

COVID-19 CADTH HORIZON SCAN

Serological Tests for COVID-19

**This report was published on
May 6, 2020**

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Service Line: Horizon Scan
Issue: 188
Publication Date: May 2020
Report Length: 13 Pages

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Cite As: *Serological Tests for COVID-19*. Ottawa: CADTH; 2020 May. (CADTH Horizon Scan; No. 188).

ISSN: 1488-6324 (online)

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Funding: CADTH receives funding from Canada's federal, provincial, and territorial governments, with the exception of Quebec.

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Key Messages

- Health Canada is reviewing serological COVID-19 tests through the expedited access route.
- Based on the available literature, the performance and role of these tests in clinical settings have not been completely demonstrated.
- Evidence to confirm that individuals have immunity to COVID-19 or are protected from reinfection is lacking.
- If accurate, antibody-based serological tests may provide information on who has COVID-19, who has been infected, and who may have immunity.
- Serological tests may be used to indicate who could be prioritized to return to work or serve as front line health workers.
- Rapid point-of-care serological tests may provide results in approximately 10 to 15 minutes.

Context

The early diagnosis of coronavirus disease 2019 (COVID-19) plays a critical role in optimizing supportive care for individuals with severe illness¹ and in containing the transmission of the infection through case identification, isolation, and contact tracing.² The primary method used in Canada for identifying COVID-19 is the laboratory-based polymerase chain reaction (PCR) test using a nose-throat swab. This test identifies the presence of antigens expressed early in infections.³

Serological testing measures the level of antibodies present in the blood. Antibodies are proteins produced by the immune system to protect the body from infection.⁴ Unlike the deep nasal or throat swab detection methods, serological tests are intended to confirm suspected cases of COVID-19 after individuals have recovered and developed antibodies that may protect them from future infection and to identify asymptomatic carriers of the virus.⁵

In the European Union⁶ and some countries, including the US⁷ and Australia,⁸ some serology tests are available and have been officially approved by their regulatory bodies with conditional use.^{6,7,8} In Canada, serological tests are being reviewed by Health Canada via the expedited access pathway to determine their validity.⁹ There is concern that inadequate testing may fail to identify individuals with the infection or may mislabel individuals as having recovered from the disease when they have never been infected. Validation ensures test accuracy and reliability, and helps prevent the further spread of the disease.⁷

Information from the test, if accurate, could provide insight into the transmission of COVID-19 and may inform policy decisions on return to work, the use of personal protective equipment, the continuation of social distancing practices, and attendance at large gatherings.¹⁰ The loosening of restrictions put into place due to the COVID-19 pandemic will be influenced by the characteristics of different community populations and will be linked to their vulnerability and immunity to the infection.¹¹

At least three provinces are considering using serological tests as a means of easing COVID-19 restrictions and social distancing measures.¹¹ There may be significant medical, public health, societal, and economic policy implications related to the deployment of these tests.

A government-funded COVID-19 immunity task force has been established to oversee the coordination of a series of country-wide serological test surveys. Data from these surveys will provide insight into the extent of the spread of the virus, its impact on populations at higher risk, and potential immunity.¹²

About This Document

This rapid Horizon Scan summarizes information identified through a limited literature search. It is not a systematic review, it was not peer-reviewed, and a critical appraisal of studies was not undertaken. It is not intended to provide recommendations. Care has been taken to ensure the information is accurate and complete, but it should be noted that international scientific evidence about COVID-19 is changing and growing rapidly. This document will be updated as additional evidence or guidance becomes available.

The Technology

Serological testing measures antibodies — specifically immunoglobulin M and immunoglobulin G — present in the blood when the body responds to a specific infection. Serology tests for COVID-19 are not designed to detect the virus in newly infected individuals; instead, they are intended to detect the virus after the infection has matured and mounted an antibody response.⁵ Current knowledge suggests that antibodies become detectable in blood somewhere between seven and 14 days after exposure to the virus, although some patients may develop antibodies sooner.¹³

Serology-based tests are being used in some hospitals to complement molecular-based testing as part of a recovery criteria and discharge requirement.¹⁴ This may be important because the sensitivity of some PCR-based tests may be compromised if specimens are taken too early in the disease process or if the specimen collection is inadequate.¹⁴

The strength of antibody response depends on several factors, including age, nutritional status, severity of disease, and certain medications or infections like HIV that suppress the immune system.¹⁵

Scientific understanding on COVID-19 immunity after infection is limited and evolving. It is unclear how long antibodies last (and if it will be the same for everyone), how much antibody is required to protect the immune system, the role of immunity in interrupting transmission, and if individuals who have recovered from the virus can be reinfected.¹⁶ Data from China, South Korea, and Japan suggest that reinfection may be possible. However, these cases may not be well-substantiated and the issue may be influenced more by testing inadequacies than by genuine reinfections.¹⁷

