



Ethiopian Public Health Institute (EPHI)  
Knowledge Translation Directorate,

Ethiopian Knowledge Translation Group for  
Health: A JBI Affiliated Group



## EVIDENCE SUMMARY

### Antibody tests during COVID-19 Pandemic

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#### Question

What is the best available evidence regarding antibody tests in detecting SAR-COV-2 infection?

#### Background

Numbers of molecular and serological testing kits are currently available and being developed to mitigate the transmission of the coronavirus disease (CDC, 2020a; World Health Organization, 2020b). Currently, the only available means and gold-standard testing method for active infection by SARS-COV-2 remains to be nucleic acid real-time reverse transcriptase-polymerase chain reaction (rRT-PCR) assay (Corman et al., 2020; World Health Organization, 2020b). This test detects the presence of SARS-CoV-2 infection from individuals suspected of having Covid-19 disease. However, the test determines only the presence of the virus during the infection period and does not indicate if the individual was infected, recovered, or cleared the virus. It also required long turnaround times to generate results, certified laboratories with a trained technician. A report of false-negative results is also additional concerns about this type of test (Li et al., 2020; Patel et al., 2020; Xie, 2020). These limitations hinder the widespread testing effort across the world in a different setting to control the outbreak.

Serology tests are blood-based tests that identify indirectly whether a person has been exposed to SARS-COV-2 infection by looking at their immune response (CDC, 2020b; Johns Hopkins Center for Health, 2020). These tests detect the presence of antibodies in response to recent infection. Studies indicate that majority of patients start to develop antibodies after the first week of the onset of the illness. This means that, unlike molecular tests, serologic tests are not suitable to identify active infection cases around pick transmission and viral shedding time (Lou et al., 2020; Okba et al., 2020; Wölfel et al., 2020). But validated serological tests are very important to understand the evolution of the infection across the population, for surveillance, epidemic forecasting, vaccine development, and determination of the virus immunity (Johns Hopkins Center for Health, 2020; World Health Organization, 2020a).

Therefore validated fast, simple to perform and accurate laboratory testing of SAR-COV-2 is essential to rapidly identify a large number of infected and asymptomatic cases to prevent and

manage the blowout of the outbreak in time. In this review, we have summarized the evidence concerning antibody tests in detecting SAR-COV-2 infection.

- ⦿ A systematic review and meta-analysis conducted to explore the feasibility of rapid diagnostic tests in the management of the COVID-19 outbreak showed that a pooled sensitivity of 64.8% (95% CI; 54.5-74.0), and specificity of 98.0% (95% CI; 95.8-99.0), with high heterogeneity and risk of reporting bias. The authors conclude that: (1) rapid diagnostic tests for COVID-19 are necessary, but should be adequately sensitive and specific; (2) few studies have been carried out to date; (3) the studies included are characterized by low numbers and low sample power, and (4) in light of these results, the use of available tests is currently questionable for clinical purposes and cannot substitute other more reliable molecular tests, such as assays based on RT-PCR (Riccò et al., 2020). (Level 3)
- ⦿ A systematic review and meta-analysis of the diagnostic accuracy of currently available SARS-CoV-2 serological tests and their real-world performance suggests that the use of serological tests for large-scale prevalence surveys (or to grant “immunity passports”) is currently only justified in hard-hit regions, while they should be used with caution elsewhere (Caini et al., 2020). (Level 3)
- ⦿ A systematic review and meta-analysis evaluating diagnostic tests (IgM and IgG) sensitivity and specificity based on Enzyme-linked immunosorbent assay (ELISA), Chemiluminescence Enzyme Immunoassays (CLIA), Fluorescence Immunoassays (FIA), and the Lateral Flow Immunoassays (LFIA) showed IgG tests perform better compared to IgM ones and show better sensitivity when the samples were taken one week after the onset of symptoms. A combined IgG/IgM tests were found to be a better choice in terms of sensitivity than measuring either antibody alone. All methods yield high specificity with ELISA and LFIA reaching levels around 99%. ELISA- and CLIA-based methods perform better in terms of sensitivity (90%–94%) followed by LFIA and FIA with sensitivities ranging from 80% to 89%. The finding indicates ELISA tests could be a safer choice at this point in the pandemic. LFIA tests are particularly attractive for large seroprevalence (antibody prevalence)

