

BRIEF REPORT

IMPLICATIONS OF FALSE POSITIVE SARS-COV-2 BY PCR TEST IN THE HEALTH CARE WORK FORCE

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ABSTRACT:

The novel nature of the SARS-CoV-2 virus inherently creates a paucity of reliable and validated data. Implementing evidence-based and data-driven protocols have been exceedingly difficult. As new information is released and integrated into the complex system, the health care delivery workflow must adapt. Incorporating changes on a frequent, if not daily basis, has led to confusion, frustration and loss of confidence among clinicians across the nation. This report illustrates the negative impact that false-positive COVID-19 results can have on the health delivery workforce and the emotional implications that false-positive results cast on health care providers

INTRODUCTION

Mark Twain once said, "Facts are stubborn things, but statistics are pliable." This statement rings a note of truth in the current COVID-19 pandemic, which has undoubtedly changed the landscape of health care delivery. The novel nature of the SARS-CoV-2 virus inherently creates a paucity of reliable and validated data. Implementing evidence-based and data-driven protocols has been exceedingly difficult, if not impossible. As new information is released and integrated into the complex system, the health care delivery workflow must adapt. Incorporating changes on a frequent basis has led to confusion, frustration and loss of confidence among clinicians across the nation. This report illustrates the negative impact that false-positive COVID-19 results can have on the health delivery workforce and the emotional implications that false-positive results cast on health care providers.

The COVID-19 pandemic has affected the very core of human existence. Health care workers are at the front and center of this phenomenon. The spotlight affixed to the health care workers has illuminated many of the obstacles in providing care for patients with COVID-19. It has also highlighted the burdens of delivering care with limited treatment options and increased personal risk of disease contraction. A current Centers for Disease Control and Prevention (CDC) report highlights the disproportionately increased risk of infection contraction for health care workers, as they account for about 11% of the COVID-19 infections in the United States.¹ These combined features are translating

to various levels of psychological strain that may last long after the COVID-19 pandemic has abated.² Health care institutions are taking extra measures to ensure the staff's safety through personal protective equipment (PPE). Due to shortages in PPE supplies, algorithms have been developed to ration PPE. Risk stratifications patient testing/screening for SARS-CoV-2 by reverse-transcription polymerase chain reaction (RT-PCR) is also a critical element of the hospital's response.³ The standard procedure for patients showing symptoms or those who test positive includes the immediate institution of a rigid isolation protocol with corresponding recommendations for specific PPE. Health care workers suspected of exposure may be required to be tested and quarantined.^{1,3} However, little attention has been paid to the potential frequency and impacts of false positives in the health care workforce.

QUALITY OF TESTING

Currently, minimal data is assessing the quality assessments of RT-PCR assays of this RNA virus. All the current RT-PCR assays used have received emergency use authorization from the FDA. Due to the time constraints and need for testing, there has been no way to complete the usual rigorous validation testing. The estimates provided by the supplier may not accurately provide the false-positive rates and estimates in relation to population prevalence and asymptomatic ratio. The CDC RT-PCR diagnostic panel contains three primer-probes that evaluate for two virus nucleocapsid genes and the human RNase P gene to detect human nucleic acids.⁴ A sensitive test will correctly identify people with the disease. Sensitivity measures correct positive results. If a check is 90% sensitive, it will accurately identify 90% of infected people—called a true positive. However, 10% of infected and tested people would get a false negative result—they have the virus, but the test says they don't.

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A specific test will accurately identify people without the disease. Specificity measures the correct negatives. There is prior knowledge that results from RT-PCR using primers in different genes can be affected by viral RNA sequence variation. False negatives can be resultant of genetic diversity and the rapid evolution of this novel coronavirus. Additionally, the specimen collection source can have implications for affecting the sensitivity and specificity of PCR testing.⁵ Wang et al. completed an analysis of 205 symptomatic known COVID-19 patients, including over 1000 specimen samples from various collection sources. They demonstrated that bronchoalveolar lavage fluid specimens showed the highest positive rates; this is improved accuracy from the current widely tested nasopharyngeal swabs. There is also variability in primer's ability to utilize specimens from different sources.

