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TechFlash: Rapid antigen tests for diagnosis of COVID-19

October 2020

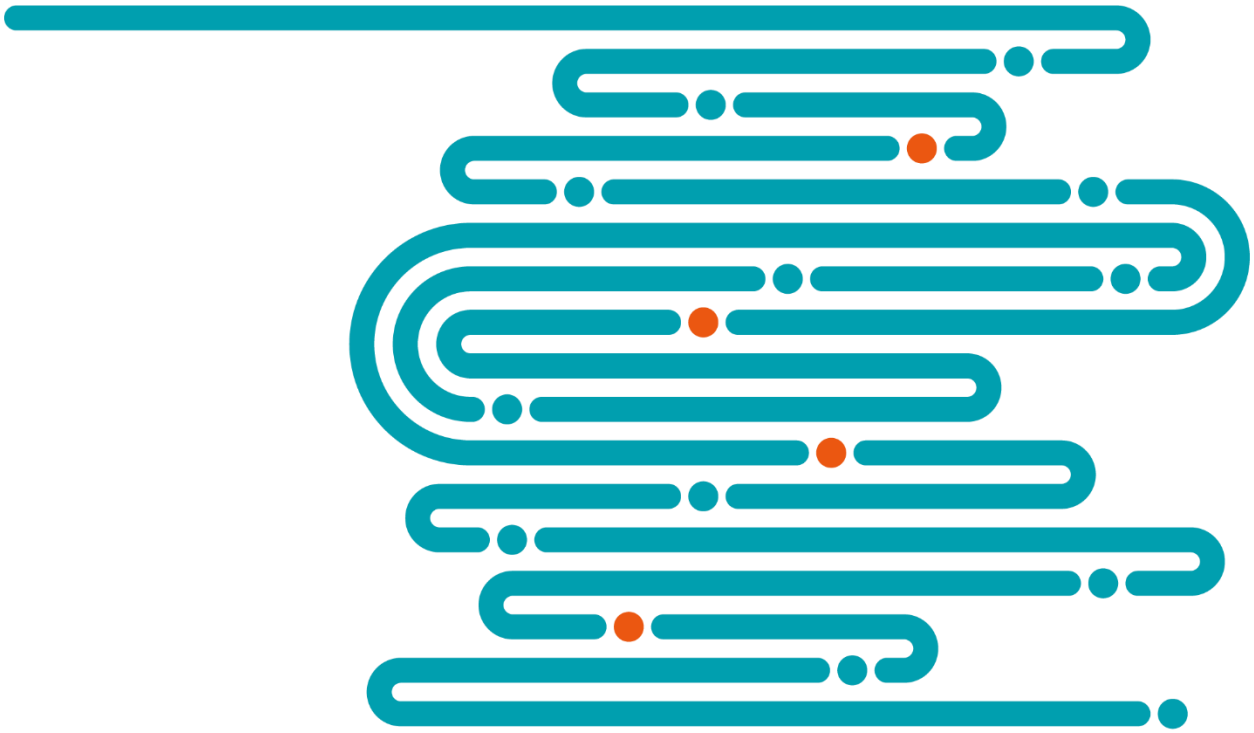

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Table of contents

This report comprises a review of abstracts identified through a search of the recent biomedical literature and does not constitute a comprehensive analysis. The report focus is on clinical evidence and outcomes.

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Technology overview and status

Rapid antigen testing for the SARS-CoV-2 virus is an emerging high-impact diagnostic technology. Potential advantages of these tests include low cost, easy sample collection, minimal infrastructure, portability and rapid results. Fast results can lead to better patient management decisions and more effective isolation recommendations to help stop the spread of COVID-19. Importantly, these tests can be more readily mass produced, which may address the high testing volume needed to cope during the pandemic.

As of October 15, 2020, the Food and Drug Administration (FDA) had granted Emergency Use Authorization (EUA) to five different rapid antigen tests for COVID-19. These include:

- BD Veritor system (Becton, Dickinson and Co.; San Diego, California)
- BinaxNOW COVID-19 Ag Card (Abbot Diagnostics Inc.; Scarborough, Maine)
- CareStart COVID-19 Antigen Test (Access Bio, Inc.; Somerset, New Jersey)
- LumiraDx SARS-CoV-2 Ag Test (LumiraDx UK Ltd.; United Kingdom)
- Sofia/Sofia 2 SARS Antigen FIA (Quidel Corp.; Athens, Ohio)

The first EUA for an antigen test was received by Quidel in May 2020. The latest EUA approvals and widespread availability of the rapid antigen tests, however, began mostly in July and August 2020. Quidel also received an EUA for a combined rapid SARS antigen/influenza test in October 2020. The CareStart test was the latest to receive emergency use authorization on October 8, 2020. Many more rapid antigen test EUAs may be expected in the near future.

