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Clinical impact of rapid molecular tests in patients with viral respiratory symptoms: a systematic literature review

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BACKGROUND & OBJECTIVE

- Viral respiratory infections may be misdiagnosed as bacterial infections, which may lead to inappropriate use of antibiotics. Even when bacterial infections are ruled out, challenges remain in identifying the exact viral pathogen, due to shared clinical signs and symptoms. Early and accurate detection of viral respiratory infections, such as COVID-19 and influenza, reduces their spread, severity, and duration.
- Levels of antibodies against viral pathogens rise too slowly to be detectable for a timely serological diagnosis of an acute (i.e., current) infection. Molecular tests and antigen tests provide more reliable alternatives.
- Sensitivity and negative predictive value of antigen tests are heavily dependent on viral load. As such, diagnostic performance of rapid antigen-based tests for viral infections such as influenza and COVID-19 has been found to be suboptimal compared to molecular tests.
- Rapid molecular tests are defined as tests with results available in less than three hours, which can be conducted in laboratory or at point of care (PoC). Previous systematic literature reviews (SLRs) have described evidence on the diagnostic performance of these tests; however, few have summarized evidence on their impact on therapeutic decisions and patient outcomes.
- As the evidence base has evolved over the course of the COVID-19 pandemic, this study aimed to provide an updated understanding of the most current evidence on the clinical impact of rapid molecular diagnostic tests compared to standard laboratory molecular tests and antigen tests in adults suspected of respiratory virus infections.

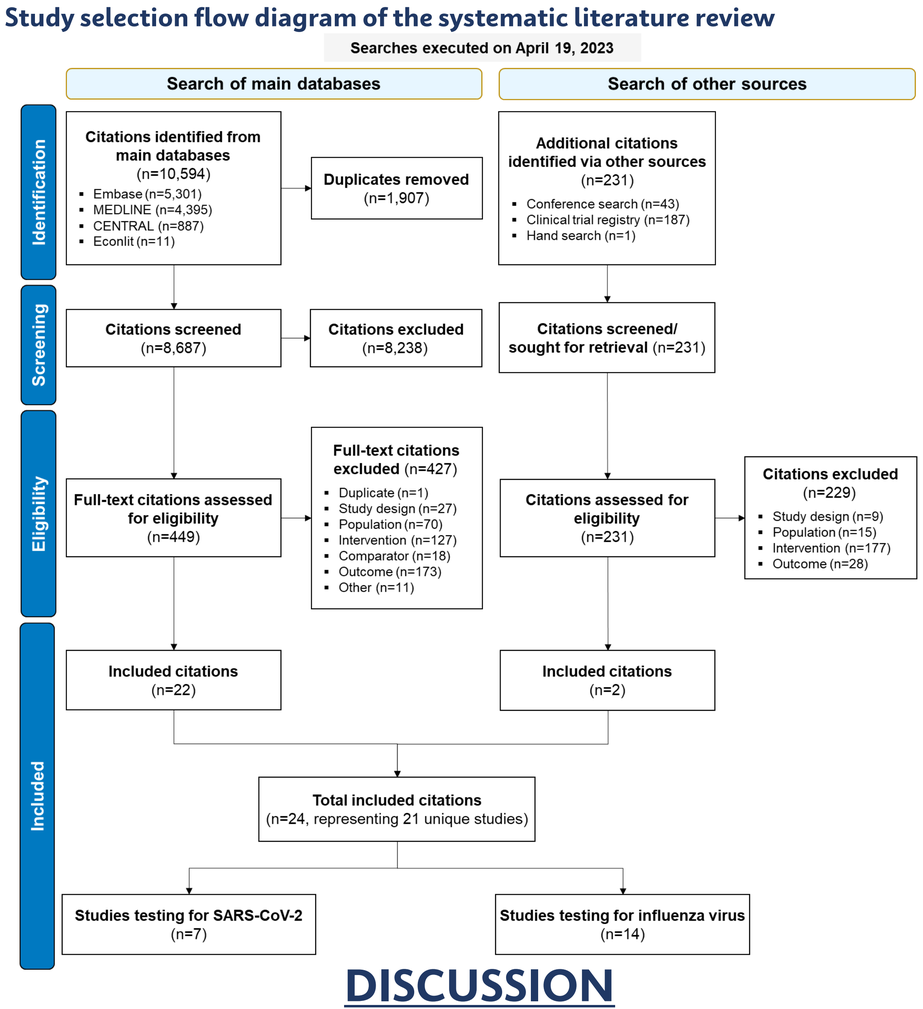
METHODS

- An SLR was conducted on April 19, 2023 to identify randomized and non-randomized controlled trials as well as multicohort prospective and retrospective observational studies, published in English from 2019 through 2023, that compared the clinical outcomes of rapid molecular tests versus standard (i.e., non-rapid) molecular tests and rapid antigen detection tests (RADTs) for the diagnosis of influenza A virus, influenza B virus, SARS-CoV-2, and respiratory syncytial virus (RSV) in adult patients suspected of viral respiratory infections.

