive Value

Proportion of truly negative cases among the negative cases detected by the test.

"If I have a negative test, what are the chances I don't have the disease?"

Negative Predictive Value=*NPV*=d/(c+d)

NPV=740/750=0.99=99%

		Diagnosis by Mental Health Professional		
		Positive	Negative	
GAD 2	≥3(+ve)	63	152	215
	<3(-ve)	10	740	750
	Total	73	892	965

Comparison of Sensitivity, Specificity and Positive Predictive Value

- Sensitivity and specificity are independent of prevalence of a disease.
- Positive predicative value depends upon prevalence. Increasing the prevalence increases the positive predictive value.

Receiver Operating Characteristics Curve (ROC)

- For tests that produce results on continuous or ordinal scale, we need a cut-off value to calculate sensitivity and specificity.
- We plot a graph of sensitivity vs. 1-specificity for different cut-off values.
- ROC curves are used to compare the results of different diagnostic tests.

Likelihood Ratios

- A single summary statistic
- Positive Likelihood Ratio (LR+)
  - (prob. of positive test given the disease)/(prob. of positive test without the disease)=sensitivity/(1-specificity)
- Negative Likelihood Ratio (LR-)
  - (prob. of negative test given the disease)/(prob. of negative test without the disease)=(1-sensitivity)/specificity

Likelihood Ratios

$$LR(+)=[a/(a+c)]/[b/(b+d)]$$
$$LR(-)=[c/(a+c)]/[d/(b+d)]$$

		Gold Standard		
		Positive	Negative	
Diagnostic test	Positive	a	b	
	Negative	c	d	
	Total	**a+c**	**b+d**	**n=a+b+c+d**

Example of Likelihood Ratios

LR(+)=0.86/(1-0.83)=5.06

A high GAD2 score is 5.1 times as likely to occur in a patient with, as opposed to a patient without, GAD.

LR(-)=(1-0.86)/0.83=0.17

		Diagnosis by Mental Health Professional		
		Positive	Negative	
GAD 2	≥3(+ve)	63	152	215
	<3(-ve)	10	740	750
	Total	73	892	965

Advantages of Likelihood Ratio

Knowing the likelihood of a disease gives a way to estimate how likely is someone to have a disease, if one knows the prevalence or probability of the disease before the test. The LR indicates by how much a given diagnostic test result will raise or lower the pretest probability of the target disease.

A Rough Guide for Interpretation of LR from Pretest to Posttest Probabilities

- >10 or <0.1 imply conclusive change from pretest probability to post test probability.
- Between 5 and 10 and 0.1 to 0.2 imply moderate shifts.
- Between 2 and 5 and 0.5 to 0.2 generate small changes.
- Between 1 and 2 and 0.5 to 1 rarely alter the probability

User's Guide to the Medical Literature :III. How to Use an Article About a Diagnostic Test: B. What are the Results and Will They Help Me in Caring for My Patients. JAMA 1994

http://synergymedical.org/med_program/ross/EpiBiostats/JAMA_Users_Guide-Diagnosis_PartII.pdf

Bayes' Theorem

- Posttest odds=pretest odds × LR
  - Pretest odds=73/892=0.082
  - LR(+)=5.06
  - Posttest odds=5.06 × 0.082=0.4149
- Posttest probability=Posttest odds/(1+Posttest odds)
- Posttest Probability=0.4149/1.4149=0.293=29%
- Posttest probability is the Positive Predictive Value

		Diagnosis by Mental Health Professional		
		Positive	Negative	
GAD 2	≥3(+ve)	63	152	215
	<3(-ve)	10	740	750
	Total	73	892	965

