COVID-19 Living Rapid Review
Rapid Antigen Testing
Expedited Draft Summary #3

(Version 3: 31 January 2022)

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)

PROSPERO registration: CRD42021284168

This research was funded by the Health Research Board through Evidence Synthesis Ireland [HRB Grant Number CBES-2018-001]. The living rapid reviews were also funded by The Strategy for Patient-Oriented Research Evidence Alliance (SPOR EA) which is supported by the Canadian Institutes of Health Research (CIHR) under the Strategy for Patient-Oriented Research (SPOR) initiative.

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 searches were conducted on October 26, 2021, December 20, 2021 and January 20, 2022. The searches will continue to be updated monthly for a limit of 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 7,601 references. To date, 5701 of these references have been reviewed at the title and abstract stage and 917 articles have been included for full-text review. We have reviewed 697 of these full-text articles and **16 studies have been included to date**. **One new study was included** in 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	Study (Author and Year)	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.
	Incidence	Young 2021 **(New)**	Daily anterior nasal self-testing for 7 days vs. Self-isolation for 10 days	Antigen-based daily testing for school-based contacts was non-inferior to self-isolation for the control of COVID-19 incidence.
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.
		Courtellemont 2021	Professionally collected nasopharyngeal vs. Professionally collected oropharyngeal vs. Professionally collected salivary	Compared to antigen tests using nasopharyngeal swabs, antigen tests on oropharyngeal or salivary samples had large decreases in sensitivity.
		Ishii 2021	Nasopharyngeal samples vs. Saliva samples	Accuracy varied by the type of antigen test, as well as the swab sampling location. The chemiluminescent enzyme test showed similar accuracy for both sample types. The immunochromatography test had high specificity for both sample types, but reduced sensitivity when using saliva swabs.
		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	Saliva samples had a worse diagnostic performance for antigen testing when compared to antigen tests performed with

			nasopharyngeal (wet and dry swab approaches)	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.
		Mak 2021	Nasopharyngeal vs. Combined nasopharyngeal and throat	Antigen tests showed similar sensitivities with nasopharyngeal swabs and with combined nasopharyngeal swabs.
		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.
		Osterman 2021	Professionally collected nasopharyngeal vs. Professionally collected oropharyngeal	Diagnostic accuracy of antigen tests had no apparent dependence on sampling site.
		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.

		Chiu 2021	Self-collected (supervised) nasal bilateral anterior vs. Professionally collected nasal bilateral anterior	The overall percentage agreement between antigen tests and PCR was similar for health care provider and self-collected specimens.
		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.
	Incidence	Young 2021 **(New)**	Daily anterior nasal self-testing for 7 days vs. Self-isolation for 10 days	Antigen-based daily testing for school-based contacts was non-inferior to self-isolation for the control of COVID-19 incidence.
Test Location (e.g., physical location of test site)				
	No evidence found			
Other Testing Strategies				

Interval between sampling and last contact with index case	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 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

New Studies:

Young[1] 2021

Young and colleagues carried out a cluster-randomized, controlled trial in secondary schools and further education colleges in England to examine the effect of an antigen testing strategy for school-based COVID-19 contacts. 201 schools were randomized to either (1) self-isolation of contacts for 10 days (control) or (2) to voluntary daily lateral flow device (LFD) testing for 7 days with LFD-negative contacts remaining at school (intervention). Contacts in the intervention schools self-tested by swabbing their anterior nasal cavity and samples were tested by school staff using a SARS-CoV-2 antigen LFD (Orient Gene, Huzhou, China). Results: The incidence of PCR-confirmed infection in the control group was 657 cases in 7,782,537 total days-at-risk (59.1 per 100 000 per week) and in the intervention group the incidence was 740 cases in 8 379 749 days-at-risk (61.8 per 100 000 per week). Adjusting for the randomization strata, participant type and the community rate of SARS-CoV-2 infection in the previous week, there was no evidence of difference between study groups in symptomatic PCR-confirmed infection, with an adjusted incidence rate ratio of 0.96 ((95% CI: 0.75–1.22), p=0.72). The authors concluded that the antigen-based daily testing strategy for school-based contacts was non-inferior to self-isolation for the control of COVID-19 transmission.

Previously Included Studies:

Basso[2] 2021

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.

Chiu 2021[3]

Chiu et al. conducted a prospective clinical evaluation study of the INDICAID COVID-19 rapid antigen test in three US clinical sites and measured real-world implementation across 12 emergency outbreak testing centers in Hong Kong. For the clinical evaluation component, three swabs were obtained from the nasal (bilateral anterior) cavity from each participant (n=329 participants total). The first swab was self-sampled by participants under supervision, followed by two samples taken from health care professionals. RT-PCR (Curative SARS-CoV-2 assay or FDA EUA BioCollections worldwide SARS-CoV-2 assay) was performed on one of the professionally obtained samples to serve as the reference standard for the positive percent agreement (PPA) and negative percent agreement (NPA) of the antigen tests. Results: When sample collection by performed by a healthcare professional, the PPA between the antigen tests and RT-PCR was 85.3% (95% CI: 75.6%-91.6%) and the NPA was 94.9% (95% CI: 91.6%-96.9%). When sample collection was self-performed by the participant, the PPA was lower at 82.7% (95% CI: 72.6%-89.6%), while the NPA

was 96.4% (95% CI: 93.4%-98.0%). The overall percentage agreement for health care provider- and self-collected specimens was 92.8% and 93.4%, respectively.

