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Bayes' theorem, COVID19, and screening tests

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ABSTRACT

The COVID19 crisis has provided a portal to revisit and understand qualities of screening tests and the importance of Bayes' theorem in understanding how to interpret results and implications of next actions.

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1. Brief commentary

During the coronavirus disease 2019 (COVID19) crisis, there has been public outcry for mass screening of the population in hopes to control an actively unfolding event which may directly impact Emergency Departments (EDs) as frontline healthcare providers. Headline news associating mass testing with better control of this pandemic may be spurious because testing in its current form without thoughtful next steps are consequential. In order to adequately assess the implications of increased testing we should revisit Bayes' theorem and its importance in interpreting test results.

To this date, there is one test that has assisted in the current crisis, real-time reverse transcriptase polymerase chain reaction (rRT-PCR). Although becoming more readily available, there are short comings to the test when placed in real world situations. Attributes which limit its sensitivity as a screening tool are stage of COVID19 illness, quality of sampling, and bodily fluid selection. Sensitivities of the most practical and common methods of testing in real world scenarios has been published as 63% for a nasopharyngeal swab and 31% for a throat swab [1].

The ideas that good screening tests with high sensitivity permitting a high degree of true positives while allowing a permissive number of false positives in order to “rule out” disease and tests with high specificity (low rate of false positives) are good “rule in” tests is an oversimplification of a complex dynamic. Although sensitivity and specificity are test attributes important to understand, Bayes' theorem allows the health care provider to convert the results of a test to the probability

of having disease. At best, as it stands with a sensitivity of 63% and a presumed specificity of >99% [2] rRT-PCR is a poor screening test because it has limited ability to rule out disease.

The ability to “rule out illness” given a negative test result using Bayes' theorem can be interpreted by the negative predictive value (NPV) of a test; in other words, given a negative test result: what is the probability of being free of disease? Unfortunately, calculating an NPV relies on prevalence of disease. Prevalence, in this calculation would act as the pre-test or prior probability of disease and combined with the NPV would generate a post-test probability for any patient (all-comers) regardless of the individual's risks.

Unlike NPV, a negative likelihood ratio (LR-) uses Bayes' theorem to facilitate interpretation of a test for a given individual regardless of prevalence by assigning prior probabilities/odds in order to determine post probabilities/odds for a given data point, in this case the LR-

$$LR- = \frac{1 - \text{sensitivity}}{\text{specificity}}$$

$$0.374 = \frac{1 - 0.63}{0.99}$$

To understand the power of Bayes' theorem we will envision 3 patients: low, moderate, and high pre-test probability of COVID19 infection. Asymptomatic individuals in a presumed low prevalence environment would constitute a low pre-test probability (10–20%) of COVID19 infection, whereas an individual with cough and fever in a city/jurisdiction with known cases of COVID19 may be assigned a moderate pre-test probability (40–60%) of disease. A high pre-test probability (80–90%) of COVID19 may include a patient with fever, cough, shortness of breath, with a known close contact with confirmed

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Table 1
Probability odds conversion for negative likelihood ratio of 0.374.

Pre-test probability	Pre-test odds	Post-test odds = (pre-test odds × LR-)	Post-test probability
0.10	0.11	0.04	0.04
0.20	0.25	0.09	0.09
0.30	0.43	0.16	0.14
0.40	0.67	0.25	0.20
0.50	1.00	0.37	0.27
0.60	1.50	0.56	0.36
0.70	2.33	0.87	0.47
0.80	4.00	1.49	0.60
0.90	9.00	3.36	0.77

COVID19. For each of these individuals, a negative rRT-PCR test result will have different implications, namely post-test odds (which can be converted to a probability for ease of interpretation). Similarly, utilizing the Fagan nomogram will provide a visual estimate of post-test probabilities based on LR [3].

Because LR- is a ratio of odds, pre-test probabilities need to be converted into odds and then the resultant odds need to be reverted back to

probabilities, where: $odds = \frac{probability}{1 - probability}$ and $probability = \frac{odds}{odds + 1}$.

Table 1 and Fig. 1 provides a visual gauge of how a LR- (0.374) changes post-test probabilities given a particular pre-test probability.