Antibody-Based Serological Testing Techniques

The various types of antibody-based serological tests include rapid diagnostic tests (e.g., lateral flow immunoassay [LFIA]), chemiluminescence immunoassay (CLIA), enzyme-linked immunosorbent assay (ELISA), and neutralization assay. Commonly using colloidal gold as a label, LFIAs are rapid tests that can be used at the point of care to yield qualitative readings (i.e., positive or negative readings as indicated by coloured lines).¹⁸ As a lab-based test requiring venipuncture samples, ELISA can yield qualitative or quantitative readings (i.e., colour or fluorescence-based), which can detect the amount of viral protein and patient antibody complexes.¹⁸ Being a technique that more closely resembles ELISA than LFIA, CLIAs require a lab-based analyzer to yield quantitative readings proportional to the amount

of antibodies detected.^{5,19} Finally, neutralization assays rely on cell cultures of the virus, with blood samples to determine if patients have active antibodies to help prevent reinfections.¹⁸ Further test details are presented in Table 1.

Table 1: Antibody-Based Serological Testing Techniques

Type of immunoassay	Antibody assessment	Sampling method	Length of time for results	Setting
Rapid diagnostic test (e.g., LFIA with colloidal gold)	IgG, IgM, IgA	Finger prick or venipuncture (i.e., whole blood, serum, or plasma)	10 to 30 minutes	Point-of-care testing
CLIA	IgG, IgM, IgA	Venipuncture	30 minutes	Lab
ELISA	IgG, IgM, IgA	Venipuncture	1 to 5 hours	Lab
Neutralization assay	Active neutralizing antibodies	Venipuncture	3 to 5 days	Lab

CLIA = chemiluminescence immunoassays; ELISA = enzyme-linked immunosorbent assay; IgA = immunoglobulin A; IgG = immunoglobulin G; IgM = immunoglobulin M; LFIA = lateral flow immunoassay.

Availability

Currently, no serology tests have been approved in Canada. Health Canada is actively assessing such tests within the expedited access process. Health Canada is collaborating with the National Microbiology Laboratory to validate testing and research, and consulting with national and international experts to guide the regulation of serological tests.²⁰

In the US, the FDA has approved 12 serological tests intended for use in clinical laboratories under the Emergency Use Authorization (EUA).⁷ Initially, serology tests did not require an EUA submission. Instead, the FDA required that manufacturers validate tests themselves and notify the FDA of this action. The FDA also required manufacturers to label tests or test reports. The labelling must indicate that the serology test has not been reviewed by the FDA, that negative results do not rule out COVID-19 infection, that follow-up molecular testing should be considered, and that serological testing should not be used as the sole basis for diagnosing COVID-19.²¹

The FDA has acknowledged some concerns about the quality of some of these tests that do not require FDA approval.²² Since the issuance of the new FDA policy, more than 100 test manufacturers have notified the FDA that they have serology tests available that are intended for the diagnosis of COVID-19. The FDA is aware that some manufacturers have made false claims that their tests are FDA-approved or -authorized.²³ As well, some test providers have been exposed for making fraudulent claims that their tests diagnose COVID-19 antibodies when they do not.²³

The FDA has subsequently revised its policy on serology tests. As of May 4, 2020, manufacturers already marketing serology tests will be required to prepare and submit an EUA with their validation data within 10 business days from the date they notified the FDA of their validation testing. As well, the FDA has outlined recommendations for performance thresholds for test accuracy.²⁴

The WHO currently recommends against the use of point-of-care immunodiagnostic tests for COVID-19 in the clinical setting.²⁵

Cost

A rapid serological test developed in Canada by BTNX Inc. sells for approximately \$US10.00 per test.²⁶

Evidence

To date, of the more than 70 serological test suppliers that have notified the FDA, 12 antibody-based serology tests have been granted EUA.²⁷ Datasheets from four suppliers²⁸⁻³¹ are summarized in this report. In addition, relevant articles with clinical data are also included.