Rapid antigen tests are commonly used in healthcare settings at the point-of-care for the detection of various common illnesses, like influenza, respiratory syncytial virus and strep throat. The COVID-19 antigen tests work using lateral flow immunoassay methods that are similar to these other tests, but they target a specific SARS-CoV-2 protein (i.e., antigen). All of the current COVID-19 antigen tests target the viral nucleocapsid (N) protein because of its relative abundance, but subsequent antigen tests may target other SARS-CoV-2 antigens, like the spike (S), membrane (M) or envelope (E) proteins.

During the antigen test procedure, a swab is used to obtain a sample of anterior nasal secretions or another validated specimen. Typically, liquid reagents or buffers are applied to the swab and the swab and/or liquid sample is placed in a well on a small plastic card. As the sample flows through the card matrix, immobilized, engineered antibodies capture the target antigen in the test area, which is indicated by the appearance of a concentrated visual or fluorescent dye. (see Figure 1) Unconjugated samples are captured further along the matrix and serve as a control indicator. The typical test takes about 10 to 15 minutes to provide a positive or negative qualitative result.

Figure 1. BinaxNow™ test card. Abbott Inc.

Some systems (e.g., BD Veritor, LumiraDx and Sofia) require a special instrument to read the indicator. This may potentially improve test readout consistency by eliminating manual interpretation, especially for samples around the positive cutoff point. The Abbott BinaxNOW test was the first authorized test that did not require analytic instrumentation for readout, followed by the Access Bio CareStart test. BinaxNOW is, however, paired with an optional free mobile app, called Navica, that registers and stores test results. This

app is intended for use as a “digital passport” to provide secure verification and subsequent access to various locations (e.g., work, air travel) based on test status and timing.

Though similar, the COVID-19 rapid antigen tests have some unique differences with respect to their analysis methodology, instrumentation, specimen requirements and test performance. (See Table 1) Differentiating factors to consider may include regulatory status and labeling, manufacturer validation data and methodology, specimen type and collection requirements, ease-of-use and costs. At this time, however, it is unknown if there are comparative advantages between systems secondary to these characteristics.

Notably, antigen tests tend to be less sensitive than molecular tests that use polymerase chain reaction (PCR) to amplify the target before analysis. Thus, they may have a high false negative rate in patients with a low viral load. Thus, usage typically includes labeling for symptomatic patients within about 5 to 7 days from symptom onset when the viral load is high. Positive tests in symptomatic patients are highly presumptive of SARS-CoV-2 infection; though high false positive rates may occur in settings with a low pre-test probability (prevalence) of COVID-19 and in asymptomatic patients. CDC guidelines for rapid antigen testing recommend confirmatory PCR testing for both negative and positive results when the clinical context and setting suggests the test results may not be accurate.

Table 1. SARS-CoV-2 rapid antigen tests.

Test	Latest EUA	Methodology/Analysis	Sample/Timing from symptom onset	Reported accuracy (IFU)
Abbott BinaxNOW	08/26/2020	Lateral Flow Visual Read	nasal swabs 7 days	PPA: 97.1% NPA: 98.5%
BD Veritor	07/23/2020	Chromatographic Digital Immunoassay, Instrument Read	nasal swabs 5 days	PPA: 85% NPA: 100%
AccessBio CareStart	10/8/2020	Lateral Flow Chromatographic Immunoassay, Visual Read	NP swabs 5 days	PPA: 88.4% NPA: 100%
LumiraDx	08/18/2020	Microfluidic Immunofluorescence Assay, Instrument Read	nasal swabs 12 days	PPA: 97.6% NPA: 96.6%
Quidel Sofia	07/17/2020	Lateral Flow, Fluorescence, Instrument Read	nasal swabs 5 days	PPA: 96.7% NPA: 100%

Abbreviations: EUA=emergency use authorization, PPA=positive percent agreement, NPA=negative percent agreement, NP=nasopharyngeal specimen, IFU=instructions for use manual

Technology significance

Diagnostic testing for COVID-19 is a very high clinical and financial impact technology due to the number of tests involved. As of mid-October, about 115 million total COVID-19 diagnostic tests have been conducted in the U.S.[1] The number of tests has grown rapidly from a few hundred available from the CDC in February and is currently around 1 million tests per day or 25 million monthly in the U.S.