### How this Evidence Summary was prepared?

The methods used to prepare in this rapid evidence review was adopted from the JBI Evidence summary:

<https://wiki.joannabriggs.org/display/JSW/Updating+Evidence+Summaries>

Evidence summaries are defined as a synopsis that summarizes existing international evidence on healthcare interventions or activities. These summaries are based on structured searches of the literature and selected evidence-based healthcare databases (JBI Database of Systematic Reviews, Cochrane Library, PubMed, and Epistemonikos). Following the search, all studies are assessed for internal validity using an abridged set of critical appraisal tools.

### Levels of evidence for the effectiveness

Level 1-(Experimental Designs:

a systematic review of RCTs, systematic review of RCTs and other study designs, & RCTs)

Level 2-(Quasi-experimental Designs:

a systematic review of quasi-experimental studies & systematic review of quasi-experimental and other lower study designs)

Level 3-(Observational analytic designs:

a systematic review of comparable cohort studies)

Level 4-(Observational descriptive studies:

a systematic review of descriptive studies, cross-sectional studies)

Level 5-(Expert Opinion:

a systematic review of expert opinion, expert consensus)

(Munn et al., 2015)

### Grades of Recommendation:

Grade A: A ‘strong’ recommendation, where there is evidence of adequate quality supporting its use

Grade B: A ‘weak’ recommendation, where there is evidence supporting its use, although this may not be of high quality

(Joanna Briggs Institute, 2013a, and b)

studies but show lower sensitivity; therefore, the authors noted that the estimation should be taken into account when designing and performing seroprevalence studies. Furthermore, even if tests are highly accurate, much about protective immunity is unknown, and the true presence of antibodies might not mean that people are immune to re-infection (Kontou et al., 2020). (Level 3)

- ⦿ A single primary study evaluating rapid antibody IgG/IgM based testing system in the community setting concluded and recommended not to rely on an antibody-based rapid test for public health measures such as community screenings, given the low sensitivity (Döhla M, Boesecke C, Schulte B, 2020). (Level 4)
- ⦿ The World Health Organization does not recommend the use of serological assays for case detection. However, their use in surveillance and research setting is recommended. The WHO states serological tests should not be used in any other setting, including for clinical decision-making, until evidence supporting use for specific indications is available (World Health Organization, 2020a). (Level 5)
- ⦿ The Center for Disease Control and Prevention (CDC) does not recommend using antibody testing to diagnose acute infection in clinical and public health settings. It recommends using a viral (nucleic acid or antigen) test to diagnose acute infection. CDC states serologic testing should not be used to determine immune status in individuals until the presence, durability, and duration of immunity is established. The test can be offered as a method to support the diagnosis of acute COVID-19 illness for persons who present late. It can be ordered in addition to recommended direct detection methods such as PCR. This will maximize sensitivity as the sensitivity of nucleic acid detection is decreasing and serologic testing is increasing during this period. Testing should be offered as a method to help establish a diagnosis when patients present with late complications of COVID-19 illness (CDC, 2020b). (Level 5)
- ⦿ CDC has also stated that the protective measures should be continued by everyone, until scientists get more data on whether antibodies protect against reinfection with this virus, even if they have had a positive antibody test. This type of test results should not be used to determine if someone can return to work or to group people together in settings such as schools, dormitories, and correctional facilities (CDC, 2020b). (Level 5)
- ⦿ The U.S. Food and Drug Administration (FDA) recommends that health care providers continue to use an antibody-based serological test intended to detect antibodies to SARS-CoV-2 to help identify people who may have been exposed to the SARS-CoV-2 virus or have recovered from the COVID-19 infection. However, they should be aware of the test limitations and the risk if the test results used on its own for the diagnosis of COVID-19. The FDA is not aware of an antibody test that has been validated for diagnosis of SARS-CoV-2 infection based on the underlying scientific principles of antibody tests and does not expect that an antibody test can be shown to definitively diagnose or exclude SARS-CoV-2 infection (U.S Food and Drug Administration, 2020). (Level 5)

