Amid the ongoing coronavirus disease 2019 (COVID-19) pandemic, the issue of diagnostic testing has been front and center. Testing capacity has been woefully insufficient for clinical testing of high-risk individuals, much less for epidemiologic evaluation of prevalence, community spread, and the consequences of public health interventions, such as social and physical distancing, school closures, and geographic shutdowns. We need more testing capacity.

However, missing from this intense focus on testing appears to be a discussion of test characteristics including sensitivity, specificity, and diagnostic yield. Information about sensitivity is critical for understanding the risk of false-negatives in the context of community transmission and variable clinical symptoms. By providing insight into false-positives, test specificity also poses implications for how policy makers understand the true scope of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). No test is ironclad, and thoughtful approaches require considering the limitations of whatever testing capacity is created.

The salience of these points has been highlighted in several analyses evaluating the diagnostic yield of SARS-CoV-2 tests. A study published in JAMA from a research group in China reported yield from reverse transcription–polymerase chain reaction testing—the most widely used test to date—collected from different sources among 205 hospitalized patients with COVID-19. The proportion of positive tests varied by source, ranging from 93.3% (14 of 15) for bronchoalveolar lavage to 69.2% (72 of 104) for sputum, 62.5% (5 of 8) for nasal, and 31.7% (126 of 398) for pharyngeal samples. Although the study possessed several limitations and could not determine reverse transcription–polymerase chain reaction testing sensitivity because of the lack of a criterion-standard comparison, it nonetheless raised questions about test performance and highlighted several overarching priorities in the US approach to SARS-CoV-2 testing.

Test Characteristics and Yield

To date, media reports and announcements describing new tests have not been accompanied by easily accessible information regarding their characteristics or diagnostic yield. This information is also difficult to find independently via web searches. While we are in the early stages of a fight against an unfamiliar foe, the focus on test characteristics and diagnostic yield should not be lost in the shuffle of ramping up testing capacity. Instead, these data should be prioritized in research and made widely available by all groups performing and interpreting tests as quickly as possible. For instance, policy makers should ensure that steps taken to speed the expansion of test capacity (eg, emergency use authorizations for new tests) incorporate processes that require both calculation and timely release of test characteristic information.

Potentially Poor Yield or Test Performance

Results based on tests with poor yield or performance characteristics could inadvertently provide inappropriate reassurance to policy makers, public health officials, clinicians, and patients. The caveats of existing analyses notwithstanding, they bring into question the utility of nasopharyngeal swabs as a widely used and promulgated testing option.
In health care settings, false-negatives could lead to premature abandonment of precautions—a particularly problematic issue given current and projected nationwide shortages in personal protective equipment. Appropriate precautions and protective equipment are needed to prevent both viral transmission to the health care workforce and to other otherwise unexposed patients via this frontline group. These are top priority efforts that would be aided by more information regarding diagnostic test characteristics and yield.

In community settings, the issues of poor sensitivity and/or test yield may become more relevant with the increased availability of home testing kits, as understandably inexperienced individuals may drive false-negatives by failing to adequately self-swab. Given the consequences of community viral transmission, the implications of using such tests to rule out individuals who in fact have disease could be staggering if negative test results prompt them to inappropriately relax social distancing practices.

A solution being promulgated by policy makers and institutions is serial testing (eg, discontinuing precautions based on sequentially negative tests). This approach could be beneficial for tests with low or unknown sensitivity or specificity and would align with influenza testing guidelines. Using multiple tests from different sampling sites would be another alternative. Data on the benefit of these approaches, which are currently lacking, are needed.

Balancing Patient Care and Clinician Safety

Testing strategies for SARS-CoV-2 can and should evolve as we continue to learn more about the virus and associated disease. As this occurs, it should be a top priority to balance the benefits of diagnosing cases with maintaining clinician safety. For example, the US Centers for Disease Control and Prevention currently recommends diagnosis via lower respiratory tract specimens, such as lower respiratory tract aspirate or bronchoalveolar lavage. While it would be straightforward to obtain samples from intubated patients and yield may be higher for these sample types than others, both would be aerosolizing procedures that potentially increase the risk of transmission to health care professionals.

The balance between diagnostic benefits and workforce safety is likely to vary by clinical scenario. For instance, even acknowledging their risks, lower respiratory aspirates may be needed in populations such as hospitalized patients who have more severe disease and high suspicion of disease despite negative tests based on nasopharyngeal swabs. In contrast, less invasive nasopharyngeal tests could be more appropriate for individuals with lower risk.

Ultimately, testing policies should be informed by data about test characteristics and yield given the clinical salience of test results. For instance, test results in the outpatient setting can affect counseling with respect to home isolation, while results in the hospital setting can guide specific laboratory testing (eg, interleukin 6), experimental therapy (eg, tocilizumab), and decisions related to intubation, droplet isolation precautions, and clearance of infection.

Conclusion

We are in uncharted territory trying to mitigate the consequences of an unfamiliar foe affecting populations the world over. However, policy makers and leaders have the opportunity to implement thoughtful testing policies as they increase testing capacity. Information about test characteristics and yield from different sample sites is needed to balance diagnostic benefit and clinician safety and to form the basis for testing policies that can help us most effectively respond to the COVID-19 pandemic.
ARTICLE INFORMATION

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Corresponding Author: Leah M. Marcotte, MD, Department of Medicine, University of Washington, 1959 Pacific St, Seattle, WA 98105 (leahmar@uw.edu).

Author Affiliations: Department of Medicine, University of Washington, Seattle (Marcotte, Liao); Value and Systems Science Lab, University of Washington Medicine Center for Scholarship in Patient Care Quality and Safety, Seattle (Marcotte, Liao); Leonard Davis Institute of Health Economics, University of Pennsylvania, Philadelphia (Liao).

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