Estimates of test production capacity project the potential availability of more than 70 million tests per month in the U.S. by the end of 2020 and more than 200 million tests per month by early 2021.[2] This amounts to approximately seven million tests per day or a factor of seven increase in testing in a short period of just a

few months. A large part of this expected increase in capacity is due to the marketing approval and mass manufacturing of rapid antigen tests.

The rapid antigen tests may have particular utility in settings where PCR tests are not readily available, like smaller or rural hospitals, decentralized settings, clinics and long-term care facilities and during off hours when hospital labs may not be fully operational.[3] Similarly, they may be helpful in testing scenarios where the turn-around time (TAT) for molecular testing is known to be sub-optimal and the delay may affect immediate clinical treatment decisions or the use of more rigorous infection control measures.

A surge in the number of COVID-19 tests during an outbreak can often overwhelm the testing capacity leading to long TATs. Rapid antigen testing at the point-of-care may be helpful in surge scenarios to provide immediate results for epidemic control decisions. In some cases, rapid results and the capability for frequent repeated testing may be more important than high test sensitivity.[4] Since those with a low viral load are less likely to be contagious, rapid antigen tests may be adequate for infection control purposes. Of note, the U.S. government has recently purchased more than 150 million rapid antigen tests from Abbott with the major intended usage for rapid deployment in surge and cluster scenarios, such as in long-term care facilities.[5]

Disadvantages of the rapid antigen tests include lower accuracy compared to the gold standard test. In some scenarios, a negative antigen test will still require confirmation with a PCR test, leading to test duplication and increased resource utilization. Further, because these tests have waived status and are conducted at the point-of-care, they may be more subject to user errors, like improper sample collection, test procedural mistakes and misinterpretations. This may lead to local variability in accuracy results.

Finally, because the technology is newly emerging, there remain many unknowns regarding test performance in the real-world and appropriate patient selection criteria. Further evidence development will be needed to define the safe and effective role of rapid antigen testing in different scenarios.

Current practice and alternatives

There are three main types of in vitro tests for COVID-19 that are differentiated by their test target: genetic, antibody and antigen.[6-11] Genetic tests, also known as molecular assays, target specific sequences of viral ribonucleic acid (RNA), usually using some type of PCR test. Antibody tests, also called serological tests, use immunoassay techniques to identify specific IgG and/or IgM antibodies circulating in the blood that are created by the body's immune system in response to infection. Antibody tests are an indirect test for COVID-19 that indicate if there was past exposure to the virus and therefore are not typically used as a diagnostic test for an active infection.[12]

Molecular tests are the current "gold standard" for COVID-19 diagnostic testing. There are hundreds of different FDA authorized commercial and laboratory-derived molecular tests for COVID-19. Significant differences may exist for these tests regarding test sensitivity, specificity, dynamic range, reproducibility, reagent consumption, equipment, cost, throughput and ease-of-use.[13] Generally, these tests have been validated on a diverse array of samples and have high sensitivity and specificity. Actual test TAT may be a few hours, but sample transportation requirements and lab backlogs can sometimes delay results for days.

PCR molecular tests designed for near-patient or point-of-care use are also commercially available. They typically utilize smaller, less-expensive instruments that require less operator training. Accuracy may be comparable to lab-based PCR techniques under controlled circumstances, though some issues related to false negatives have been reported for these devices during the COVID-19 pandemic.[14] TAT may be as short as 10 to 15 minutes, which is comparable to rapid antigen tests.

In addition to the currently available rapid antigen tests, there are more than fifty rapid antigen tests in development worldwide.[15, 16] Some of these require analytic instrumentation and others are standalone. For example, Roche has developed an instrument-free rapid chromatographic immunoassay now available in European markets. Like Abbott, Roche expects to be able to scale manufacturing to around 50 million tests monthly. Some other examples of rapid antigen tests in development include: E25Bio, Iceni Diagnostics, Maxim Biomedical, OraSure, Pinnacle, SD Biosensor, Sona Nanotech, and Qiagen.