Lateral Flow Immunoassay

Literature on the use of LFIA for the detection of antibodies against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was identified in two supplier-provided datasheets^{30,31} and three articles.³²⁻³⁴ Granted EUA by the FDA, the Cellex qSARS-CoV-2 IgG/IgM Rapid Test³¹ and ChemBio DPP COVID-19 IgM/IgG System³⁰ detects IgG and IgM against the nucleocapsid protein of SARS-CoV-2. Tested in 128 reverse transcription PCR (RT-PCR)-confirmed SARS-CoV-2 patients and 250 negative patients, the Cellex-supplied datasheet stated a positive percent agreement (PPA) and negative percent agreement (NPA) of 93.75% (95% CI, 88.06 to 97.26%) and 96.40% (95% CI, 92.26 to 97.78%), respectively.³¹ Tested in 31 RT-PCR–confirmed patients and 41 negative patients, the ChemBio test had a PPA and an NPA of 93.5% (95% CI, 79.3 to 98.2%) and 90.2% (95% CI, 77.5 to 96.1%), respectively.³⁰ Two primary studies involving the use of LFIAs included 397 and 128,³³ and 38 and 12,³⁴ hospital-based patients who tested positive and negative by RT-PCR, respectively. The IgM/IgG test developed by Li et al. (2020)³³ resulted in a sensitivity of 88.66% and a specificity of 90.63%, while the VivaDiag COVID-19 IgM/IgG Rapid Test³⁴ resulted in a sensitivity of 18.4% and a specificity of 91.7%. The IgM/IgG test supplied by Zhuhai Livzon Diagnostics Inc. was tested in 76 RT-PCR–positive patients and 37 negative patients with a clinical diagnosis of SARS-CoV-2 in the hospital setting.³² At one to seven, eight to 14, and 15 days or more after the onset of symptoms, this IgM/IgG test resulted in sensitivities of 11.1%, 92.9%, and 96.8%, respectively.³²

Chemiluminescence Immunoassay

Literature on the use of CLIA for the detection of antibodies against SARS-CoV-2 was identified in three articles.^{19,35,36} Tested in 43 RT-PCR–confirmed patients and 33 suspected patients, the CLIA provided by Shenzhen YHLO Biotech Co., Ltd. resulted in sensitivities of 48.1% and 88.9%, and specificities of 100% and 90.9%, to IgM and IgG, respectively.¹⁹ Tested in 37 RT-PCR–confirmed patients and showing a rapid increase in IgM and IgG six days after the onset of symptoms, the MAGLUMI 2000 Plus CLIA system resulted in sensitivities of 100% and 88% for IgG and IgM, respectively, on day 12.³⁵ Additionally, a review article included data for the Caris 200 Automatic Chemiluminescence Analyzer, which resulted in a sensitivity of 94.8% and specificity of 99.7% for the total antibody level (IgM, IgG, and IgA).³⁶

Enzyme-Linked Immunosorbent Assay

Literature on the use of ELISA for the detection of antibodies against SARS-CoV-2 was identified in two supplier-provided datasheets^{28,29} and three articles.³⁷⁻³⁹ Granted EUA by the FDA, the Mount Sinai COVID-19 ELISA IgG Antibody Test²⁸ and VITROS Immunodiagnostic

Products Anti-SARSCoV-2 Total Reagent Pack²⁹ detects the presence IgM and total IgG, respectively. The sensitivity and specificity data were not available for the Mount Sinai COVID-19 ELISA IgG Antibody Test.^{18,28} Tested in 36 and 400 confirmed positive and negative samples, respectively, the VITROS Immunodiagnostic Products Anti-SARSCoV-2 Total Reagent Pack resulted in a sensitivity of 83% and a specificity of 100%.²⁹ Tested in 173 SARS-CoV-2–confirmed patients, the ELISA provided by Beijing Wantai Biological Pharmacy Enterprise Co., Ltd. showed seroconversion rates of 93.1%, 82.7%, and 64.7% for total antibody, IgM, and IgG, respectively.³⁷ Furthermore, the median times for seroconversion were 11, 12, and 14 days for total antibody, IgM, and IgG, respectively.³⁷ Tested in 82 RT-PCR–confirmed patients and 58 probable patients (i.e., RT-PCR–negative but symptomatic), the ELISA protocol developed by Guo et al. (2020)³⁹ showed seroconversion rates of 75.6% and 93.1% for IgM in the confirmed and probable groups, respectively. Tested in serum samples collected at least 14 days after the onset of symptoms in 16 RT-PCR–confirmed patients, the ELISA test developed by To et al. (2020)³⁸ showed seroconversion rates of 94% for anti-nucleoprotein (NP) IgG, 88% for anti-NP IgM, 100% for anti-surface spike protein receptor binding domain (RBD) IgG, and 94% for anti-RBD IgM.

Additional Studies and Ongoing Trials

Two articles were identified that compared LFIA, CLIA, and/or ELISA.^{40,41} Using 37 serum samples from 22 RT-PCR–confirmed hospital patients, Gao et al. (2020)⁴⁰ compared three IgM/IgG tests developed by Beier Bioengineering Co., Ltd.: LFIA with colloidal gold as label, CLIA, and ELISA.⁴¹ Serum samples were collected at three stages of infection onset: 10 samples from early stage (one to seven days after), 13 from middle stage (eight to 14 days after), and 14 from late stage (14 to 24 days after).⁴¹ LFIA with colloidal gold resulted in the highest positive rate of IgM detection (50.0%, 38.5%, and 64.3% in early, middle, and late stages), while ELISA resulted in the highest positive rate of IgG detection (40.0%, 61.5%, and 85.7% in early, middle, and late stages).⁴¹ Tested in 48 RT-PCR–confirmed patients, 47 negative patients, and 36 suspected patients in a hospital setting, Lippi et al. (2020)³⁹ compared the MAGLUMI 2019-nCoV IgM/IgG CLIA to the EUROIMMUN IgA/IgG ELISA.⁴⁰ Despite exhibiting an overall 90% agreement in IgG detection, the two tests resulted in variable positivity rates at different stages of symptom onset.⁴⁰ The MAGLUMI 2019-nCoV IgM/IgG CLIA and EUROIMMUN IgA/IgG ELISA resulted in IgG-positive detection rates of 10.0%, 53.8%, 100%, and 0%, 15.4%, and 100%, respectively, at less than five days, at greater than five days to 10 days, and at greater than 10 days to 21 days.⁴⁰

