Update: Guidelines on the Preoperative Diagnostic Workup for COVID-19

A rapid review commissioned by RACS

10 May 2022

Royal Australasian College of Surgeons

Update: Guidelines on the Preoperative Diagnostic Workup for COVID-19 (April 2022)

Authors

Deanne Forel,[1*] Meegan Vandepeer,[1*] Jonathan Henry W. Jacobsen,[1] David R. Tivey,[1,2] Wendy J. Babidge,[1,2] Trevor G. Collinson,[3] Jen Kok,[4] Vanessa S. Beavis,[5] Andrew D.MacCormick,[6,7] Peter J. Hewett,[2] Thomas J. Hugh,[8,9] Henry H. Woo,[10] Robert T. Padbury,[11,12] David A. Scott,[13,14] Mark Frydenberg,[15,16] Guy J. Maddern[1,2,17]

* Authors contributed equally

Affiliation

1. Australian Safety and Efficacy Register of New Interventional Procedures – Surgical, Royal Australasian College of Surgeons, Adelaide, South Australia, Australia.
2. Discipline of Surgery, The Queen Elizabeth Hospital, University of Adelaide, Adelaide, South Australia, Australia.
3. General Surgeons Australia, Adelaide, South Australia, Australia
4. Centre for Infectious Diseases and Microbiology Laboratory Services, New South Wales Health Pathology-Institute of Clinical Pathology and Medical Research, Westmead Hospital, Sydney, New South Wales, Australia
5. Anaesthesia and Operating Rooms, Auckland City Hospital, Auckland, New Zealand
6. Department of Surgery, South Auckland Clinical School, University of Auckland, Auckland, New Zealand
7. Department of Surgery, Counties Manukau District Health Board, Auckland, New Zealand
8. Northern Clinical School, University of Sydney, Sydney, New South Wales, Australia
9. Surgical Education, Research and Training Institute, Royal North Shore Hospital, Sydney, New South Wales, Australia
10. Sydney Adventist Hospital, University of Sydney, Sydney, New South Wales, Australia
11. Flinders University, Adelaide, South Australia, Australia
12. Division of Surgery and Perioperative Medicine, Flinders Medical Centre, Adelaide, South Australia, Australia
13. Department of Anaesthesia and Acute Pain Medicine, St Vincent's Hospital, Melbourne, Victoria, Australia

14. Anaesthesia Perioperative and Pain Medicine Unit, Melbourne Medical School, University of Melbourne, Melbourne, Victoria, Australia
15. Department of Urology, Cabrini Institute, Cabrini Health, Melbourne, Victoria, Australia
16. Department of Surgery, Central Clinical School, Monash University, Melbourne, Victoria, Australia
17. Basil Hetzel Institute for Translational Health Research, Adelaide, South Australia, Australia

Acknowledgments

Jo Vabolis, copyeditor

DISCLAIMER AND EXCLUSION OF LIABILITY

This Report (and the rapid review and the data analysis contained in it) have been prepared in accordance with a specific request and terms of reference. It is necessarily general in nature and does not constitute advice relating to any specific or general circumstances, condition, or situation.

Information provided in this Report is a summary of the available evidence identified through the application of a rapid review methodology at the time of writing. Further, the information furnished is reasonably believed to be accurate and reliable. However, it is not a comprehensive review of all available evidence.

In providing this report, neither RACS nor any officer or staff of RACS shall be liable for any omission, errors of judgement, action or non-action made by the Recipient of this Report or its agents, based on the information contained. RACS does not represent, warrant, undertake or guarantee that the use of the guidance in the Report will lead to any particular outcome or result. It is the responsibility of the recipient to have express regard to the particular circumstances of each case and the application of the Report and analysis in each case.

The Report is only applicable at the time of writing, or if updated by RACS, at the time of publication of its update. Material developed by third parties used in this Report may be reviewed and updated from time to time. RACS does not take responsibility for reviewing the Report after it has been published or submitted to a recipient unless it has explicitly agreed to do so. It is the responsibility of the recipient to ensure that they have obtained the current version or are aware of more recent or more appropriate information or material.

The Report has been prepared to have regard to the information available at the time of its preparation, and the recipient should therefore have regards to any information, research or other material which may have been published or become available subsequently. RACS takes no responsibility for matters arising from changed circumstances or information or material which may have become available subsequently.

EXCLUSION OF LIABILITY

To the maximum extent permitted by law, RACS and its officers, employees, agents, consultants, licensors, partners, and affiliates exclude all liability to you or any other person for any loss, cost, expense, claim or damage (whether arising in contract, negligence, tort, equity, statute or otherwise, and for any loss, whether it be consequential, indirect, incidental, special, punitive, exemplary or otherwise, including any loss of profits, loss or corruption of data or loss of goodwill) arising directly or indirectly out of, or in connection with, this Report or the use of this Report by you or any other person.

Recommendations

1. Patient history should be thoroughly examined for symptoms compatible with, and exposure to (especially close contact with infected persons) severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection, and equal weight should be given to these findings as to clinical presentation.
2. Hyposmia (decrease in sense of smell), hypogeusia (decrease in sense of taste), fever, cough, dyspnoea, malaise, fatigue, and sputum/respiratory secretions and/or expectoration should be considered important in considering the potential for SARS-CoV-2 infection.
3. Assessment of patient symptoms is insufficient as a sole method of diagnosing coronavirus disease (COVID-19), although it can inform necessary adjunctive investigations.
4. Patients suspected of having COVID-19 based on either symptoms and/or high-risk exposure history should undergo testing with nucleic acid amplification tests (NAATs; most commonly reverse transcription polymerase chain reaction [RT-PCR][a]), the gold standard test for diagnosing SARS-CoV-2 infection. Depending on testing demand, the results of NAATs are generally available within 24-48 hours in Australia and Aotearoa New Zealand.
5. There is considerable postoperative morbidity and mortality associated with operating on patients with an active SARS-CoV-2 infection. Thus, any surgical operation that can be delayed without adverse effects to patients should await the testing results prior to undertaking surgery in patients suspected of SARS-CoV-2 infection.
6. Rapid antigen point-of-care tests (RATs) and rapid NAATs are both available in Australia and Aotearoa New Zealand to diagnose SARS-CoV-2 infection.
    a. RATs may be performed outside the laboratory (including self-testing at home), and have been shown to be less sensitive than NAATs. As such, RATs are not recommended to be used alone for confirmation of SARS-CoV-2 infection, but may be used to complement and preserve NAAT, particularly when laboratory testing capacity is overwhelmed. There is emerging evidence that RATs have reduced analytical sensitivity in detecting the Omicron compared to the Delta variant. Surgeons should consult their local health

[a] RT-PCR also includes transcription mediated amplification (TMA) technology. TMA is used in some commercial NAAT assays. The analytical performance of TMA is equivalent to RT-PCR.

authorities with regard to RATs as jurisdictions may have different guidelines on their use.

   b. Rapid NAATs should be considered where an urgent result is required (within 1-2 hours) to inform whether a patient needs to be treated or transferred, and where access to laboratory testing is not available (i.e. in rural and remote communities). Where there are substantial delays in laboratory-based or rapid NAAT results, RATs may be useful if positive. The positive predictive value of RATs improves as the prevalence of infection increases.

7. Antibody testing is not recommended for the acute diagnosis of COVID-19, but may help clarify inconclusive NAAT results. The detection of SARS-CoV-2 IgG against the spike (S) but not nucleocapsid proteins may be affected by prior SARS-CoV-2 vaccination.
8. Chest imaging (computed tomography, ultrasound, or X-ray) alone is not recommended for the diagnosis of COVID-19.
9. Non-SARS-CoV-2-specific laboratory tests (such as haematology and biochemistry tests) have no utility in the diagnostic workup of potential SARS-CoV-2 infection; however, they may be used for prognosis and monitoring.
10. For patients who cannot (due to urgent/emergency surgery) or refuse to undergo SARS-CoV-2 diagnostic tests, operative staff should assume patients are COVID-positive and act in accordance with state health authorities and hospital guidelines.
11. Preoperative testing for SARS-CoV-2 in patients with no symptoms or risk factors varies between health jurisdictions in Australia and Aotearoa New Zealand, and will likely change based on the community prevalence of COVID-19. Operative staff need to check with their health departments for current recommendations.

Table 1 Proposed preoperative diagnostic workup for COVID-19 (updated March 2022)

Features of patient history	Advised preoperative investigation
Patient is asymptomatic and is not a close contact	**Refer to local health authority or health departments** [#]
Patient has been previously diagnosed with COVID-19	**Refer to Delaying Surgery for Patients Recovering from COVID-19**
Any risk of potential SARS-CoV-2 exposure, including: • Close contact[##] with a confirmed case of COVID-19 in the past 2 weeks • Close contact with someone who displays symptoms of hyposmia (loss of smell), hypogeusia (loss of taste), fever, cough, dyspnoea, malaise, fatigue, and sputum/respiratory secretions and/or expectoration in the past 2 weeks (including in the 3 days prior to onset of symptoms) • Travel from area of high COVID-19 prevalence in the past 2 weeks or close contact with such a traveller* • Presence within an aged care facility in the past 2 weeks, either as a resident, worker, or visitor • Presence within a detention facility in the past 2 weeks, either as a resident, worker, or visitor • Presence within a group residential setting in the past 2 weeks, either as a resident, worker, or visitor • Presence within other facilities that have relatively high risk of COVID-19 transmission • Profession that includes regular interaction with potential COVID-19 cases (e.g. workers in healthcare, allied health facilities, border staff, supermarkets, schools, delivery, factories, farming, or transport) **Where surgery can be delayed for 24 hours without adverse effects**	**NAAT assay** **(await result)**
Any of the following symptoms in the past two weeks: • Hyposmia • Hypogeusia • Cough • Fever • Dyspnoea • Malaise or fatigue • Sputum production/expectoration **Where surgery can be delayed for 24 hours without adverse effects**	**NAAT assay** **(await result)**
Surgery required within 24 hours AND presence of ANY of the above history features	**Commence preoperative investigation for SARS-CoV-2 infection using conventional NAAT assay or rapid NAAT** and carry on with perioperative course† until a result is returned.** **Whilst a negative RAT result does not exclude SARS-CoV-2 infection, a positive result may be helpful when the prevalence of infection is high or when there are substantial delays in NAAT results**

Abbreviations

COVID-19 = Coronavirus disease 2019; **NAAT** = nucleic acid amplification test; **SARS-CoV-2** = severe acute respiratory syndrome coronavirus 2; **RAT** = rapid antigen point-of-care tests.