Clinical evidence summary

The Medline/PubMed bibliographic database, MedRxiv preprint server for health sciences and ClinicalTrials.gov database of registered clinical studies were searched in October 2020 to identify clinical evidence related to the use of authorized rapid antigen tests. Keywords used in the literature search strategy included: *rapid, antigen, test*, COVID-19, SARS-CoV-2, coronavirus* and/or specific product names.

The primary source of information for rapid antigen test performance characteristics is derived from the material submitted by the manufacturer to the FDA as part of the EUA process. Methodology and clinical performance are provided in the instructions for use (IFU) for each product: BD Veritor IFU, BinaxNOW IFU, CareStart IFU, LumiraDx IFU, Sofia IFU. Of note, clinical performance data in the IFU may be updated through an FDA amendment process; thus, the most recent product labeling should be obtained. Clinical performance data for the authorized tests as of October 2020 are summarized in Table 2.

Abbott BinaxNOW clinical performance was derived from 102 nasal swab samples collected at seven U.S. sites from suspected COVID-19 symptomatic patients within seven days of symptom onset. COVID-19 was present in 34% (35/102) of samples. Results showed a positive percent agreement (PPA) of 97.1% (95% confidence interval, CI= 85.1% - 99.9%) and a negative percent agreement of 98.5% (95% CI= 92.0% - 100%). Tests were performed more than seven days after symptom onset in a small adjunctive sample of 28 patients. PPA in this cohort was only 75% and NPA dropped to 92%.

The BD Veritor clinical performance was derived from testing 226 direct nasal swab samples collected from suspected COVID-19 symptomatic patients within five days of symptom onset. Samples were collected in 21 different sites across the U.S., with RT-PCR used as the gold standard. Results showed a PPA of 84% (95% CI= 67% - 93%), NPA of 100% (95% CI= 98% - 100%) and an overall percent agreement (OPA) of 98% (CI= 95% - 99%). COVID-19 was present in 13.7% (31/226) of samples. Positive predictive value (PPV) for this prevalence was 100% and negative predictive value (NPV) was 97.5%.

LumiraDx clinical performance was derived from 257 samples collected within 12 days of symptom onset. COVID-19 prevalence was 32.3% (83/257) in the sample cohort. Overall PPA was 97.6% (CI=91.6% - 99.3%), NPA was 96.6% (CI= 92.7% - 98.4%) and OPA was 96.9% (CI= 94.0% - 98.4%). PPV was 93.1% (CI= 85.8% - 96.8%) and NPV was 98.8% (CI= 95.8% - 99.7%).

The Quidel Sofia clinical performance was shown in 209 direct nasal swab samples collected within five days of symptom onset at five different locations. Disease prevalence was 14.4% (30/209). PPA was 96.7% (95% CI= 83.3% - 99.4%) and NPA was 100% (95% CI= 97.9% - 100%). PPV was 100% (95% CI= 88.3% - 100%) and NPV was 99.4% (95% CI= 96.9% - 99.9%).

The Access Bio clinical performance was determined using 106 retrospective frozen NP swab samples and 20 contrived samples (10 positive and 10 negative). In the retrospective sample, the test demonstrated a PPA of 88.37% (95% CI= 75.5% - 94.9%) and NPA of 100% (95% CI= 94.3% – 100%). A prospective

performance study at five U.S. sites using NP swabs and collection within five days of symptom onset is reportedly underway and results are expected to be included in updated future labeling.

Table 2. Clinical performance data for antigen tests.

Test	Sample size	Pre-valence	Sample type	Symptom onset	Clinical performance PPA	NPA	OPA	LOD (TCID50/mL)
BinaxNOW	102	34%	nasal	≤ 7 days	97.1%	98.5%	98%	22.5
Veritor	226	13.7%	nasal	≤ 5 days	85%	100%	98%	140
CareStart	106	36%	NP	≤ 5 days	88.4%	100%	95.2%	800
LumiraDx	257	32.3%	nasal	≤ 12 days	97.6%	96.6%	96.9%	32
Sofia	209	14.4%	nasal	≤ 5 days	96.7%	100%	99.5%	113

Abbreviations: PPA=positive percent agreement, NPA=negative percent agreement, OPA=overall percent agreement, NP=nasopharyngeal specimen, LOD=estimated limit of detection, $TCID_{50}$=50% tissue culture infection dose

