
Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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REVIEW

# A systematic review comparing at-home diagnostic tests for SARS-CoV-2: Key points for pharmacy practice, including regulatory information

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ABSTRACT

*Background:* Home-based rapid diagnostic testing can play an integral role in controlling the spread of coronavirus disease 2019 (COVID-19).
*Objectives:* This review aimed to identify and compare at-home diagnostic tests that have been granted Emergency Use Authorizations (EUAs) and convey details about COVID-19 diagnostic tests, including regulatory information, pertinent to pharmacy practice.
*Methods:* The Food and Drug Administration (FDA) online resources pertaining to COVID-19 tests, EUAs, and medical devices were consulted, as were linked resources from FDA's webpages. Homepages of the 9 COVID-19 home tests with EUAs were comprehensively reviewed. PubMed literature searches were performed, most recently in May 2021, to locate literature about the identified home tests, as were searches of Google Scholar, medRxiv, and bioRxiv. Studies were included if they were performed at home or if subjects self-tested at study sites. Samples were collected by a parent or guardian for patients under 18 years of age. Positive percent agreement (PPA) and negative percent agreement (NPA) for the clinical diagnosis of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) virus was evaluated.
*Results:* Limited data have been published for these home tests given that they are available through EUAs that do not require clinical trials. Fifteen studies were located from searching the literature, but only 2 met the inclusion criteria. Review of the home tests' websites yielded a single study for each test, with the 3 BinaxNOW platforms using the same study for their EUAs. The 9 COVID-19 home tests with EUAs as of May 7, 2021, include 3 molecular tests and 6 antigen tests. These tests had similar performance on the basis of PPA ranging from 83.5% to 97.4% and NPA ranging from 97% to 100%.
*Conclusion:* The 9 SARS-CoV-2 home tests demonstrated satisfactory performance in comparison with laboratory real time reverse-transcription polymerase chain reaction tests. The convenience and ease of use of these tests make them well-suited for home-based rapid SARS-CoV-2 testing.


Feelings of being unprepared and overwhelmed rippled throughout the world in the early days of the coronavirus disease 2019 (COVID-19) pandemic. As infections rapidly spread, scientists struggled to develop and distribute reliable diagnostic tests and establish meaningful testing protocols.[1] In a scramble to develop diagnostic tests for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the Food and Drug Administration (FDA) expanded its Emergency Use Authorization (EUA) process to allow for more applicants to seek approval for tests.[2] Even with these measures, unacceptable delays in testing continue and have furthered the confusion and panic caused by the pandemic.

Although vaccines are being administered in many countries, it is recognized that the world will need to contend with SARS-CoV-2 for the foreseeable future. With

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**Key Points**

**Background:**

- Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) screening and diagnostic tests are a critical tool to help reduce disease transmission, and there is a crucial need for widely available rapid diagnostic tests for consumer use.
- Several test types have been utilized under Emergency Use Authorizations (EUAs), including molecular, antigen, and serology tests.

**Findings:**

- Nine diagnostic tests have been granted EUA for at-home use, including 3 molecular tests: Lucira coronavirus disease 2019 (COVID-19) all-in-one test kit, Lucira CHECK-IT COVID-19 test kit, and Cue COVID-19 test for home and over-the-counter (OTC) use; and 6 antigen tests: BinaxNOW COVID-19 Ag card home test, BinaxNOW COVID-19 antigen self-test, BinaxNOW COVID-19 Ag card 2 home test, QuickVue at-home COVID-19 test, QuickVue at-home OTC COVID-19 test, and Ellume COVID-19 home test.
- The 9 at-home tests currently available under EUAs show high positive percent agreement and negative percent agreement for identifying SARS-CoV-2.

this reality, a critical need remains to diagnose COVID-19 quickly and accurately. Until more is known about immunity durability after infection and vaccination, tests allowing for minimal interaction of symptomatic individuals with others are needed. Several testing platforms have been utilized over the first year of the pandemic to improve testing access and reduce disease transmission risks (e.g., drive-thru testing centers). Although these services allow for high-volume, socially distanced testing, these models are somewhat inconvenient for patients and usually rely on polymerase chain reaction (PCR) tests that may have unacceptably long turnaround times.[3,4] To improve convenience, diagnostic laboratories have developed at-home collection kits allowing individuals to collect specimens at home to then send to a designated laboratory for testing, with 50 having EUAs as of May 7, 2021.[5] Although these kits provide convenience and social distancing, their turnaround times are suboptimal. Since November 2020, multiple manufacturers have received EUA for complete at-home testing platforms.[5,6] In theory, these tests offer optimal efficiency and convenience while maintaining maximal social distancing. These home tests are a dramatic shift from early pandemic testing models, so little is known about them. The purpose of this systematic review is to identify at-home diagnostic tests for SARS-CoV-2 that currently have EUA in the United States and evaluate their diagnostic accuracy. Regulations impacting testing and key considerations that clinicians should be familiar with regarding these home tests are also discussed.

## Regulatory matters

The Clinical Laboratory Improvement Amendments of 1988 (CLIA) established national quality standards for nonresearch laboratory testing performed on human-derived specimens. Under these regulatory standards for laboratory tests performed for the purposes of health assessment or for "diagnosis, prevention, or treatment,"[7-9] CLIA defines roles for the Centers for Disease Control and Prevention (CDC), Center for Medicare and Medicaid Services (CMS), and FDA in supporting laboratory testing.[7] Under CLIA, CMS is responsible for certifying laboratories and other facilities, including pharmacies, and ensuring compliance with testing standards.[8,10] CDC is responsible for technical oversight, developing technical standards, and maintaining laboratory quality.[7] In this role, various guidelines are issued to ensure safety and quality. CDC's *Interim Guidelines for Collecting, Handling, and Testing Clinical Specimens for COVID-19* provides critical information for health care providers offering point-of-care (POC) testing and specifies that pharmacists are considered health care providers under this guidance.[11] FDA reviews and approves medical devices brought to the market.[7] Once a medical test receives FDA approval, it is categorized on the basis of the complexity of methods required to run the test. Numerous factors are considered when assigning test complexity, including user interpretation requirements, calibration and quality control requirements, degree of independent judgment needed, difficulty of performance calculations, intricacy of methodologies, and degree of training needed to operate and run the test. On the basis of these elements, many tests are assigned moderate or high-level complexity and can only be run by laboratories certified to run tests of these complexities. A company may apply for a waived complexity status (i.e., CLIA-waived) if they believe that their test is simplistic enough, does not require training other than review of a product insert to perform, requires no or minimal interpretation or judgment, and presents little risk of erroneous results.[12] By obtaining CLIA-waived status, a test may be performed in a nontraditional laboratory setting in possession of a CMS Certificate of Waiver,[13] with pharmacies demonstrating a surge in these waivers since the pandemic began.[14] In addition, manufacturers of CLIA-waived devices may seek clearance for home-use.[15]

Typically, the approval process for a new test takes about 3-7 years.[16] Section 564 of the Federal Food, Drug, and Cosmetic Act enables the FDA Commissioner to allow unapproved medical products or unapproved uses of approved medical products to be used in emergency situations. This process is referred to as EUA and allows FDA to facilitate the availability and use of medical measures needed during public health emergencies.[2,17] Granting EUA is different from FDA approval of a device. EUA may only be granted after a declaration by the U.S. Department of Health and Human Services (HHS) Secretary that circumstances exist justifying the authorization.[17] In addition, FDA must determine that the following statutory criteria have been met: (1) use "for a serious or life-threatening condition," (2) "evidence of effectiveness," (3) favorable "risk-benefit analysis," and (4) "no alternatives" exist.[17] For FDA approval, a high standard of proof of effectiveness is required. For EUA, the standard of "may be

effective" is considered;[17] therefore, data from controlled clinical trials need not be available. For in vitro diagnostic devices, performance data to support the intended use may be derived from testing "fresh, contrived, banked, or archived specimens."[17]

All devices granted EUA are only authorized for use while the emergency declaration exists. Once an EUA declaration is terminated, all devices authorized during the emergency declaration are no longer available for use and must be removed from the market. However, after EUA termination, the device manufacturer may continue or initiate an FDA review for device approval.[17]

Under the *Public Readiness and Emergency Preparedness (PREP) Act,* the HHS Secretary issued an emergency declaration for COVID-19 that provides "limited liability for activities related to medical countermeasures against COVID-19."[18] Included in this are EUA devices.[18] Following this emergency declaration, as of May 2021, FDA has issued 370 EUAs for qualifying in vitro diagnostics tests targeting SARS-CoV-2.[2] As of May 7, 2021, 270 of the tests are molecular tests, and 13 meet criteria for CLIA-waived status; 24 are antigen detection tests, and 19 meet criteria for CLIA-waived status; 76 are serology tests to detect SARS-CoV-2 antibodies, and 7 meet criteria for CLIA-waived status.[5,19] Since the initial emergency declaration, multiple amendments have been introduced, and *General Counsel Advisory Opinions* and *Guidance* documents from the HHS have been issued.[20] Of particular significance for pharmacists are the *Third Amendment* and HHS *Guidance* documents that clarify the roles of pharmacists, pharmacy interns, pharmacy technicians, and pharmacies, which indicate that they are all covered under the PREP Act when performing POC diagnostic testing, vaccinations, and services considered SARS-CoV-2 countermeasures, provided regulatory requirements are met.[21-25]

