**TAKE-HOME MESSAGE**

Although newer rapid influenza tests have improved our ability to rule out disease, they are still better at ruling in influenza. Change in management should be considered before testing.

**Update: Can Newer Rapid Influenza Tests Rule Out Disease?**

**EBEM Commentators**

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**Results**

Pooled diagnostic accuracy for 3 types of commercially available rapid influenza tests.

<table>
<thead>
<tr>
<th>Test</th>
<th>No. of Studies</th>
<th>Sensitivity, % (95% CrI)</th>
<th>Specificity, % (95% CrI)</th>
<th>Positive LR</th>
<th>Negative LR</th>
<th>Influenza A</th>
<th>Influenza B</th>
<th>Influenza A</th>
<th>Influenza B</th>
</tr>
</thead>
<tbody>
<tr>
<td>RIDT</td>
<td>130</td>
<td>54.4 (48.9–59.8)</td>
<td>99.4 (99.1–99.7)</td>
<td>96.1; 0.5</td>
<td>319.4</td>
<td>99.4 (99.7–99.9)</td>
<td>99.8 (97.9–99.9)</td>
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<tr>
<td>DIA</td>
<td>19</td>
<td>80.0 (73.4–85.6)</td>
<td>98.3 (97.4–98.9)</td>
<td>47.1; 0.2</td>
<td>59.7</td>
<td>98.7 (97.5–99.4)</td>
<td>99.4 (98.7–99.4)</td>
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</tr>
<tr>
<td>Rapid</td>
<td>13</td>
<td>91.6 (84.9–95.9)</td>
<td>99.2 (98.6–99.7)</td>
<td>116.0; 0.1</td>
<td>166.4</td>
<td>99.4 (98.9–99.8)</td>
<td>99.9 (98.9–99.9)</td>
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<tr>
<td>NAAT</td>
<td></td>
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</tbody>
</table>

*Crit, Credibility intervals; RIDT, rapid influenza diagnostic test; DIA, digital immunoassay; NAAT, nucleic acid amplification test.*

*Pooled estimates.*

Of the 162 studies included for full-text review, 38 were excluded for not reporting influenza A and B results separately, leaving 124 articles for quantitative analysis. Overall, the new rapid influenza tests, digital immunoassays, and rapid nucleic acid amplification tests demonstrated strikingly higher sensitivities for influenza A and B compared with the more traditional rapid influenza diagnostic tests. The pooled sensitivities varied widely between test types (ranging from 53% to 95%), whereas the pooled specificities were consistently greater than 98.3%.

In assessment of risk of bias according to the Quality Assessment of Diagnostic Accuracy Studies,1 more than half of studies involving rapid influenza diagnostic tests and rapid nucleic acid amplification tests had selection bias or were at high risk of bias. Analysis suggests that bias could have been introduced through lack of blinding to the reference test (with the highest risk of bias in the non-automated rapid influenza diagnostic tests, and differences in other covariates (ie, industry sponsorship, point-of-care testing, and commercial brand). Although the heterogeneity identified in rapid test sensitivity could not be fully explained by underreporting of clinical
Influenza affects 25 million illnesses, 310,000 hospitalizations, and 12,000 deaths and predict that the 2017 to 2018 season will be more severe. Although influenza affects all populations, those at highest risk for serious outcomes include patients at extremes of age, those with chronic medical conditions, immunosuppression, and pregnant patients. Influenza symptoms are nonspecific; therefore, having a more accurate diagnostic test could improve patient outcomes by facilitating timely antiviral initiation to high-risk populations while potentially decreasing antibiotic overuse. In addition, early identification or ruling out of influenza could facilitate throughput and admission processes while also using isolation space appropriately.

A previous 2012 systematic review examined only traditional rapid influenza diagnostic tests and reported excellent specificity of 98.2%, but poor sensitivity of only 62.3%, indicating these tests could be used to rule in influenza but not exclude the diagnosis. This updated review examines the diagnostic accuracy of 2 newer types of rapid influenza tests (digital immunoassays and rapid nucleic acid amplification tests) in addition to the traditional rapid influenza diagnostic tests. Similar to the rapid influenza diagnostic tests, the newer tests can be performed rapidly at the point of care, and do not require laboratory personnel to operate. The key finding was that digital immunoassays and rapid nucleic acid amplification tests offer markedly higher sensitivities (ranging from 76.8% to 95.4%), with similarly high specificities (>98%). The rapid nucleic acid amplification tests had an overall negative LR less than 0.1, making them the only test that could usefully rule out influenza; however, performance varied widely among different commercial assays, making this finding inconclusive. The authors of this systematic review reported that the rapid nucleic acid amplification tests cost 2 to 5 times more than the rapid influenza diagnostic tests or digital immunoassays.

Current guidelines from the Centers for Disease Control and Prevention recommend testing patients for influenza only if test results would change clinical management or if patients are being admitted to the hospital. Therefore, clinicians should use the newer rapid influenza diagnostic tests in the context of each patient encounter, understanding that although the newer tests have improved the ability to rule out disease, they are still better at ruling in disease. Before a local influenza epidemic has been identified, given the extremely high positive LR, rapid diagnostic testing would rule in disease when results were positive. Once the local health department has announced the onset of an epidemic, routine diagnostic testing for influenza may not be required and empiric treatment could be considered for high-risk populations.

The findings should be interpreted with caution because of the risk of bias introduced by industry sponsorship. The majority of the digital immunoassay (68%) and rapid nucleic acid amplification test (62%) studies were sponsored by industry, and a sensitivity analysis found that industry sponsorship was associated with higher sensitivities. Of note, the systematic review itself was funded in part by a rapid influenza test company. The medical literature is clear that industry-sponsored research tends to favor the industry’s product and affects how physicians practice medicine; therefore, further research on rapid tests is warranted.

Editor’s Note: This is a clinical synopsis, a regular feature of the Annals’ Systematic Review Snapshots (SRS) series. The source for this systematic review snapshot is: Merckx J, Wall R, Schiller I, et al. Diagnostic accuracy of novel and traditional rapid tests for influenza infection compared...


*Michael Brown, MD, MSc, Jestin N. Carlson, MD, MS, and Alan Jones, MD, serve as editors of the SRS series.*