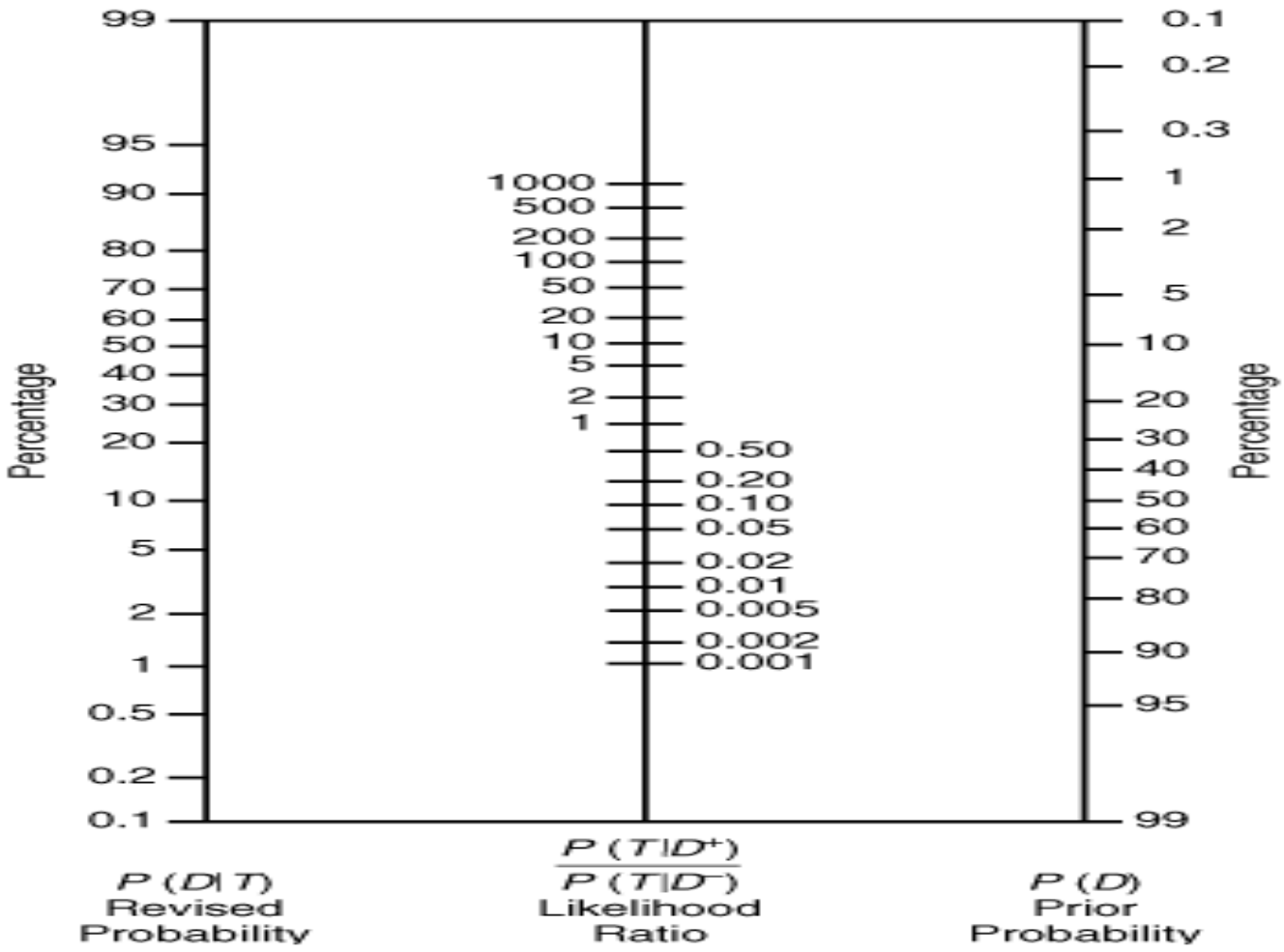
Another Example: PIOPED Study

	Pulmonary Embolism				
	Present		Absent		
V/Q Scan Results	No.	Proportion	No.	Proportion	Likelihood Ratios
High Probability	102	102/251=0.408	14	14/630=0.022	18.3
Intermediate Probability	105	105/251=0.418	217	217/630=0.344	1.2
Low Probability	39	39/251=0.155	273	273/630=0.433	0.36
Normal/near normal	5	5/251=0.020	126	126/630=0.200	0.10
Total	251		630		