- ⦿ According to Johns Hopkins Center for Health release, serology tests will be an important tool for public health workers to estimate the prevalence of the disease, including those that may be asymptomatic or have recovered. However, currently, many of these tests have been approved for research use only, which indicates that they are not yet approved for use as a public health diagnostic tool or at-home diagnosis. Validated, accurate tests are in short supply and are under development (Johns Hopkins Center for Health, 2020). (Level 5)
- ⦿ An evidence review conducted by the Canadian Agency for Drugs and Technologies in Health (CADTH) on available literature regarding the serological test for COVID-19 indicated that the performance and role of these tests in clinical settings have not been completely demonstrated. Evidence that confirms individuals have immunity to COVID-19 or are protected from reinfection is currently missing. An accurate antibody-based serological test may provide information on who has COVID-19, who has been infected, and who may have immunity. The test may be used to indicate who could be prioritized to return to work or serve as front line health workers. but rigorous analytical and clinical testing is needed first before consideration for the general population-based used (Canadian Agency for Drugs and Technologies in Health, 2020). (Level 5)

### Best Practice Recommendation

- 👉 Serological tests are not recommended to be used solely to diagnose the presence of SARS-COV-2 infection. (Grade B)
- 👉 Due to a lack of evidence and accurate antibody-based serological tests against SARS-COV-2, it is not recommended to use this type of test to determine individuals who have immunity to COVID-19 and can return to work or who may donate convalescent plasma. (Grade B)
- 👉 There is still uncertainty regarding the accuracy and role of the use of these tests for widespread of the population. (Grade B)
- 👉 It is recommended serology tests to be used in surveillance and research laboratory setting. It should not be used in any other setting, including for clinical decision-making, until evidence supporting use for specific indications is available. (Grade B)