## Overview of SARS-CoV-2 test types and performance measures

In addition to understanding the regulatory matters surrounding SARS-CoV-2 testing, a basic understanding of SARS-CoV-2 test types and performance parameters is important for pharmacists who may be involved in test administration, distribution, and patient counseling. The 3 test types currently available include molecular tests, antigen tests, and serology tests.[26]

Molecular diagnostic tests amplify and detect pathogen-specific genetic targets, detecting target SARS-CoV-2 genetic material in the case of COVID-19.[26] For diagnosing SARS-CoV-2, PCR assays are most prevalent and typically exhibit high sensitivity, with sensitivity indicating the percentage of true positive results detected by the test [low false negative rate].[27,28] Testing during the first few days of infection when viral loads may be small, or when there may be inadequate specimens, can lead to false negatives because there is inadequate SARS-CoV-2 genetic material for the tests to detect.[29] A meta-analysis found an average test sensitivity of 95% for the studied rapid molecular assays.[30] The same meta-analysis found an average test specificity of 98.9%,[30] with specificity being the probability that a negative test result is truly negative (low false positive rate).[27,28] Although PCR-based tests have excellent sensitivity and specificity, they require expensive equipment and are prone to contamination.[31] In addition, these tests are sometimes criticized as being too sensitive because they do not discriminate between viable pathogens and residual genetic fragments from nonviable virus.[32] In other words, these tests can determine whether the disease is present in a patient but cannot determine whether it is contagious or not.

Antigen diagnostic tests detect proteins such as the spike protein, nucleocapsid protein, or both from viable virus.[27] These assays are typically based on less expensive lateral flow technology.[33] Many of these tests do not require analyzers or readers and are, therefore, less expensive and highly portable.[34] The trade-off is that they tend to have lower analytical sensitivities, "i.e., require greater amounts of virus material to turn positive" than PCR tests.[34] A meta-analysis found a wide range of test sensitivities for the studied antigen tests, with an average sensitivity of 56.2%. This same meta-analysis found good test specificity, with an average of 99.5% for the antigen tests studied.[30] Even with low sensitivities, Larremore, an infectious disease modeler and proponent of frequent rapid testing for SARS-CoV-2 infection indicated, "Even low-sensitivity tests, which only catch people at the early and most-contagious stage of infection, could still be useful."[35] Indeed, antigen tests when administered when there are peak viral loads, when individuals are most likely to be infectious, reportedly exhibit sensitivity comparable to PCR tests.[34]

Serologic tests detect antibodies to a virus, thus indicating whether there has been a recent or past infection. These tests, also called antibody tests, are not meant to detect active infection but rather can identify individuals who have already had the virus.[26] Figure 1 depicts approximations of tests' ability to detect viral infection as time progresses from infection onset through 4 weeks after infection.

With the use of rapid diagnostic tests, it is essential to understand the impact of their performance characteristics as the intended use and pretest probability of disease fluctuate. When the sensitivity of a test is *low* and the pretest probability of disease is *high*, the test may return a higher rate of false negative results. This correlates with the negative predictive value (NPV) of a test or how good it is at ruling out a disease. In this scenario, one should confirm a negative test result when there is a high suspicion of disease with a more sensitive test like a laboratory-based PCR test, so a true infection is not missed.[7] Conversely, a test with a relatively high specificity may result in a high rate of false positive tests when the pretest probability of disease is *low*. This correlates with the positive predictive value (PPV) of a test or how good the test is at ruling in a disease. In this case, it is prudent to confirm a positive result in an asymptomatic individual with a laboratory-based PCR test in an effort not to misdiagnose someone with COVID-19.[7]

As the COVID-19 pandemic continues and SARS-CoV-2 continues to circulate for the foreseeable future, manufacturers have begun to expand access to tests for the general public. One solution is to enable individuals to collect and test specimens at home, allowing for complete at-home testing. Currently, 6 antigen tests and 3 PCR test have received EUAs for at-home testing.[5]

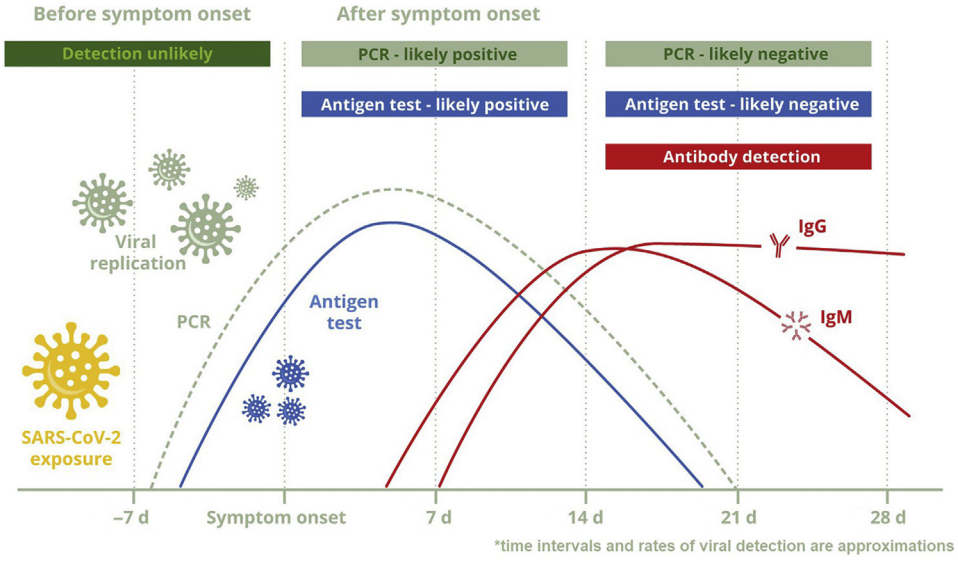


**Figure 1.** Test method versus progression of infection. Abbreviations used: IgG, immunoglobulin G; IgM, immunoglobulin M; PCR, polymerase chain reaction; SARS-Cov-2, severe acute respiratory syndrome coronavirus 2. Image reused with permission from Spring Healthcare. Copyright 2020 Spring Healthcare. https://springhealthcare.org/sars-cov-2-antigen-rapid-test-swab/.

## Methods

### *Search strategies*

FDA website documents and linked resources pertaining to COVID-19 tests, EUAs, and medical devices were consulted. Websites of the 9 COVID-19 home tests with EUAs were comprehensively reviewed. PubMed, Google Scholar, medRxiv, and bioRxiv literature searches were most recently performed in May 2021 for home tests issued EUAs. Database search details can be found in Appendix 1.

### *Inclusion criteria*

To detect literature about the SARS-CoV-2 home tests with current EUAs, all PubMed, Google Scholar, medRxiv, and bioRxiv results that specifically mentioned one or more tests' proprietary name(s) were extracted for review. Studies were included if the samples were self-collected (or collected by a parent or guardian for patients under 18 years of age) and evaluated the positive percent agreement (PPA) and negative percent agreement (NPA) for the clinical diagnosis of SARS-CoV-2 virus. Studies from the home tests manufacturers' websites were also selected for inclusion because EUA does not require clinical trials and limited data is available for these tests.

## Results

Searches of PubMed, Google Scholar, medRxiv, and bioRxiv yielded 15 unique studies after de-duplication.[36-50] Studies identified can be found in Appendix 2. Fourteen of the studies examined the BinaxNOW platform, and 1 examined the Cue COVID-19 Test. Two studies met inclusion criteria.[41,49] Seven studies were identified in the manufacturers' EUA labeling.[51-59] The 3 at-home BinaxNOW platforms all used the same study for their EUA.[51-53] Data from all 7 manufacturers' studies were included in the qualitative systematic review.[51-59]

### *Risk of bias*

Because all of the tests have been made available through EUA, the data used to obtain the EUAs were from interim analyses;[51-59] therefore, the sample sizes were smaller, leading to issues with selection bias and potential issues with the ability to extrapolate the data to expanded populations. In addition, the clinical data have only been published in the manufacturers' literature, so while FDA has reviewed it, it has not gone through the rigorous peer-review process that occurs when studies are published in medical journals. In addition, many of the details needed to fully assess bias are missing (e.g., missing demographic data make it difficult to know which patient populations are represented in the studies). Therefore, there is a high risk of bias in the studies included in this systematic review.

### *Synopsis of test characteristics*

There are 9 COVID-19 home tests at the time this article was written, some of which are the same testing platform with different availabilities or indications.[5,51-59] Three of the tests are molecular (2 Lucira and 1 Cue),[55-57] and 6 are antigen-based (Ellume, 3 BinaxNOW, and 2 QuickVue).[51-54,58,59] A full comparison of the molecular tests can be found in Table 1, and a full comparison of the antigen tests can be found in Table 2.