Due to the clinical implications of false negatives, much of the discussion around testing focuses on these concerns. Similarly, much of the conversation regarding testing is around sensitivity; this is because PCR related testing usually has near-perfect specificity. The primer design selection for the genomic sequence of SARS-CoV-2 aids in the accuracy and reliability of the positive results with reported in-vitro analytical specificity of >98%. Despite this, false positives are still possible. They can arise from several technical errors and reagent contamination. The most common included contamination with previously amplified DNA. This can carry implications when screening healthy, asymptomatic patients. Clinical decision making is impeded by assuming all positive results are correct.^{5,6}

DISCUSSION

Responses and protocols for COVID-19 are similar across counties, states and countries, but the disease prevalence of COVID-19 is varied. In areas of low prevalence, false positives are more likely than in areas with more disease.^{4,5} High false-positive rates are typical of RT-PCR assays of RNA viruses, which may not be as reliable for testing varied prevalence. The CDC recognizes that in the absence of SARS-CoV transmission worldwide, the probability that a positive test result will be a "false positive" is high. To decrease the possibility of a false-positive result, testing should be limited to patients with a high index of suspicion for having SARS-CoV disease.⁷

Failure to recognize the implications of the frequency of false positives and the consequent unreliability of positive test results could result in 1) unnecessary removal of frontline health care workers from service for quarantine; 2) myopic focus on COVID-19 patients and development of bias that results in decreased attention to other pathologies; 3) delay in treatment; 4) increase burn rate of PPE unnecessarily due to misinterpretation of positive result; 5) psychological effects on the health care force and their families. The implications of each of these and the proposed mitigation processes will be discussed.

The CDC quarantine recommendations for health care workers who have had actual or possible contact with infected patients without proper personal protective equipment (PPE) has been dynamic. This includes asymptomatic patients who have tested positive with RT-PCR assays.¹ This has caused a rapid surge in

the number of health care workers placed on self-quarantine. At a single hospital in California, more than 200 workers were forced to go under quarantine due to their possible exposure to a COVID-19 positive patient, who officials believe to be the first documented case of community transmission in the U.S. When this patient was eventually transferred to a tertiary medical center, an additional 90 or more workers who might have exposure were placed under quarantine.^{4,5} The conspicuous implications of numerous health care workers under quarantine leave a shortage of available personnel needed to care for the sick. Some hospitals require multiple negative RT-PCR tests for their employees before returning to work.

Unclear efficacy and exact specificity of the test becomes an additional barrier to caring for the ill and meeting the increasing demand for health care workers during this pandemic.^{4,5} Moreover, real-time RT-PCR does not discriminate against viable versus neutralized virus leads to higher false-positive rates, which causes further delays in quarantined health care workers' return to the workforce.⁴ There is a strong sentiment across health care institutions that reexamine this policy as it can affect staffing levels and, overall, impede the health care delivery capacity. It is simply not sustainable to provide appropriate care to patients during this difficult time with a health care workers' shortage.

Routine use of surgical face masks and the addition of protective eyewear with goggles or face shield helps prevent exposures and the need for self-quarantine but adds an additional layer of discomfort to staff. Next, the positive COVID-19 test leads to a myopic focus on COVID-19 rather than comprehensive care required to accurately identify and treat other diagnoses promptly. This is especially true when there is a compromised workforce to provide comprehensive care. There is already a shortage of health care workers due to the growing number of hospitalized COVID-19 patients. Physicians are trained to treat patients, not as a diagnosis. Even under optimal circumstances, it is often challenging to deliver complete care, especially with complex, critically ill patients.

Most institutions limit the number of patients the health care providers are assigned to, depending on the acuity of care that the patient requires. At our institution, ICU nurses are capped at a maximum of two patients, while medical/surgical ward nurses are assigned to a maximum of four patients during any given shift. On the other hand, physicians do not have as well-defined limitations on how many patients they can treat. This can lead to upwards of 20 patients for physicians.^{8,9} However, with the additional workforce in quarantine due to positive COVID-19 tests, the ratio of available health care workers to inpatients is rapidly decreasing.^{8,9} This limits the time allotted to each patient, which may lead to compromises in providing comprehensive care.

Moreover, patients who are COVID-19 positive or sick enough to be hospitalized are more likely to have other comorbidities. Heightened focus on COVID-19 positive status, even in false-positive patients, unintentionally creates a bias and deters attention from promptly diagnosing other pathologies.