Notes

[#] Screening requirements may differ between states and territories and reflect the local rates of community transmission, refer to local health authority for screening advice. [##]The definition of a 'close contact' is outlined in Appendix A. *States have different screening policies for interstate travellers. For information relevant to each state consult the following site: https://www.health.gov.au/health-

alerts/covid-19/domestic-travel. **May include rapid NAAT. Test type is dependent on what is currently listed on the Australian Register of Therapeutic Goods. Rapid NAAT assays that provide results within 1 to 2 hours (after the specimen is received in the testing laboratory) that are currently in use includes the Xpert® Xpress SARS-CoV-2 (Cepheid, United States)[b] and Cobas® Liat® (Roche Diagnostics, Germany).

†Proceed to surgery with surgical staff wearing full personal protective equipment and taking appropriate intraoperative precautions, especially for potential aerosol-generating procedures if test result cannot be obtained prior to surgery or if a positive result is returned.[c,d,e]

[b] New South Wales Health. *Rapid PCR testing for SARS-CoV-2 on GeneXperts: Clinician fact sheet*. Published 28 July 2021, cited 1 December 2021. Available from: Rapid PCR testing for SARS-CoV-2 on GeneXperts: Clinician factsheet - Communities of practice (nsw.gov.au)

[c] Royal Australasian College of Surgeons. *Surgery Triage: Responding to the COVID-19 Pandemic*. 2nd edition., cited 9 June 2020. Available from: https://www.surgeons.org/-/media/Project/RACS/surgeons-org/files/news/covid19-information-hub/2020-04-22_racs-triage-of-surgery-web.pdf?rev=c28712668d7f45f19ca9df53b77011ea&hash=82A77A9AD9B8A5E23807E449386B80E1%20(accessed%2026%20September%202020

[d] Royal Australasian College of Surgeons. *Guidelines for Personal Protective Equipment*. 1st edition., cited 9 June 2020. Available from: https://www.surgeons.org/-/media/Project/RACS/surgeons-org/files/COVID-PDFs/2020-08-11-PPE-Guidelines-updated-V3_.pdf?rev=3fc9a83b24d64ee29c229de2be8d437b&hash=0591E61633B00EDE5B966D6B1AA9B3DF

[e] Royal Australasian College of Surgeons. *Guidelines for Safe Surgery: Open versus Laparoscopic*. 1st edition., cited 9 June 2020. Available from: https://www.surgeons.org/-/media/Project/RACS/surgeons-org/files/COVID-PDFs/Recommendations-on-safe-surgery-laparoscopic-vs-open-V3.pdf?rev=8898aea1d1e34829a40dc8b0fa81ecda&hash=B308660E3B9802543DA711317B62D51F

Balancing the diagnostic workup of COVID-19 with surgical urgency

Given the considerable postoperative morbidity and mortality associated with operating on COVID-19 patients,[f,g] as well as the need to minimise the risk of spreading COVID-19 to healthcare workers and other patients, it is imperative that all surgical patients suspected of SARS-CoV-2 infection undergo appropriate testing prior to their operation; however, this need for diagnostic evaluation must be balanced with the urgency of surgery to ensure optimal outcomes for the patient, and surgery should not be delayed unnecessarily.

Fortunately, within Australia and Aotearoa New Zealand, depending on testing demand, it is possible for patients to have same-day return of results for the conventional RT-PCR assays, meaning that surgery should be delayed by no more than 24-48 hours while awaiting a laboratory result for potential SARS-CoV-2 infection (not accounting for scheduling details within individual institutions). Other rapid tests (see below) can return accurate results within 1 hour.

With the emergence of rapid NAAT, turnaround times for accurate SARS-CoV-2 results that are comparable to conventional assays may be further reduced to 1–2 hours (after the sample is received in the testing laboratory). Many laboratories serving hospitals where surgery is performed (including in rural and regional areas) have introduced these tests.

This means that protocols for surgical triage during both the initial and any successive phases of the COVID-19 pandemic[h,i,j] can be implemented with modification to incorporate an appropriate diagnostic workup.

---

[f] Nepogodiev D, Glasbey JC, Li E, et al. Mortality and pulmonary complications in patients undergoing surgery with perioperative SARS-CoV-2 infection: an international cohort study. *The Lancet*. 2020.

[g] Lei S, Jiang F, Su W, et al. Clinical characteristics and outcomes of patients undergoing surgeries during the incubation period of COVID-19 infection. *EClinicalMedicine*. 2020; 10.1016/j.eclinm.2020.100331:100331.

[h] Royal Australasian College of Surgeons. *Surgery Triage: Responding to the COVID-19 Pandemic*. 2nd edition., cited 9 June 2020. Available from: https://www.surgeons.org/-/media/Project/RACS/surgeons-org/files/news/covid19-information-hub/2020-04-22_racs-triage-of-surgery-web.pdf?rev=c28712668d7f45f19ca9df53b77011ea&hash=82A77A9AD9B8A5E23807E449386B80E1%20(accessed%2026%20September%202020, *op. cit.*

[i] Brindle ME, Doherty G, Lillemoe K, Gawande A. Approaching Surgical Triage During the COVID-19 Pandemic. *Ann Surg*. 2020; 10.1097/SLA.0000000000003992.

[j] Argenziano M, Fischkoff K, Smith CR. Surgery Scheduling in a Crisis. *N Engl J Med*. 2020; 382:e87.

As outlined in previous RACS rapid reviews on this topic, emergency surgery should not be delayed whilst awaiting confirmation of COVID-19 in suspected patients.[k] Commencement of preoperative investigation for SARS-CoV-2 infection should occur, and surgery should proceed as needed, with surgical staff wearing full personal protective equipment (PPE)[l] and undertaking appropriate intraoperative precautions.[m] In order to optimise the efficient use of medical resources, surgery that can be delayed for up to 24-48 hours (the likely maximum duration to complete COVID-19 testing) without adversely affecting patient morbidity or mortality, should await test results prior to surgery where SARS-CoV-2 infection is suspected. This process of deliberation is summarised in **Box 1**.

Box 1. Balancing the diagnostic workup with surgical urgency when COVID-19 is suspected

Possible to delay surgery for 24-48 hours	**Impossible to delay surgery for 24-48 hours**
• Delay surgery for 24-48 hours to facilitate appropriate preoperative testing for SARS-CoV-2 infection • Refer to Proposed Preoperative Diagnostic Workup for COVID-19 (***Table 1***) for appropriate diagnostic pathway depending on clinical presentation and exposure history	• Commence appropriate testing for SARS-CoV-2 infection preoperatively • Proceed to surgery with surgical staff wearing full PPE and appropriate intraoperative precautions taken, especially for potential aerosol-generating procedures[n,o,p] • Isolate patient postoperatively and await test result

[k] Royal Australasian College of Surgeons. *Surgery Triage: Responding to the COVID-19 Pandemic*. 2nd edition., cited 9 June 2020. Available from: https://www.surgeons.org/-/media/Project/RACS/surgeons-org/files/news/covid19-information-hub/2020-04-22_racs-triage-of-surgery-web.pdf?rev=c28712668d7f45f19ca9df53b77011ea&hash=82A77A9AD9B8A5E23807E449386B80E1%20(accessed%2026%20September%202020, *op. cit.*

[l] Royal Australasian College of Surgeons. *Guidelines for Personal Protective Equipment*. 1st edition., cited 9 June 2020. Available from: https://umbraco.surgeons.org/media/5302/2020-05-05-covid19-ppe-guidelines.pdf, *op. cit.*

[m] Royal Australasian College of Surgeons. *Guidelines for Safe Surgery: Open versus Laparoscopic*. 1st edition., cited 9 June 2020. Available from: https://umbraco.surgeons.org/media/5214/2020-04-15-recommendations-on-safe-surgery-laparoscopic-vs-open.pdf, *op. cit.*

[n] Royal Australasian College of Surgeons. *Surgery Triage: Responding to the COVID-19 Pandemic*. 2nd edition., cited 9 June 2020. Available from: https://umbraco.surgeons.org/media/5254/2020-04-22_racs-triage-of-surgery-web.pdf, *op. cit.*

[o] Royal Australasian College of Surgeons. *Guidelines for Personal Protective Equipment*. 1st edition., cited 9 June 2020. Available from: https://umbraco.surgeons.org/media/5302/2020-05-05-covid19-ppe-guidelines.pdf, *op. cit.*

[p] Royal Australasian College of Surgeons. *Guidelines for Safe Surgery: Open versus Laparoscopic*. 1st edition., cited 9 June 2020. Available from: https://umbraco.surgeons.org/media/5214/2020-04-15-recommendations-on-safe-surgery-laparoscopic-vs-open.pdf, *op. cit.*

Executive summary

Introduction

In July 2020, in response to the Coronavirus disease 2019 (COVID-19) pandemic, a rapid review was conducted to evaluate the literature surrounding the clinical, laboratory and radiological methods used to diagnose severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). This review was used to inform evidence-based guidance for surgeons in Australia and Aotearoa New Zealand on the preoperative diagnostic workup necessary for patients with suspected COVID-19 (published as *Guidelines on the Preoperative Diagnostic Workup for COVID-19*). The current rapid review was conducted to update these recommendations, where necessary, and reflect contemporary information.

Methodology

The rapid review methodology utilised in the original guideline document was repeated by researchers from the RACS Evidence Support for Advocacy Team (ASERNIP–S and Research, Audit & Academic Surgery). The PubMed database was searched from May 2020 (the end search date from the original report) to September 2021 for literature evaluating the diagnostic accuracy of various COVID-19 tests, as well as common COVID-19 symptoms. Searches were limited to systematic reviews, meta-analyses, and guidelines. The systematic searches were supplemented with targeted searches of PubMed and Google. Recent Australian guidelines from Communicable Diseases Network Australia (CDNA) and the Public Health Laboratory Network (PHLN) were also reviewed to harmonise recommendations from expert groups.

Results

Common symptoms associated with COVID-19 include: hyposmia, hypogeusia, fever, cough, dyspnoea, malaise, fatigue, and sputum production/expectoration (coughing up phlegm). In general, symptoms are more common in adults than children; however, symptoms alone are insufficient for diagnosing COVID-19 but rather should be a prompt for further diagnostic investigation.

Nucleic acid amplification tests (NAATs), with reverse transcription polymerase chain reaction (RT-PCR) the most common type performed, remains the gold standard test for detection of SARS-CoV-2 infection. Antibody tests and chest imaging are still not recommended.

