COVID-19 Living Rapid Review
Rapid Antigen Testing
Expedited Draft Summary #1
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Andrew Beck[1], Nicole Shaver[1], Alexandria Bennett[1], Gabrielle Zitiktye[1], Niyati Vyas[1], Barbara Whelan[2], Rhea O'Regan[2], Aileen Conway[2], Becky Skidmore[3], David Moher[1,4] and Julian Little[1]

1 Knowledge Synthesis and Application Unit, School of Epidemiology and Public Health, Faculty of Medicine, University of Ottawa, Ottawa, Ontario, Canada
2 Evidence Synthesis Ireland, School of Nursing and Midwifery, National University of Ireland, Galway, Ireland
3 Independent Information Specialist, Ottawa, Ontario
4 Clinical Epidemiology Program, Ottawa Hospital Research Institute, Ottawa, Ontario, Canada

Corresponding Author: Andrew Beck (andrew.beck@uottawa.ca)

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Question

What is the effectiveness of different COVID-19 rapid testing strategies[1] including self-administered versus supervised testing, and different testing frequencies (e.g., one off compared to serial testing at different intervals for different lengths of time) at detecting infectiousness or reducing transmission?

Methods Summary

A detailed peer-reviewed search strategy was developed by an information specialist in consultation with the review team. Electronic databases searched include MEDLINE, Embase, and Cochrane CENTRAL. The initial search was conducted September 12, 2021 and updated on October 26, 2021. The search will continue to be updated monthly for six months.

All reviewers independently conducted a training exercise based on 50 articles for title and abstract screening and 10 articles for full-text review before beginning study selection to ensure agreement between reviewers. One reviewer independently screened titles and abstracts and then full-text studies for relevant articles. For data extraction, all reviewers completed a training exercise based on 5 articles before beginning data extraction. One reviewer independently extracted data from included studies with a second reviewer verifying study inclusion and extracted data. Critical appraisals and analyses of the included studies have not been completed and will be available in the final manuscript.

Findings

We present a summary of evidence in Table 1, study characteristics in Table 2 and a descriptive summary of the included studies.

Overall, the searches retrieved 4,762 references. After review at the title and abstract stage, 772 articles were included for full-text review. We have reviewed 218 full-text articles and **10 studies have been included** so far and these were used to complete this expedited draft summary.

[1] *This review does not focus on the comparison of rapid antigen detection tests with a reference standard reverse transcription polymerase chain reaction (RT-PCR) test or the choice of individual tests.*

Table 1: Summary of effectiveness of different COVID-19 rapid testing strategies by outcome

Rapid Antigen Test Strategy	Outcome	Author	Intervention and Comparator	Effectiveness of Strategy *[as reported by study authors]*
Testing Frequency/ Interval				
	Detecting Infectiousness	Pickering 2021	Longitudinal antigen testing with nasopharyngeal sampling vs. Longitudinal RT-PCR testing with nasopharyngeal sampling	In two patients with RT-PCR confirmed mild disease symptoms/asymptomatic disease, all antigen tests failed to detect infection at the time of initial testing. The authors highlighted the importance of repeated antigen testing to detect infectiousness.
		Smith 2021	Testing interval every 3 days vs. Testing interval weekly	For both antigen and RT-qPCR testing, protocol sensitivity was >98% if testing was performed at least every third day. Protocol sensitivity was significantly lower for antigen tests than RT-qPCR tests when testing was only applied once weekly.
Location of Sampling (e.g., where swab is collected from)				
	Detecting Infectiousness	Basso 2021	Self-collected salivary vs. Professionally collected nasopharyngeal	Antigen testing with self-sampled saliva had limited sensitivity, while antigen testing with professionally collected nasopharyngeal samples