For FDA EUA clearance, an antigen test is required to have PPA ≥ 80% compared to the reference standard in a cohort with at least 30 positive results.[17] All of the authorized tests exceed this threshold, suggesting there is diagnostic value associated with using these tests in appropriate settings. However, false negatives compared to laboratory-based PCR tests may occur and should be considered when clinical suspicion is high. Agreement is expected to be better at high viral loads, which usually occurs in the pre-symptomatic (1 to 3 days before symptom onset) and early symptomatic phases (first 5 to 7 days after symptom onset).[18] Agreement with PCR improves at low cycle threshold (Ct) values (e.g., Ct ≤ 25) consistent with a dependence on viral load.

Clinical performance of the BD Veritor test has been further reported compared to laboratory-based PCR.[19] In this study, 251 nasal samples were collected within seven days of symptom onset and tested with the BD Veritor system. These were compared to nasopharyngeal (n=217) or oropharyngeal (n=34) samples from the same participants placed in universal transport medium and shipped to a reference lab for PCR testing. For the overall cohort with samples collected through five days of symptom onset, the PPA was 83.9%. PPA dropped slightly to 82.4% through six days of symptom onset and 76.3% through seven days. NPA was 99.5% to 100% for all cohorts. Discordant results showed nine false negatives and one false positive for BD Veritor compared to PCR. Follow-up analysis suggested false negatives were associated with the Ct score.

In a secondary study from the same group as above, the BD Veritor test was compared to the Sofia 2 rapid antigen test in samples collected within five days from symptom onset from 377 symptomatic participants at five U.S. sites.[19] Overall, BD Veritor showed a PPA of 97.4%, NPA of 98.1% and OPA of 98.1% compared to Sofia 2. The authors concluded that there was good agreement between these two rapid tests and that the labeled difference in sensitivity (see Table 2, 96.7% vs. 85%) was not supported by their study.

It has been proposed that the high sensitivity of PCR can detect the presence of viral RNA in very small amounts, even if the virus is no longer infectious. In these cases, PCR may report false positives for contagious virus and the lower sensitivity of antigen tests may correlate better with contagiousness.

To test this hypothesis, a study was performed where 38 PCR positive specimens were cultured for active virus.[20] Overall, 28 of 38 PCR-positive specimens were also positive by culture methods. Testing with the

BD Veritor antigen test was positive in 27 of the 28 PCR+/culture+ samples. In the 10 culture negative samples, the antigen test was positive in two cases and negative in eight cases. Though the PCR test had higher overall diagnostic sensitivity, the positive predictive value was only 73.7% for culture positivity compared to 90% for the antigen test.

The Sofia SARS antigen test performance was reported in a study using 64 nasopharyngeal samples (32 positive, 32 negative) collected withing the first five days after symptom onset.[21] Two false negatives and one false positive were found compared to PCR resulting in a sensitivity of 93.8% and specificity of 96.9%. Sensitivity reportedly improved for samples with high viral loads with no false negatives in samples with Ct < 30. Though patient samples were different than typical clinical usage, these results are consistent with results obtained from direct nasal swabs.

An ongoing, multi-center clinical trial evaluating the performance of the LumiraDx COVID-19 antigen test was identified (clinical trials identifier: NCT04557046). This study intends to enroll 400 participants at six different point-of-care sites, including physician offices, urgent care centers, emergency departments, outpatient clinics and drive through testing sites. Results are expected by December 2020.

AdventHealth in Florida was an early adopter of rapid antigen testing in May and June of 2020. They reported preliminary results from a validation study on 1,172 patients tested using both rapid antigen testing and PCR.[22] In the overall cohort, 107 false negatives and six false positives were noted compared to PCR testing, resulting in a reported sensitivity of 76.7% and specificity of 99.2%.

In a subsequent pilot study, AdventHealth began screening healthcare workers with significant exposure to COVID-19 patients.[22] A total of 497 staff participated in the pilot (358 asymptomatic, 139 symptomatic). In asymptomatic staff, 2% (7/358) were positive on antigen testing. In symptomatic staff, 11% (15/139) were positive on antigen testing. Symptomatic staff negative on antigen testing could have a confirmatory PCR test and this identified another 5 COVID+ staff members. Staff with a low risk exposure, no symptoms and a negative antigen test were allowed to return to work.