User's Guide to the Medical Literature :III. How to Use an Article About a Diagnostic Test: B. What are the Results and Will They Help Me in Caring for My Patients. JAMA 1994

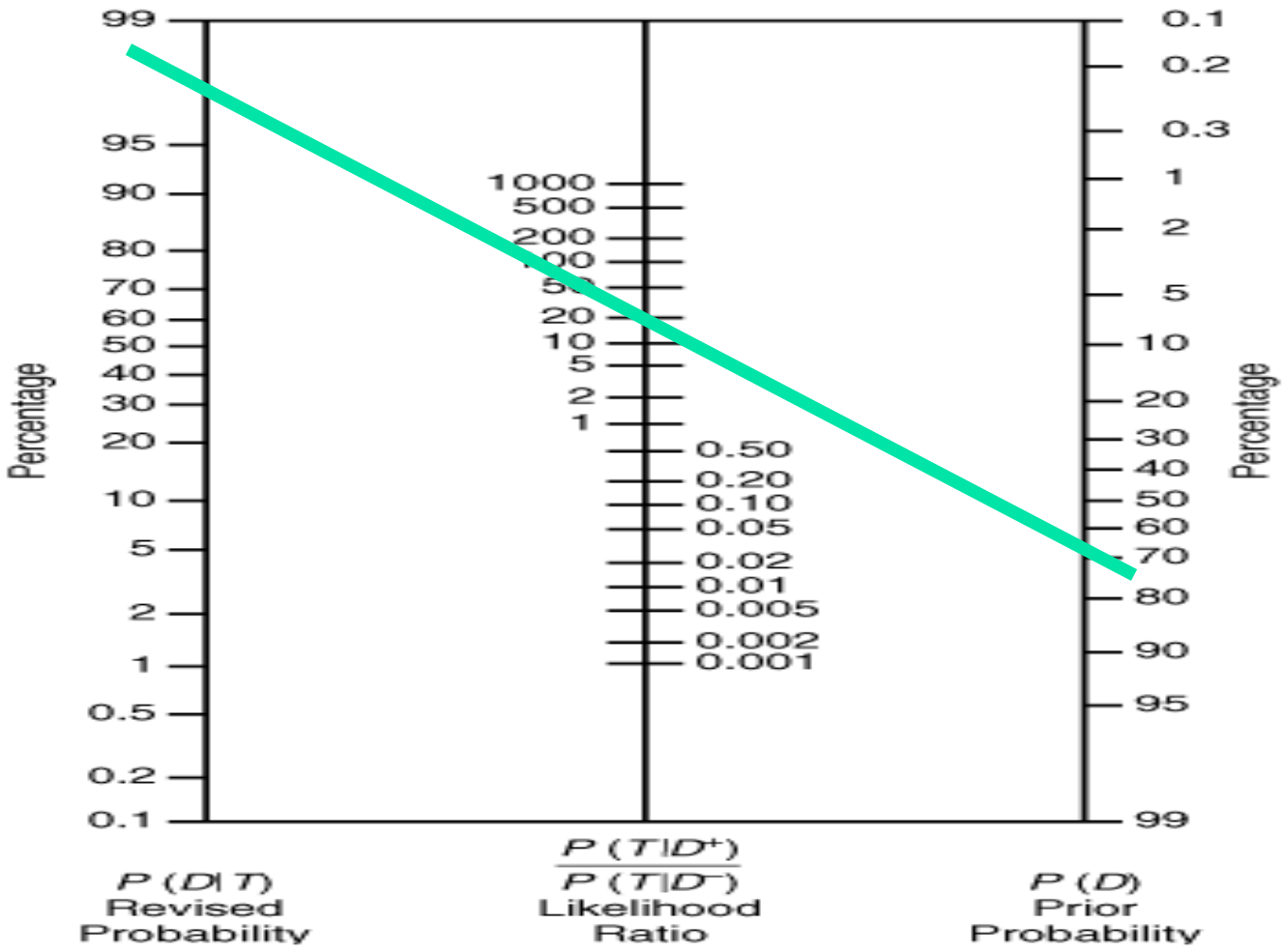
http://synergymedical.org/med_program/ross/EpiBiostats/JAMA_Users_Guide-Diagnosis_PartII.pdf