As depicted in Table 1 and Fig. 1, individuals with a low pre-test probability (10–20%) of disease and a negative rRT-PCR test with a LR- of (0.374) results in a lower post-test probability (4–9%). Those

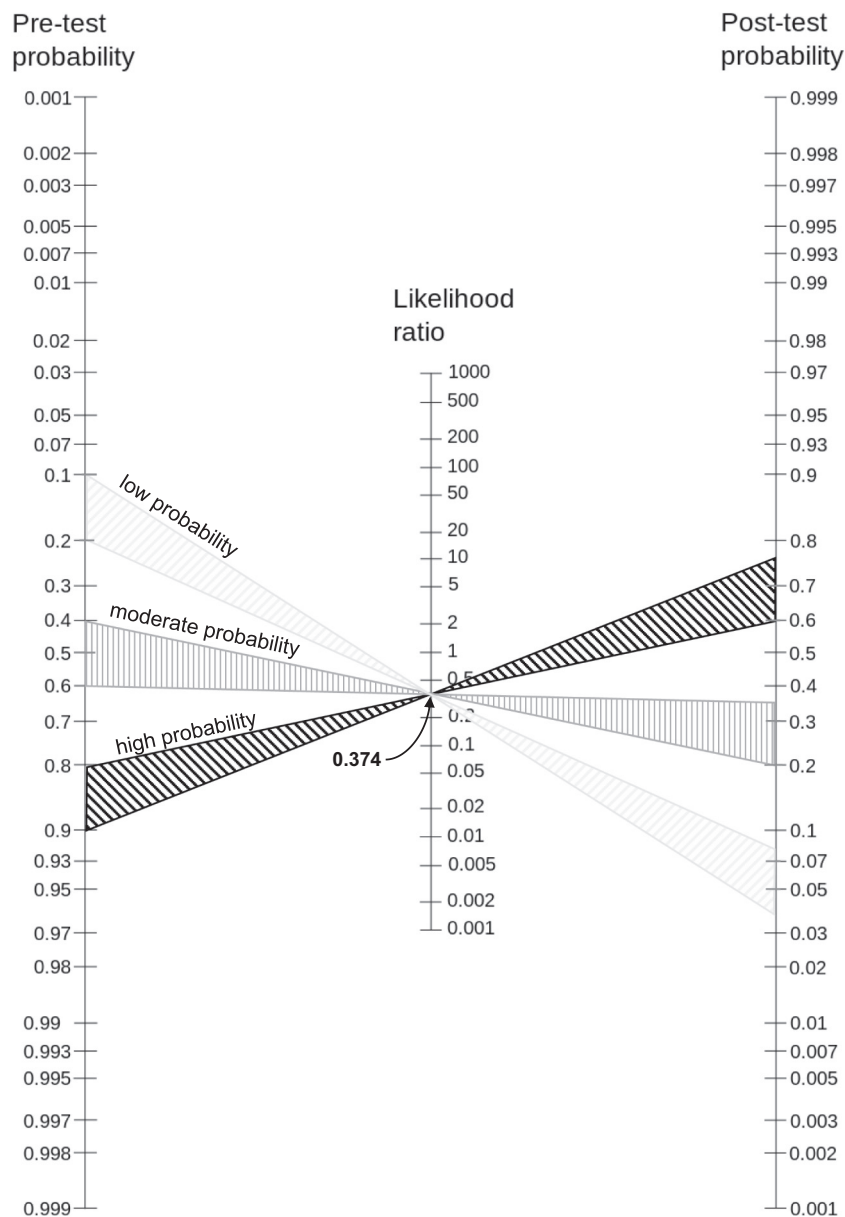


Fig. 1. Fagan nomogram with LR- 0.374 [4].

individuals with moderate pre-test probability (40–60%) and a negative rRT-PCR test have a reduction in post-test probability of COVID19 (Table 1 and Fig. 1 20–36%), but not to an insignificant amount.

Given a high enough pre-test probability (>80%) and negative test result, post-test probabilities remain elevated (Table 1 and Fig. 1 60–77%), and clinicians should be wary of informing a patient that a “negative” test has ruled out COVID19.

Given these three scenarios, subsequent actions and recommendations from EDs rely heavily on post test probabilities, not the categorical outcomes of either “positive” or “negative”. Therefore, a negative test without knowing an individual's post-test probability of disease can limit the ability of clinicians to perform appropriate next actions and dispositions (i.e. discharge instructions, admission to which ward, etc.). For all screening tests, whether for COVID19 or other diagnoses, the understanding of predictive values and likelihood ratios with the help of Bayes' theorem will ensure sound interpretation and resultant recommendations and actions by clinicians and stake-holders. A negative test result, in this paradigm, is never absolutely negative. Rather it adjusts the pre-test probability of having disease lower.

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Declaration of competing interest

None.

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