RESULTS

- A total of 23 citations (representing 21 unique studies) were included in the SLR. Of the 21 included studies, seven and 14 tested patients for SARS-CoV-2 and influenza virus (with or without RSV), respectively (**Figure 1**). Of the seven studies testing for SARS-CoV-2, two were non-randomized controlled trials, two were prospective implementation studies, and three were retrospective studies. Of the 14 studies testing for influenza virus, one was a randomized controlled trial, two were prospective implementation studies, and 11 were retrospective studies.
- Studies evaluating rapid molecular tests often did so at PoC (rather than laboratory).
- There was considerable heterogeneity in the design, patient eligibility criteria, and evaluated outcomes across the included studies. **Table 1** and **Table 2** summarize the reported outcomes in the studies testing for SARS-CoV-2 and for influenza virus (with or without RSV), respectively.

Figure 1: Study selection flow diagram of the systematic literature review



DISCUSSION

- Compared to standard molecular tests, rapid molecular tests reduced the rates of ancillary tests, such as chest X-rays and blood cultures, in patients presenting with COVID-19 and influenza-like symptoms.
- Rapid molecular tests reduced unnecessary patient isolation, bay closures and length of stay at emergency departments and hospitals compared to standard molecular tests and RADTs.
- Compared to standard molecular tests, rapid molecular tests reduced the time that uninfected patients spent in the hospital under investigation (exposure time).
- Rapid molecular tests reduced use of antibiotics and oseltamivir in those with negative test results for influenza and/or RSV.
- Rapid molecular tests also led to decreased time to test results and lower hospitalization rates in patients testing for SARS-CoV-2 and the influenza virus compared to standard molecular tests and RADTs.

CONCLUSIONS

- By accelerating the patient characterization process and with a positive impact on patient treatment and discharge decisions, rapid molecular tests optimize patient flow and improve patient bed management, thereby increasing isolation room availability and expediting access to hospital procedures, resulting in more timely clinical decision-making.
- By reducing exposure time, rapid molecular tests may lower hospital-acquired infections and related costs.
- By decreasing inappropriate use of antibiotics and antivirals in patients with negative test results and increasing appropriate oseltamivir use in patients at high risk of influenza complications, rapid molecular tests improve antimicrobial stewardship.

Table 1: Summary of outcomes in studies testing for SARS-CoV-2

Outcomes	Summary of outcomes (number of studies)
LoS at the ED	• Median LoS in all-comers (n=4) o 3.2-8 hours (rapid mol.) vs 3.7-28.8 hours (standard mol.) • Median LoS in hospitalized patients (n=1) o 7.6 hours (rapid mol.) vs 20.6 (standard mol.); p<0.001 • Mean LoS in all-comers (n=1) o Rapid mol. vs RADT: decreased by 15 minutes (95% CI: 7.6-37.6)
Anti-microbial prescriptions in patients with negative test	None of the included studies testing for SARS-CoV-2 reported this outcome.
Admission to hospital	• % admission in all-comers (n=2) o 81.7% (rapid mol.) vs 86.3% (standard mol.); p<0.001 o 50.5% (rapid mol.) vs 51.6% (RADT); NS • % admission in patients with negative test (n=1) o 25.7% (rapid mol.) vs 31.2% (RADT); p<0.05
LoS at the hospital	• Median LoS in all-comers (n=1) o 5.1 days (rapid mol.) vs 4.2 days (standard mol.); p=0.017 [a] • Mean LoS in all-comers (n=1) o 6.7 days (rapid mol.) vs 6 days (RADT); NS • Mean LoS in patients with negative test (n=1) o 5.1 days (rapid mol.) vs 5.8 days (RADT); p=0.01
LoS under medical observation	• Median time from admission to definitive bed placement (n=1) o 17.1 hours (rapid mol.) vs 23.4 hours (standard mol.); p=0.02 • Median time from test order to first treatment space re-assignment after a negative result (n=1) o 6.6 hours (rapid mol.) vs 19.2 hours (standard mol.); p<0.001
Ancillary testing	• % patients undergoing chest X-ray (n=1) o Rapid mol. vs standard mol.: decreased by 7% (95% CI: 4%-9%)
Time to test results	• Median time to test results (n=6) o 0.18-3.8 hours (rapid mol.) vs 4.3-35.9 hours (standard mol.)

Notes: a) Study investigators noted that the higher observed value in the rapid molecular group was likely due to the higher prevalence of SARS-CoV-2-positive patients in that group (39.5%) compared to that of the standard molecular group (27.9%). **Abbreviations:** CI, confidence interval; ED, emergency department; LoS, length of stay; mol., molecular test; NS, not statistically significant; molecular, polymerase chain reaction; RADT, rapid antigen detection test.