				had a better diagnostic performance.
		Klein 2021	Self-collected (supervised) nasal mid-turbinate vs. Professionally collected nasopharyngeal	Both sampling methods yielded comparable sensitivity and specificity results.
		Kritikos 2021	Professionally collected salivary vs. Professionally collected nasopharyngeal (wet and dry swab approaches)	Saliva samples had a worse diagnostic performance for antigen testing when compared to antigen tests performed with nasopharyngeal samples (both wet and dry).
		Lindner 2021	Self-collected (with instruction) nasal mid-turbinate vs. Professionally collected nasopharyngeal	Supervised self-sampling from the nose was concluded to be a reliable alternative to professional nasopharyngeal sampling for antigen testing.
		Nikolai 2021	Professionally collected nasal mid-turbinate vs. Professionally collected anterior nasal	Anterior nasal and nasal mid-turbinate sampling are equivalently accurate at detecting infectiousness in ambulatory symptomatic adults.
		Yokota 2021	Professionally collected salivary vs. Professionally collected nasopharyngeal	Positivity rates were higher in nasopharyngeal samples for antigen tests, than in saliva samples.
Sampler (e.g., individual administering test)				
	Detecting Infectiousness	Basso 2021	Self-collected salivary vs. Professionally collected nasopharyngeal	Antigen testing with self-sampled saliva had limited sensitivity, while antigen testing with professionally collected nasopharyngeal samples

				had a better diagnostic performance.
		Klein 2021	Self-collected (supervised) nasal mid-turbinate vs. Professionally collected nasopharyngeal	Both sampling methods yielded comparable sensitivity and specificity results and authors suggested antigen nasal self-sampling could be useful in population testing.
		Lindner 2021	Self-collected (with instruction) nasal mid-turbinate vs. Professionally collected nasopharyngeal	Supervised self-sampling from the nose was concluded to be a reliable alternative to professional nasopharyngeal sampling for antigen testing.
		Nikolai 2021	Self-collected nasal mid-turbinate vs. Professionally collected nasopharyngeal sampling	Self-sampled nasal mid-turbinate was equally as sensitive at detecting infectiousness, as professionally collected nasopharyngeal sampling; specificity was slightly lower for nasal mid-turbinate self-sampling.
	Feasibility	Nikolai 2021	Self-sampling [no comparator]	Participants are reliably and easily able to perform nasal mid-turbinate sampling on themselves, following instructions.
Test Location (e.g., physical location of test site)				
	No evidence found			
Other Testing Strategies				
Interval between sampling and last	Detecting Infectiousness	Schuit 2021	<5 days between sampling vs. > 5 days between sampling	The sensitivity of antigen tests was higher when there were <5 days between sampling and the last contact with the index case

contact with index case				compared to when there was an interval of >5 days. Specificity remained high regardless of interval of last contact with an index case.
Practicality when Antigen Testing	Detecting Infectiousness/User Friendliness	Yin 2021	Various antigen tests	Most diagnostic performances of different antigen tests are similar and, therefore, antigen testing strategies should maximize user friendliness and practical aspects (e.g., opening caps while wearing gloves, ensuring biosafety outside a laboratory and instructions targeting non-laboratory operators).

Descriptive Summaries:

Basso 2021[1]
Basso and colleagues performed a prospective cohort study with 234 patients recruited from an Italian hospital. The diagnostic accuracy of two lateral flow immunochromatographic antigen assays (Espline® SARS-CoV-2 (Fujirebio®) or PanbioTM COVID-19 Ag Rapid Test) was assessed through paired samples from each patient. Samples were collected through 1) salivary self-sampling and 2) nasopharyngeal samples collected from trained nurses. Salivary and nasopharyngeal samples were tested for COVID-19 via the two antigen assays and also assessed with rRT-PCR (TaqPath) to serve as the reference test for diagnostic accuracy. Results: Antigen testing with self-sampled saliva had limited sensitivity (13%) with rRT-PCR as the reference standard. Antigen testing with nasopharyngeal samples had a better diagnostic performance (sensitivity: 48% and 66%; specificity: 100% and 99% for Espline and Abbott, respectively), depending on viral loads.