Since the original guidance, research has been published on new tests for the detection of SARS-CoV-2, in particular rapid NAATs and rapid antigen tests (RATs) that can be used at

the point-of-care (POC). Several rapid NAATs and many RATs are listed on the Australian Register of Therapeutic Goods (ARTG). With respect to RATs, different Australian regulatory agencies have stated that these should not be used as the definitive test for the diagnosis of SARS-CoV-2 infection owing to their lower sensitivity compared with laboratory-based RT-PCR. False positive RAT results may also occur when the pre-test probability or prevalence of infection is low. Rapid RT-PCR however, have comparable sensitivity and specificity with laboratory-based RT-PCR. The Xpert® Xpress SARS-CoV-2 test (Cepheid, United States) and Cobas® Liat® (Roche Diagnostics, Germany) are examples of rapid RT-PCR tests that are currently being used in many jurisdictions in Australia. Rapid RT-PCR are useful when rapid turnaround times are required. Rapid RT-PCR may provide a result within 1-2 hours (after the sample is received in the testing laboratory) for high-risk patients to inform clinical management and where access to laboratory-based testing is not available, such as in rural and remote communities.

Conclusions

Patient symptoms and exposure history are equally important in determining which patients should undergo preoperative COVID-19 testing. If patients with suspected COVID-19 based on symptoms and/or exposure history and surgery can be delayed for 24-48 hours without adverse effects, patients should undergo a laboratory-based NAAT.

For patients who cannot wait for a COVID-19 test result (due to urgent/emergency surgery), preoperative testing should be initiated (using conventional RT-PCR or rapid NAATs where appropriate), and operative staff should proceed with surgery assuming the patient is COVID-positive and act in accordance with hospital guidelines (e.g. personal protective equipment and isolation of the patient).

At the time of writing, the need for preoperative testing of patients without symptoms varies between health jurisdictions. Operative staff need to check with their health departments for current recommendations, as these may change based on the community prevalence of COVID-19.

Introduction

The Coronavirus disease 2019 (COVID-19) global pandemic has caused considerable disruption to surgical care across Australia and Aotearoa New Zealand. Although worldwide research efforts have produced a sizeable literature base in a relatively short time, the causative virus—severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)—and its effects on healthcare systems at both an individual and systemic level, are still not completely understood.

In 2020, the international COVIDSurg Collaborative published an article that demonstrated the importance of appropriate and effective preoperative diagnostic protocols for patients with suspected SARS-CoV-2 infection.[1] They found that surgical patients with perioperative SARS-CoV-2 infection experienced a postoperative pulmonary complication rate of 51.2%, which was associated with high mortality.[1] Subsequent studies have reported perioperative mortality rates of 14.8% to 16.7% in patients with SARS-CoV-2 infection, significantly greater than SARS-CoV-2 negative subjects.[2 3] As such, an effective and reliable diagnostic workup, in an Australian and Aotearoa New Zealand context, was recognised as necessary to appropriately triage surgical patients with COVID-19 and reduce postoperative morbidity and mortality.

In July 2020, the Royal Australasian College of Surgeons published guidelines to assist surgeons on the appropriate preoperative diagnostic workup of surgical patients with suspected COVID-19.[4] To inform this guidance, a rapid review of the literature surrounding the clinical, laboratory and radiological methods used to diagnose active SARS-CoV-2 infection in **low COVID-19 prevalence settings** was carried out. The intention of the current guidance document is to update the previous rapid review, incorporate new testing technologies and evidence into the report, and amend the recommendations as the prevalence of COVID-19 in Australia and Aotearoa New Zealand has increased considerably since the previous guidelines were published. The current rapid review provides the first update of the guidelines with the evidence available up until April 2022.

Methodology

A rapid review methodology[5] was utilised to search for available literature. PubMed was systematically searched for articles published between 6 May 2020 and 27 September 2021 to update the evidence included in the original guidance document. Owing to the large quantity of available literature, a systematic review filter was applied to the original search terms to capture higher-level evidence (see ***Appendix B*** for search strategy). The search was supplemented with targeted searches of peer-reviewed and grey literature using PubMed and Google (up to April 2022). Targeted searches were also used to identify guidelines and regulatory advice on the diagnostic tests.

Study selection was performed by two ASERNIP–S researchers (MV and DF) using Rayyan.[6] Systematic reviews that meta-analysed the largest number of studies/patients were prioritised for inclusion first. Comparative studies, case series and case reports, as well as systematic reviews without meta-analyses, were excluded. There were no language restrictions.

Study extraction used a standard template, with each extraction performed by a single reviewer (MV, DF) and a random sample checked by a second reviewer.

Results

Search results

The systematic search identified 3,821 studies. After title and abstract screening, 157 studies were reviewed at full text. Thirty-two studies were included from the systematic and non-systematic searches.

COVID-19 caseload in Australia and New Zealand

As of 30 March 2022, 4,196,055 cases of COVID-19 have been reported in Australia, including 5,928 deaths.[7] Of these cases, 473,140 were considered active cases at the time of writing.[7] In Aotearoa New Zealand, as of 29 March, there have been 538,532 cases of COVID-19, including 278 deaths.[8] Of these cases, 105,065 were considered active cases at the time of writing.[8] These numbers have increased considerably since the last report was published.

At the time of writing, Australia had partially opened its borders with several states allowing fully vaccinated international travellers to arrive with limited or no quarantining. Likewise, Aotearoa New Zealand has opened its boarders to citizens and international travellers. It is likely once unrestricted international travel resumes, COVID-19 case numbers will increase.

Clinical presentation of COVID-19

Summary

- Patients at high risk of acquiring COVID-19 based on exposure history should be treated with extra caution. These include travellers who have recently been on planes or cruise ships, residents in aged care settings, people in detention facilities, people in group residential settings, and those who have been in close contact with someone who has COVID-19.
- The most common COVID-19 symptoms are fever (51% in children; 79% in adults; 83% in adults aged >60 years) and cough (41% in children; 54% in adults; 60% in adults aged >60 years). This remains unchanged from the original guidance.
- Additional common symptoms identified in the update include fatigue and sputum production and/or expectoration (coughing up phlegm). These symptoms more frequently occurred in adults compared to children.
- Data on symptoms caused by the new Omicron variant and whether they differ from other variants is not yet available.
- The diagnostic accuracy of COVID-19 symptoms is low; consequently, they should not be used as the sole criteria when determining diagnosis.
- Approximately 42% of COVID-19 cases showed no symptoms at the time of testing (asymptomatic or pre-symptomatic). Thus, patient history should be thoroughly examined for potential exposure to SARS-CoV-2 with equal weight given to exposure history and clinical presentation.
- Healthcare professionals need to check with their health departments regarding whether patients who are not exhibiting symptoms should be tested.

The importance of exposure history for COVID-19

A considerable proportion of COVID-19 cases exhibit no symptoms.[9] For example, of 104,058 laboratory confirmed COVID-19 cases, 42.8% of individuals exhibited no symptoms at the time of testing.[10] This figure consists of truly asymptomatic patients as well as those with pre-symptomatic infections. Children (0 to 18 years old) with SARS-CoV-2 infection were significantly more likely to appear asymptomatic compared to adults ≥60 years old (46.6% vs.19.7%, respectively).[10] Both asymptomatic and pre-symptomatic individuals are able to transmit the SARS-CoV-2 virus.[11] It is thus imperative to thoroughly examine all patients' histories for potential sources of SARS-CoV-2 exposure and to give equal weight to these findings as well as their clinical presentation. At the time of writing this report there was no information on whether the new SARS-CoV-2 variant, Omicron, results in higher levels of asymptomaticity than other variants.

Despite the relatively high proportion of asymptomatic or pre-symptomatic COVID-19 patients, **when the prevalence of COVID-19 in the community is low**, the accuracy of COVID-19 diagnostic tests in patients with no symptoms is reduced and may lead to more false positives than true positives. Further, a multicentre Australian study on 3,010 elective surgery patients with no symptoms of, or exposure to SARS-CoV-2, found that no patient returned a positive reverse transcription polymerase chain reaction (RT-PCR) test. This indicates that routine preoperative screening for SARS-CoV-2 in elective surgery patients with low pre-test probability is not recommended;[12 13] however, several health authorities recommend all elective surgery patients get tested prior to their operation.[14 15] As such, operative staff should check with their health departments regarding current recommendations on testing of patients who are not exhibiting symptoms.

Patients without symptoms from population groups considered at high risk of contracting COVID-19 should be treated with extra caution regarding the use of PPE and triage considerations,[16 17] and they should undergo RT-PCR testing for potential SARS-CoV-2 infection. In Australia and Aotearoa New Zealand, these groups include travellers who have recently been on planes or cruise ships, residents in aged care facilities, people in detention facilities, people in group residential settings, and those who identified as close contacts of someone with COVID-19 (including the 2 to 3 days prior to symptom onset in the SARS-CoV-2 infected person).[18 19] Further, people in 'essential' professions that place them in regular contact with people who may have COVID-19 (e.g. healthcare, allied health facilities, supermarkets, schools, borders, deliveries, factories, farming and transport workers)[20] should also be treated with caution and undergo RT-PCR testing.

Symptoms associated with COVID-19

The original guidance document identified the following symptoms most frequently associated with COVID-19: fever, cough, sore throat, dyspnoea (including shortness of breath or tachypnoea), diarrhoea, nausea or vomiting, and myalgia (muscle pain) or arthralgia (joint pain).[4]

The update search identified additional symptoms and delineated symptoms by age (≤18 years of age). A summary of the most common symptoms (occurring in ≥20% of patients) identified in the new evidence is reported in ***Table 2*** (for a complete list of symptoms, refer to ***Appendix C***); however, note that there is substantial heterogeneity in the prevalence of different symptoms for all 3 age categories.

Table 2 COVID-19 symptom prevalence

Symptom	Prevalence (%)		
	Children (≤18 years)	Adults	Older adults (>60 years)
Fever[21-23]	51.0	78.8	83.0
Cough[21-23]	41.0	53.9	60.0
Dry cough[23]	NR	NR	56.0
Malaise[21]	NR	37.9	NR
Fatigue[21-23]	12.0	32.2	33.0
Anorexia[21 23]	NR	14.0	31.0
Chest pain/discomfort[22-24]	3.0	9.0	26.0
Sputum production[23 25 26]	6.0	25.0	28.0
Hyposmia[25 27]	3.5	25.0	NR
Expectoration[21 27]	15.0	24.2	NR
Dyspnoea[23 25 28]	7.0	23.0	42.0
Myalgia[21-23]	12.0*	21.3	15.0

Abbreviations
NR = not reported.
Notes
Symptoms not identified in the original guidance document are highlighted in grey. *Reported with fatigue.