Table 2: Summary of outcomes in studies testing for influenza and/or respiratory syncytial virus

Outcomes	Summary of outcomes (number of studies)
LoS at the ED	• Median LoS in all-comers (n=5) o 3.7-11 hours (rapid mol.) vs 3.8-11.9 hours (standard mol.) • Median LoS in patients with positive test (n=4) o 3.6-10.3 hours (rapid mol.) vs 3.8-12.9 hours (standard mol.) • Mean LoS in patients with positive test (n=1) o 3.4 hours (rapid mol.) vs 4.9 hours (standard mol.); p<0.01
Anti-microbial prescriptions in patients with negative test	• % antibiotic prescription (n=5) o 36.3% (rapid mol.) vs 48.2% (standard mol. #1) & 47.5% (standard mol. #2); p<0.0001 o 49% (rapid mol.) vs 61% (standard mol.); p<0.0001 o 56.5% (rapid mol.) vs 57.1% (standard mol.); NS o 44.5% (rapid mol.) vs 37.7% (RADT reflexed on standard mol.); NS o 46.6% (post-rapid mol.) vs 50% (pre-rapid mol.); NS • % oseltamivir prescription (n=6) o 0.2% (rapid mol.) vs 1.7% (standard mol. #1) & 6.6% (standard mol. #2); p<0.0001 o 14.9% (rapid mol.) vs 27.5% (standard mol.); p=0.0135 o 0.6% (rapid mol.) vs 5.0% (standard mol.); p<0.0001 o 1.7% (rapid mol.) vs 3.9% (RADT and/or standard mol.); p<0.001 o 2.3% (rapid mol.) vs 13.1% (RADT reflexed on standard mol.); p<0.005 o 1.7% (post-rapid mol.) vs 26.4% (pre-rapid mol.); p<0.0001
Admission to hospital	• % admission in all-comers (n=3) o 54.0% (rapid mol.) vs 75.8% (standard mol. #1) & 61.7% (standard mol. #2); p<0.0001 o 74.5% (rapid mol.) vs 91.3% (standard mol.); p=0.000 o 73.3% (rapid mol.) vs 77.7% (standard mol.); p<0.001 • % admission in patients with negative test (n=5) o 57.9% (rapid mol.) vs 77.4% (standard mol. #1) & 65.2% (standard mol. #2); p<0.0001 o 81.8% (rapid mol.) vs 95.3% (non-rapid); no hypothesis testing o 80.0% (rapid mol.) vs 93.0% (non-rapid); p<0.0001 o 76.5 (rapid mol.) vs 77.7% (non-rapid); p<0.05 o 71.6% (post-rapid mol.) vs 71.0% (pre-rapid mol.); NS
LoS at the hospital	• Median LoS in all-comers (n=1) o 4.2 days (rapid mol.) vs 4.2 days (standard mol.); NS • Mean LoS in all-comers (n=2) o 6.5 days (rapid mol.) vs 11.5 days (standard mol.); p=0.000 o Rapid mol. vs standard mol.: decreased by 3.4 hours; NS • Mean LoS in patients with negative test (n=3) o 10.2 days (rapid mol.) vs 16.0 days (standard mol.); p<0.05 o 4.8 days (rapid mol.) vs 4.2 days (standard mol.); NS o Rapid mol. vs standard mol.: increase by 1.0 hour; NS
LoS under medical observation	• Mean time on the open bay prior to isolation (n=1) o 4.0 hours (rapid mol.) vs 20.9 hours (standard mol.); p<0.001
Ancillary testing	• % all-comer patients undergoing chest X-ray (n=2) o 66% (rapid mol.) vs 82.3% (standard mol. #1) & 79.4% (standard mol. #2); p<0.0001 o 24.4% (rapid mol.) vs 26.9% (standard mol.); NS • % patients with a positive test undergoing chest X-ray (n=1) o 62.2% (rapid mol.) vs 86.0% (standard mol. #1) & 80.7% (standard mol. #2); p<0.0001 • % patients with a negative test undergoing chest X-ray (n=1) o 67.6% (rapid mol.) vs 79.8% (standard mol. #1) & 78.7% (standard mol. #2); p<0.0001 • % patients receiving blood culture test (n=1) o 56.0% (rapid mol.) vs 62.8% (standard mol.); p<0.001
Time to test results	• Median time to test results (n=8) o 1-3.5 hours (rapid mol.) vs 18.2-29.2 hours (standard mol.) (n=6) o 29 minutes (rapid mol.) vs (RADT [16 minutes] and standard mol. [29 hours]) o 2.4 hours (rapid mol.) vs 9.9 hours (RADT and/or standard mol.); p<0.05 • Mean time to test results (n=2) o 2.9 hours (rapid mol.) vs 31.2 hours (standard mol.); p<0.001 [a] o 3.5 hours (rapid mol.) vs 27 hours (standard mol.); p<0.01

Notes: a) Turnaround time was defined for rapid molecular as the number of hours between admission to the ward and notification of the test result, and for standard molecular as the number of hours between admission to the ward and electronic transcription of the results. **Abbreviations:** ED, emergency department; LoS, length of stay; mol., molecular test; NS, not statistically significant; molecular, polymerase chain reaction; RADT, rapid antigen detection test.

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