Klein 2021[2]
Klein and colleagues studied 290 participants in a prospective cohort study conducted at a drive-in testing center in Germany. They compared the sensitivity and specificity between a supervised, self-collected nasal mid-turbinate swab and a professionally collected nasopharyngeal swab, using the PanbioTM antigen rapid diagnostic test (Abbott). Standard reverse transcription polymerase chain reaction (RT-PCR) using Tib Molbiol® (Berlin, Germany) was used as the reference standard for both sampling methods. Results: The sensitivity of Panbio antigen testing with nasal mid-turbinate sampling was 84.4% (95% CI: 71.2–92.3%) and 88.9% (95% CI: 76.5–95.5%) with nasopharyngeal sampling. Specificity was equivalent in both sampling methods (99.2%, 95% CI: 97.1–99.8%). The authors concluded that the sampling methods yielded comparable results and that nasal self-sampling could be useful in population antigen testing.

Kritikos 2021[3]
Kritikos et al. conducted a prospective cohort study among COVID-19 hospitalized patients in a Swiss tertiary university hospital. The diagnostic performance of two antigen tests were examined (One Step Immunoassay Exdia® COVID-19 Ag (Precision Biosensor, Daejeon, Korea) and Standard Q® COVID-19 Rapid Antigen Test (Roche-Switzerland)), using RT-PCR (Cobas 6800, Roche-Switzerland, Basel, Switzerland) as the reference standard. For each test, the performance of two different sampling locations were assessed: 1) a nasopharyngeal sample (both wet and dry swab approaches) and 2) a saliva sample, both sampled by trained personnel. Results: The rapid antigen tests with nasopharyngeal swabs had sensitivities of 35% and 41% for the Standard Q® and Exdia® assays, respectively, when a wet-swab approach was used (i.e., the swab was diluted in the viral transport medium before testing). The dry-swab nasopharyngeal sampling approach had a marginally improved sensitivity of 47%. Saliva samples had a worse diagnostic performance when used for antigen testing (sensitivities of 4% and 8%, respectively). Rapid antigen testing using either approach was concluded not to be ideal for hospitalized patients.

Lindner 2021[4]
Lindner and colleagues conducted a prospective cohort study with 289 participants recruited from an outpatient COVID-19 testing center in Germany. The diagnostic performance of a rapid antigen test (STANDARD Q (SD Biosensor, Inc. Gyeonggi-do, Korea)) was assessed using two sampling procedures: 1) a self-collected (with instruction) nasal mid-turbinate swab and 2) a nasopharyngeal

swab collected by a trained health care worker. A RT-PCR (Roche Cobas (Pleasanton, CA, USA) or TibMolbiol (Berlin, Germany)) with a combined nasopharyngeal/oropharyngeal swab served as the reference standard for both tests. Results: The STANDARD Q antigen test with nasal mid-turbinate sampling had a sensitivity of 74.4% (95% CI: 58.9–85.4%) and specificity of 99.2% (95% CI: 97.1–99.8%). With nasopharyngeal sampling, the test sensitivity was 79.5% (95% CI: 64.5–89.2%) and specificity was 99.6% (95% CI: 97.8–100%). Supervised self-sampling from the nose was concluded to be a reliable alternative to professional nasopharyngeal sampling for antigen testing.

Nikolai 2021[5]
Nikolai et al. carried out a prospective cohort study with 228 participants from a German outpatient COVID-19 testing facility. The diagnostic performance of the STANDARD Q COVID-19 antigen test was calculated (SD Biosensor, Inc. Gyeonggi-do, Korea)) with real-time polymerase chain reaction (RT-PCR) as the reference standard. To determine the effect of localization on antigen test performance, professionally collected anterior nasal swabs and nasal mid-turbinate swabs were compared. Additionally, to examine the effectiveness of self-sampling, the performance of the antigen test with a self-collected nasal mid-turbinate swab was compared against antigen test performance with professional nasopharyngeal sampling. Results: Antigen testing with professional anterior nasal and nasal mid-turbinate showed equivalent sensitivities of 86.1% (95% CI: 71.3–93.9%) and equivalent specificities of 100.0% (95% CI: 95.7–100%), when compared with RT-PCR. Antigen testing with self-sampled nasal mid-turbinate and professional nasopharyngeal sampling also yielded an identical sensitivity of 91.2% (95% CI: 77.0–97.0%). Specificity was slightly lower with nasal mid-turbinate self-sampling than nasopharyngeal sampling (98.4% (95% CI: 91.4–99.9%) and 100.0% (95% CI: 94.2–100%), respectively. Self-sampling was also reported to be feasible, with 85.3% of participants stating that the nasal mid-turbinate self-sampling was easy to perform.