Of the symptoms identified in the original guidance document for the general population, the new evidence supports their presentation across all ages, albeit with different prevalence. Fever and cough remain the 2 most common symptoms experienced in all age cohorts.

Symptoms not reported in the original guidance that now appear in the updated literature include dry cough, malaise, fatigue, sputum production and/or expectoration, chest pain and anorexia. Fatigue and sputum production (and/or expectoration) occurs more commonly in adults and individuals over 60 years of age, compared with children. Chest pain and anorexia are more common in those over 60 years of age. Less common symptoms, not included in ***Table 2***, include nausea, vomiting, abdominal pain, diarrhoea, and cutaneous manifestations of COVID-19.

COVID-19 symptoms that persist long-term (>3 weeks) are being increasingly reported in the literature. For further information regarding Long COVID please refer to the *RACS Delay to Surgery for Patients Recovering from COVID-19 Report*.

At the time of writing, data on the prevalence of symptoms for the Omicron variant and whether symptoms differ between Omicron and other SARS-CoV-2 variants were not available.

Diagnostic accuracy of COVID-19 symptoms

A systematic review by the Cochrane Collaboration (Struyf et al 2020[29]) aimed to assess the diagnostic accuracy of various signs and symptoms to determine if an individual presenting for care (primary care or hospital outpatient settings) has COVID-19. Individual symptoms associated with COVID-19 had poor diagnostic accuracy (low sensitivity or specificity) and thus should not be used as a diagnostic tool (***Table 3***). The analysis was subject to selection bias and heterogeneity.

Table 3 Diagnostic accuracy of signs and symptoms for COVID-19

Symptom	Number of studies	Number of patients	Pooled summary estimate	
			Sensitivity	Specificity
Cough	25	15,459	67%	35%
Fever	7	5,548	54%	67%
Anosmia	11	9,552	28%	93%
Ageusia	6	7,393	25%	91%
Anosmia or ageusia	6	8,143	41%	91%
Sore throat	20	15,876	21%	70%
Myalgia	13	8,105	27%	83%
Fatigue	12	5,553	36%	75%
Headache	6	6,171	22%	80%
Dyspnoea	24	14,913	25%	77%
Diarrhoea	20	13,016	12%	91%

Abbreviations
COVID-19 = coronavirus disease.
Source
Struyf et al 2020[29]

Laboratory findings associated with COVID-19

Summary

- Laboratory tests that measure haematological, renal, and hepatic function have limited utility in diagnosing COVID-19 but are used for patient monitoring.

As stated in the original report, laboratory tests (such as haematology or biochemistry [e.g. renal and hepatic function tests]) have limited utility in the diagnosis of COVID-19. NSW Health Pathology recommends a set of tests for patients presenting with COVID-19 with the results guiding subsequent clinical management. The test panels reflect different disease stages and include COVID-initial panel prognosis and COVID-ICU (intensive care unit) and non-ICU inpatient monitoring;[30] however, NSW Health Pathology notes that early accurate prognosis is not possible given deterioration can occur in weeks 2 and 3 of COVID-19. Currently, the markers with the best positive predictive value remain clinical observations (e.g. oxygen saturation and respiratory rate).[30]

Laboratory-based testing

Summary

- Reverse transcription polymerase chain reaction (RT-PCR) remains the gold standard test for the diagnosis of COVID-19.
- Nasopharyngeal, oropharyngeal and bilateral deep nasal swabs are the preferred upper respiratory tract specimens for RT-PCR testing, having the highest sensitivity and specificity.
- Antibody tests should not be used for the diagnosis of acute COVID-19 infection.

Reverse transcription polymerase chain reaction

RT-PCR is a form of NAAT that detects the presence of SARS-CoV-2 RNA in a specimen. The Therapeutic Goods Administration (TGA) and Public Health Laboratory Network (PHLN) (***Table 4***) consider RT-PCR to be the gold standard test for the diagnosis of COVID-19 in Australia.

Table 4 Position statements on RT-PCR

Organisation	Updated	Comments
Therapeutic Goods Administration[31]	12 January 2022	'While rapid antigen tests can provide a result within 15 to 30 minutes, they are generally considered to be less sensitive than a PCR test which is still currently the gold-standard in SARS-CoV-2 diagnosis.'
Public Health Laboratory Network – Communicable Diseases Network Australia[32] Joint Statement on SARS-CoV-2 Rapid Antigen Tests	Version 2.2 25 January 2022	'Nucleic acid amplification testing (NAAT) (for example, using reverse transcription polymerase chain reaction (RT-PCR) or transcription-mediated amplification (TMA)) is the gold standard for diagnosing acute symptomatic SARS-CoV-2 infection.'

Abbreviations
PCR = polymerase chain reaction; **RT-PCR** = reverse transcription polymerase chain reaction; **SARS-CoV-2** = severe acute respiratory syndrome coronavirus 2.

The sensitivity and specificity of RT-PCR are summarised in ***Table 5***. The results demonstrate that the site of sample collection influences test outcome. Pharyngeal swabs result in the highest sensitivity and specificity, whereas faecal, blood and urine samples have very poor sensitivity. The results for saliva were heterogenous, and while the specificity was high, the sensitivity was lower compared to pharyngeal swabs. Due to its lower performance, the PHLN advises against routine use of saliva for COVID-19 testing in adults or children, except in specific situations.[33] Repeat testing (especially of lower respiratory tract specimens) of persons with suspected COVID-19 is recommended by the PHLN following an initial negative result.[34]

Table 5 Sensitivity and specificity of RT-PCR using different samples for diagnosing COVID-19

Test sample	Study	Number of studies	Sensitivity (95% CI)	Specificity (95% CI)
Pharyngeal swabs[a]	Au et al 2021[35]	13	96.1% (91.5 to 98.3)	94.7% (88.1 to 97.8)
Saliva[b]	Tsang et al 2021[36]	13	85.0% (75.0 to 93.0)	99.0% (98.0 to 99.0)
	Ricco et al 2020[37]	15 (for sensitivity) 10 (for specificity)	83.5% (73.1 to 90.4)	97.7% (93.8 to 99.2)
Sputum	Mohammadi et al 2020[38]	11 Days after symptom onset 0–7 = 4 8–14 = 4 >14 = 4	71.0% (61 to 80) Days after symptom onset 0–7 = 98% (89 to 100) 8–14 = 69% (57 to 80) >14 = 46% (23 to 70)	NR
Stool/faeces/rectal	Boger et al 2021[39]	4	24.1% (16.7 to 33.0)	NR
Blood	Boger et al 2021[39]	3	7.3% (4.1 to 11.7)	NR
Urine[c]	Boger et al 2021[39]	4	0.00% (0.00 to 3.7)	NR
	Bwire et al 2020[40]	3	0.08% (-0.07 to 2.4)	NR

Abbreviations

CI = Confidence intervals; **COVID-19** = coronavirus disease; **NR** = not reported; **RT-PCR** = reverse transcription polymerase chain reaction.

Notes

a = The recommended site of sampling for RT-PCR diagnosis of COVID-19.

b = There was only 1 study in common in the meta-analyses from the 2 reviews.

c = Studies included in the meta-analyses of the 2 reviews differed.

Laboratory-based RT-PCR requires specialist platforms and must be conducted by qualified pathologists or medical laboratory scientists in a laboratory accredited by the National

Association of Testing Authorities (NATA).[41] The PHLN state that with respect to NAAT, most diagnostic laboratories use either commercial or in-house assays for testing with turnaround times being generally less than 24 hours after receipt of the specimen in the testing laboratory.[34]

The Communicable Diseases Network Australia (CDNA) *National Guidelines for Public Health Units* (Version 6.7, 22 March 2022)[42] states that Australian laboratories use highly accurate SARS-CoV-2 assays and where required have procedures in place to confirm test results. They note that when there is active COVID-19 in the community, the positive predictive value of NAAT is very high; however, indeterminate or suspected false positive SARS-CoV-2 test results may still occur.[43] Where an indeterminate or inconclusive NAAT result is obtained, the CDNA state that Public Health Units (PHUs) should contact the laboratory microbiologist to discuss the results and decide whether further testing is required.[42] Laboratory microbiologists should also be contacted in the situation where a false positive result is suspected, such as in jurisdictions with low or no community transmission, where pre-test probability of SARS-CoV-2 infection is low, before designating the result a false positive. The laboratory microbiologist will investigate whether there is evidence of a laboratory error or non-specific reactivity in the NAAT to ascertain whether further testing is required.[42] Given the reported poor outcomes of surgery in COVID-19 patients,[1] the correct test result is imperative to appropriately triage patients.

Antibody testing

Serology tests detect whether an individual has antibodies specific to SARS-CoV-2 produced in response to prior infection or vaccination.[44] Laboratory-based antibody tests detect SARS-CoV-2-specific immunoglobulin G (IgG), M (IgM) or total antibody in serum, plasma, whole blood or dried blood spot samples using either lateral flow, enzyme-linked immunosorbent assay (ELISA) or other chemiluminescent methods.[45] Immunofluorescent antibody and neutralization tests are also available in reference laboratories.

The original guidance document found the limited diagnostic utility of serological tests. These results did not confirm nor exclude the diagnosis of COVID-19 infections or provide information on the potential infectivity of an individual, because the detection of antibodies may be due to a past infection and/or vaccination. In addition, antibody tests may not be useful to diagnose a current infection because it can take 1 to 3 weeks after infection before antibodies are detectable.[44]

The TGA and Centers for Disease Control and Prevention (CDC) still advise against using antibody testing for COVID-19 diagnosis (TGA, January 2022; CDC, January 2022).[45] [46] The

PHLN state that, ‘While serological assays have no role in the detection of acute COVID-19 infection, they can be helpful for the retrospective diagnosis of infection.’[34] Examples provided by the PHLN of when serological assays may be useful include where the result will influence individual or outbreak management, such as testing patients who have had symptoms consistent with COVID-19 but:

- are RT-PCR negative,
- were not tested,
- have unexpected positive or inconclusive results on RT-PCR assays or,
- had an epidemiological risk factor for COVID-19 but remained asymptomatic.[34]

Point-of-care (POC) tests for COVID-19

Summary

- Rapid antigen point-of-care tests (RATs) are being widely used in the community as a diagnostic test for COVID-19; however, RT-PCR remains the gold standard for healthcare settings, given the potential for false negative RAT results.
- Rapid NAATs are being used in several health jurisdictions in Australia. They are particularly indicated for use in high-risk patients where an urgent result is required (within 1 to 2 hours) to inform clinical management or where access to laboratory-based testing is not available such as in rural and remote communities.
- Antibody POC tests should not be used for acute diagnosis of COVID-19.
- Guidance provided by the National Pathology Accreditation Advisory Council (NPAAC) should be followed when performing POC tests.

