34 Use of Risk Factors to Guide Treatment

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Introduction

Accurate, generalizable prediction tools are an important aspect of consistent, high-quality patient care. Risk calculators and clinical decision rules are now common in diagnosis, prognosis, and treatment of disease. Terminology and mathematics behind clinical testing is sometimes complex, but there are a few simple ideas that can be incorporated into everyday practice to improve understanding of literature and enhance patient care. Diagnostic test accuracy is usually summarized by *sensitivity*, *specificity*, *positive predictive value*, and *negative predictive value*. Although less commonly used, *likelihood ratios* are a more clinically relevant measure of test performance and can be applied to an individual patient's test results to guide care. Multiple tests can be combined using statistical models to generate *prediction rules* or *clinical risk calculators* that provide prognostic information about diagnosis or treatment. This chapter will briefly review the terminology and mathematics behind test accuracy, the use of diagnostic tests to guide clinical practice, and the creation and use of risk calculators [1].

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Diagnostic Tests: Sensitivity, Specificity, and Likelihood Ratios

One of the most important early applications of statistics to biomedical science was in the assessment of test performance: when a patient has a disease, how often is the test positive, and when the patient does not have the disease, how often is it negative? *Sensitivity* is the probability that a test will be positive given the presence of disease (helps to *rule out* disease). (Fig. 34.1). *Specificity* is the probability that the test will be negative in the absence of disease (helps to *rule in* disease) [2]. These measures are particularly useful because they are characteristics of the test, and are mathematically independent of the population they are applied to. *Positive predictive value* and *negative predictive value* are the respective probabilities that a positive or negative test result came from a person with (or without) the disease, but they are dependent on the prevalence in the population that they are applied to and have little direct clinical utility. A *likelihood ratio* (LR) is population-independent measure of test performance calculated from the sensitivity and specificity using Bayes' Theorem. Every test has a positive LR for positive results and a negative LR for negative results. (Fig. 34.1). The major advantage of LRs is that when the patient's pre-test probability of disease is estimable or known, the appropriate LR can be used to calculate the patient's post-test probability of disease. Online calculators and simple nomograms are available

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		Disease +	Disease -
Test	+	**A** (TP)	**B** (FP)
	-	**C** (FN)	**D** (TN)

Name	Formula	Population-dependent?
Sensitivity	**A/(A+C)**	No
Specificity	**D/(B+D)**	No
Positive Predictive Value	**A/(A+B)**	Yes
Negative Predictive Value	**D/(D+C)**	Yes
Positive Likelihood Ratio	**Sensitivity/(1-Specificity)**	No
Negative Likelihood Ratio	**(1-Sensitivity)/Specificity**	No

TP = true positives
FP = false positives
TN = true negatives
FN = false negatives

Fig. 34.1 Test performance parameters for a binary test: sensitivity, specificity, positive predictive value, negative predictive value, positive likelihood ratio, and negative likelihood ratio

to assist with converting pre-test to post-test probabilities using LRs [3] (Fig. 34.2).

Clinical Risk Calculators and Decision Guides

Clinical risk calculators and decision guides are mathematical models based on patient data that are used to provide prognostic information to doctors and patients and assist in treatment decisions. A clinical risk calculator is the principle of a multivariable model in reverse: instead of using the experience of multiple patients to estimate the risk associated with particular exposures, individual patient exposures are entered into a model, and the patient's individual risk of some outcome, e.g., opioid dependence, is calculated [4]. Clinical decision guides utilize a similar strategy to identify patients that will benefit from a particular treatment, e.g., cervical facet joint pain [5]. Risk calculators and clinical decision guides often assign "points" to each individual risk factor and the total number of points is associated with a particular risk. This strategy increases usability and comprehensibility at the cost of some precision. The validity and accuracy of risk calculators and clinical decision guides is limited by the source population and computational methods used, which may or may not be apparent to the user. Subjective measures of exposure and outcome, common in chronic pain medicine, may also limit validity and accuracy. Models openly published in peer-reviewed journals are preferable to those whose formulae are kept secret.