No literature was identified regarding the performance of neutralization assays; therefore, no summary can be provided. As of March 20, 2020, approximately 100 immunoassay submissions were received by the Foundation for Innovative New Diagnostics (FIND).⁴² With results pending, FIND is in the process of reviewing 27 serological tests specific to SARS-CoV-2 antibodies.⁴² Additionally, numerous non-peer-reviewed preliminary reports and ongoing clinical trials on serological tests have been registered on the medRxiv and ClinicalTrials.gov websites, respectively.

Overall Evidence Conclusion

Due to the scarcity of published large clinical studies and the standardization of performance testing of antibody-based serology tests against SARS-CoV-2, there remains uncertainty regarding the accuracy and role of the use of these tools. The identified literature suggested a wide range of test sensitivity and specificity across different antibody-based serological techniques. As not all test developers have published their data, and with some making

unfounded claims regarding their tests, there may also be a lack of transparency in the accuracy and performance of serology tests in clinical settings.^{5,43} In addition to variable sensitivities and specificities, the clinical performance (i.e., positive and negative predictive value) of different antibody-based serological tests are likely lower because of the low presumed prevalence of SARS-CoV-2 infections.⁴⁴ Thus, the interpretation of test results should take into consideration the prevalence of SARS-CoV-2 infections in different settings (e.g., long-term care versus overall population).⁴⁵ Furthermore, as an antibody response against SARS-CoV-2 may take several days after infection to develop, antibody-based serological test accuracy is dependent on the time of sampling and may not be useful in the early days of infection because of the risk of false-negative results.^{13,46} There is also the risk of false-positive results due to cross-reactivity from a previous or current infection with other non-SARS-CoV-2 human coronaviruses.⁴⁷ Additionally, evidence is lacking for immunity from reinfection in those who have antibodies after recovering from COVID-19.⁴⁸

With the current available evidence, the WHO does not recommend the use of rapid antibody-based serological tests for patient care.⁴⁹ The FDA's recommendations to health care providers state that an antibody-based serological test may be used to help determine if a patient may have been exposed to SARS-CoV-2, but it should not be used on its own for the diagnosis of COVID-19.⁵⁰ Nonetheless, antibody-based serological testing may have a role to play in contact tracing, therapeutic studies, return-to-work decisions, and serological surveillance.^{13,51,52} The combination of RT-PCR and antibody-based serological tests may enhance the accuracy of infection detection.^{33,39} The Alberta Health Services COVID-19 Scientific Advisory Group acknowledges that the development of and access to validated serological tests may help in the testing of priority groups such as health care providers.¹⁷ Further research investigating the analytical and clinical accuracy of antibody-based serological tests, especially with standardized validation protocols and large clinical studies, would provide an additional knowledge base for clinicians, researchers, and decision-makers.

Implications

The deployment of validated serological tests across Canada may have medical, public health, societal, and socioeconomic implications. While serological testing may be beneficial for decisions about easing the COVID-19 restrictions and social isolation, there is concern that their rollout may also exacerbate inequalities and may compromise some individual liberties.⁵³

Medical

There are several medical-related implications of serological tests for COVID-19 that extend beyond their immediate diagnostic capabilities. Some of the uses of these tests may include:

- These tests may identify fully recovered individuals who are willing to donate their antibodies for transfusion into patients who are critically ill from COVID-19 as part of studies investigating the use of convalescent plasma therapy as treatment.⁵⁴
- Data from serological surveillance programs may help to develop vaccines⁵⁵ by establishing optimal antigens⁵⁶ and checking vaccine efficacy.⁵⁷
- Vaccination policies may use serology test data to identify who does not have COVID-19 antibodies and should be prioritized for vaccination,⁵⁸ and to help establish a “globally fair vaccine-allocation” policy.⁵⁹

Public Health

Serological testing may provide answers to important epidemiological questions about the scope of the infection, including its transmissibility, virulence, actual fatality rates,^{13,60} and to validate if measures put in place to stop the spread were effective.⁶¹

Epidemiologists may be able to use the serology results to determine the resistance of a population to a secondary wave of infection and prepare a response that is tailored to protect those in high-risk groups.⁶⁰

