

# Evidence-Based Medicine

## Likelihood Ratios

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"I propose we leave math to the machines and go play outside." Calvin

### Case Presentation

A 28 year-old medical resident comes to see you to discuss her feelings of being overwhelmed. She states that she feels tired all of the time and has little interest in doing things outside of her ward rotation. She spends most of the time on her days off sleeping or doing laundry. She eats poorly and has stopped exercising. She finds it hard to concentrate on simple things like reading journal articles or watching golf on television. Her friends have noticed that she is talking and moving very slowly (Trumboism). She denies suicidal ideation. She wonders if she has major depression and would be eligible for disability pay and some time off.

What is your pretest probability that she has major depression?

Having recently perused a copy of JGIM (J Gen Intern Med 2001; 16:606-613), you recall a study by Kroenke et al. of the PHQ-9 Depression severity measure and you decide to try it out.

How will your knowledge of likelihood ratios help you to sort out her problem?

**Definition:** A Likelihood Ratio is the likelihood that a given test result would be expected in a person with a particular disorder compared to the likelihood that the same test result would be expected in a person without that disorder.

	Disease +	Disease -	
Test +	a	b	a + b
Test -	c	d	c + d
	a + c	b + d	a + b + c + d

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

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

The likelihood for a positive test LR (+) is easily calculated as follows:

$$\text{LR (+)} = \text{sensitivity}/(1-\text{specificity})$$

Similarly, the likelihood for a negative test LR (-) can be derived as follows:

$$\text{LR (-)} = (1 - \text{sensitivity})/\text{specificity}$$

Let's go over an example to make things more clear. From the article by Kroenke et al. looking at the PHQ, we can calculate Likelihood ratios for each category of severity.

Table 2. Distribution of PHQ-9 Scores According to Depression Diagnostic Status\*

Level of Depression Severity, PHQ-9 Score	Major Depressive Disorder (N = 41)	Other Depressive Disorder (N = 65)	No Depressive Disorder (N = 474)
	n (%)	n (%)	n (%)
Minimal, 0-4	1 (2.4)	8 (12.3)	348 (73.4)
Mild, 5-9	4 (9.8)	23 (35.4)	93 (19.6)
Moderate, 10-14	8 (19.5)	17 (26.1)	23 (4.9)
Moderately severe, 15-19	14 (34.1)	14 (21.5)	8 (1.7)
Severe, 20-27	14 (34.1)	3 (4.6)	2 (0.4)

\* Depression diagnostic status was determined in 580 primary care patients by having a mental health professional who was blinded to the PHQ-9 score administer a structured psychiatric interview.

For the most severe category ( PHQ = 20-27), the likelihood ratio is calculated as the percentage of people with major depression scoring in the severe category divided by the percentage of people without depression scoring in the severe category.

$$LR = 14/41 \div 5/539 = 36.80$$

Diagnostic test result (PHQ)	Target disorder – Major Depression (based on reference standard)		Likelihood Ratio
	Present n	Absent n	
20 – 27 (severe)	14	5	36.80
15 – 19 (mod. severe)	14	22	8.37
10 – 14 (moderate)	8	40	2.63
5 – 9 (mild)	4	116	0.45
0 – 4 (minimal)	1	356	0.04
Totals	41 patients with major depression	539 patients without major depression	580 patients in the study

For the above study, it would be more useful to group findings according to scores above or below a certain level in order to create a simple positive or negative test with pre-defined positive and negative likelihood ratios.

If we set the bar for diagnosing major depression at a score of  $\geq 10$ , then the test would have the following characteristics:

Sensitivity =  $TP/TP + FN = 36/41 = 88\%$   
 Specificity =  $TN/TN + FP = 472/539 = 88\%$   
 $LR(+) = \text{Sensitivity}/1 - \text{Specificity} = 0.88/(1 - 0.88) = 7.33$   
 $LR(-) = 1 - \text{Sensitivity}/\text{Specificity} = (1 - 0.88)/0.88 = 0.14$

Diagnostic test result PHQ	Target disorder - Depression (based on reference standard)		Likelihood Ratio
	Present n	Absent n	
Positive = PHQ $\geq 10$	36 TP	67 FP	7.33 LR(+)
Negative = PHQ $< 10$	5 FN	472 TN	0.14 LR(-)
Totals	41 TP + FN	539 FP + TN	

Similarly, if we set the bar higher (PHQ  $\geq 15$ ), then our parameters change slightly with decreased sensitivity ( $28/41 = 68\%$ ) and increased specificity ( $512/539 = 95\%$ ) with a stronger LR(+) and slightly weaker LR(-).

Diagnostic test result PHQ	Target disorder - Depression (based on reference standard)		Likelihood Ratio
	Present n	Absent n	
Positive = PHQ $\geq 15$	28	27	13.6
Negative = PHQ $< 15$	13	512	0.34
Totals	41	539	

**So now that I am an expert at calculating likelihood ratios, how does this help me?**

The likelihood ratio, when combined with your pretest probability can then help you to estimate your post-test probability of the condition that you are considering.

For the example considered above, refer to the nomogram on the next page. If your pretest probability for the resident having major depression is 50%, then a PHQ score of 10 would increase your post-test probability of depression to approx. 86%. If she scored 15 or higher, then the post-test probability increases to about 93%. For a negative result (PHQ < 10), your pretest probability for major depression would then decrease to somewhere between 10 and 20%. Thus the PHQ becomes a very helpful instrument in sorting out the situation.

Just as important, the likelihood ratios for given conditions have been established for many conditions and tests and can be calculated from other studies that you come across. This knowledge can be instrumental in your decision on whether or not to order a test in the first place.