Six of the tests are available OTC, and 3 are only available via prescription.[51-59] The BinaxNOW Ag Card, QuickVue at-Home, and Lucira All-in-One tests are only indicated for patients suspected of having COVID-19 (e.g., symptomatic),[51,55,58] and the remaining 6 tests are indicated for both symptomatic and asymptomatic patients.[52-54,57,59] All test results can be

**Table 1**
Comparison of at-home molecular COVID-19 tests[51-59]

| Device characteristic | Lucira COVID-19 all-in-one test kit | Lucira CHECK-IT COVID-19 test kit | Cue COVID-19 test for home and OTC use |
|---|---|---|---|
| Emergency Use Authorization date | November 17, 2020 | April 9, 2021 | March 20, 2021 |
| Manufacturer | Lucira | Lucira | Cue Health |
| Requires prescription | Yes | No (OTC version of Lucira COVID-19 all-in-one test kit) | No |
| Principle of test procedure | Qualitative molecular amplification | Qualitative molecular amplification | Qualitative molecular amplification |
| Specimen sample | Nasal swab | Nasal swab | Nasal swab |
| Authorized age for use | Self-collected: ≥14 y | Self-collected: ≥14 y | Self-collected: ≥18 y |
| | | Adult-collected: ≥2 y | Adult-collected: ≥2 y |
| Requires observation by telehealth proctor | No | No | No |
| Indication for use | Suspected COVID-19 by health care provider | With or without symptoms or other epidemiologic reason to suspect COVID-19 | With or without symptoms or other epidemiologic reason to suspect COVID-19 |
| Instructions for use | Open kit | Open kit | Set up Monitoring System |
| | Insert batteries | Insert batteries | Open kit |
| | Insert vial into test unit | Insert vial into test unit | Insert test cartridge into reader |
| | Nasal swab | Nasal swab | Nasal swab with wand |
| | Inset nasal swab in vial | Inset nasal swab in vial | Insert nasal swab into cartridge |
| | Stir vial contents | Stir vial contents | |
| | Close vial and press down | Close vial and press down | |
| Results | Appears on display | Appears on display | Appears in mobile app |
| Results automatically reported to public health authorities | No | No | Yes |
| Differentiates between SARS-CoV-1 and SARS-CoV-2 | Yes | Yes | No |
| Endogenous interfering substance at tested concentrations | None | None | None |
| Cross-reactivity with other organisms | No | No | No |
| Time to result | 11–30 min | 11–30 min | approximately 20 min |
| Requirements | None | None | Cue Health Monitoring System |
| | | | Mobile smart device |
| | | | Cue Health mobile app |
| Price | $55 | $55 | Not set yet |
| When and how available | Currently available; kit sent to home after provider submits prescription | Currently commercially available | Availability unknown |
| Same test available for nonhome POC use | Yes | Yes | Yes |

Abbreviations used: COVID-19, coronavirus disease 2019; OTC, over-the-counter; POC = point of care; SARS-CoV-1, Severe acute respiratory syndrome coronavirus 1; SARS-CoV-2, Severe acute respiratory syndrome coronavirus.

read on the test platform's display or in their mobile application.[51-59] Although results for Cue will appear in the mobile application, patients will need to insert the cartridge into an external reader.[57] BinaxNOW Ag Card and Ag Card 2 also have an external step where the results will only appear in the mobile application after they have been interpreted by an outside individual, although there is an unofficial visual reader on the card.[51,52] All the tests should be stored at room temperature and can be discarded in the trash with proper disposal of the batteries for the machines requiring their use.[51-59] Patients should not discard the external reader for the Cue test as it will be needed to read all subsequent Cue tests.[57]

Patients can get technical support for help using the devices from the respective manufacturer.[51-59] The selection of an at-home test will be largely dependent on availability and patient characteristics and preferences. All the tests have some limitations of use as well, which can vary depending on the type of test. False negative results can occur with all the tests, particularly if they are not performed correctly. False negatives can also occur with the antigen tests if the antigen level is below the detection level of the test. Positive test results cannot be used to rule out the presence of other pathogens. In addition, the antigen tests can detect viable and nonviable virus, so patients may test positive even if they do not have an active infection. Finally, the predictive values of the test can be impacted by the prevalence of the disease, so the reliability of the test results can be significantly different in regions where the prevalence is high compared with areas where the prevalence is low.

### *Synopsis of test performances*

Given the current nature of COVID-19 testing and the lack of a consensus gold standard reference test, the manufacturers of these home tests used validation standards required by FDA for EUAs.[51-59] As a result, the measures of sensitivity and

**Table 2**
Comparison of at-home antigen COVID-19 tests[51-59]

| Device characteristic | Ellume COVID-19 home test | BinaxNOW COVID-19 Ag card home test | BinaxNOW COVID-19 Ag card 2 home test | BinaxNOW COVID-19 antigen self-test | QuickVue at-home COVID-19 test | QuickVue at-home OTC COVID-19 test |
|---|---|---|---|---|---|---|
| Emergency use authorization date | December 15, 2020 | December 16, 2020 | March 31, 2021 | March 31, 2021 | March 1, 2021 | March 31, 2021 |
| Manufacturer | Ellume | Abbott | Abbott | Abbott | Quidel | Quidel |
| Requires prescription | No | Yes | No | No | Yes | No |
| Principle of test procedure | Qualitative lateral flow immunoassay | Qualitative lateral flow immunoassay | Qualitative lateral flow immunoassay | Qualitative lateral flow immunoassay | Qualitative lateral flow immunoassay | Qualitative lateral flow immunoassay |
| Specimen sample | Midturbinate nasal swab | Nasal swab | Nasal swab | Nasal swab | Nasal swab | Nasal swab |
| Authorized age for use | Self-collected: ≥16 y | Self-collected: ≥15 y | Self-collected: ≥15 y | Self-collected: ≥15 y | Self-collected: ≥14 y | Self-collected: ≥14 y |
| | Adult-collected: ≥2 y | Adult-collected: ≥4 y | Adult-collected: ≥2 y | Adult-collected: ≥2 y | Adult-collected: ≥8 y | Adult-collected: ≥2 y |
| Requires observation by telehealth proctor | No | Yes | Yes | No | No | No |
| Indication for use | With or without symptoms or other epidemiologic reasons to suspect COVID-19 | Suspected COVID-19 by health care provider within first 7 d of symptom onset | Screening use with serial testing in patients with or without symptoms or other epidemiologic reasons to suspect COVID-19 | Screening use with serial testing in patients with or without symptoms or other epidemiologic reasons to suspect COVID-19 | Suspected COVID-19 by health care provider within first 6 d of symptom onset | Screening use with serial testing in patients with or without symptoms or other epidemiologic reasons to suspect COVID-19 |
| Instructions for use | Open kit | Open kit | Open kit | Open kit | Open kit | Open kit |
| | Open app/answer questions | Open app/answer questions | Open app/answer questions | Add reagent to top of card | Open tube | Open tube |
| | Connect analyzer to phone | Add reagent to top of card | Add reagent to top of card | Nasal swab | Nasal swab | Nasal swab |
| | Apply processing fluid to dropper | Nasal swab | Nasal swab | Insert nasal swab to bottom card | Insert nasal swab in tube | Insert nasal swab in tube |
| | Nasal swab | Insert nasal swab in card | Insert nasal swab to bottom card | Perform test twice over 3 d with 36 h between tests if serial testing | Insert test strip into tube | Insert test strip into tube |
| | Insert nasal swab in dropper | Scan results with app | Scan results with app | | Remove test strip | Remove test strip |
| | Apply dropper fluid to analyzer | | Perform test twice over 3 d with 36 h between tests if serial testing | | | Perform test twice over 2–3 days with 24–36 h between tests if serial testing |
| Results | Appear in mobile app | Unofficial: visual read on card | Unofficial: visual read on card | Visual read on card | Visual read on strip | Visual read on strip |
| | | Official: appears in mobile app after outside interpretation | Official: appears in mobile app after outside interpretation | | | |
| Results automatically reported to public health authorities | Yes | Yes | Yes | No | No | No |
| Differentiates between SARS-CoV-1 and SARS-CoV-2 | No | No | No | No | No | No |
| Endogenous interfering substance | None | Mupirocin | Mupirocin | Mupirocin | None | None |
| Cross-reactivity with other organisms | No | No | No | No | No | No |

(*continued on next page*)

**Table 2** (*continued*)

| Device characteristic | Ellume COVID-19 home test | BinaxNOW COVID-19 Ag card home test | BinaxNOW COVID-19 Ag card 2 home test | BinaxNOW COVID-19 antigen self-test | QuickVue at-home COVID-19 test | QuickVue at-home OTC COVID-19 test |
|---|---|---|---|---|---|---|
| Time to result | 15 min | Unofficial: 15 min<br>Official: approximately 20 min | 15 min | 15 min | 10 min | 10 min |
| Requirements | Smart phone with iOS or Android Ellume COVID-19 application | Smart phone with iOS or Android Navica application | Smart phone with iOS or Android Navica application | N/A | N/A | N/A |
| Price | $38.99 | $50/1 test; $150/6-pack | Not set yet | $20–24 | Not set yet | Not set yet |
| When and how available | Currently available at select CVS stores | Currently available from Optum (1) or eMed (6) | Availability unknown | Currently commercially available | Availability unknown | Availability unknown |
| Same test available for nonhome POC use | No | Yes | Yes | Yes | Yes | Yes |

Abbreviations used: POC, point of care; COVID-19, coronavirus disease 2019; OTC, over-the-counter; SARS-CoV-1, Severe acute respiratory syndrome coronavirus 1; SARS-CoV-2, Severe acute respiratory syndrome coronavirus; iOS, internet operating system; N/A, not applicable.

specificity may not be appropriate to use in some situations.[60] Similar statistics can be used in place of sensitivity and specificity to show that the tests were evaluated using comparable tests rather than a true reference standard. In this scenario, sensitivity is replaced with PPA, and specificity is replaced with NPA.