Two meta-analyses including antigen testing for COVID-19 were identified. A Cochrane systematic review conducted in May 2020 considered 5 different studies comprising 943 samples and eight different tests.[23] The average sensitivity was 56.2% (95% CI= 29.5% - 79.8%) and average specificity was 99.5% (95% CI= 98.1% - 99.9). Available trials on antigen testing was noted to be highly limited. A more recent meta-analysis from a European collaborative also noted the low quality and scarcity of available data from independent sources.[24]

Financial issues

The cost of COVID-19 testing is highly variable and may depend on a lot of different factors.[25] On the low end, the initial cost for the Abbott BinaxNOW test cartridge is reportedly $5 during the initial rollout phase. Costs for other rapid antigen tests have typically ranged from about $15 to $50.[26] Some of the antigen tests incur costs for the cartridge and the reader, which may be up to a few thousand dollars. In addition, there may be a variable cost associated with administering the test that can add about $15 to $100. In general, antigen tests typically cost less overall than PCR tests due to less expensive instrumentation, fewer reagents and reduced processing steps.

Antigen test costs are covered by most insurance plans, Medicare and Medicaid when they are conducted using authorized tests in symptomatic patients for diagnostic purposes. Reimbursement rates, however, are highly dependent on payer. Federal laws enacted during the COVID-19 pandemic, including the Families

First Coronavirus Response Act (FFCRA) and the Coronavirus Aid, Relief, and Economic Security (CARES) Act, have eliminated patient cost-sharing (e.g., co-payment, co-insurance or deductibles) requirements as well. A new Current Procedural Terminology (CPT®) code 87426 was created on June 25, 2020 to facilitate reimbursement coding specific to antigen testing.

Because they are in the early stages of dissemination, there remain many unknowns surrounding the economic effects of these diagnostic technologies. Further study is needed, therefore, to better delineate the inputs for financial modeling. If these technologies are associated with improved outcomes secondary to rapid TAT, there is potential for a highly favorable cost benefit. The societal benefit associated with reduced spread of infection due to better decisions for when to isolate a positive patient may be deemed a sufficient reason to make rapid testing available even without rigorous cost-effectiveness modeling.

The total cost of COVID-19 testing has been estimated at $6 billion to $25 billion annually in the U.S.[27] Assumptions at the low end include use of current testing levels limited by supply availability. The high end assumes tripling of current test volumes due to mass screening initiatives needed as part of return to work and school safety measures. Increased testing due to fluctuating local surges and decreases in COVID-19 prevalence, e.g., from a second wave, are difficult to predict in these modeling scenarios; but could have a large effect on testing volumes. Vaccine availability with widespread dissemination could also have a significant impact leading to decreased testing volumes and associated costs.

Patient selection criteria

FDA EUA labeling defines the patients and conditions under which the test has been validated. Best results may be expected when adhering rigorously to the product labeling. At this time, antigen tests are indicated for diagnostic testing in symptomatic patients with suspected COVID-19 within a specified short duration of symptom onset (usually 5 to 7 days). Off-label usage may also be expected, with the caveat that the healthcare provider needs to thoroughly consider the device performance limitations and clinical circumstances in order to effectively use the results.

Other than use in symptomatic patients in high prevalence populations, there are limited published data defining appropriate patient selection algorithms for antigen testing. Further appropriateness criteria may be premised on usage when test results would reasonably be expected to lead to more immediate clinical decisions or infection control measures. Some reasonable scenarios may include:[3, 18, 28]

- Targeted testing in areas with a current surge in cases and expected high disease prevalence
- Outbreak control in healthcare settings, long-term care sites, schools or other congregate settings
- Contact tracing with serial antigen testing in high-risk settings, like frontline healthcare facilities, or for those with high-risk exposure to known positive cases
- Remote and rural healthcare settings with limited access to rapid testing, where results may be later confirmed through PCR testing

Similarly, there may be a relative contraindication for antigen testing in asymptomatic patients, in areas with a very low COVID-19 prevalence and for routine, widespread screening or surveillance.

Future developments

Continued development of clinical evidence is expected and needed in the near future. There is a particular need for large, independent, real-world studies confirming the clinical performance of the rapid antigen tests in symptomatic populations. Further guidance on the conditions for follow-up PCR testing for potential false negatives and false positives may be derived from these future studies. Rapid antigen test usage in asymptomatic cases and screening scenarios is also likely, but there is very limited data on clinical performance under these conditions. Further study in nursing homes, long-term care facilities and other similar settings is needed to better define test value for these populations.