Fagan's Nomogram



Source: Dawson B, Trapp RG: *Basic & Clinical Biostatistics*, 4th Edition: http://www.accessmedicine.com

Fagan's Nomogram for PIOPED Example



Source: Dawson B, Trapp RG: *Basic & Clinical Biostatistics*, 4th Edition: http://www.accessmedicine.com

Computing Sensitivity and Specificity

Table 5.—Comparison of the Results of Diagnostic Test (Ventilation-Perfusion Scan) With the Result of Reference Standard (Pulmonary Angiogram) Assuming Only High-Probability Scans Are Positive (Truly Abnormal)*

	Angiogram	
Scan Category	Pulmonary Embolus Present	Pulmonary Embolus Absent
High probability	102	14
Others	149	616
Total	251	630

*Sensitivity, 41%; specificity, 98%; likelihood ratio of a high-probability test result, 18.3; likelihood ratio of other results, 0.61.

Table 5. Comparison of the Results of Diagnostic Test (Ventilation-Perfusion Scan) With the Result of Reference Standard (Pulmonary Angiogram) Assuming Only High-Probability Scans Are Positive (Truly Abnormal)

Changing Threshold of Positive vs. Negative

Table 6.—Comparison of the Results of Diagnostic Test (Ventilation-Perfusion Scan) With the Result of Reference Standard (Pulmonary Angiogram) Assuming Only Normal/Near-Normal Scans Are Negative (Truly Normal)*

Scan Category	Angiogram: Pulmonary Embolus Present	Angiogram: Pulmonary Embolus Absent
High, intermediate, and low probability	246	504
Near normal/normal	5	126
Total	251	630

*Sensitivity, 98%; specificity, 20%; likelihood ratio of high, intermediate, and low probability, 1.23; likelihood ratio of near normal/normal, 0.1.

Table 6. Comparison of the Results of Diagnostic Test (Ventilation-Perfusion Scan) With the Result of Reference Standard (Pulmonary Angiogram) Assuming Only Normal/Near-Normal Scans Are Negative (Truly Normal)

Comparison of Likelihood Ratios with Sensitivity and Specificity

- With sensitivity and specificity we loose important information.
- We have to calculate sensitivity and specificity with every cut point.
- For likelihood ratio method just need to know one number.
- Likelihood ratios can be used on individual's level.

Assumptions

All summary statistics are based upon:

- The diseases or diagnoses being considered are mutually exclusive and include the actual diagnosis.
- The result of each diagnostic test are independent from the results of all other tests.

Reading and Reporting Diagnostic Tests

- Always report confidence intervals of measures.
- Always report the prevalence of the condition.
- Report how the subjects were selected.
- Question whether treatment would be changed depending on the results of a test.

Helpful Articles

- Users' Guides to the Medical Literature: III. How to Use an Article About a Diagnostic Test: A. Are the Results of the Study Valid?

http://www-archive.thoracic.org/sections/meetings-and-courses/mecor-courses/resources/level2/DiagnosisA.pdf

- User's Guide to the Medical Literature :III. How to Use an Article About a Diagnostic Test: B. What are the Results and Will They Help Me in Caring for My Patients. JAMA 1994

http://synergymedical.org/med_program/ross/EpiBiostats/JAMA_Users_Guide-Diagnosis_PartII.pdf

- Statistical Guidance on Reporting Results from Studies Evaluating Diagnostic Tests
  http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm071287.pdf

Thank you!

Questions/Comments

Rizwana.Rehman@va.gov

(919) 286-0411 ext: 5024

For more information, program materials, and to complete evaluation for CME credit visit

www.epilepsy.va.gov/Statistics