Interpreting COVID-19 Test Results: a Bayesian Approach

J Gen Intern Med 35(8):2490–1
DOI: 10.1007/s11606-020-05918-8

INTRODUCTION

As physicians care for patients with contact history and symptoms that might represent coronavirus disease 2019 (COVID-19), interpreting the results of polymerase chain reaction (PCR) assays from nasal and pharyngeal swabs is crucial. While a positive result in an acutely ill patient is straightforward, how should physicians interpret negative tests in patients with suspected COVID-19 infection?

Physicians and patients often place inappropriate confidence in test results, even when those tests are imperfect.[1] Specifically, physicians may minimize their own clinical reasoning (e.g., their pre-test probability of disease) and defer to a test result that may not be correct. With PCR testing for COVID-19, false negative tests are particularly concerning, potentially leading to an inappropriate sense of security regarding infectivity.

To accurately interpret test results, one needs to know the positive and negative predictive values of a test in the setting applied, which depend on its sensitivity and specificity, along with prevalence or pre-test probability. Although the specificity of PCR assays for COVID-19 appears to be close to 100%, documenting its sensitivity is surprisingly elusive.[2] Real-world sensitivity of the COVID-19 assay is especially impacted by difficulty in sampling technique for obtaining specimens using nasopharyngeal swabs.[3] One recent unpublished (non-peer reviewed) study based on the experience in China suggested a sensitivity of 70%.[4]

We believe that Bayes theorem can be applied to the interpretation of negative PCR results in patients with suspected COVID-19 infection. To illustrate, we simulate two patient scenarios with differing contact history and clinical presentations.

METHODS

We applied a Bayesian analysis to interpret negative and positive COVID-19 PCR assay results for two clinical scenarios. For both scenarios, we assumed a PCR assay specificity of 99.9% and varied the sensitivity from 70 to 90%.[4, 5]

Scenario 1 (high pre-test probability of COVID-19 infection): A 32-year-old nurse presents with 2 days of fevers to 102°, cough, and subjective dyspnea. She works in an emergency room that has evaluated numerous COVID-19 patients. She reports using appropriate personal protective equipment. We estimated a pre-test probability of COVID-19 infection at 90% (but varied it to as low as 70%).

Scenario 2 (low pre-test probability of COVID-19 infection): A 25-year-old male presents with subjective fevers (no temperature taken), cough, and subjective dyspnea. He has no significant exposures but lives where COVID-19 infections were reported; he has worked at home for the past month with occasional shopping for food. He reports frequent hand washing and practices social distancing. We estimated a pre-test probability of COVID-19 infection at 5% (but varied it to as high as 10%).

RESULTS

For the high-risk scenario with our estimated 90% pre-test probability, the post-test probability of a false negative test ranged from 47 to 73% (Table 1). With a 70% pre-test probability, the post-test probability of a false negative ranged from 19 to 41%. For a low-risk scenario with a pre-test probability of 5–10%, the post-test disease probability with a negative test ranged from 0.5 to 3.2%. Disease likelihood with a positive test remained > 99.9% in the high-risk scenario and > 97.4% in the low-risk patient.

DISCUSSION

We applied a Bayesian approach to illustrate the interpretation of COVID-19 negative tests based on the clinical suspicion of disease probability. A positive test in both high pre-test and low pre-test scenarios most likely represents acute infection. Likewise, a negative test in a low pre-test probability case

Table 1 Estimates for Post-Test Probability of Acute COVID-19 Infection for Simulated Patient Scenarios

Clinical Scenarios	Pre-test probability (%)	PCR assay sensitivity (%)	Post-test probability of acute COVID-19 infection	
			Positive test (%)	Negative test (%)
Patient 1: high pre-test probability	70	70	100	41.2
		90	100	18.9
	90	70	100	73.0
		90	100	47.4
Patient 2: low pre-test probability	5	70	97.4	1.6
		90	97.9	0.5
	10	70	98.7	3.2
		90	99.0	1.1

Received April 22, 2020
Accepted May 6, 2020
Published online June 3, 2020

indicates a low likelihood of acute infection. However, when COVID-19 infection is likely, such as in a healthcare worker with significant exposure, a negative test should not rule out acute infection. In this case, as recommended by the CDC,[6] repeat testing or further evaluation should be considered.

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Compliance with Ethical Standards:

Conflict of Interest: *The authors declare that they do not have a conflict of interest.*

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