All manufacturers' studies of the home test kits' performances were prospective studies.[51-59] The PPA for the 9 home tests ranged from 83.5% (QuickVue At-Home) to 97.4% (Cue COVID-19), and the NPA ranged from 97% (Ellume) to 100% (BinaxNOW). It is important to note that all 3 at-home BinaxNOW tests use the same platform, so the same data sets were used to receive their EUA. See Table 3 for a summary of the studies and additional statistics.

Given that the BinaxNOW tests (home and nonhome) all use the same platform, 2 studies using the nonhome version of BinaxNOW (BinaxNOW Ag Card) met inclusion criteria for this systematic review. One study evaluated the BinaxNOW Ag Card test in asymptomatic, college-aged students in November 2020.[41] Students (n = 2638) were instructed to self-swab under the direct observation of trained individuals at a college screening event. Whereas the NPA was the same for the home tests (100%; [95% CI 99%–100%]), the PPA was significantly lower (53.3%; [95% CI 39.1%–67.1%]). This suggests that a negative test in asymptomatic patients may not be effective in ruling out the disease. Similar findings were found by Shah et al.[49] who studied the BinaxNOW Ag Card test in a community testing site where patients were observed self-swabbing. In both symptomatic and asymptomatic patients, they found a PPA of 77.2% (95% CI, 72.4%– 81.6%) and an NPA of 99.6% (95% CI 99.2%–99.8%). The PPA for asymptomatic patients was 78.6% (73.4%–83.3%) compared with 81.9% (95% CI 76.5%–86.5%) in patients who had symptoms within 7 days of testing. In addition, they evaluated the potential benefits of serial testing in the same visit. They only found a similar PPA (81.4%; [95% CI 76.8%–85.5%]) for the repeat test, suggesting that serial testing at the same visit is not warranted (Table 3).

## Discussion

Perfection is defined as "an unsurpassable degree of accuracy or excellence."[61] In medicine and science, we are trained to seek perfection in our instruments, analytical approach, and solutions. Unfortunately, we can become obsessed with striving for perfection and lose sight of our true goals. During World War II, Sir Robert Alexander Watson-Watt, developer of the early warning radar system used in Britain, was a believer in the "cult of the imperfect."[62] He was often quoted as saying, "Give them the third best to go on with; the second best comes too late, the best never comes."[62] This suggests that rather than waiting for the perfect, which may never come, we can succeed using an imperfect option. This idea holds true now, as we grapple with controlling the spread of SARS-CoV-2. If we wait for development of the perfect SARS-CoV-2 test, the loss of life and prevention of spread would be horrific. Therefore, we need to embrace the technologies we have at our disposal and use them to optimize their value.

Many in vitro SARS-CoV-2 diagnostic tests have received EUA since the beginning of the pandemic. These tests employ methods including PCR and antigen detection using a variety of platforms requiring a range of technical expertise,

**Table 3**
Test performance versus laboratory molecular comparator[51-59]

| Study element | BinaxNOW COVID-19 Ag card home test, BinaxNOW COVID-19 Ag 2 card home test, BinaxNOW COVID-19 antigen test[a] | Ellume COVID-19 home test | QuickVue at-home COVID-19 test | QuickVue At-Home OTC COVID-19 test | Lucira COVID-19 all-in-one test kit | Lucira CHECK-IT COVID-19 test kit | Cue COVID-19 test for home and OTC use |
|---|---|---|---|---|---|---|---|
| Study design | United States multisite prospective | United States multisite prospective | United States multisite prospective | United States prospective | Prospective | Prospective | United States multisite prospective |
| Population | Present with COVID-19 sx within 7 d of onset | All-comers study (asx and sx), age ≥ 2 y | Present with COVID-19 sx within 6 d of onset | Present with COVID-19 sx within 6 d of onset | Present with COVID-19 sx | All-comers (asx and sx) | All-comers (asx and sx), age ≥ 2 y |
| No. self-tested samples | 53 sx pts | 198 pts (64 sx, 134 asx) | 161 sx pts | 306 sx pts 44 asx pts | 101 sx pts | 404 pts | 273 pts |
| Main efficacy results | PPA: 91.7% (95% CI 73%–98.9%) | Overall PPA: 95% (95% CI 82%–99%) | PPA: 84.8% (95% CI 71.8–92.4%) | PPA: 83.5% (95% CI 74.9%–89.6%) | PPA: 94.1% (95% CI 85.5%–98.4%) | Overall PPA: 91.7% (95% CI 85.6%–95.8%) | Overall PPA: 97.4% (95% CI 86.5%–99.5%) |
| | NPA: 100% (87.7%–100%) | Overall NPA: 97% (95% CI 93%–99%) | NPA: 99.1% (95% CI 95.2%–99.8%) | NPA: 99.2% (95% CI 97.2%–99.8%) | NPA: 98% (95% CI 89.4%–99.9%) | Overall NPA: 98.2% (95% CI 95.8–99.4%) | Overall NPA: 99.1% (95% CI 96.9%–99.8%) |
| | | Sx PPA 96% (95% CI 81%–99%) | | | | Sx: PPA: 94.1% (95% CI 85.5%–98.4%) | Sx PPA: 96.4% (95% CI 82.3%–99.4%) |
| | | Sx NPA 100% (95% CI 91%–100%) | | | | Sx: NPA: 98% (95% CI 89.4%–99.9%) | Sx NPA: 98.2% (95% CI 93.6%–99.5%) |
| | | Asx PPA 91% (95% CI 62%–98%) | | | | Asx PPA 90.1% (95% CI 81.5%–95.6%) | Asx PPA: 100% (95% CI 72.23%–100%) |
| | | Asx NPA 96% (91%–98%) | | | | Asx NPA: 98.2% (95% CI 95.5%–99.5%) | Asx NPA: 100% (95% CI 97.0%–100%) |
| Results based on days of symptoms | Self-tested: not studied | Sx: PPA 100% up to 6 d, then 96%, NPA 100% up to > 7 d | Not studied | Not studied | Not studied | Not studied | Not studied |
| Additional efficacy results[b] | PPV: 100% (95% CI not calculated) | Overall PPV: 87.5% (74.6%–94.3%) | PPV: 97.5% (84.7%–99.6%) | PPV: 97.6% (91%–99.4%) | PPV: 98% (87.3%–99.7%) | Overall PPV: 96% (91%–98.3%) | Overall PPV: 94.9% (82.3%–98.7%) |
| | NPV: 93.3% (78.8%–98.2%) | Overall NPV: 98.7% (95.3%–99.7%) | NPV: 94.2% (89.2%–97%) | NPV: 94% (90.9%–96.1%) | NPV: 94.2% (84.5%–98%) | Overall NPV: 96% (93.2%–97.7%) | Overall NPV: 99.6% (97.1%–99.94%) |
| | LR +: infinity | Overall LR +: 30.5 (12.8–72.4) | LR +: 97.5 (13.8–688.9) | LR +: 105.63 (26.49–421.3) | LR+: 47.06 (6.75–327.97) | LR+: 49.87 (20.89–119.02) | LR+: 113.43 (28.51–451.32) |
| | LR−: 0.083 (0.022–0.314) | Overall LR−: 0.06 (0.01–0.21) | LR−: 0.15 (0.08–0.3) | LR−: 0.17 (0.11–0.26) | LR−: 0.06 (0.02–0.18) | LR−: 0.08 (0.05–0.15) | LR−: 0.03 (0–0.18) |
| | | Sx PPV: 100% (95% not calculated) | | | | Sx PPV: 98% (87.3%–99.7%) | Sx PPV: 93.1% (77.3%–98.2%) |
| | | Sx NPV: 97.4% (84.8%–99.6%) | | | | Sx NPV: 94.2% (90.2%–98.9%) | Sx NPV: 99.1% (94%–99.9%) |
| | | Sx LR+: infinity | | | | Sx LR+: 47.06 (6.75–327.97) | Sx LR+: 53.04 (13.41–209.79) |
| | | Sx LR−: 0.04 (0.01–0.26) | | | | Sx LR−: 0.06 (0.02–0.18) | Sx LR−: 0.04 (0.01–0.25) |
| | | Asx PPV: 66.7% (45.4%–82.8%) | | | | Asx PPV: 94.8% (87.3%–98%) | Asx PPV: 100% (95% CI not calculated) |
| | | Asx NPV: 99.2% (90.5%–98.3%) | | | | Asx NPV: 96.5% (93.4%–98.1%) | Asx NPV: 100% (95% CI not calculated) |

(*continued on next page*)

**Table 3** (*continued*)

| Study element | BinaxNOW COVID-19 Ag card home test, BinaxNOW COVID-19 Ag 2 card home test, BinaxNOW COVID-19 antigen test[a] | Ellume COVID-19 home test | QuickVue at-home COVID-19 test | QuickVue At-Home OTC COVID-19 test | Lucira COVID-19 all-in-one test kit | Lucira CHECK-IT COVID-19 test kit | Cue COVID-19 test for home and OTC use |
|---|---|---|---|---|---|---|---|
| | | Asx LR+: 22.36 (9.29–53.84) | | | | Asx LR+: 50.02 (18.89–132.45) | Asx LR+: infinity |
| | | Asx LR−: 0.09 (0.01–0.61) | | | | Asx LR −: 0.1 (0.05–0.19) | Asx LR−: 0 (95% CI not calculated) |

Abbreviations used: Asx, asymptomatic; LR−, likelihood ratio for negative test result; LR+, likelihood ratio for positive test result; NPV, negative predictive value; PPV, positive predictive value; Sx, symptomatic; COVID-19, coronavirus disease 2019; OTC, over-the-counter; PPA, positive percent agreement; NPA, negative percent agreement.