Societal

There are some broad societal implications related to serology-based testing. The tests may be used to ease social distancing directives for different populations based on vulnerability and immunity to the infection.^{11,62} The tests may be used to inform strategies on the reopening of schools,⁶³ to identify requirements for personal protective equipment,¹⁰ and to determine populations considered safe to travel.⁶⁴

Some countries, such as the US, the UK, Italy, and Germany are considering using serology-based tests as the basis for developing “immunity certificates” to loosen social distancing measures.^{65,66} In these countries, the certificates are intended to provide individuals with conditional access to society. These types of certificates may have implications related to the stigmatization and marginalization of some populations.⁶⁶ As well, these types of certificates may have some broader privacy-related issues, including those related to the protection of medical data.⁵³

Socioeconomic

Serological testing may be used to inform strategic staffing decisions about the return to work of essential workers, such as health care professionals, who are presumed to be immune and may not require certain types of protective equipment. The test may also help to overcome people’s fears of contracting the virus from co-workers.⁶⁷

Once priority groups have been tested, serological tests may be used to stimulate sectors of the economy that are contingent on the gathering of people.⁶⁸ Since individuals who do not have immunity may require regular PCR testing to prove that they are not infected, there is concern that they may be classified less favourably than those with immunity by employers.⁵³ As well, there are concerns that some people may deliberately attempt to expose themselves to COVID-19, with the hope that they will experience mild symptoms, so that they can return to work more quickly.⁵³

Final Thoughts

Rigorous testing to determine analytical and clinical sensitivity and specificity is required before serological testing can be considered for widespread population-based use. As the utility of serological testing for COVID-19 immunity is predicated on the fact that immunity will last for some time and that reinfection is not possible, emerging evidence on immunity duration and reinfection will have to be reviewed and updated as new evidence becomes available. If serology tests prove to have clinical utility, initially, while production ramps up, there may not be enough serology tests for everyone; to ensure the most judicious distribution of these tests, policy-makers may want to consider priority group-based rollout of the test.

Literature Search Methods

A limited literature search was conducted on the concepts of serology and COVID-19 using the following bibliographic databases: MEDLINE and Embase via Ovid, Scopus, and the Cochrane Library. Grey literature was identified by searching relevant sections of the *Grey Matters* checklist (<https://www.cadth.ca/grey-matters>). No filters were applied to limit the retrieval by study type. The search was also limited to English-language documents published between January 1, 2017 and April 17, 2020.