Courtellemont[4] 2021
Courtellemont and colleagues conducted a prospective cohort study with 248 samples from hospitalized patients or individuals voluntarily accessing the COVID- 19 screening department of a regional French hospital. Sensitivity of the COVID- VIRO® (AAZ) immunochromatography assay rapid antigen test was assessed through comparison with RT- qPCR as the reference test (TaqPath Covid- 19 Multiplex RT- PCR, Thermo Fisher Scientific). Trained healthcare personnel obtained paired nasopharyngeal samples from each participant. Additionally, a subset of participants had oropharyngeal (n=34) and/or saliva (n=14) swabs taken to determine the impact of swab location on antigen test sensitivity. Results: Using nasopharyngeal swabs, the sensitivity of specificity of the antigen test was 96.7% (CI: 93.5%–99.9%) and 100%, respectively. Tests on oropharyngeal or salivary samples had large decreases in reliability (sensitivities of 70.6% and 0%, respectively. The authors noted that nasopharyngeal samples should be used for the diagnosis of SARS- CoV- 2.

Ishii[5] 2021
Ishii et al. performed a prospective cohort study on 486 samples obtained from patients at a Japanese university medical center. The diagnostic accuracy of two antigen tests (Espline immunochromatography and Lumipulse quantitative chemiluminescent enzyme immunoassay) was obtained through comparison to RT-PCR as the standard. Swabs were obtained for both nasopharyngeal and saliva samples for each test. Results: The Lumipulse antigen test showed high sensitivity for both saliva swabs (88.9%) and nasopharyngeal swabs (91.7%). Specificities were also high for nasopharyngeal swabs and saliva samples at 99.6% and 96.9%, respectively. The sensitivity of the Espline test was 90.9% for nasopharyngeal swabs and 33.3% for saliva samples, whereas the specificity was 100% for both sample types.

Klein[6] 2021
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[7] 2021
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[8] 2021
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.

Mak[9] 2021
Mak and colleagues performed a retrospective cohort study on 70 samples collected by the Public Health Laboratory Services Branch in Hong Kong. The test performance for two antigen tests for detecting SARS-CoV- 2 was evaluated (an automated antigen detection (AAD) test, Elecsys SARS-CoV-2 Antigen (Roche, Germany) and a SARS- CoV-2 Rapid Antigen Test (SD Biosensor, Korea)) using RT-PCR as the reference standard. Samples were collected via nasopharyngeal swab and combined nasopharyngeal swab and throat swab. Results: The Elecsys SARS-CoV-2 Antigen test had a sensitivity of 85.7% when nasopharyngeal swabs were used and a sensitivity of 88.6% when combined nasopharyngeal swab and throat swabs were used.

Nikolai[10] 2021
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.

Osterman[11] 2021
Osterman and colleagues carried out a diagnostic evaluation study of two rapid antigen tests in 833 patients and health care workers at two University Hospitals in Germany. Diagnostic accuracy of the SARS-CoV-2 Rapid Antigen Test (RAT) from Roche Diagnostics and the SD Biosensor Standard F COVID-19 Ag fluorescent immunoassay was obtained through comparison with RT- PCR samples. Healthcare workers obtained nasopharyngeal or oropharyngeal samples from each patient. Results:

Both antigen tests showed a comparable specificity: 97.78% for FIA and 97.67% for RAT. The SARS-CoV-2 Rapid Antigen Test (RAT) had a clinical sensitivity and specificity of 50.3% and 97.7%, respectively, whereas the SD Biosensor Standard F COVID-19 Ag test had a sensitivity and specificity of 45.4% and 97.8%. The authors noted that the diagnostic accuracy of either test had no apparent dependence on patients' age or sampling site.