For example, when considering a diagnosis of DVT, we often group patients into high, intermediate and low risk categories based on our clinical suspicions. An understanding of differing test characteristics will help you in ordering the proper test. For a patient who is at very low risk, one might consider obtaining a d-dimer test with a LR(-) of 0.09 prior to ordering an ultrasound. If negative, this might provide sufficient evidence that a DVT is not present and would obviate the need for further testing such as ultrasound.

TARGET DISORDER	SIGN, TEST, SYMPTOM	REFERENCE STANDARD	PATIENT, POPULATION, SETTING	LR+ (95% CI)	LR- (95% CI)
Deep venous thrombosis (DVT) <sup>1</sup>	Compression ultrasound (USS) in all patients	Venography	Hospital patients	39	0.23
	USS in high risk	Venography	Hospital patients	∞	0.09
	USS in moderate risk	Venography	Hospital patients	53	0.39
	USS in low risk	Venography	Hospital patients	24	0.34
DVT <sup>2</sup>	Homan's sign (positive if no dorsiflexion of the foot on squeezing the calf muscles)		Hospital patients	1.5	0.6
Deep venous thrombosis (DVT) <sup>3</sup>	D-dimer analysis alone	Duplex ultrasound scanning	Patients with suspected DVT. Set in a university hospital in Basel, Switzerland.	2.0	0.3
	D-dimer analysis plus clinical assessment			1.8	0.09

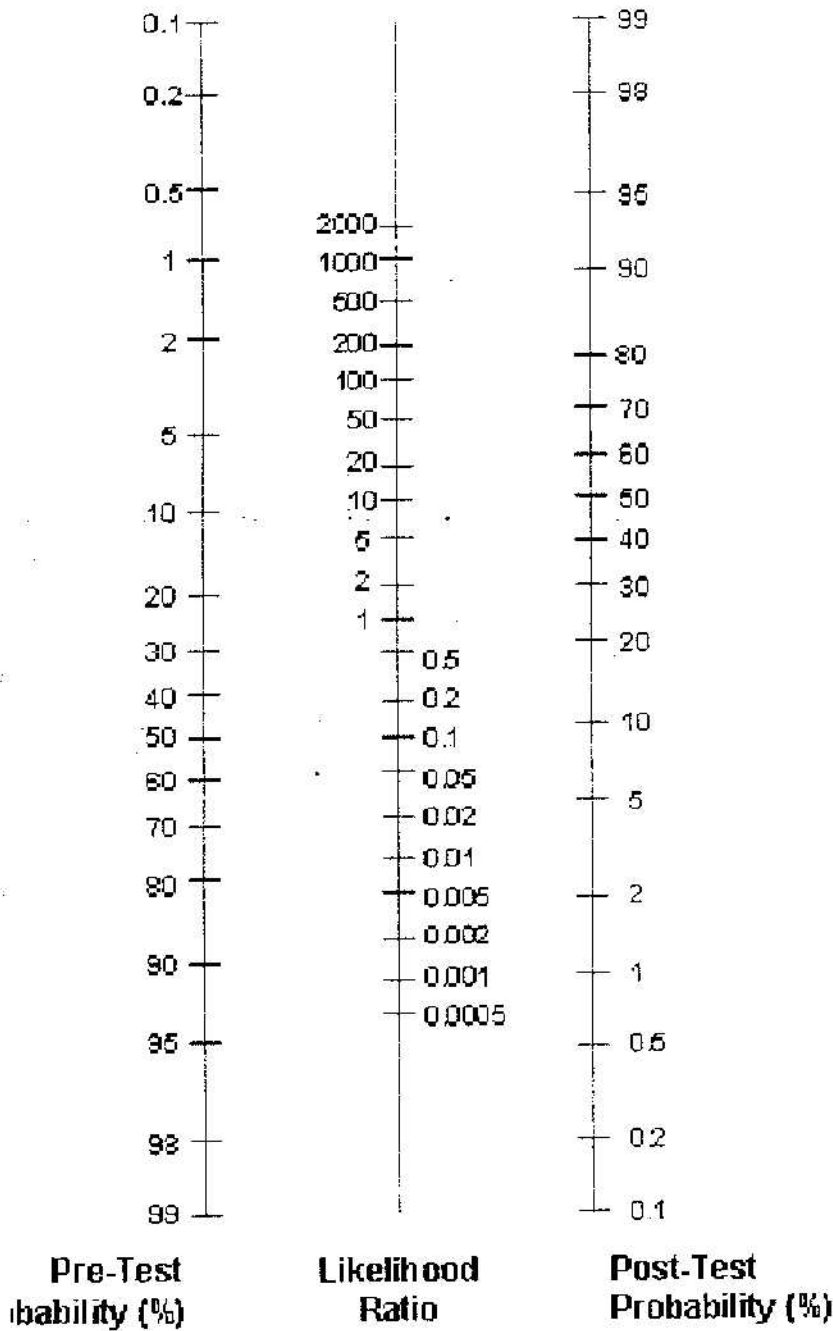
The Centre for Evidence Based medicine is a helpful resource that is web accessible and free. It contains a list of diagnostic tests for which likelihood ratios have been established (as above). It also offers helpful devices such as the nomogram pictured on the next page and stats calculators that do the math for you. Check them out at [www.cebm.utoronto.ca](http://www.cebm.utoronto.ca).

**“It was clear as mud, but it cover de ground, and de confusion made me brain go round.”**

**Harry Belafonte, The Piaba song**

Nomogram for converting Pre-test Probabilities to Post-test Probabilities for a diagnostic test result with a given Likelihood Ratio.

([http://www.cebm.net/likelihood\\_ratios.asp](http://www.cebm.net/likelihood_ratios.asp))



$$PPV = \frac{TP}{TP + FP}$$