References

1. Government of Canada. Clinical management of patients with moderate to severe COVID-19 - interim guidance. 2020; <https://www.canada.ca/en/public-health/services/diseases/2019-novel-coronavirus-infection/clinical-management-covid-19.html>. Accessed 2020 Apr 20.
2. Udugama B, Kadhiresan P, Kozlowski HN, et al. Diagnosing COVID-19: the disease and tools for detection. *ACS nano*. 2020;Mar 30:acs.nano.0c02624.
3. Government of Canada. Coronavirus disease (COVID-19): for health professionals. 2020; <https://www.canada.ca/en/public-health/services/diseases/2019-novel-coronavirus-infection/health-professionals.html>. Accessed 2020 Apr 20.
4. Premier Biotech. PCR and serology based testing explained. 2020; <https://premierbiotech.com/innovation/pcr-and-serology-based-testing-explained/>. Accessed 2020 Apr 20.
5. Abbasi J. The promise and peril of antibody testing for COVID-19. *JAMA*. 2020;Apr 17.
6. An overview of the rapid test situation for COVID-19 diagnosis in the EU/EEA. Solna (SE): European Centre for Disease Prevention and Control; 2020; <https://www.ecdc.europa.eu/sites/default/files/documents/Overview-rapid-test-situation-for-COVID-19-diagnosis-EU-EEA.pdf>. Accessed 2020 May 1.
7. U.S. Food & Drug Administration. Coronavirus (COVID-19) update: serological test validation and education efforts. 2020; <https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-serological-test-validation-and-education-efforts>. Accessed 2020 Apr 22.
8. Australian Government Department of Health. COVID-19 point-of-care tests. 2020; <https://www.tga.gov.au/covid-19-point-care-tests>. Accessed 2020 May 1.
9. Health Canada. Diagnostic devices for use against coronavirus (COVID-19). 2020; <https://www.canada.ca/en/health-canada/services/drugs-health-products/medical-devices/covid-19.html>. Accessed 2020 Apr 20.
10. Pavlides SC, Furman AC. Prudent use of SARS-CoV- antibody testing: avoiding false assumptions. Plymouth Meeting (PA): ECRI Institute; 2020; https://assets.ecri.org/PDF/COVID-19-Resource-Center/COVID-19-Clinical-Care/COVID-Position-Paper_Antibody-Testing-2.pdf. Accessed 2020 Apr 20.
11. Canadian Press. Return to normal hinges on immunity, say those pushing for new COVID-19 blood tests. *CBC News* 2020 Apr 17; <https://www.cbc.ca/news/health/immunity-tests-coronavirus-1.5535855?cmp=rss>. Accessed 2020 Apr 20.
12. Justin Trudeau Prime Minister of Canada. Prime Minister announces new support for COVID-19 medical research and vaccine development. 2020 Apr 23; <https://pm.gc.ca/en/news/news-releases/2020/04/23/prime-minister-announces-new-support-covid-19-medical-research-and>. Accessed 2020 Apr 24.
13. Patel R, Babady E, Theel ES, et al. Report from the American Society for Microbiology COVID-19 International Summit, 23 March 2020: Value of Diagnostic Testing for SARS-CoV-2/COVID-19. *mBio*. 2020;11(2):26.
14. Tahamtan A, Ardebili A. Real-time RT-PCR in COVID-19 detection: issues affecting the results. *Expert Rev Mol Diagn*. 2020;10.1080/14737159.2020.1757437.
15. World Health Organization. Advice on the use of point-of-care immunodiagnostic tests for COVID-19. 2020; <https://www.who.int/news-room/commentaries/detail/advice-on-the-use-of-point-of-care-immunodiagnostic-tests-for-covid-19>. Accessed 2020 Apr 20.
16. McKenna S. What immunity to COVID-19 really means. *Scientific American* 2020 Apr 10; <https://www.scientificamerican.com/article/what-immunity-to-covid-19-really-means/>. Accessed 2020 Apr 21.
17. Key research question: can people with previous COVID-19 infection become re-infected by the virus? Edmonton (AB): Alberta Health Services; 2020; <https://www.albertahealthservices.ca/assets/info/ppih/ff-ppih-covid-19-reinfection-rapid-review.pdf>. Accessed 2020 Apr 21.
18. Johns Hopkins Bloomberg School of Public Health. Serology-based tests for COVID-19. 2020; <https://www.centerforhealthsecurity.org/resources/COVID-19/serology/Serology-based-tests-for-COVID-19.html#sec1>. Accessed 2020 Apr 21.
19. Jin Y, Wang M, Zuo Z, et al. Diagnostic value and dynamic variance of serum antibody in coronavirus disease 2019. *Int J Infect Dis*. 2020;94:49-52.
20. Health Canada. Serological tests for use against COVID-19. 2020; <https://www.canada.ca/en/health-canada/services/drugs-health-products/medical-devices/covid-19/serological-testing.html>. Accessed 2020 Apr 22.
21. Johnson M. FDA fleshes out emergency guidance for coronavirus test developers. *Modern Healthcare* 2020 Mar 26; <https://www.modernhealthcare.com/politics-policy/fda-fleshes-out-emergency-guidance-coronavirus-test-developers>. Accessed 2020 Apr 22.
22. U.S. Food & Drug Administration. Coronavirus (COVID-19) update: daily roundup April 15, 2020. 2020; <https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-daily-roundup-april-15-2020>. Accessed 2020 Apr 22.
23. U.S. Food & Drug Administration. Coronavirus (COVID-19) update: serological tests. 2020; <https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-serological-tests>. Accessed 2020 Apr 22.
24. Insight into FDA's Revised Policy on Antibody Tests: Prioritizing Access and Accuracy. 2020.
25. World Health Organization. Advice on the use of point-of-care immunodiagnostic tests for COVID-19: scientific brief. 2020; <https://www.who.int/news-room/commentaries/detail/advice-on-the-use-of-point-of-care-immunodiagnostic-tests-for-covid-19>. Accessed 2020 Apr 22.
26. Crowe K. Why Canada is taking so long to start testing blood for COVID-19. *CBC News* 2020 Apr 2; <https://www.cbc.ca/news/health/rapid-blood-test-await-approval-in-canada-1.5518485>. Accessed 2020 Apr 20.