Impact Studies

Verification is an important part of diagnostic testing and the use of risk calculators and clinical decision guides. Validity and accuracy may change with alterations in populations, disease burden, diagnosis, and treatment. With the use of any new tool, it is important to study the short-term and long-term impact on patient care and determine whether revised or new models should be implemented.

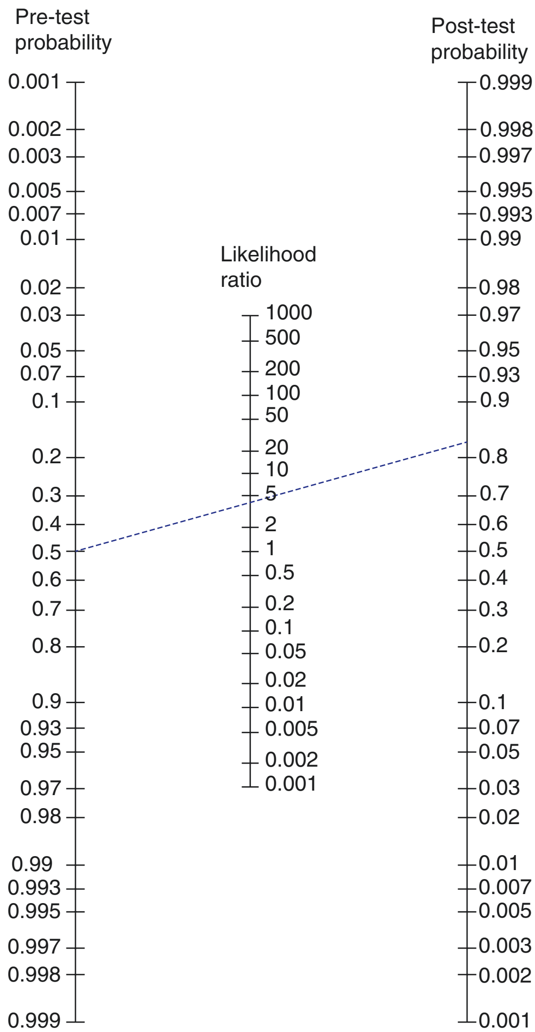

Fig 34.2 Fagan nomogram for converting pre-test probabilities to post-test probabilities using likelihood ratios. In the example in the figure, a test with a positive likelihood ratio of 5 is applied to a patient with a pre-test probability of disease of 0.5, resulting in a post-test probability of 0.833. (Source: https://commons.wikimedia.org/wiki/File:Fagan_nomogram.svg)

High Yield Points

- Test performance is summarized by sensitivity, specificity, positive predictive value, negative predictive value, and likelihood ratios.
- Likelihood ratios are the most clinically useful measure of test performance; a likelihood ratio can be used to calculate a post-test probability of disease from a pre-test probability of disease using Bayes' Theorem or a Fagan Nomogram.
- Clinical risk calculators provide physicians and patients with important prognostic information, but they are often limited by the source population the calculator was derived from.
- Development of accurate and precise diagnostic tools in chronic pain is difficult because of the subjective nature of pain and patient experience.

Questions

A new clinical test is designed for predicting whether facet joint pain will improve with steroid injection. The rule was developed and validated at a single, large academic medical center in Europe with a low prevalence of facet joint pain.

1. Compared to the original population, if the test is applied to a population with a higher prevalence of facet joint pain, a positive result will have:
   A. Lower specificity
   B. Higher likelihood ratio
   C. Greater positive predictive value
   D. Higher sensitivity
   Answer: C
2. An independent investigator finds that a positive result does not significantly change the likelihood of facet joint pain responding to injection. This is most consistent with a likelihood ratio of:
   A. 0.01
   B. 0.1
   C. 1
   D. 10
   Answer: C
3. The test is applied to validation cohort of 100 patients with facet joint pain and the results were compared to each patient's actual response to injection. Of 44 patients with a positive test, 30 experienced improvement in pain following injection. Of 56 patients with a negative test, 4 experienced improvement in pain following injection. What is the sensitivity of the test for predicting improvement in pain based on this result?
   A. 68%
   B. 79%
   C. 88%
   D. 93%
   Answer: B

References

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