[a] Because all BinaxNOW diagnostic tests are the same platform with different Emergency Use Authorizations, the same data sets were used to support each test's Emergency Use Authorization.

[b] Calculated using the MedCalc Diagnostic Test Evaluation Calculator (2021). https://www.medcalc.org/calc/diagnostic_test.php.

equipment, and expense. If we seek perfection, the question should be asked as to what makes a test perfect. Is perfection based on sensitivity and specificity of the assay? What if, in order to obtain analytical perfection, the procedures use an expensive analyzer and take 3 days to get results? Would that test still be considered perfect? If a comparator test had lower sensitivity and specificity but only cost $5 to perform and gave results within 15 minutes, would that test be imperfect? A companion philosophy to the cult of the imperfect that we as clinicians should embrace is the concept of situational relevancy.[63] Simply put, situational relevancy is the realization that there is not a single correct solution to a problem with multiple variables. Rather, the correct solution for a given problem changes as the variables change. As an example, think about 2 SARS-CoV-2 testing scenarios. In the first scenario, we wish to detect SARS-CoV-2 in a limited number of hospitalized patients exhibiting symptoms of COVID-19. The goal for this scenario is to identify infected individuals for quarantine. Given these conditions, it seems that a test with high sensitivity and specificity would be important, and we may be willing to sacrifice turnaround time to improve these characteristics. In addition, because we would only be using this test on a relatively small population and given that the cost of a patient in an isolation room would be high, we may find that using a more expensive test would be cost-effective if performance characteristics were maximized. In the second scenario, we wish to screen asymptomatic individuals for SARS-CoV-2 to minimize the chance that they would infect co-workers. In this scenario, we understand that the pretest probability of having SARS-CoV-2 is low and the likelihood of detecting an individual with infection is low. In addition, people are to be screened 3 times a week before they may enter a building. Under this set of variables, being able to rule out the presence of the virus would seem more important that detecting the actual virus. Since the pretest probability of being infected with SARS-CoV-2 is low, any positive test result would likely need confirmation to rule out a false positive. Furthermore, because individuals are being tested 3 times a week, cost would be an appreciable consideration regarding the long-term application of a test system. Lastly, if a negative result is needed before a worker is allowed to go into a workspace, then speed is a critical factor in determining the utility of a test. Thus, even though the underpinning goal of detecting SARS-CoV-2 is the same in the 2 scenarios, the desirable characteristics of the "perfect" test is highly situational.

The best indicator of situational value is likely to be the PPV and NPV associated with the tests rather than their sensitivity and specificity. Sensitivity and specificity are fixed performance characteristics of each of the tests and do not account for pretest probability of the patient having or not having SARS-CoV-2. Therefore, they provide limited information on the real-world utility of the tests. Examples of the situational relevance of SARS-CoV-2 antigen tests was recently demonstrated in 2 studies examining the performance of antigen tests for SARS-CoV-2.[47,64] In both reports, the PPV and NPV were high among symptomatic individuals (high pretest probability). Similarly, the PPV decreased and NPV increased for each test among those with no symptoms.[47,64] These observations yield important information regarding use of these tests that can be extrapolated to home

**Table 4**
Pharmacy care model[51-59]

| COVID-19 home testing pharmacy care model: Key counseling points | |
|---|---|
| What are the symptoms of COVID-19? | Fever, acute respiratory illness (cough, dyspnea), chills, myalgias, headache, sore throat, loss of taste/smell, nausea and vomiting, or diarrhea |
| Do I need to have symptoms of COVID-19 in order to home test myself? | Lucira all-in-one, BinaxNOW Ag Card, QuickVue at-home: COVID-19 must be suspected by health care provider<br>Lucira check-it, Cue, Ellume, BinaxNOW Ag Card 2, BinaxNOW antigen self-test, QuickVue at-home OTC: with or without COVID-19 symptoms |
| Do I need a prescription to get a COVID-19 home test? | The current at-home tests that do NOT require a prescription are Lucira check-it, Cue, Ellume, BinaxNOW 19 Ag Card 2, BinaxNOW antigen self-test, and QuickVue at-home OTC (the tests that are available for both symptomatic and asymptomatic testing are the ones that do not require a prescription). |
| How do I administer a COVID-19 home test with the nasal swab? | Stick the nasal swab into one nostril. Rotate swab for about 5 seconds and repeat process within the other nostril. It is important to insert the same swab into both nostrils for an accurate sample with most tests. |
| I'm worried about administering a COVID-19 home test without someone's help. | If you're worried about doing the test alone, BinaxNOW Ag Card and Ag Card 2 require a telehealth proctor to be present to assist with proper nasal swab technique along with reading results. Feel free to also ask your local pharmacist for guidance on how to administer or look online for administration videos on the manufacturer website. |
| Does the nasal swab hurt? | No. The nasal swab may cause some discomfort or tickling feeling, but it should not cause puncturing or any sharp pains. Do not insert the swab any further if experiencing pain. |
| Which home testing device is the most efficacious? | All home testing kits with a current EUA are similar in efficacy, with QuickVue at-home having the lowest positive percent agreement rate (83.5%), and Cue COVID-19 test for home and OTC use having the highest (97.4%). Ellume has the lowest negative percent agreement (97%), and the 3 BinaxNOW home tests have the highest (100%). |
| How long will it take to receive results? | Results vary on the basis of test, ranging from 11−30 min. |
| The test is positive, now what? | Tell your health care provider and stay in contact with them throughout the illness. To avoid spreading the virus, follow CDC recommendations and isolate yourself from others. Potential for a PCR-based confirmatory test may be indicated. |
| The test is negative, now what? | A negative result means the SARS-CoV-2 was not found in your specimen. If you took the test while experiencing symptoms, a negative result usually means your current illness is not COVID-19. False negatives are possible, meaning you are positive for COVID-19, even though the test result stated negative. Discuss your symptoms and test results with your health care provider to determine whether follow-up testing is necessary |
| The test is invalid or there was an error, now what? | If the display shows invalid result or test error, the test didn't perform properly. Refer to the package insert and contact the manufacturer for assistance |

COVID-19, coronavirus disease 2019; SARS-Cov-2, severe acute respiratory syndrome coronavirus 2; CDC, Centers for Disease Control and Prevention; PCR, polymerase chain reaction; OTC, over-the-counter.

tests. Among symptomatic individuals, a positive test result is highly predictive of the presence of SARS-CoV-2 and can help diagnose an infection. However, because the NPV of tests under these circumstances is less than 100%, a negative test in a patient with symptoms should be confirmed with a laboratory-based PCR test. On the other hand, if a home test were to be used for screening in an asymptomatic population, their value as a diagnostic test would decrease (lower PPV). Therefore, a positive test result would likely need confirmation with laboratory-based PCR. However, in this scenario, a negative test can provide a strong indication that infection is not present, and the likelihood that the individual is infectious is low (high NPV).

Currently, some home tests are only authorized for use among those who are symptomatic or suspected of having COVID-19; they have the potential to assist in making a diagnosis. Accordingly, the use of these tests in a home environment in an asymptomatic individual would be outside the EUA of these tests. However, there is a reasonable probability that these tests may be used outside of their authorizations, not just those with EUAs for both symptomatic and asymptomatic individuals. One element that will require constant attention is the performance of these tests against emerging SARS-CoV-2 variants. Although the known variants are believed to only possess alterations in spike proteins, the impact of these changes on the performance of the current home-use tests is not fully known. Furthermore, additional structural and genetic changes are likely to occur, so constant evaluation of tests against new variants must continue to maintain the performance integrity of the tests.

Despite several possible shortcomings, home tests are likely to play a large role during the COVID-19 pandemic. There is a major convenience factor of home tests, considering the capability to purchase a test before symptom onset. Having a test readily available reduces the fear burden for vulnerable patients, those without transportation, and the risk of a long result time. The ability of individuals to run a test at home without venturing into public for testing and risking viral exposure or exposing others to SARS-CoV-2 is an important advantage of these tests. In addition, the convenience, quick results, and relatively low-cost of home tests are ideal for frequent, longitudinal screenings to clear individuals for work, school, or travel. Laboratory or pharmacy-based testing are inferior to home tests with respect to these variables.

Insurance companies may reimburse patients who purchase at-home tests. With rapid changes occurring throughout the pandemic, it is too soon to recommend one test over the other. All tests have their various efficacies, and which test is chosen should be based on patient preference, ease, and symptomatology.

Because some at-home tests require a prescription and others can be purchased OTC at local pharmacies, it is important that pharmacists be familiar with these tests. Table 4 lists common questions that pharmacists may be asked regarding these tests. Because only BinaxNOW requires the user to be supervised by a telehealth proctor, many questions related to specimen collection, test interpretation, and post-test actions may arise. Pharmacists should be able to address these questions for the currently authorized tests and be prepared for the marketplace entry of more SARS-CoV-2 home tests. In addition, pharmacists should be aware of the regulatory stipulations, particularly CLIA regulations, and understand them before physically assisting with specimen collection and test interpretation. A CLIA Certificate of Waiver may be necessary to perform or assist with performing these tests, and physically assisting with these tests may be precluded, even in CLIA-waived settings, because tests authorized for home use are not automatically authorized for use in CLIA-waived settings. Finally, the pharmacist must be able help patients understand when confirmatory testing is required and where that can be completed.