Pickering[12] **2021**
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[13] **2021**
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[14] **2021**
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[15] **2021**

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[16] **2021**

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 to November 2020	Italy	Hospital (inpatient or outpatient)	234 Participants	Symptomatic or Asymptomatic	Variable (<7 to >14 days)
Chiu 2021	Prospective Cohort	November 2020 to March 2021	USA and Hong Kong	Clinical sites/emergency outbreak testing centers	329 samples [for clinical evaluation]	Symptomatic or Asymptomatic	Tested within 5 days of symptoms
Courtellemont 2021	Prospective Cohort	October 2020	France	Hospital setting	248 samples analyzed	Symptomatic or Asymptomatic	Not Reported
Ishii 2021	Prospective Cohort	August to September 2020	Japan	University medical center	486 samples analyzed	Symptomatic or Asymptomatic	Variable (range 0-14 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)
Mak 2021	Retrospective Cohort [Laboratory Evaluation Study]	January to March 2021	Hong Kong	Public Health Laboratory Services Branch	70 samples analyzed	Not Reported	Not Reported
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)
Osterman 2021	Prospective Cohort	March to December 2020	Germany	University Hospitals	833 samples analyzed	Symptomatic	Not Reported
Pickering 2021	Retrospective Cohort [Laboratory Evaluation Study]	March to October 2020	UK	Hospital (inpatient or outpatient)	241 Samples (n=100 sensitivity, n=141 positivity sample)	Symptomatic or Asymptomatic	Variable (ranged from -1 to 37 days)
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)
Young	Cluster-randomised trial	April to June 2021	England	Secondary schools and further education colleges	201 schools randomized	Symptomatic or Asymptomatic	Daily testing following confirmation of exposure for contacts in intervention schools

*No study reported on vaccination status of included participants.

References of included studies

1. Young, B. C. *et al.* Daily testing for contacts of individuals with SARS-CoV-2 infection and attendance and SARS-CoV-2 transmission in English secondary schools and colleges: an open-label, cluster-randomised trial. *The Lancet* **398**, 1217–1229 (2021).
2. Basso, D. *et al.* Salivary SARS-CoV-2 antigen rapid detection: A prospective cohort study. *Clin. Chim. Acta* **517**, 54–59.
3. Chiu, R. Y. T. *et al.* Evaluation of the INDICAID COVID-19 Rapid Antigen Test in Symptomatic Populations and Asymptomatic Community Testing. *Microbiol. Spectr.* **9**, (2021).
4. Courtellemont, L. *et al.* High performance of a novel antigen detection test on nasopharyngeal specimens for diagnosing SARS- CoV- 2 infection. *J. Med. Virol.* **93**, 3152–3157 (2021).
5. Ishii, T. *et al.* Immunochromatography and chemiluminescent enzyme immunoassay for COVID-19 diagnosis. *J. Infect. Chemother.* **27**, 915–918 (2021).
6. Klein, J. A. F. *et al.* Head-to-head performance comparison of self-collected nasal versus professional-collected nasopharyngeal swab for a WHO-listed SARS-CoV-2 antigen-detecting rapid diagnostic test. *Med. Microbiol. Immunol. (Berl.)* **210**, 181–186.
7. Kritikos, A. *et al.* Sensitivity of Rapid Antigen Testing and RT-PCR Performed on Nasopharyngeal Swabs versus Saliva Samples in COVID-19 Hospitalized Patients: Results of a Prospective Comparative Trial (RESTART). *Microorganisms* **9**, 09.
8. Lindner, A. K. *et al.* Head-to-head comparison of SARS-CoV-2 antigen-detecting rapid test with self-collected nasal swab versus professional-collected nasopharyngeal swab. *Eur. Respir. J.* **57**, 04 (4).
9. Mak, G. C. K. *et al.* Evaluation of automated antigen detection test for detection of SARS-CoV-2. *Diagn. Microbiol. Infect. Dis.* **101**, 115490 (2021).

10. Nikolai, O. *et al.* Anterior nasal versus nasal mid-turbinate sampling for a SARS-CoV-2 antigen-detecting rapid test: does localisation or professional collection matter? *Infect. Dis.* 1–6.
11. Osterman, A. *et al.* Evaluation of two rapid antigen tests to detect SARS-CoV-2 in a hospital setting. *Med. Microbiol. Immunol. (Berl.)* **210**, 65–72 (2021).
12. Pickering, S. *et al.* Comparative performance of SARS-CoV-2 lateral flow antigen tests and association with detection of infectious virus in clinical specimens: a single-centre laboratory evaluation study. *Lancet Microbe* **2**, e461–e471.
13. Schuit, E. *et al.* Diagnostic accuracy of rapid antigen tests in asymptomatic and presymptomatic close contacts of individuals with confirmed SARS-CoV-2 infection: cross sectional study. *BMJ* **374**, n1676.
14. Smith, R. L. *et al.* Longitudinal assessment of diagnostic test performance over the course of acute SARS-CoV-2 infection. *J. Infect. Dis.* **30**, 30.
15. Yin, N. *et al.* SARS-CoV-2 Diagnostic Tests: Algorithm and Field Evaluation From the Near Patient Testing to the Automated Diagnostic Platform. *Front. Med.* **8 (no pagination)**,.
16. Yokota, I. *et al.* Performance of qualitative and quantitative antigen tests for SARS-CoV-2 using Saliva. *Infect. Dis. Rep.* **13(3)**, 742–747 (2021).