Delay in properly diagnosing patients leads to delay in treating them. This causes an increase in morbidities and mortalities that may have been preventable with an adequate number of health care workers. In trauma, the golden hour is referred to as "the period following a traumatic injury during which there is the highest likelihood that prompt medical and surgical treatment will prevent death."¹⁰ Delaying inappropriate treatment can have an unfavorable impact, especially in high acuity illnesses that require timely intervention. Currently, the workforce is overwhelmed with a surplus of patients requiring health care workers to spread themselves too thin to treat patients.⁹ Being able to recruit quarantined health care workers due to false-positive tests would alleviate some burden off the active duty workers. This, in turn, would eliminate further delays in treatment and prevent poor outcomes.

There is already a well-known shortage of PPE nationwide, with many institutions scavenging to fulfill their supply needs.¹¹ Many rely on community donations, makeshift PPEs and even improper reuse to protect their health care workers as well as their patients. False-positive tests further devastate the shortage issue. Misinterpretation of a positive result increases the burn rate of PPE unnecessarily. Whether a patient is falsely positive or truly positive, contact, droplet and airborne precautions become effective immediately when caring for the patient. This means that any health care personnel must observe full PPE, which includes face shield/goggles, N95 or higher respirator, isolation gown and gloves.^{3,11,12} The interdisciplinary team entails doctors, nurses, nursing assistants, pharmacists, registered dieticians, social workers, case managers and physical/occupational therapists, among many other members. Even if we limit direct physical contact with the COVID-positive patients, nurses and doctors (at a minimum) are required to assess patients and provide bedside care at least several times daily. This adds to the number of PPE wasted on patients who may not have the COVID-19 virus. Not only that, putting on and taking off PPE is very time consuming and further contributes to the shortage of the workforce previously mentioned above.

Lastly, the negative psychological ramifications of false-positive tests have on health care personnel and their family members are endless. It is not uncommon for us to encounter news articles about health care workers staying in hospital call rooms or other temporary housing, including tents set up in their garages to avoid exposing their families to the potential risk of contracting the virus. The fear is further intensified if that health care worker was exposed to a positive patient or ended up with a false-positive test. A cross-sectional study conducted in Spain revealed that out of 3,480 people who participated in an online survey, 18.7% revealed depressive, 21.6% anxiety and 15.8% PTSD symptoms.² Severe manifestations can even lead to sleep disturbances and suicidality. Besides the apparent mental distress caused by directly caring for the ill, false-positive tests keep health care workers out of the workforce with the current protocol. This often entails being without paid time off. This can place a financial burden on health care workers, especially those who have family members who are financially dependent on these workers' hourly wages.

SOLUTIONS

So how can we mitigate the negative consequences false-positive COVID-19 tests impose on our already compromised workforce? First and foremost, it is crucial to establish a regimented protocol that is universal across all institutions. Given the constant emergence of new data regarding the novel virus, guidelines are viewed more like suggestions than stringent rules. Even within the same institution, regulations regarding exposure to asymptomatic COVID-positive patients vary case by case basis. Health care workers' quarantine status depends on multiple factors, including PPE applied during exposure, symptomology, duration of exposure and the consulting infectious disease professional on the case.

What we need is a multi-step screening tool involving multiple laboratory tests to increase specificity. It would be more beneficial if the screening tests utilized have a rapid turnover rate so that the duration of quarantine can be as minimal as possible. Another solution would be to limit the number of team members in direct contact with patients until their COVID-19 status has been verified. New data surrounding the virus is continually developing, which will help us better handle this pandemic. Lastly, we propose sufficient resources for mental health and financial support options, including counseling, support groups and disability insurance coverage. Health care workers are the backbones of our communities and are crucial to combating and navigating through the pandemic. We must be sensitive and cognizant of the psychological burden COVID-19 may impose to protect our frontline workers so that they can continue to fight and take care of our patients.

It is incredibly important that we are aware of available data regarding COVID-19 and consider that one size does not fit all, particularly if its prevalence is varied. Statistical analyses in a clinical setting are paramount when making decisions for the already overstretched workforce. Additionally, the discussion must continue on the validity and reliability of data to make sound clinical decisions.

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