Pickering 2021[6]
Pickering and colleagues conducted a laboratory evaluation study using stored samples previously obtained from inpatients/outpatients at a UK hospital. Samples were tested with real-time polymerase chain reaction (RT-PCR) (AusDiagnostics multiplexed-tandem PCR assay) to confirm COVID-19 infection. To investigate how antigen test results vary over time, a subset of sequential longitudinal nasopharyngeal samples from five infected patients with varying levels of disease severity was assessed. Four rapid antigen tests were used to evaluate the samples: Innova Rapid SARS-CoV-2 Antigen Test, Encode SARS-CoV-2 Antigen Rapid Test Device, SureScreen COVID-19 Rapid Antigen Test Cassette and SureScreen COVID-19 Rapid Fluorescence Antigen Test. Results: All four tests identified infectious samples as positive, with the exception of one sample tested by SureScreen-F. However, in two patients (one asymptomatic and one with mild symptoms), RT-PCR results showed infection, while all antigen tests indicated a negative result at the time of initial testing. The authors highlighted the importance of repeat testing with rapid antigen tests, rather than one-off testing.

Schuit 2021[7]
Schuit and colleagues conducted a prospective cross-sectional study in 4274 participants across four public health COVID-19 test sites in the Netherlands. They assessed the diagnostic test accuracy of two rapid antigen tests (Veritor System (Beckton Dickinson) and Biosensor (Roche Diagnostics)) in the close contacts of infected individuals, as well as how the interval (days) between sampling and last contact with index case impacted diagnostic test performance. Reverse-transcriptase polymerase chain reaction (RT-PCR) (Roche cobas 6800/8800 platforms) was used as a reference standard to determine test performance. Results: In Veritor and Biosensor antigen tests, test sensitivity was higher when there were <5 days between sampling and the last contact with the index case (69.6%, 95% CI: 55.9 to 81.2 and 75.0%, 95% CI: 50.9 to 91.3 respectively), compared to when there was an

interval of >5 days (56.5%, 95% CI: 41.1 to 71.1 and 69.2%, 95% CI: 38.6 to 90.9, respectively). In both antigen tests, specificity remained high regardless of interval of last contact with an index case.

Smith 2021[8]
Smith et al. carried out a prospective cohort study of 43 adults newly infected with COVID-19 at a US research university. The longitudinal performance of a rapid antigen test (Quidel SARS Sofia antigen fluorescent immunoassay (FIA)) and RT-qPCR (Thermo Taqpath coronavirus disease 2019 (COVID-19) assay) tests were compared through daily testing during early infection. Participants collected their own nasal swabs for antigen testing and nasal/saliva samples for RT-qPCR testing. Results: For both antigen and RT-qPCR testing the protocol sensitivity (ability of each of test platform to detect infected individuals was affected by differences in testing frequencies) remained >98% as long as testing was performed at least every third day. Protocol sensitivity was significantly lower for antigen tests than PCR tests measured with either saliva or nasal swabs, when testing was applied weekly (Antigen: 79.7%, 95% CI: 74.7–84.1; Nasal RT-qPCR: 98.7%, 95% CI, 96.6–99.6; Saliva RT-qPCR: 96.3, 95% CI: 93.6–98.2). The authors concluded that the best alternative, if rapid serial RT-qPCR testing is unavailable, is frequent serial antigen testing (at least every 3 days or twice weekly).