There is continued development in the area of POC technologies for diagnosing COVID-19, including CRISPR (clustered regularly interspaced short palindromic repeats).[47] They can be potentially performed at, or near the place where a specimen is collected and provide results within minutes rather than hours as required with laboratory-based RT-PCR tests. Antibody, NAAT and RATs POC have also been developed.[48]

The TGA notes that due to the urgent nature of the COVID-19 pandemic a number of these tests have undergone expedited assessment based on the clinical and performance data available at the time to enable their legal supply in Australia.[46] Currently, 71 POC test are listed on the Australian Register of Therapeutic Goods (ARTG) with RATs the most prevalent.[49] The TGA is conducting post-market reviews of all approved COVID-19 tests to provide updated evidence to support the ongoing safety and performance of the tests.[46]

The NPAAC has provided guidance on the use of POC tests (published 2021) to reduce the risk of patients receiving incorrect results due to poorly performed tests and to ensure tests are used for their intended purpose.[50]

Rapid antigen point-of-care tests

RATs work by identifying SARS-CoV-2 antigens (such as nucleoprotein) in nasopharyngeal or nasal swab specimens, thus implying current viral infection. Most of the currently approved RATs return results in 15 to 30 minutes.[31]

Many RATs have been approved for supply in Australia by the TGA.[49] The TGA has released a guidance document for implementation and a checklist for businesses using RATs for COVID-19 in the workplace. This document outlines the general considerations for use and test choice consideration.[51]

The pooled diagnostic accuracy of 12 RATs (5 of which are on the ARTG) is reported in ***Table 6***.[52] The pooled estimates of sensitivity and specificity of the 12 tests were 72.1% (95%CI, 68.8 to 75.3) and 99.0% (95% CI, 98.7 to 99.2), respectively. Test sensitivity and specificity was reduced in asymptomatic individuals, in individuals tested ≥7 days from onset of symptoms and in people ≥18 years of age. In addition, not following 'instructions for use' significantly lowered the diagnostic accuracy.[52] The sensitivity of anterior nasal/mid-turbinate and nasopharyngeal samples was much higher than for oropharyngeal and saliva samples.

The sensitivity and/or specificity of 15 individual RATs (6 of which are on the ARTG) are reported in ***Table 7***. Specificity was above 98% for all tests except for the Standard F (SD BIOSENSOR Inc, South Korea) and Lumipulse G SARS-CoV-2 Ag (Fujirebio, Japan). The highest sensitivity was observed for the SARS-CoV-2 Antigen Test (LumiraDx, United Kingdom) and the Lumipulse G SARS-CoV-2 Ag (Fujirebio, Japan), with both above 97%.

A recent study evaluated the diagnostic accuracy of one of the RATs on the ARTG, the Abbott Panbio™ COVID-19, in 3 Australian hospitals during a period of low COVID-19 prevalence.[53] Specificity was high (99.96%) and sensitivity was dependent on the duration of symptoms, ranging from 77.3% (1–33 day of symptom duration) to 100% (<7 day symptom duration). The authors concluded that given the test's high specificity it has utility in the rapid triaging of public health and hospital resources while awaiting confirmatory RT-PCR; however, its adoption in a low-prevalence population requires further consideration.[53]

Position statements or guidance on the use of RATs are summarised in ***Table 8***. In its latest guidance, the World Health Organization (WHO) recommends the use of tests that meet the pre-defined target product profiles,[54] such as minimum sensitivity and specificity requirements (≥80% sensitivity and ≥97% specificity).[55] They further state that these tests perform best in individuals with high viral load, early in the course of infection. Of the RATs listed in ***Table 7*** and included on the ARTG, none meet the WHO specifications (as of January 2022). PHLN CDNA and the TGA note that RATs are not as accurate as RT-PCR. The RCPA reiterates this position, however, acknowledges RATs may be used for surveillance in COVID-19 hotspots and surges. The PHLN and CDNA list the principles, requirements and recommendations for use of RATs.[32]

State and territory health departments have also recently published their own guidance on the use of these RATs for community testing (***Table 9***). This has been in response to the increased pressure on laboratory-based testing capacities as a result of the large increase in COVID-19 cases that occurred in December 2021. Several state and territories have noted a positive RAT does not require a subsequent RT-PCR to confirm diagnosis. A positive result from a RAT needs to be registered with the relevant public health authority.

Table 6 Pooled sensitivity and specificity of 12 rapid antigen tests for diagnosing COVID-19 and subgroup analyses of sample type, instructions-for-use conformity, age and asymptomatic or symptomatic

	Number of datasets	Number of samples	Sensitivity (95% CI)	Specificity (95% CI)
Pooled estimates	119	71,424	72.1% (68.8 to 75.3)	99.0% (98.7 to 99.2)
IFU conformity				
IFU conforming	81	49,643	76.3% (73.1 to 79.2)	99.1% (98.8 to 99.4)
IFU nonconformity	75	31,416	65.9% (60.6 to 70.8)	98.3% (97.7 to 98.8)
Sample type				
Anterior nasal/mid-turbinate	32	25,814	75.5% (70.4 to 79.9)	99.2% (98.8 to 99.5)
Nasopharyngeal	122	59,810	71.6% (68.1 to 74.9)	98.9% (98.5 to 99.1)

Table 7 Sensitivity and specificity of individual rapid antigen tests for diagnosing COVID-19

Test name	Approved by TGA	Number of datasets	Number of samples	Sensitivity (95% CI)	Specificity (95% CI)
Tests analysed by bivariate analyses					
SARS-CoV-2 Antigen Test (LumiraDx, UK)	N	4	1,373	88.2% (59.0 to 97.5)	98.6% (96.2 to 99.5)
Lumipulse G SARS-CoV-2 Ag (Fujirebio, Japan)	N	5	3, 532	87.2% (78 to 92.9)	96.7% (88.6 to 99.1)
Sofia SARS Antigen FIA (Quidel, US)	Y	5	2,197	77.4% (74.2 to 80.3)	99.1 (98.3 to 99.5)
Standard Q (SD BIOSENSOR, South Korea)	Y	33	1,6478	74.9% (69.3 to 79.7)	98.6% (97.8 to 99.2)
Standard Q nasal (SD BIOSENSOR, South Korea)	N	6	2,271	80.2% (70.3 to 87.4)	99% (97.7 to 99.6)
Panbio COVID-19 Ag (Abbott Laboratories, US)	Y	35	24,472	71.8% (65.4 to 77.5)	99.4% (99.1 to 99.7)
BIOCREDIT Covid-19 (RapiGEN, South Korea)	Y	6	2,116	62.0% (46.7 to 75.2)	98.5% (94.0 to 99.6)
COVID-19 Ag Respi-Strip (Coris BioConcept, Belgium)	N	5	729	40% (28.7 to 52.4)	98.5% (95.4 to 99.5)
Standard F (SD BIOSENSOR, South Korea)	N	6	2,692	68.1% (55.5 to 78.5)	97.7% (96.6 to 98.5)
BD Veritor (BD, US)	Y	6	6,661	63.5% (49.3 to	99.5% (98.8 to

Test name	Approved by TGA	Number of datasets	Number of samples	Sensitivity (95% CI)	Specificity (95% CI)
				75.8)	99.8)
BinaxNOW (Abbott Laboratories, US)	N	4	8,163	61.8% (48.0 to 74.0)	99.8% (99.5 to 99.9)
CLINITEST (Siemens, Germany)	N	4	740	62.3% (47.4 to 75.2)	98.9% (97.1 to 99.6)
Tests analysed by univariate analyses					
INNOVA SARS-CoV-2 (Innova Medical Group, US)	N	10[a] 4[b]	2,686[a] 8,668[b]	76.1% (68.1 to 84.1)	99.4% (96.7 to 100)
NADAL COVID-19 Ag Test (nal von minden, Germany)	N	4	1,492	58.4% (29.2 to 87.6)	NR
COVID-19 Rapid Antigen Visual Read (SureScreen Diagnostics, UK)	Y	4	269	65.9% (58.4 to 73.3)	NR

Abbreviations

CI = confidence interval; **COVID-19** = coronavirus disease; **NR** = not reported; **POC** = point of care; **SARS-CoV-2** = severe acute respiratory syndrome coronavirus 2; **UK** = United Kingdom; **US** = United States.

Notes

a = sensitivity

b = specificity

Source

Brummer 2021[52]

Table 8 Position statements/guidance on rapid antigen testing

Organisation	Updated	Comments
The Royal College of Pathologists of Australasia Position Statement – COVID-19 Antigen and Point of Care Testing[56]	January 2022 (next review June 2022)	'Rapid antigen tests have an important place supporting PCR tests in surveillance monitoring of COVID-19 infections at the present high prevalence stage of the pandemic in Australia and New Zealand.' 'Rapid Antigen Tests have inherent performance limitations, particularly the sensitivity of the tests in asymptomatic people, leading to significant levels of false negatives (compared to PCR testing).' 'PCR testing should be used for symptomatic people.' 'The RCPA highlights the lower sensitivity and specificity of RATs, which ideally should not be used alone for diagnostic purposes. Authorities may need to use RATs for surveillance purposes in circumscribed agreed settings in COVID-19 hotspots and surges, and regrettably for diagnosis if timely PCR testing is not available during a surge.'
Therapeutic Goods Administration[31]	January 2022	'Rapid antigen point-of-care tests detect the presence of viral protein from the SARS-CoV-2 virus. While rapid antigen tests can provide a result within 15-30 minutes, they are generally considered to be less sensitive than a PCR test which is still currently the gold-standard in SARS-CoV-2 diagnosis.'
Public Health Laboratory Network (PHLN) – Communicable Diseases Network Australia (CDNA) Joint Statement on SARS-CoV-2 Rapid Antigen Tests [32]	Version 2.2 January 2022	'At this time, in the context of widespread community transmission, PHLN and CDNA recommend deployment of RATs to enhance and preserve laboratory-based testing capacity.' 'Currently, there is considerable variability in the performance between different RATs, and they are less sensitive compared to the gold standard NAA for the diagnosis of COVID-19. This represents a potential risk in environments with low community transmission where the accuracy of every single test counts.' '1. RATs may be used for public health investigation where the pre-test probability is high. For example: where a NAA confirmed case has been identified in a closed setting, • to rapidly identify an outbreak in a closed setting where there are a number of symptomatic • individuals and rapid access to NAA is not available, or • where community transmission has been established. 2. Rapid antigen testing may be considered for use where NAA is unavailable or where an extensive delay in result TAT is anticipated. 3. RATs may be used for screening purposes at an interval sufficient to mitigate the reduced sensitivity of the test. This interval is test and prevalence specific, therefore a set interval cannot be applied across all such devices. 4. In low community transmission environments, public health authorities should consider the potential