## Conclusion

SARS-CoV-2 tests authorized for home use are not perfect; however, they represent a valuable resource in our effort to halt the current pandemic. The SARS-CoV-2 home tests examined in this review demonstrated satisfactory performance in comparison with laboratory RT-PCR tests. Owing to their simplicity, speed, and cost, they can help patients make informed decisions about the need to seek care and the infection risk they pose to others (Table 4).

## References

1. Ketchum K, O'Connor L. COVID-19 testing problems started early, U.S. still playing from behind. Modern Healthcare. Available at: https://www.modernhealthcare.com/technology/covid-19-testing-problems-started-early-us-still-playing-behind. Accessed January 27, 2021.
2. U.S. Food and Drug Administration. Emergency use authorization. Available at: https://www.fda.gov/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/emergency-use-authorization. Accessed January 27, 2021.
3. Smith A. What it's like to get a drive-through COVID-19 test. *Pharmacy Times*. Available at: https://www.pharmacytimes.com/news/what-its-like-to-get-a-drive-through-covid-19-test. Accessed February 6, 2021.
4. Good Life Medical Services. Drive-thru testing for coronavirus. Available at: https://www.goodlifemedicalservices.com/drivethru-testing. Accessed February 6, 2021.
5. U.S. Food and Drug Administration. Coronavirus (COVID-19) update: May 7, 2021. Available at: https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-may-7-2021. Accessed May 11, 2021.
6. U.S. Food and Drug Administration. Coronavirus (COVID-19) update: FDA authorizes first COVID-19 test for self-testing at home. Available at: https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-fda-authorizes-first-covid-19-test-self-testing-home. Accessed May 11, 2021.
7. U.S. Food and Drug Administration. Clinical laboratory improvement amendments (CLIA). Available at: https://www.fda.gov/medical-devices/ivd-regulatory-assistance/clinical-laboratory-improvement-amendments-clia. Accessed January 27, 2021.
8. Centers for Medicare & Medicaid Services. How to apply for a CLIA certificate, including international laboratories. Available at: https://www.cms.gov/Regulations-and-Guidance/Legislation/CLIA/How_to_Apply_for_a_CLIA_Certificate_International_Laboratories. Accessed February 10, 2021.
9. Centers for Disease Control and Prevention. COVID-19: calls for clinical laboratory partners. Available at: https://www.cdc.gov/clia/index.html. Accessed February 10, 2021.
10. Ginter LW, Fink JL. Point-of-care testing. *Pharmacy Times*. Available at: https://www.pharmacytimes.com/publications/issue/2018/july2018/pointofcare-testing. Accessed February 10, 2021.
11. Centers for Disease Control and Prevention. Interim guidelines for collecting and handling of clinical specimens for COVID-19 testing. Available at: https://www.cdc.gov/coronavirus/2019-ncov/lab/guidelines-clinical-specimens.html. Accessed May 11, 2021.
12. U.S. Food and Drug Administration. CLIA categorizations. Available at: https://www.fda.gov/node/365445. Accessed January 27, 2021.
13. Department of Health & Human Services, Centers for Medicare & Medicaid Services. Clinical laboratory improvement amendments application for certification. Available at: https://www.cms.gov/Medicare/CMS-Forms/CMS-Forms/Downloads/CMS116.pdf. Accessed January 27, 2021.
14. Klepser NS, Klepser DG, Adams JL, Adams AJ, Klepser ME. Impact of COVID-19 on prevalence of community pharmacies as CLIA-Waived facilities [e-pub ahead of print]. *Res Social Adm Pharm*. https://doi.org/10.1016/j.sapharm.2020.12.003; accessed May 11, 2021.
15. U.S. Food and Drug Administration. CLIA waiver by application. Available at: https://www.fda.gov/medical-devices/ivd-regulatory-assistance/clia-waiver-application. Accessed May 11, 2021.
16. Van Norman GA. Drugs, devices, and the FDA: part 2: an overview of approval processes: FDA approval of medical devices. *JACC Basic Transl Sci*. 2016;1(4):277–287.
17. U.S.Food and Drug Administration. Emergency use authorization of medical products and related authorities. Available at: https://www.fda.gov/regulatory-information/search-fda-guidance-documents/emergency-use-authorization-medical-products-and-related-authorities. Accessed February 5, 2021.
18. Kadlec R, Department of Health & Human Services. Declaration under the Public Readiness and Emergency Preparedness Act for medical countermeasures against COVID-19. *Fed Regist*. 2020;85(52):15198–15203. Available at: https://www.federalregister.gov/documents/2020/03/17/2020-05484/declaration-under-the-public-readiness-and-emergency-preparedness-act-for-medical-countermeasures. Accessed January 27, 2021.
19. U.S. Food and Drug Administration. In vitro diagnostics EUAs. Available at: https://www.fda.gov/medical-devices/coronavirus-disease-2019-covid-19-emergency-use-authorizations-medical-devices/vitro-diagnostics-euas. Accessed May 11, 2021.
20. U.S. Department of Health and Human Services. Office of the Assistant Secretary for Preparedness and Response. Public health emergency: Public Readiness and Emergency Preparedness Act. Available at: https://www.phe.gov/Preparedness/legal/prepact/Pages/default.aspx. Accessed February 11, 2021.
21. U.S. Department of Health and Human Services, Office of the Assistant Secretary for Health. Guidance for licensed pharmacists, COVID-19 testing, and immunity under the PREP Act. Available at: https://www.phe.gov/Preparedness/legal/prepact/Documents/pharmacist-guidance-COVID19-PREP-Act.pdf. Accessed May 11, 2021.
22. United States Department of Health and Human Services. Office of the Assistant Secretary for Preparedness and Response. Guidance for licensed pharmacists and pharmacy interns regarding COVID-19 vaccines and immunity under the PREP Act. Available at: https://www.phe.gov/Preparedness/legal/prepact/Documents/pharmacist-guidance-COVID19-vaccines-immunity.pdf. Accessed February 11, 2021.
23. U.S. Department of Health and Human Services, Office of the Assistant Secretary for Preparedness and Response. Guidance for PREP Act coverage for qualified pharmacy technicians and state-authorized pharmacy interns for childhood vaccines, COVID-19 vaccines, and COVID-19 testing. Available at: https://www.hhs.gov/sites/default/files/prep-act-guidance.pdf. Accessed February 11, 2021.
24. U.S. Department of Health and Human Services, Office of the Assistant Secretary for Preparedness and Response. PREP Act authorization for pharmacies distributing and administering certain covered countermeasures. Available at: https://www.hhs.gov/guidance/sites/default/files/hhs-guidance-documents//prep-act-authorization-pharmacies-administering-covered-countermeasures.pdf. Accessed February 11, 2021.