Yin 2021[9]
Yin and colleagues conducted a retrospective cohort study among 1568 recently symptomatic patients of five University Hospitals. The performance and user friendliness assessment of four COVID-19 antigen rapid diagnostic tests (Panbio COVID-19 Ag Rapid Test Device (Abbott Rapid Diagnostics), Germany, BD Veritor SARS-CoV-2 (Becton-Dickinson and Company, USA)m COVID-19 Ag Respi-Strip (Coris BioConcept, Belgium), SARS-CoV-2 Rapid Antigen Test (SD Biosensor, Republic of Korea)) compared to RT-PCR (Abbott Molecular, USA) were evaluated. Samples were retrieved using nasopharyngeal swabs. Results: The authors failed to find a significant difference between the clinical performances of the four antigen rapid diagnostic tests. They focused on user-friendliness as a main criterion of choice of test. Only one test had a less satisfactory rating (Coris COVID-19 Ag Respi-strip) due to practicality issues of a "strip-in-a-tube" format, making result reading difficult. The authors underlined practical aspects such as opening caps while wearing gloves, ensuring biosafety outside a laboratory and instructions targeting non-laboratory operators.

Yokota 2021[10]
Yokota et al. conducted a retrospective study using samples from a Japanese hospital to evaluate the performance of an immunochromatographic antigen test (Espline SARS-CoV-2 (Fujire- bio, Tokyo, Japan)) and a chemiluminescent enzyme immunoassay LUMIPULSE G1200 (Fujirebio, Tokyo, Japan). Frozen samples were previously analyzed using StepOnePlus Real Time PCR System (Thermo Fisher Scientific, Waltham, MA, USA) and included 34 PCR-positive samples (17 saliva and 17 nasopharyngeal swabs) and 309 PCR-negative samples. Results: Of the samples confirmed positive by RT-PCR, positivity rates were higher in nasopharyngeal samples for both Espline and Lumipulse antigen tests (24%, 95% CI: 7–50 and 95% CI: 82%, 57–96, respectively), than in saliva samples (59%, 95% CI: 33–82 and 100%, 95% CI: 80–100). However, positivity rates were much higher for the Lumipulse chemiluminescent antigen test than the Espline immunochromatographic test for either sampling strategy.

Table 2: Study characteristics

Author & Year of Publication	Study Design	Dates	Location	Setting	Sample Size	Symptom Status	Time of Test in Relation to Symptom Onset
Basso 2021	Prospective Cohort	August 2020 to November 2020	Italy	Hospital (inpatient or outpatient)	234 Participants	Symptomatic or Asymptomatic	Variable (<7 to >14 days)
Klein 2021	Prospective Cohort	December 2020 to January 2021	Germany	COVID-19 drive-in test center	290 Participants	Symptomatic or Asymptomatic	Variable (mean duration of symptoms of 3.8 days (SD=5.4) on test day)
Kritikos 2021	Prospective Cohort	December 2020 to February 2021	Switzerland	Tertiary university hospital	58 Participants	Symptomatic or Asymptomatic	Variable (5 days after positive PCR test)
Lindner 2021	Prospective Cohort	September to October 2020	Germany	Hospital (outpatient COVID-19 test center)	289 Participants	Symptomatic or Asymptomatic	Variable (average duration of symptoms of 4.4 days (SD=2.7) on test day)
Nikolai 2021	Prospective Cohort	November 2020 to January 2021	Germany	Hospital (outpatient COVID-19 test center)	228 Participants	Symptomatic or Asymptomatic	Variable (average duration of symptoms of 3.4 days (SD=3.0) on test day)
Pickering 2021	Retrospective Cohort [Laboratory	March to October 2020	UK	Hospital (inpatient or outpatient)	241 Samples (n=100 sensitivity,	Symptomatic or Asymptomatic	Variable (ranged from -1 to 37 days)

	Evaluation Study]				n=141 positivity sample)		
Schuit 2021	Prospective Cohort	December 2020 to February 2021	Netherlands	Four Public Health COVID-19 test centers	4274 Participants	Symptomatic or Asymptomatic	Variable (tested ≥5 days after exposure and asymptomatic at time of test request)
Smith 2021	Prospective Cohort	Not Reported	USA	Research University	43 Participants	Symptomatic or Asymptomatic	Not Reported
Yin 2021	Retrospective Cohort	July to September 2020	Belgium	Five University Hospitals	1568 Participants (99 samples for antigen testing)	Symptomatic	< 7 days
Yokota 2021	Retrospective Cohort	Not Reported	Japan	Hospital	343 Samples	Symptomatic	Variable (median duration of symptoms of 9 days (range 2-14) on test day)

*No study reported on vaccination status of included participants.

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