Organisation	Updated	Comments
		impact: • of false negative results from RATs used in outbreak settings, i.e., a small proportion of cases may initially be missed. This may have an adverse impact on outbreak control and public confidence. • on public health resources of false positive results from RATs when used without careful integration in the SARS-CoV-2 detection workflow.'
World Health Organization interim guidance Antigen-detection in the diagnosis of SARS-CoV-2 infection[a][55]	6 October 2021	'Ag-RDTs perform best in individuals with high viral load, early in the course of infection, and will be most reliable in settings where SARS-CoV-2 prevalence is ≥ 5%. When there is no transmission, or low transmission, the positive predictive values of Ag-RDTs will be low, and in such settings NAATs are preferable for first-line testing or for confirmation of Ag-RDT positive results.' 'WHO recommends the use of Ag-RDTs that meet minimum performance requirements of ≥ 80% sensitivity and ≥ 97% specificity. Ag-RDTs are less sensitive than NAAT, particularly in asymptomatic populations, but careful selection of cohorts for testing can mitigate this limitation.' 'Ag-RDTs should be prioritized for use in symptomatic individuals meeting the case definition for COVID-19, and to test asymptomatic individuals at high risk of infections, including contacts and health workers, particularly in settings where NAAT capacity is limited.' 'Clinical discretion considering epidemiological context, clinical history and presentation and available testing resources should determine if negative Ag-RDT results require confirmatory testing with NAAT or repeat testing with Ag-RDTs (within 48 hours) if NAAT is not readily available.'

Abbreviations

Ag-RDTs = antigen-detecting rapid diagnostic tests; **CDNA** = Communicable Diseases Network Australia; **COVID-19** = coronavirus disease; **NAAT** = nucleic acid amplification test; **PCR** = polymerase chain reaction; **PHLN** = Public Health Laboratory Network; **POC** = point of care; **RATs** = rapid antigen tests; **RT-PCR** = reverse transcription polymerase chain reaction; **SARS-CoV-2** = severe acute respiratory syndrome coronavirus 2.

Notes

Only key comments have been listed from these documents.

Table 9 State guidance/recommendations on the use of rapid antigen tests

State/territory	Updated	Recommendations/guidance
Aotearoa New Zealand https://www.health.govt.nz/covid-19-novel-coronavirus/covid-19-health-advice-public/assessment-and-testing-covid-19/rapid-antigen-testing-rat	29 March 2022	'Rapid antigen tests (RATs) are currently Aotearoa New Zealand's primary testing tool for people with COVID-19 symptoms or household contacts.'
Australian Capital Territory https://www.covid19.act.gov.au/stay-safe-and-healthy/symptoms-and-getting-tested/when-to-get-tested	06 April 2022	'Most people can now use a RAT to confirm they are positive for COVID-19. Occasionally, RATs may not pick up that you do have COVID-19 infection. If you have COVID-19 symptoms you should have a PCR test. RATs are currently NOT recommended for children under 2 years of age. It is recommended that children under 2 years of age have a PCR test.'
New South Wales https://www.nsw.gov.au/covid-19/stay-safe/testing/how-testing-works/rapid-antigen-self-tests-for-community#toc-who-should-do-a-rapid-antigen-test	29 March 2022	'If you are at higher risk of severe illness you should get a PCR test as they are more accurate. If you are not at higher risk of severe illness, do a rapid antigen test unless your doctor tells you to have a PCR test. Specific testing advice is available for residents of age care facilities.'
Northern Territory https://coronavirus.nt.gov.au/stay-safe/symptoms-testing#get-rat	07 April 2022	'The NT COVID-19 testing procedure is to use a Rapid Antigen Test to confirm a positive diagnosis of COVID-19. PCR tests are no longer required to validate a Rapid Antigen Test result and will only be used if clinically required or requested by an authorised officer.'
Queensland https://www.health.qld.gov.au/__data/assets/pdf_file/0019/1141084/covid-19-rats-hhs-guidance.pdf	3 February 2022	'For asymptomatic patients who are close contacts, the use of RATs as guided by the Isolation for diagnosed cases of COVID-19 and management of close contacts direction is preferred. For symptomatic patients, HHSs should use a flexible approach to testing based on the following: • For vulnerable clients or those living or working with vulnerable people at any time and for all when PCR testing turn-around times are prolonged, RAT may be preferred as an initial test, with PCR performed on those who test negative on RAT (or in parallel to RAT if preferred) • Where PCR testing turn-around times are < 24 hours and clients are not vulnerable and do not live or work with vulnerable people, PCR alone may be the preferred test.'
South Australia https://www.sahealth.sa.gov.au/wps/wcm/connect/public+content/sa+health+internet/conditions/infectious+diseases/covid-19/testing+and+tracing/rapid+antigen+testing+rat+for+covid-19	11 March 2022	Use RATs 'if you are a close contact and have no COVID-19 symptoms, you can access rapid antigen tests to complete your required tests. You should get a PCR test as soon as you develop any COVID-19 symptoms. This applies to all people, including close contacts.

State/territory	Updated	Recommendations/guidance
		If you are a close contact with no COVID-19 symptoms, you can also get a PCR test. You must also get a PCR test if you have COVID-19 symptoms and test negative using a rapid antigen test to confirm your result. In South Australia, rapid antigen tests are now used as a test to diagnose COVID-19. This means that if you test positive using a rapid antigen test, your result does not need to be confirmed with a PCR test.'
Tasmania https://www.coronavirus.tas.gov.au/keeping-yourself-safe/testing-for-covid-19/rapid-antigen-tests-rats https://www.coronavirus.tas.gov.au/keeping-yourself-safe/testing-for-covid-19	09 March 2022 11 April 2022	'If you are required to get tested, RAT kits are available at no cost. Get tested if you: • have COVID-19 symptoms • are a close contact of a confirmed COVID-19 case • are directed to by Public Health You should get a PCR test at a testing clinic when: • you are having difficulty accessing or using a RAT, • you get an invalid result after taking a RAT, • you get a negative RAT result and have ongoing symptoms • your GP or medical practitioner recommends you get a PCR test. Public Health advise the following people should have a PCR test, rather than a rapid antigen test (RAT): • People with immunodeficiency • People receiving immunosuppressive therapy • People who receive dialysis • People who have end stage renal failure • People who are not fully vaccinated referred by their GP due to risk factors'
Victoria https://www.coronavirus.vic.gov.au/rapid-antigen-tests	09 April 2022	'Most people should take a rapid antigen test as their first option, particularly if you have symptoms or you are a contact of someone who has COVID-19. If you have symptoms or you are a contact of someone who has COVID-19, and you can't access a rapid antigen test, you can get a PCR test. • If you do not have symptoms and you are not a contact, and you test positive on a rapid antigen test, we recommend you get a PCR test to confirm that result. We do not recommend this if you have symptoms or you are a contact.'
Western Australia https://www.wa.gov.au/government/covid-19-coronavirus/covid-19-coronavirus-rapid-antigen-tests	30 March 2022	'RATs are recommended for use if: • attending a large gathering in a crowded place such as a wedding or funeral • visiting a person who is vulnerable to risks of COVID-19

State/territory	Updated	Recommendations/guidance
		• visiting a high-risk setting, e.g. an aged care facility, hospital or disability group home • need to check quickly for COVID-19 • recommended by the Department of Health.'

Abbreviations

COVID-19 = coronavirus disease; **GP** = general practitioner; **NSW** = New South Wales, **NT** = Northern Territory, **PCR** = polymerase chain reaction, **RAT** = rapid antigen test.

Nucleic acid amplification tests

NAATs work by detecting and amplifying segments of the SARS-CoV-2 genome, if present, in upper or lower respiratory tract specimens.[57] In response to the pandemic, a range of NAATs have become available. These include rapid RT-PCR NAATs, which use small, table-top devices and return a result much quicker (15–60 minutes) than laboratory-based RT-PCR, and non-RT-PCR NAATs, such as loop isothermal amplification tests, which use a different technique for amplification of the virus' genetic material.[58] RT-PCR tests are generally considered better at detecting the presence of the SARS-CoV-2 virus.[46] Currently 6 rapid molecular tests have been approved by the TGA.[49]

Table 10 reports the sensitivity and specificity of 5 rapid NAATs identified in the updated search (2 of which are currently listed on the ARTG). The overall sensitivity of the tests reported was above 90% and the overall specificity was above 97%. With respect to the diagnostic performance of the individual tests, those with a sensitivity and specificity greater than 95% included Xpert® Xpress SARS-CoV-2, BioFire COVID-19, and SAMBA II. Of these, the Xpert® Xpress SARS-CoV-2 is included on the ARTG.