25. U.S. Department of Health and Human Services, Office of the Assistant Secretary for Health. Third amendment to declaration under the PREP act for medical countermeasures against COVID−19. Available at: https://www.govinfo.gov/content/pkg/FR-2020-08-24/pdf/2020-18542.pdf. Accessed February 11, 2021.
26. U.S. Food and Drug Administration. FDA combating COVID-19 with medical devices. Available at: https://www.fda.gov/media/136702/download. Accessed May 11, 2021.
27. Altman E, Mounir I, Najid FZ, Perlaza SM. On the true number of COVID-19 infections: effect of sensitivity, specificity and number of tests on prevalence ratio estimation. *Int J Environ Res Public Health*. 2020;17(15):5328.
28. Trevethan R. Sensitivity, specificity, and predictive values: foundations, pliabilities, and pitfalls in research and practice. *Front Public Health*. 2017;5:307.
29. Yüce M, Filiztekin E, Özkaya KG. COVID-19 diagnosis -a review of current methods. *Biosens Bioelectron*. 2021;172:112752.
30. Dinnes J, Deeks JJ, Adriano A, et al. Rapid, point-of-care antigen and molecular-based tests for diagnosis of SARS-CoV-2 infection. *Cochrane Database Syst Rev*. 2020;8(8):CD013705.
31. Yu CY, Chan KG, Yean CY, Ang GY. Nucleic acid-based diagnostic tests for the detection SARS-CoV-2: an update. *Diagnostics (Basel)*. 2021;11(1):53.
32. Hosseini A, Pandey R, Osman E, et al. Roadmap to the bioanalytical testing of COVID-19: from sample collection to disease surveillance. *ACS Sens*. 2020;5(11):3328−3345.
33. Tang YW, Schmitz JE, Persing DH, Stratton CW. Laboratory diagnosis of COVID-19: current issues and challenges. *J Clin Microbiol*. 2020;58(6):e00512−e00520.
34. Mina MJ, Andersen KG. COVID-19 testing: one size does not fit all. *Science*. 2021;371(6525):126−127.
35. McDermott A. Inner workings: researchers race to develop in-home testing for COVID-19, a potential game changer. *Proc Natl Acad Sci U S A*. 2020;117(42):25956−25959.
36. Aranda-Diaz A, Imbert E, Strieff S, et al. Implementation of rapid and frequent SARS-CoV2 antigen testing and response in congregate homeless shelters. Available at: https://www.medrxiv.org/content/10.1101/2021.04.20.21255787v1.full. Accessed May 11, 2021.
37. Donato LJ, Trivedi VA, Stransky AM, et al. Evaluation of the Cue Health point-of-care COVID-19 (SARS-CoV-2 nucleic acid amplification) test at a community drive through collection center. *Diagn Microbiol Infect Dis*. 2021;100(1):115307.
38. Forde JE, Ciupe SM. Quantification of the tradeoff between test sensitivity and test frequency in a COVID-19 epidemic-a multi-scale modeling approach. *Viruses*. 2021;13(3):457.
39. James AE, Gulley T, Kothari A, Holder K, Garner K, Patil N. Performance of the BinaxNOW coronavirus disease 2019 (COVID-19) antigen card test relative to the severe acute respiratory coronavirus virus 2 (SARS-CoV-2) real-time reverse transcriptase polymerase chain reaction (rRT-PCR) assay among symptomatic and asymptomatic healthcare employees [e-pub ahead of print]. *Infect Control Hosp Epidemiol*. https://doi.org/10.1017/ice.2021.20; accessed May 11, 2021.
40. Kuo P, Realegeno S, Pride DT. Comparison of two nucleic acid amplification tests (NAATs) and two antigen tests for detection of SARS-CoV-2 from upper respiratory specimens. *J Clin Virol Plus*. 2021;1(1):100011.
41. Okoye NC, Barker AP, Curtis K, et al. Performance characteristics of BinaxNOW COVID-19 antigen card for screening asymptomatic individuals in a University setting. *J Clin Microbiol*. 2021;59(4):e03282−e03290.
42. Peng J, Mann SA, Mitchell AM, et al. Estimation of secondary household attack rates for emergent SARS-CoV-2 variants detected by genomic surveillance at a community-based testing site in San Francisco. Available at: https://www.medrxiv.org/content/10.1101/2021.03.01.21252705v1. Accessed May 11, 2021.
43. Perchetti GA, Huang ML, Mills MG, Jerome KR, Greninger AL. Analytical sensitivity of the Abbott BinaxNOW COVID-19 Ag Card. *J Clin Microbiol*. 2021;59(3). e02880−20.
44. Pilarowski G, Lebel P, Sunshine S, et al. Performance characteristics of a rapid severe acute respiratory syndrome coronavirus 2 antigen detection assay at a public plaza testing site in San Francisco. *J Infect Dis*. 2021;223(7):1139−1144.
45. Pilarowski G, Marquez C, Rubio L, et al. Field performance and public health response using the BinaxNOW TM Rapid SARS-CoV-2 antigen detection assay during community-based testing [e-pub ahead of print]. *Clin Infect Dis*. https://doi.org/10.1093/cid/ciaa1890; accessed May 11, 2021.
46. Pollock NR, Jacobs JR, Tran K, et al. Performance and implementation evaluation of the Abbott BinaxNOW Rapid Antigen Test in a high-throughput drive-through community testing site in Massachusetts. *J Clin Microbiol*. 2021;59(5). e00083−21.
47. Prince-Guerra JL, Almendares O, Nolen LD, et al. Evaluation of Abbott BinaxNOW Rapid Antigen Test for SARS-CoV-2 infection at two community-based testing sites - Pima County, Arizona, November 3−17, 2020 [published correction appears in *MMWR Morb Mortal Wkly Rep*. 2021;70(4):144]. *MMWR Morb Mortal Wkly Rep*. 2021;70(3):100−105.
48. Reddy SG, Das S. Strategies for antigen testing: an alternative approach to widespread PCR resting. Available at: https://www.medrxiv.org/content/10.1101/2021.04.05.21254024v1. Accessed May 11, 2021.
49. Shah MM, Salvatore PP, Ford L, et al. Performance of repeat BinaxNOW SARS-CoV-2 antigen testing in a community setting, Wisconsin, November-December 2020. Available at: https://www.medrxiv.org/content/10.1101/2021.04.05.21254834v1. Accessed May 11, 2021.
50. Sood N, Shetgiri R, Rodriguez A, et al. Evaluation of the Abbott BinaxNOW rapid antigen test for SARS-CoV-2 infection in children: implications for screening in a school setting. *PLoS One*. 2021;16(4), e0249710.
51. Abbott Diagnostics. Scarborough, Inc. BinaxNOW™ COVID-19 Ag card home test: healthcare provider instructions for use. Available at: https://www.fda.gov/media/144574/download. Accessed May 11, 2021.
52. Abbott Diagnostics. BinaxNOW COVID-19 Ag Card 2 home test: healthcare provider instructions for use. Available at: https://www.fda.gov/media/147259/download. Accessed May 6, 2021.
53. Abbott Diagnostics. BinaxNOW™ COVID-19 Ag card: healthcare provider instructions for use. Available at: https://www.fda.gov/media/141570/download. Accessed May 6, 2021.
54. Ellume Limited. Ellume COVID-19 Home Test: product overview for healthcare professionals. Available at: https://www.fda.gov/media/144592/download. Accessed January 10, 2021.
55. Lucira. COVID-19 all-in-one test kit. Available at: https://www.fda.gov/media/143808/download. Accessed January 10, 2021.
56. Lucira CHECK IT COVID-19 test kit: instructions for us. Available at: https://www.fda.gov/media/147494/download. Accessed May 6, 2021.
57. Cue Health, Inc. The Cue COVID-19 test for home and over the counter (OTC) use: instructions for use. Available at: https://www.fda.gov/media/146470/download. Accessed May 6, 2021.
58. Quidel. QuickVue at-home COVID-19 test: healthcare provider instructions for use. Available at: https://www.fda.gov/media/146312/download. Accessed May 6, 2021.
59. Quidel. QuickVue at-home OTC COVID-19 test: healthcare provider instructions for use. Available at: https://www.fda.gov/media/147265/download. Accessed May 6, 2021.
60. U.S. Department of Health and Human Services, Food and Drug Administration, Center for Devices and Radiological Health, Diagnostic Devices Branch, Division of Biostatistics, Office of Surveillance and Biometrics. Guidance for industry and FDA staff: statistical guidance on reporting results from studies evaluating diagnostic tests. Available at: https://www.fda.gov/files/medical%20devices/published/Guidance-for-Industry-and-FDA-Staff—Statistical-Guidance-on-Reporting-Results-from-Studies-Evaluating-Diagnostic-Tests-%28PDF-Version%29.pdf. Accessed May 11, 2021.
61. Merriam-Webster. Perfection definition. Available at: https://www.merriam-webster.com/dictionary/perfection. Accessed February 11, 2021.
62. Encyclopedia britannica. Sir Robert Alexander Watson-Watt. Available at: https://www.britannica.com/biography/Robert-Alexander-Watson-Watt. Accessed February 11, 2021.
63. Wilson P. Situational relevance. *Inform Storage Ret*. 1973;9(8):457−471.
64. Pray IW, Ford L, Cole D, et al. Performance of an antigen-based test for asymptomatic and symptomatic SARS-CoV-2 testing at two university campuses - Wisconsin, September-October 2020. *MMWR Morb Mortal Wkly Rep*. 2021;69(5152):1642−1647.