The field of COVID-19 testing is rapidly evolving, with numerous manufacturers involved and different types of tests in development. Many more rapid antigen tests are expected to be authorized throughout 2020 and 2021. For example, the National Institutes of Health (NIH), in collaboration with the Biomedical Advanced Research and Development Authority (BARDA), are also funding some rapid antigen test development and commercialization projects through their Rapid Acceleration of Diagnostics (RADx) program. In addition to support for the Quidel Sofia antigen test, recent RADx grants have been awarded to the rapid antigen test manufacturers Ellume (Valencia, California), Luminostics (Milpitas, California) and Quanterix (Billerica, Massachusetts). Of note, some of these tests are being developed for home use, which would be a major COVID-19 testing milestone.

Numerous other novel test methodologies beyond PCR, antigen and antibody testing are under development. As these potentially become authorized in the near future, they may be alternatives to the rapid antigen tests. Comparative trials will be needed to determine their relative advantages and disadvantages.

Conclusions and recommendations

The following conclusions and recommendations are based on the material presented in this report:

- COVID-19 testing is a very high impact technology and the rapid antigen tests are an emerging type of COVID-19 testing expected to have a significant role in immediate patient care decisions. Potential advantages of these tests include low cost, mass production, minimal instrumentation/infrastructure requirements and rapid results provided at the point-of-care.
- Rapid antigen tests from five different manufacturers are now commercially available and many more are expected to be authorized in the near future. These COVID-19 tests are based on lateral flow immunoassay methods that are commonly used for detection of other diseases. This test methodology has been adapted to detect a specific antigen associated with the SARS-CoV-2 nucleocapsid protein.
- There are potential differences among these tests due to different methodologies and clinical performance. However, no comparative advantages have been proven as yet. Differentiating factors to consider among tests include regulatory status and labeling, manufacturer validation data and methodology, corroborating performance data from independent sources, specimen type and collection requirements, ease-of-use and total test costs. Manufacturer reputation, proof of quality control, manufacturing capacity, efficient distribution and test availability may also be important considerations.

- The authorized rapid antigen tests have all met FDA emergency use standards for diagnostic accuracy under specified conditions. Current tests all demonstrate a PPA ≥ 80% and NPA ≥ 97% compared to the reference standard. Lower PPA values indicate the antigen tests are less sensitive than molecular tests and may result in false negatives, particularly when the viral load is low. Of note, the rapid antigen tests all provide a qualitative yes/no result rather than a quantitative result taking viral load into account.
- Further, even though reported NPAs are very high, a high rate of false positives may be expected in low prevalence scenarios. For example, even a test with a specificity (NPA) of 99% would have a false positive rate of ~16% in a test population where the prevalence is 5%. For large volume testing scenarios, like screening asymptomatic people, this could quickly add up to hundreds of false positives where the patient is incorrectly told they are positive for COVID-19 and confirmatory testing will be required.
- Rapid antigen tests may be most appropriately used in settings where immediate results are useful to direct clinical treatment decisions and/or infection control measures. Those situations where PCR tests are not readily available or the TAT for results is expected to be too long may benefit from rapid antigen testing. Some examples may include small or rural hospitals, decentralized healthcare settings, off-hours and surge conditions.
- The field of COVID-19 diagnostic testing is rapidly evolving. New devices and new studies are being added weekly. Efforts should be made to update the evidence and other material included in this report before decision-making.

Related links

Guidance documents:

CDC guidance on rapid antigen testing (Sept. 4, 2020)

WHO guidance for rapid antigen testing (Sept. 11, 2020)

FDA guidance for test manufacturers (May 2020)

APHL guidance for implementation of rapid antigen testing (Sept. 24, 2020)

IDSA guidelines for rapid testing (Sept. 4, 2020)

ICMR guidance on rapid antigen test KITS (September 25, 2020)

AHCA/NCAL guidance (Aug. 20, 2020)

FDA resources:

EUAs for antigen tests

FAQs on testing

FDA EUA letter	Fact sheets	Instructions for use
CareStart COVID-19 Antigen test	HCP Patients	IFU
Sofia 2 Flu + SARS Antigen FIA	HCP Patients	IFU
BinaxNOW COVID-19 Ag Card	HCP Patients	IFU
LumiraDx SARS-CoV-2 Ag Test	HCP Patients	IFU
BD Veritor System for Rapid Detection of SARS-CoV-2	HCP Patients	IFU
Sofia SARS Antigen FIA	HCP Patients	IFU

Product websites:

BD Veritor system (Becton, Dickinson and Co.; San Diego, California)

BinaxNOW COVID-19 Ag Card (Abbot Diagnostics Inc.; Scarborough, Maine)

CareStart COVID-19 Antigen Test (Access Bio, Inc.; Somerset, New Jersey)

LumiraDx SARS-CoV-2 Ag Test (LumiraDx UK Ltd.; United Kingdom)

Sofia/Sofia 2 SARS Antigen FIA (Quidel Corp.; Athens, Ohio)

COVID-19 test volumes:

Johns Hopkins

World in Data

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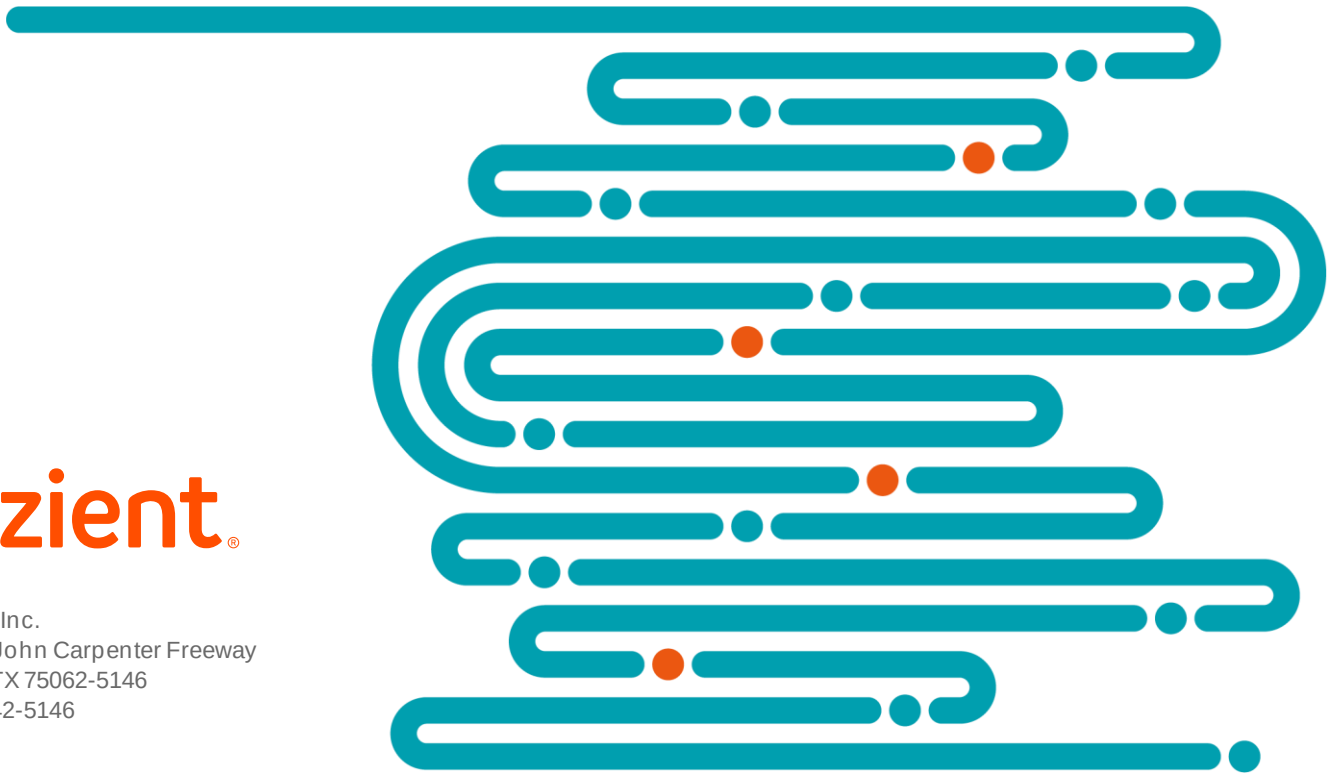

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