27. U.S. Food & Drug Administration. Emergency use authorizations: test kit manufacturers and commercial laboratories table. 2020; <https://www.fda.gov/medical-devices/emergency-situations-medical-devices/emergency-use-authorizations>. Accessed 2020 Apr 22.
28. Fact sheet for healthcare providers: COVID-19 ELISA IgG Antibody Test – Mount Sinai. New York (NY): Mount Sinai; 2020: <https://www.fda.gov/media/137030/download>. Accessed 2020 Apr 21.
29. Fact sheet for healthcare providers: VITROS immunodiagnostic products anti-SARS-CoV2 total reagent pack. Rochester (NY): Ortho-Clinical Diagnostics, Inc.; 2020: <https://www.fda.gov/media/136970/download>. Accessed 2020 Apr 21.
30. DPP COVID-19 IgM/IgG System. Medford (NY): Chembio Diagnostic Systems, Inc.; 2020: <https://www.fda.gov/media/136963/download>. Accessed 2020 Apr 21.
31. Cellex qSARS-CoV-2 IgG/IgM Rapid Test. Research Triangle Park (NC): Cellex; 2020: <https://www.fda.gov/media/136625/download>. Accessed 2020 Apr 21.
32. Pan Y, Li X, Yang G, et al. Serological immunochromatographic approach in diagnosis with SARS-CoV-2 infected COVID-19 patients. *J Infect*. 2020;10:[in press, corrected proof].
33. Li Z, Yi Y, Luo X, et al. Development and clinical application of a rapid IgM-IgG combined antibody test for SARS-CoV-2 infection diagnosis. *J Med Virol*. 2020;1-7.
34. Cassaniti I, Novazzi F, Giardina F, et al. Performance of VivaDiag COVID-19 IgM/IgG Rapid Test is inadequate for diagnosis of COVID-19 in acute patients referring to emergency room department. *J Med Virol*. 2020;30 Mar.
35. Padoan A, Cosma C, Sciacovelli L, Faggian D, Plebani M. Analytical performances of a chemiluminescence immunoassay for SARS-CoV-2 IgM/IgG and antibody kinetics. *Clin Chem Lab Med*. 2020;16 Apr.
36. Loeffelholz MJ, Tang YW. Laboratory diagnosis of emerging human coronavirus infections - the state of the art. *Emerg Microbes Infect*. 2020;9(1):747-756.
37. Zhao J, Yuan Q, Wang H, et al. Antibody responses to SARS-CoV-2 in patients of novel coronavirus disease 2019. *Clin Infect Dis*. 2020;ciaa344.
38. To KK, Tsang OT, Leung WS, et al. Temporal profiles of viral load in posterior oropharyngeal saliva samples and serum antibody responses during infection by SARS-CoV-2: an observational cohort study. *Lancet Infect Dis*. 2020;20(5):565-574.
39. Guo L, Ren L, Yang S, et al. Profiling early humoral response to diagnose novel coronavirus disease (COVID-19). *Clin Infect Dis*. 2020;21(ciaa310):[corrected proof].
40. Lippi G, Salvagno GL, Pegoraro M, et al. Assessment of immune response to SARS-CoV-2 with fully automated MAGLUMI 2019-nCoV IgG and IgM chemiluminescence immunoassays. *Clin Chem Lab Med*. 2020;16 Apr.
41. Gao HX, Li YN, Xu ZG, et al. Detection of serum immunoglobulin M and immunoglobulin G antibodies in 2019-novel coronavirus infected cases from different stages. *Chin Med J*. 2020:[epub ahead of print].
42. Foundation for Innovating Diagnostics. FIND evaluation update: SARS-COV-2 immunoassays. 2020; <https://www.finddx.org/covid-19/sarscov2-eval-immuno/>. Accessed 2020 Apr 22.
43. U.S. Food & Drug Administration. FDA statement: coronavirus (COVID-19) update: serological tests. 2020; <https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-serological-tests>. Accessed 2020 Apr 21.
44. IDSA COVID-19 antibody testing primer. Arlington (VA): Infectious Diseases Society of America; 2020: <https://www.idsociety.org/globalassets/idsa/public-health/covid-19/idsa-covid-19-antibody-testing-primer.pdf>. Accessed 2020 May 1.
45. Government of Ontario. How Ontario is responding to COVID-19. 2020; <https://www.ontario.ca/page/how-ontario-is-responding-covid-19>. Accessed 2020 May 1.
46. Zhong L, Chuan J, Gong BO, et al. Detection of serum IgM and IgG for COVID-19 diagnosis. *Sci China Life Sci*. 2020;25:777-780.
47. Cheng MP, Papenburg J, Desjardins M, et al. Diagnostic testing for severe acute respiratory syndrome-related coronavirus-2: a narrative review. *Ann Intern Med*. 2020;Apr 13.
48. World Health Organization. "Immunity passports" in the context of COVID-19: scientific brief. 2020; <https://www.who.int/news-room/commentaries/detail/immunity-passports-in-the-context-of-covid-19>. Accessed 2020 Apr 27.
49. World Health Organization. Advice on the use of point-of-care immunodiagnostic tests for COVID-19. 2020; <https://www.who.int/news-room/commentaries/detail/advice-on-the-use-of-point-of-care-immunodiagnostic-tests-for-covid-19>. Accessed 2020 Apr 24.
50. U.S. Food & Drug Administration. Important information on the use of serological (antibody) tests for COVID-19 - letter to health care providers. 2020; <https://www.fda.gov/medical-devices/letters-health-care-providers/important-information-use-serological-antibody-tests-covid-19-letter-health-care-providers>. Accessed 2020 Apr 24.
51. Okba NMA, Muller MA, Li W, et al. Severe acute respiratory syndrome coronavirus 2-specific antibody responses in coronavirus disease 2019 patients. *Emerg Infect Dis*. 2020;26(7).
52. Beeching NJ, Fletcher TE, Beadsworth MBJ. Covid-19: testing times. *BMJ*. 2020;369:m1403.