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## Appendix

**Appendix 1**
Search strategies

| Database/Website | Date of Most Recent Search | Search Terms | Search Limits | # of Results |
|---|---|---|---|---|
| PubMed | 5/5/2021 | (PCR or "polymerase chain reaction" or "nucleic acid amplification" or "SARS-CoV-2 nucleocapsid protein" or "molecular diagnostic" or "molecular diagnostics" or "molecular diagnosis" or "Pathology, Molecular" or antigen or nucleocapsid or "lateral flow immunoassay" or immunoassay or "RT-LAMP" or LAMP assay or viable or "non-viable" or "COVID-19 Testing" or "Diagnostic Techniques and Procedures" or "rapid diagnostic tests" or "rapid diagnostic testing") AND ("COVID 19 Testing" or "COVID-19 Testings" or "Testing, COVID-19" or "SARS Coronavirus 2 Testing" or "COVID-19 Virus Testing" or "COVID 19 Virus Testing" or "COVID-19 Virus Testings" or "Testing, COVID-19 Virus" or "Virus Testing, COVID-19" or "COVID19 Testing" or "COVID19 Testings" or "Testing, COVID19" or "COVID19 Virus Testing" or "COVID19 Virus Testings" or "Testing, COVID19 Virus" or "Virus Testing, COVID19" or "SARS-CoV-2 Testing" or "SARS CoV 2 Testing" or "SARS-CoV-2 Testings" or "Testing, SARS-CoV-2" or "Coronavirus Disease 2019 Testing" or "2019 Novel Coronavirus Disease Testing" or "2019 Novel Coronavirus Testing" or "2019-nCoV Disease Testing" or "2019 nCoV Disease Testing" or "2019-nCoV Disease Testings" or "Disease Testing, 2019-nCoV" or "Testing, 2019-nCoV Disease" or "2019-nCoV Infection Testing" or "2019 nCoV Infection Testing" or "2019-nCoV Infection Testings" or "Infection Testing, 2019-nCoV" or "Testing, 2019-nCoV Infection" or "COVID-19 Diagnostic Testing" or "COVID 19 Diagnostic Testing" or "COVID-19 Diagnostic Testings" or "Diagnostic Testing, COVID-19" or "Severe Acute Respiratory Syndrome Coronavirus 2 Testing" or "Coronavirus Disease-19 Testing" or "Coronavirus Disease 19 Testing" or "Coronavirus Disease-19 Testings" or "Testing, Coronavirus Disease-19" or "2019-nCoV Testing" or "2019 nCoV Testing" or "2019-nCoV Testings" or "Testing, 2019-nCoV") AND ("home test"[Title/Abstract] OR "home tests"[Title/Abstract] OR "home testing"[Title/Abstract] OR "home use"[Title/Abstract] OR "self-collect"[Title/Abstract] OR "self-collected"[Title/Abstract] OR "self-administered"[Title/Abstract] OR "Direct-To-Consumer Screening[Title/Abstract] AND Testing"[Title/Abstract] OR "at-home"[Title/Abstract] OR "Abbott BinaxNOW"[Title/Abstract] OR Abbott[Title/Abstract] OR "Ellume COVID-19 home test"[Title/Abstract] OR Ellume[Title/Abstract] OR "Lucira COVID-19 All-in-One"[Title/Abstract] OR Lucira[Title/Abstract] OR QuickVue OR "Cue COVID-19") | 10/1/2020 - | 199 |
| medRxiv & bioRxiv | 5/5/2021 | * Searching for all proprietary names with Boolean operator OR between each proprietary name caused erroneous results [BinaxNOW OR Lucira OR Ellume OR "QuickVue At Home" OR "Cue COVID-19"] so each proprietary name was searched individually | | |
| medRxiv & bioRxiv | 5/5/2021 | BinaxNOW | Date Posted: 10/1/2020 – 5/5/2021 | 41 |
| medRxiv & bioRxiv | 5/5/2021 | Lucira | Date Posted: 10/1/2020 – 5/5/2021 | 3 |
| medRxiv & bioRxiv | 5/5/2021 | Ellume | Date Posted: 10/1/2020 – 5/5/2021 | 12 |
| medRxiv & bioRxiv | 5/5/2021 | "QuickVue At Home" | Date Posted: 10/1/2020 – 5/5/2021 | 0 |
| medRxiv & bioRxiv | 5/5/2021 | "Cue COVID-19" | Date Posted: 10/1/2020 – 5/5/2021 | 0 |
| Google Scholar | 5/5/2021 | (COVID-19 OR SARS-CoV-2) AND (BinaxNOW OR Lucira OR Ellume OR "QuickVue At Home" OR "Cue COVID 19") | Articles added in the last year | 285 |

**Appendix 2**
Published studies and preprint studies examining home tests' platforms

| Author(s), Year, Publication Status | Test Platform | Included/Excluded | Inclusion/Exclusion Reason |
|---|---|---|---|
| Aranda-Diaz et al.[1], Preprint | BinaxNOW COVID-19 Antigen Card | Excluded | Not self-collection of test samples |
| Donato et al.[2], Published | Cue COVID-19 Test for Home and Over The Counter (OTC) Use | Excluded | Not self-collection of test samples |
| Forde and Ciupe[3], Published | BinaxNOW COVID-19 Antigen Card | Excluded | Modelling study |
| James et al.[4], Published | BinaxNOW COVID-19 Antigen Card | Excluded | Not self-collection of test samples |
| Kuo et al.[5], Published | BinaxNOW COVID-19 Antigen Card | Excluded | Samples from previously frozen specimens |
| Okoye et al.[6], Published | BinaxNOW COVID-19 Antigen Card | Included | Self-collection of test samples |
| Peng et al.[7], Preprint | BinaxNOW COVID-19 Antigen Card | Excluded | Not self-collection of test samples |
| Perchetti et al., 2020, Published | BinaxNOW COVID-19 Ag CARD | Excluded | Used de-identified specimens at the laboratory |
| Pilarowski et al.[8], Published | BinaxNOW COVID-19 Ag CARD | Excluded | Not self-collection of test samples |
| Pilarowski et al.[9]. Published | BinaxNOW COVID-19 Ag CARD | Excluded | Not self-collection of test samples |
| Pollock, Jacobs and Tran, 2021, Published | BinaxNOW COVID-19 Ag CARD | Excluded | Not self-collection of test samples |
| Prince-Guerra et al.[10], Published | BinaxNOW COVID-19 Ag Card | Excluded | Not self-collection of test samples |
| Reddy and Das[11], Preprint | BinaxNOW COVID-19 Ag Card | Excluded | Modelling study |
| Shah et al., 2021, Preprint | BinaxNOW COVID-19 Ag Card | Included | Self-collection of test samples |
| Sood et al.[12], Published | BinaxNOW COVID-19 Ag Card | Excluded | Not self-collection of test samples |

## Appendix References

1. Aranda-Diaz A, Imbert E, Strieff S, et al. Implementation of rapid and frequent SARS-CoV2 antigen testing and response in congregate homeless shelters. medRxiv. Published online April 27, 2021:2021.04.20.21255787. https://doi.org/10.1101/2021.04.20.21255787.
2. Donato LJ, Trivedi VA, Stransky AM, et al. Evaluation of the Cue Health point-of-care COVID-19 (SARS-CoV-2 nucleic acid amplification) test at a community drive through collection center. *Diagn Microbiol Infect Dis*. 2021;100(1):115307. https://doi.org/10.1016/j.diagmicrobio.2020.115307.
3. Forde JE, Ciupe SM. Quantification of the tradeoff between test sensitivity and test frequency in a COVID-19 epidemic—a multi-scale modeling approach. *Viruses*. 2021;13(3):457. https://doi.org/10.3390/v13030457.
4. James AE, Gulley T, Kothari A, Holder K, Garner K, Patil N. Performance of the BinaxNOW coronavirus disease 2019 (COVID-19) Antigen Card test relative to the severe acute respiratory coronavirus virus 2 (SARS-CoV-2) real-time reverse transcriptase polymerase chain reaction (rRT-PCR) assay among symptomatic and asymptomatic healthcare employees. *Infect Control Hosp Epidemiol. Published online*. 2021:1–3. https://doi.org/10.1017/ice.2021.20.
5. Kuo P, Realegeno S, Pride DT. Comparison of two nucleic acid amplification tests (NAATs) and two antigen tests for detection of SARS-CoV-2 from upper respiratory specimens. *Journal of Clinical Virology Plus*. 2021;1(1-2):100011. https://doi.org/10.1016/j.jcvp.2021.100011.
6. Okoye NC, Barker AP, Curtis K, et al. Performance characteristics of BinaxNOW COVID-19 antigen card for screening asymptomatic individuals in a University setting. *J Clin Microbiol*. 2021;59(4). https://doi.org/10.1128/JCM.03282-20.
7. Peng J, Mann SA, Mitchell AM, et al. Estimation of secondary household attack rates for emergent SARS-CoV-2 variants detected by genomic surveillance at a community-based testing site in San Francisco. medRxiv. Published online March 3, 2021:2021.03.01.21252705. https://doi.org/10.1101/2021.03.01.21252705.
8. Perchetti GA, Huang M-L, Mills MG, Jerome KR, Greninger AL. Analytical sensitivity of the Abbott BinaxNOW COVID-19 Ag Card. *J Clin Microbiol*. 2021;59(3). https://doi.org/10.1128/JCM.02880-20.
9. Pilarowski G, Lebel P, Sunshine S, et al. Performance characteristics of a rapid severe acute respiratory syndrome coronavirus 2 antigen detection assay at a public plaza testing site in San Francisco. *J Infect Dis*. 2021;223(7):1139–1144. https://doi.org/10.1093/infdis/jiaa802.
10. Pilarowski G, Marquez C, Rubio L, et al. Field performance and public health response using the BinaxNOW rapid severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) antigen detection assay during community-based testing. *Clin Infect Dis*. 2020. https://doi.org/10.1093/cid/ciaa1890 (ciaa1890).
11. Pollock NR, Jacobs JR, Tran K, et al. Performance and implementation evaluation of the Abbott BinaxNOW Rapid Antigen Test in a high-throughput drive-through community testing site in Massachusetts. J Clin Microbiol. Published online February 23, 2021. https://doi.org/10.1128/JCM.00083-21.
12. Prince-Guerra JL, Almendares O, Nolen LD, et al. Evaluation of Abbott BinaxNOW Rapid Antigen Test for SARS-CoV-2 infection at two community-based testing sites - Pima County, Arizona, November 3-17, 2020. *MMWR Morb Mortal Wkly Rep*. 2021;70(3):100–105. https://doi.org/10.15585/mmwr.mm7003e3.
13. Reddy SG, Das S. Strategies for antigen testing: an alternative approach to widespread PCR testing. medRxiv. Published online April 7, 2021:2021.04.05.21254024. https://doi.org/10.1101/2021.04.05.21254024.
14. Shah MM, Salvatore PP, Ford L, et al. Performance of repeat BinaxNOW SARS-CoV-2 antigen testing in a community setting, Wisconsin, November-December 2020. medRxiv. Published online April 9, 2021:2021.04.05.21254834. https://doi.org/10.1101/2021.04.05.21254834.
15. Sood N, Shetgiri R, Rodriguez A, et al. Evaluation of the Abbott BinaxNOW rapid antigen test for SARS-CoV-2 infection in children: implications for screening in a school setting. *PLoS One*. 2021;16(4), e0249710. https://doi.org/10.1371/journal.pone.0249710.