### References

- Caini, S., Bellerba, F., Corso, F., Díaz-basabe, A., Natoli, G., Facciotti, F., Raimondi, S., Palli, D., Mazzarella, L., & Pelicci, P. G. (2020). *Meta-analysis of diagnostic performance of serological tests for SARS-CoV-2 antibodies and public health implications*.
- Canadian Agency for Drugs and Technologies in Health. (2020). Serological Tests for COVID-19. *The Lancet*, 249(6461), 923–924. [https://doi.org/10.1016/S0140-6736\(47\)91386-X](https://doi.org/10.1016/S0140-6736(47)91386-X)
- CDC. (2020a). Center for Disease Prevention and Control: Diagnostic Test for COVID-19. *CDC*.
- CDC. (2020b). *Interim Guidelines for COVID-19 Antibody Testing*. *CDC*.
- Corman, V. M., Landt, O., Kaiser, M., Molenkamp, R., Meijer, A., Chu, D. K., Bleicker, T., Brünink, S., Schneider, J., Luisa Schmidt, M., GJC Mulders, D., Haagmans, B. L., van der Veer, B., van den Brink, S., Wijsman, L., Goderski, G., Romette, J.-L., Ellis, J., Zambon, M., ... Chantal, R. (2020). Detection of 2019 -nCoV by RT-PCR. *Euro Surveill*, 25(3), 1–8. <https://doi.org/10.2807/1560-7917.ES.2020.25.3.2000045>
- Döhla M, Boesecke C, Schulte B, et al. (2020). *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. January.
- Joanna Briggs Institute. (2013a). JBI Levels of Evidence FAME. *JBI Approach*, October, 2–6. <http://www.joannabriggs.edu.au>
- Joanna Briggs Institute. (2013b). New JBI Grades of Recommendation. *Joanna Briggs Institute*, October, 1. [http://joannabriggs.org/assets/docs/approach/JBI-grades-of-recommendation\\_2014.pdf](http://joannabriggs.org/assets/docs/approach/JBI-grades-of-recommendation_2014.pdf)
- Johns Hopkins Center for Health. (2020). Serology testing for COVID-19. *Johns Hopkins Center for Health Security*. <https://doi.org/10.1101/2020.01.28.923011>
- Kontou, P. I., Braliou, G. G., Dimou, N. L., Nikolopoulos, G., & Bagos, P. G. (2020). *Antibody Tests in Detecting SARS-CoV-2 Infection* :
- Levesque, J., & Maybury, D. W. (2020). A note on COVID-19 seroprevalence studies: a meta-analysis using hierarchical modeling. *MedRxiv*, 2020.05.03.20089201. <https://doi.org/10.1101/2020.05.03.20089201>
- Li, D., Wang, D., Dong, J., Wang, N., Huang, H., Xu, H., & Xia, C. (2020). False-negative results of a real-time reverse-transcriptase polymerase chain reaction for severe acute respiratory syndrome coronavirus 2: Role of deep-learning-based ct diagnosis and insights from two cases. *Korean Journal of Radiology*, 21(4), 505–508. <https://doi.org/10.3348/kjr.2020.0146>
- Lou, B., Li, T.-D., Zheng, S.-F., Su, Y.-Y., Li, Z.-Y., Liu, W., Yu, F., Ge, S.-X., Zou, Q.-D., Yuan, Q., Lin, S., Hong, C.-M., Yao, X.-Y., Zhang, X.-J., Wu, D.-H., Zhou, G.-L., Hou, W.-H., Li, T.-T., Zhang, Y.-L., ... Chen, Y. (2020). Serology characteristics of SARS-CoV-2 infection since exposure and post symptom onset. *The European Respiratory Journal*. <https://doi.org/10.1183/13993003.00763-2020>
- Munn, Z., Lockwood, C., & Moola, S. (2015). The Development and Use of Evidence Summaries for Point of Care Information Systems: A Streamlined Rapid Review Approach. *Worldviews on Evidence-Based Nursing*, 12(3), 131–138. <https://doi.org/10.1111/wvn.12094>
- Okba, N. M. A., Muller, M. A., Li, W., Wang, C., GeurtsvanKessel, C. H., Corman, V. M., Lamers, M. M., Sikkema, R. S., Bruin, E. de, Chandler, F. D., Yazdanpanah, Y., Hingrat, Q. Le, Descamps, D., Houhou-Fidouh, N., Reusken, C. B. E. M., Bosch, B.-J., Drosten, C., Koopmans, M. P. G., & Haagmans, B. L. (2020). SARS-CoV-2 specific antibody responses in COVID-19 patients. *MedRxiv*, March, 2020.03.18.20038059. <https://doi.org/10.1101/2020.03.18.20038059>
- Patel, R., Babady, E., Theel, E., Storch, G., Pinsky, B., George, K., Smith, T., & Bertuzzi, S. (2020). Report from the American Society for Microbiology COVID-19 COVID-19. *MBio*, 11(2), 1–5. <https://doi.org/DOI:10.1128/mBio.00722-20>
- Riccò, M., Ferraro, P., Gualerzi, G., Ranzieri, S., Henry, B. M., Said, Y. Ben, Pyatigorskaya, N. V., Nevolina, E., Wu, J., Bragazzi, N. L., & Signorelli, C. (2020). Point-of-Care Diagnostic Tests for Detecting SARS-CoV-2 Antibodies: A Systematic Review and Meta-Analysis of Real-World Data. *Journal of Clinical Medicine*, 9(5 PG-1515–1515), 1515. <https://doi.org/10.3390/jcm9051515>
- U.S Food and Drug Administration. (2020). *Important information on the use of serological (antibody) tests for COVID-19 letter to health care providers*.
- Wölfel, R., Corman, V. M., Guggemos, W., Seilmaier, M., Zange, S., Müller, M. A., Niemeyer, D., Jones, T. C., Vollmar, P., Rothe, C., Hoelscher, M., Bleicker, T., Brünink, S., Schneider, J., Ehmann, R., Zwirgmaier, K., Drosten, C., & Wendtner, C. (2020). Virological assessment of hospitalized patients with COVID-2019. *Nature*, 581(March). <https://doi.org/10.1038/s41586-020-2196-x>
- World Health Organization. (2020a). Advice on the use of point-of-care immunodiagnostic tests for COVID-19 Rapid diagnostic tests based on antigen detection. *WHO Coronavirus Disease (COVID-19) Pandemic*.
- World Health Organization. (2020b). Laboratory testing strategy recommendations for COVID-19: interim guidance, 21 March 2020. *World Health Organization*, March, <https://apps.who.int/iris/handle/10665/331509>. Lic.
- Xie, X. (2020). Chest CT for Typical Covid-19 pneumonia. *Radiology*. <https://doi.org/10.14358/PERS.81.12.21>

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