53. Immunity certificates: if we must have them, we must do it right. Harvard (MA): Edmond J. Safra Center for Ethics; 2020: <https://ethics.harvard.edu/files/center-for-ethics/files/safracenterforethicswhitepaper8.pdf>. Accessed 2020 Apr 22.
54. Duan K, Liu B, Li C, et al. Effectiveness of convalescent plasma therapy in severe COVID-19 patients. *Proc Natl Acad Sci U S A*. 2020;117(17):9490-9496.
55. Cohen J. Unprecedented nationwide blood studies seek to track U.S. coronavirus spread. *Science* 2020 Apr 7; <https://www.sciencemag.org/news/2020/04/unprecedented-nationwide-blood-studies-seek-track-us-coronavirus-spread>. Accessed 2020 Apr 21.
56. World Health Organization. Advice on the use of point-of-care immunodiagnostic tests for COVID-19: scientific brief. 2020; https://apps.who.int/iris/bitstream/handle/10665/331713/WHO-2019-nCoV-Sci_Brief-POC_immunodiagnosics-2020.1-eng.pdf. Accessed 2020 Apr 21.
57. Scholz F. Minnesota-based Laboratory Infectolab Americas Releases COVID-19 Serology on Monday the 13th of April. *BusinessWire* 2020 Apr 13; <https://www.businesswire.com/news/home/20200409005699/en/Minnesota-based-Laboratory-Infectolab-Americas-Releases-COVID-19-Serology>. Accessed 2020 Apr 21.
58. Weintraub K. What can antibody testing really tell us about COVID? *WebMD Health News* 2020 Apr 16; <https://www.webmd.com/lung/news/20200416/what-can-antibody-testing-really-tell-us-about-covid>. Accessed 2020 Apr 21.
59. Lurie N, Saville M, Hatchett R, Halton J. Developing Covid-19 vaccines at pandemic speed. *N Engl J Med*. 2020; Perspective.
60. Drake N. To start reopening shuttered nations, we need this blood test. *National Geographic* 2020 Apr 16; <https://www.nationalgeographic.com/science/2020/04/coronavirus-to-start-reopening-shuttered-nations-we-need-this-blood-test/>. Accessed 2020 Apr 22.
61. Patel NV. The coronavirus test that might exempt you from social distancing—if you pass. *MIT Technology Review* 2020 Apr 2; <https://www.technologyreview.com/2020/04/02/974964/the-coronavirus-test-that-might-exempt-you-from-social-distancing-if-you-pass/>. Accessed 2020 Apr 22.
62. Gordon A. Checking blood for coronavirus antibodies—3 questions answered about serological tests and immunity. *The Pursuit* 2020 Apr 16; <https://sph.umich.edu/pursuit/2020posts/checking-blood-for-coronavirus-antibodies.html>. Accessed 2020 Apr 23.
63. Vogel G. New blood tests for antibodies could show true scale of coronavirus pandemic. *Science* 2020 Mar 19; <https://www.sciencemag.org/news/2020/03/new-blood-tests-antibodies-could-show-true-scale-coronavirus-pandemic>. Accessed 2020 Apr 23.
64. National University Singapore. SSHSPH COVID-19 science reports. 2020; <https://sph.nus.edu.sg/covid-19/research/>. Accessed 2020 Apr 23.
65. Rodriguez A. Dr. Fauci says immunity certificates 'possible' after coronavirus pandemic. Here's what that means. *USA Today* 2020 Apr 16; <https://www.usatoday.com/story/news/health/2020/04/16/covid-19-fauci-says-immunity-certificates-possible-what-they/2987765001/>. Accessed 2020 Apr 23.
66. Siddique H. 'Immunity passports': can they end the UK coronavirus lockdown? *The Guardian* 2020 Apr 3; <https://www.theguardian.com/world/2020/apr/03/immunity-passports-can-they-end-uk-coronavirus-lockdown>. Accessed 2020 Apr 23.
67. Dewatripont M, Goldman M, Muraille E, Platteau J-P. Rapidly identifying workers who are immune to COVID-19 and virus-free is a priority for restarting the economy. *VOX CEPR Policy Portal* 2020; <https://voxeu.org/article/rapidly-identifying-workers-who-are-immune-covid-19-and-virus-free-priority-restarting-economy>. Accessed 2020 Apr 23.
68. Shierholz H, Reich R, Wurth RC, Pfeffer J. When is the right time to reopen the US economy? Our panelists' verdict. *The Guardian* 2020 Apr 16; <https://www.theguardian.com/commentisfree/2020/apr/16/when-is-the-right-time-to-reopen-the-us-economy-coronavirus-our-panelists-verdict>. Accessed 2020 Apr 23.