Table 10 Sensitivity and specificity of a range of rapid nucleic acid amplification tests for diagnosing COVID-19

Test	Approved by TGA	Number of studies	Sensitivity (95% CI)	Specificity (95% CI)
Diagnostic accuracy as reported by Ulhaq et al (2021)[59]				
Overall sensitivity and specificity of molecular tests		7 tests 12 studies 31 datasets	95.9% (93.9 to 97.2)	97.2% (95.5 to 98.3)
Individual tests				
Xpert® Xpress SARS-CoV-2 (Cepheid, US)	Y	2	95.6% (84.9 to 98.8)	96.4% (77.9 to 99.5)
ID NOW COVID-19 (Abbott, US)	Y	4	91.6% (80.5 to 96.6)	94.2% (70.8 to 99.1)
BioFire COVID-19 Test (BioFire Defense, LLC, US)	N	2	96.7 (74.3 to 99.7)	98.2 (93.1 to 99.5)

Test	Approved by TGA	Number of studies	Sensitivity (95% CI)	Specificity (95% CI)
Diagnostic accuracy as reported by Dinnes et al (2021)[60]				
Overall sensitivity and specificity of molecular tests		5 tests 29 studies 31 datasets	91.5% (90.5 to 97.6)	98.8% (98.3 to 99.2)
Individual tests (including IFU conforming and nonconforming studies)				
ID NOW COVID-19 (Abbott, US)	Y	12	78.6% (73.7 to 82.8)	99.8% (99.2 to 99.9)
ID NOW COVID-19 (Abbott, US) (IFU conforming only studies)	Y	4	73.0% (66.8 to 78.4)	99.7% (98.7 to 99.9)
Xpert Xpress SARS-CoV-2 (Cepheid, US)	Y	13	99.1% (97.7 to 99.7)	97.9% (94.6 to 99.2)
Xpert Xpress SARS-CoV-2 (Cepheid, US) (IFU conforming only studies)	Y	2	100% (88.1 to 100)[a]	97.2% (89.4 to 99.3)[a]
COVID Nudge (DNANudge,UK) (IFU conforming study)	N	1	94.4% (86.2 to 98.4)	100% (98.8 to 100)
SAMBA II SARS-CoV-2 (Diagnostics for the Real World, US)	N	2	96.0% (81.1 to 99.3)	97.0% (93.5 to 98.6)
Accula SAR-CoV-2 (Mesa Biotech, Inc., US)	N	1	68.0% (53.3 to 80.5)	100% (92.9 to 100)

Abbreviations

CI = confidence interval; **COVID-19** = coronavirus disease; **IFU** = instructions for use; **LLC** = limited liability company; **POC** = point of care; **SARS-CoV-2** = severe acute respiratory syndrome coronavirus 2; **UK** = United Kingdom; **US** = United States.

Notes

Turnaround time for the ARTG-listed tests are as follows: Xpert Xpress: 30 minutes, ID NOW: 15–20 minutes.[61]

a = Separate pooling of sensitivity or specificity

Source

Dinnes et al (2021), Ulhaq et al (2021)[59 60]

NSW Health published a factsheet on 'Rapid PCR testing for SARS-CoV-2 on GeneXperts®' in July 2021. They noted the GeneXpert® system (used for the Xpert® Xpress SARS-CoV-2 test) is used in 37 laboratories throughout NSW enabling rapid on-site SARS-CoV-2 testing in several metropolitan, regional and rural sites.[62] The indications and testing criteria for rapid NAAT as outlined by NSW Health are as follows:

- 'Rapid SARS-CoV-2 testing should only be considered in high-risk patients where an urgent result is required (within one to four hours).'
- 'Acutely unwell inpatients (including patients in the Emergency Department) with recent onset of respiratory symptoms/pneumonia (particularly if pregnant) or patients with unexplained sepsis developed in hospital.'

- ‘Requirement for a rapid result to inform clinical management (i.e. treatment or transfer).’[62]

Queensland and Western Australia uses the Xpert® Xpress SARS-CoV-2 test in its Aboriginal and Torres Strait Islander COVID-19 Point-of-Care Testing Program.[63] This program is funded by the Australian Government Department of Health and led by the Kirby Institute and Flinders University International Centre for Point-of-Care Testing.[63] This suggests the utility of rapid NAATs in settings where access to conventional RT-PCR is limited or significantly delayed (applicable to all 3 Epidemiological Zones[q]).[41] As suggested by the PHLN, these settings may include rural and remote communities or hospital ICUs.[41]

It should be noted that a severe limitation on reagent cartridge supply for the Xpert® Xpress SARS-CoV-2 test has been reported nationally, and the system is not suitable for simultaneous testing of large numbers of samples.[64] The throughput of rapid NAAT is limited as samples are tested individually (except when pooled when prevalence is low).

Antibody POC tests

Antibody POC tests are intended to detect IgG and/or IgM antibodies to SARs-CoV-2 from venous or finger prick blood samples that are placed on a test strip. Results take approximately 15 to 30 minutes.[46] Twenty-three antibody POC tests have been approved by the TGA and are listed on the ARTG; however, the PHLN, TGA, RCPA and CDC all recommend that that these tests not be used for the diagnosis of acute COVID-19 infection (***Table 11***). The TGA also notes that none of the manufacturers claim that these tests should be used as a sole basis for diagnosis of COVID-19 and advise the results need to be interpreted along with other clinical findings.[65]

Table 11 Summary of recommendations regarding POC antibody tests.

Agency	Date published	Summary of recommendation
Public Health Laboratory Network[66]	March 2020	‘There are significant limitations to the use of point-of-care serology tests and they are not recommended as first line tests for the diagnosis of acute viral infection.’
Royal College of Pathologists of Australia[67]	March 2020	‘COVID-19 IgG/IgM rapid tests have no role to play in the acute diagnosis of COVID-19 infection. COVID-19 IgG/IgM rapid tests will miss patients in the early stages of disease when they are infectious to other

[q] Epidemiological Zone 1: no community transmission, Epidemiological Zone 2: community transmission, Epidemiological Zone 3: community transmission placing burden on response capacity.[41]

Agency	Date published	Summary of recommendation
		people.'
Therapeutic Goods Administration[68]	January 2022	'Serology point-of-care COVID-19 tests cannot determine whether a person is infectious. Serology point-of-care COVID-19 tests are not able to detect if a person has been recently infected. Management of an effective COVID-19 response relies on accurate reporting of COVID-19 infections from all facilities that offer testing. It is illegal to supply or advertise these COVID-19 point-of-care tests as self-tests or tests for home in Australia.'
Therapeutic Goods Administration[65]	March 2021	'The Doherty Institute's studies, along with other evaluations performed by Australian and international laboratories confirm that the sensitivity of these tests in the early stages of infection is poor and that they shouldn't be used for the diagnosis of acute COVID-19 infection. This conclusion is consistent with current advice from the Public Health Laboratory Network, the Royal College of Pathologists of Australasia and the TGA that these tests must be used with caution due to the potential for these tests to fail to detect COVID-19 during the acute phase of the illness, prior to the development of antibodies.'
Centers for Disease Control and Prevention[45]	January 2022	'Antibody testing does not replace virologic testing and should not be used to establish the presence or absence of acute SARS-CoV-2 infection.'

Abbreviations
COVID-19 = coronavirus disease; **IgG** = immunoglobulin G; **IgM** = immunoglobulin M; **POC** = point of care; **SARS-CoV-2** = severe acute respiratory syndrome coronavirus 2; **TGA** = Therapeutic Goods Administration.

The ability of COVID-19 tests to detect emerging genetic variants of COVID-19

Summary

- Health professionals should be aware that genetic variants of SARS-CoV-2 may yield false negative results.
- The TGA is reviewing all ARTG-listed RAT and laboratory tests to verify whether they can accurately detect emerging variants of SARS-CoV-2.
- The performance of many of the NAATs against Omicron has been verified by the TGA, but the performance of RATs against this variant is still under review.

The SARS-CoV-2 virus has mutated over time resulting in genetic variation in the population of circulating virus variants.[69] 'Variants of concern' is a term used describe those strains that are thought to be more transmissible or might cause more severe infection than others.[70] Current variants of concern in Australia, as reported by the Communicable Diseases Genomics Network, are listed in ***Table 12***.

Table 12 Current and previous variants of concern[a]

WHO/CDGN	Lineage
Current	
Omicron	B.1.1.529 (including the sublineages BA.*)
Delta	B.1.617.2 and sub-lineages AY
Previous	
Alpha	B.1.1.7 and sub-lineages Q
Beta	B.1.351 and sub-lineages B.1.351
Gamma	P.1 and sub-lineages P.1

Abbreviations
WHO = World Health Organization; **CDGN** = Communicable Diseases Genomics Network.
Notes
a = As reported on 6 December 2021 by the CDGN[70]

Mutations in the SARS-CoV-2 virus can potentially change the performance of NAAT, RAT or serology tests.[69] The TGA reports that laboratory and health professionals should be aware that genetic variants of SARS-CoV-2 may yield false negative results.[71] As a result, it reviews the accuracy of all ARTG-listed POC and laboratory tests aimed at identifying individuals with COVID-19 against emerging variants of SARS-CoV-2 with at least 5% prevalence in the global population (i.e. mutations that occur in at least 5% of each viral variant). The TGA notes that monitoring of these variants will continue as they mutate.

The effect of mutations on molecular tests

SARS-CoV-2 NAATs are the most widely used COVID-19 diagnostic test in Australia.[71] The TGA notes that because NAATs directly target the viral genome, they may be particularly vulnerable to sequence mutations which could lead to negative results.[71] The TGA has reviewed the performance of approved NAAT test kits against several SARS-CoV-2 variants. NAATs listed on https://www.tga.gov.au/post-market-review-nucleic-acid-tests have been validated against:

- 'Alpha, Beta, Gamma, Delta, Delta Plus, Kappa, Epsilon, Eta, Iota, Zeta, Theta, and Lambda variants across 5% mutation prevalence as of 31 August 2021.
- Delta (B.1.617.2 and AY sub-lineages) and Mu Variants (B.1.621) across 5% mutation prevalence, as of 1 December 2021; and Omicron variant (B.1.1.529).

Those NAATs that have been cancelled, either by the TGA or the sponsor, are listed on https://www.tga.gov.au/post-market-review-nucleic-acid-tests.

The effect of mutations on antigen and rapid antigen point-of-care tests

Rapid antigen tests that the TGA have deemed as having evidence to support their continued performance with specific variants are listed on https://www.tga.gov.au/post-market-review-antigen-and-rapid-antigen-tests. One test, CovClear COVID-19 Antigen Test (ARTG 374063), has been suspended from the ARTG by the TGA due to safety and performance concerns. It should be noted that not all test kits for all variants are listed, due to their lower prevalence, recent emergence or because the data is still being reviewed. There are suggestions that the analytical performance of the RATs in detecting the Omicron variant is less compared to that of the Delta variant.[72 73]

The effect of mutations on serology tests

Information on the effect of mutations on the performance of serology test kits were not available at the time of updating this report, but the TGA noted it will be published as soon as it becomes available.[71]

Imaging for COVID-19

Summary

- Computed tomography (CT), X-ray and ultrasound of the chest are not recommended for the diagnosis of COVID-19.

No new guidelines or position statements were identified by the update search; as such, the recommendation remains that imaging should not be used for COVID-19 diagnosis. Results from a recent meta-analysis on the diagnostic accuracy of thoracic imaging tests (CT, X-ray and ultrasound of the lungs) for the evaluation of people with suspected COVID-19 are presented in ***Table 13***.[74] This review states, 'At this stage, despite its limitations, RT-PCR remains the best tool for diagnosing COVID-19.[74] Individual imaging test results are discussed below.

Computed tomography

The authors reported that chest CT is sensitive and moderately specific for the diagnosis of COVID-19. They concluded it may have more utility for excluding COVID-19 infection rather than distinguishing it from other respiratory conditions.[74] An additional 8 meta-analyses reported the poor specificity of CT for diagnosing COVID-19.[39 75-81]

Table 13 Sensitivity and specificity of chest imaging for the diagnosis of COVID-19

Test	Number of studies	Number of patients	Sensitivity (95% CI)	Specificity (95% CI)
Chest CT	41	16,133	87.9% (84.6 to 90.6)	80.0% (74.9 to 84.3)
Chest X-ray	9	3,694	80.6% (69.1 to 88.6)	71.5% (59.8 to 80.8)
Ultrasound	5	446	86.4% (72.7 to 93.9)	54.6 (35.3 to 72.6)

Abbreviations

CI = confidence interval; **COVID-19** = coronavirus disease; **CT** = computed tomography; **NR** = not reported.

Source

Islam et al (2021)[74]

Chest X-ray

The authors noted that chest X-ray is moderately sensitive and specific for the diagnosis of COVID-19, but due to the limited availability of data, the accuracy estimate of chest X-ray is uncertain and should be interpreted with caution (***Table 13***).

Ultrasound

The authors noted that ultrasound of the lungs is sensitive but not specific for the diagnosis of COVID-19. Again, the authors noted that due to the limited availability of data, the

accuracy estimate of ultrasound is uncertain and should be interpreted with caution. An indirect comparison of chest X-ray and ultrasound did not show any differences in specificity or sensitivity.[74]

Conclusions

The recommendations for diagnostic workup prior to surgery remain mostly unchanged from the original guidance. Patient symptoms and exposure history continue to be equally important in determining who should get tested, and laboratory-based RT-PCR remains the gold standard test if a patient is suspected of having COVID-19.

Fever and cough remain the 2 most common COVID-19 symptoms. Symptoms not reported in the original guidance but identified by the update search include fatigue and sputum production/expectoration, both of which occur more commonly in adults and individuals aged over 60 years.

In the previous report, the testing of patients without symptoms was not recommended due to the potential for increased false positives in communities with low SARS-CoV-2 prevalence. As of March 2022, several health jurisdictions are recommending that all patients get tested prior to elective surgery. Given that the incidence of COVID-19 has increased in Australia following the reopening of borders, lifting of restrictions and the emergence of the Omicron variant, it is likely other health jurisdictions may adopt these recommendations. It is advised that operative staff routinely check with their state health departments about current recommendations.

Since the original guidance, a significant amount of literature has been published on rapid NAAT that can be done at the POC and RAT that can be used for self-testing at home, rather than samples being sent to a laboratory unlike the earlier phases of the COVID-19 pandemic. This has been motivated by the need to expedite testing and the availability of time critical results for clinical management. Several of these POC tests, including antigen, antibody and molecular, are approved for use in Australia; however, antibody POC tests are not recommended for the diagnosis of acute COVID-19 infection for the purposes of pre-operative care. Of the POC tests, rapid NAAT have been found to have the highest sensitivity and specificity.

Since the original report, new variants of SARS-CoV-2 have emerged. The TGA is conducting post-market reviews of all ARTG-approved COVID-19 tests against these new variants to verify whether the tests can accurately detect them.[71]

References

1. Mortality and pulmonary complications in patients undergoing surgery with perioperative SARS-CoV-2 infection: an international cohort study. *Lancet* 2020;396(10243):27-38. doi: 10.1016/s0140-6736(20)31182-x
2. Haffner MR, Le HV, Saiz AM, Jr., Han G, Fine J, Wolinsky P, Klineberg EO. Postoperative In-Hospital Morbidity and Mortality of Patients With COVID-19 Infection Compared With Patients Without COVID-19 Infection. *JAMA Netw Open* 2021;4(4):e215697. doi: 10.1001/jamanetworkopen.2021.5697
3. Knisely A, Zhou ZN, Wu J, Huang Y, Holcomb K, Melamed A, Advincula AP, Lalwani A, Khoury-Collado F, Tergas AI, St Clair CM, Hou JY, Hershman DL, D'Alton ME, Huang YY, Wright JD. Perioperative Morbidity and Mortality of Patients With COVID-19 Who Undergo Urgent and Emergent Surgical Procedures. *Ann Surg* 2021;273(1):34-40. doi: 10.1097/sla.0000000000004420
4. Royal Australasian College of Surgeons. Guidelines on the Preoperative Diagnostic Workup for COVID-19 2020. Available from: https://www.surgeons.org/-/media/Project/RACS/surgeons-org/files/news/covid19-information-hub/Guidelines-on-the-Preoperative-Diagnostic-Workup-for-COVID-19.pdf accessed November 16 2020.
5. Watt A, Cameron A, Sturm L, Lathlean T, Babidge W, Blamey S, Facey K, Hailey D, Norderhaug I, Maddern G. Rapid versus full systematic reviews: validity in clinical practice? *ANZ J Surg* 2008;78(11):1037-40. doi: 10.1111/j.1445-2197.2008.04730.x
6. Ouzzani M, Hammady H, Fedorowicz Z, Elmagarmid A. Rayyan-a web and mobile app for systematic reviews. *Syst Rev* 2016;5(1):210. doi: 10.1186/s13643-016-0384-4
7. Australian Government Department of Health. Coronavirus (COVID-19) case numbers and statistics. Available from: https://www.health.gov.au/news/health-alerts/novel-coronavirus-2019-ncov-health-alert/coronavirus-covid-19-case-numbers-and-statistics accessed March 30 2022.
8. Ministry of Health New Zealand. COVID-19: Current cases. Available from: https://www.health.govt.nz/our-work/diseases-and-conditions/covid-19-novel-coronavirus/covid-19-data-and-statistics/covid-19-current-cases accessed March 29 2022.
9. Day M. Covid-19: four fifths of cases are asymptomatic, China figures indicate. *BMJ* 2020;369:m1375. doi: 10.1136/bmj.m1375
10. Sah P, Fitzpatrick MC, Zimmer CF, Abdollahi E, Juden-Kelly L, Moghadas SM, Singer BH, Galvani AP. Asymptomatic SARS-CoV-2 infection: A systematic review and meta-analysis. *Proc Natl Acad Sci USA* 2021;118(34):1-26.
11. Wu P, Liu F, Chang Z, Lin Y, Ren M, Zheng C, Li Y, Peng Z, Qin Y, Yu J, Geng M, Yang X, Zhao H, Li Z, Zhou S, Ran L, Cowling BJ, Lai S, Chen Q, Wang L, Tsang TK, Li Z. Assessing Asymptomatic, Presymptomatic, and Symptomatic Transmission Risk of Severe Acute Respiratory Syndrome Coronavirus 2. *Clin Infect Dis* 2021;73(6):e1314-e20. doi: 10.1093/cid/ciab271
12. Coatsworth N, Myles PS, Mann GJ, Cockburn IA, Forbes AB, Gardiner EE, Lum G, Cheng AC, Gruen RL. Prevalence of asymptomatic SARS-CoV-2 infection in elective surgical patients in Australia: a prospective surveillance study. *ANZ J Surg* 2021;91(1-2):27-32. doi: 10.1111/ans.16564
13. Watters DA. Preoperative screening and testing for COVID-19 during Victoria's second wave. *ANZ J Surg* 2021;91(1-2):6-8. doi: 10.1111/ans.16465
14. Epworth. COVID-19 update for patients 2021. Available from: https://www.epworth.org.au/who-we-are/coronavirus-update/for-patients accessed 20 December 2021.
15. Government of South Australia SA Health. Testing for COVID-19 2021. Available from: https://www.sahealth.sa.gov.au/wps/wcm/connect/Public+Content/SA+Health+Intern

et/Conditions/Infectious+diseases/COVID-19/Testing+and+tracing/Testing+for+COVID-19 accessed 20 December 2021.
16. Babidge WJ, Tivey DR, Kovoor JG, Weidenbach K, Collinson TG, Hewett PJ, Hugh TJ, Padbury RTA, Hill NM, Maddern GJ. Surgery triage during the COVID-19 pandemic. *ANZ J Surg* 2020;90(9):1558-65. doi: https://doi.org/10.1111/ans.16196
17. Royal Australasian College of Surgeons. Guidelines for Personal Protective Equipment 2020. Available from: https://umbraco.surgeons.org/media/5302/2020-05-05-covid19-ppe-guidelines.pdf.
18. He X, Lau EHY, Wu P, Deng X, Wang J, Hao X, Lau YC, Wong JY, Guan Y, Tan X, Mo X, Chen Y, Liao B, Chen W, Hu F, Zhang Q, Zhong M, Wu Y, Zhao L, Zhang F, Cowling BJ, Li F, Leung GM. Temporal dynamics in viral shedding and transmissibility of COVID-19. *Nat Med* 2020;26(5):672-75. doi: 10.1038/s41591-020-0869-5
19. HealthDirect Australian Government. Groups at higher risk of developing COVID-19 2020. Available from: https://www.healthdirect.gov.au/coronavirus-covid-19-groups-at-higher-risk-faqs accessed November 16 2021.
20. The Lancet. The plight of essential workers during the COVID-19 pandemic. *The Lancet* 2020;395(10237):1587. doi: 10.1016/S0140-6736(20)31200-9
21. Li J, Huang DQ, Zou B, Yang H, Hui WZ, Rui F, Yee NTS, Liu C, Nerurkar SN, Kai JCY, Teng MLP, Li X, Zeng H, Borghi JA, Henry L, Cheung R, Nguyen MH. Epidemiology of COVID-19: A systematic review and meta-analysis of clinical characteristics, risk factors, and outcomes. *J Med Virol* 2021;93(3):1449-58.
22. Cui X, Zhao Z, Zhang T, Guo W, Guo W, Zheng J, Zhang J, Dong C, Na R, Zheng L, Li W, Liu Z, Ma J, Wang J, He S, Xu Y, Si P, Shen Y, Cai C. A systematic review and meta-analysis of children with coronavirus disease 2019 (COVID-19). *J Med Virol* 2021;93(2):1057-69.
23. Singhal S, Kumar P, Singh S, Saha S, Dey AB. Clinical features and outcomes of COVID-19 in older adults: a systematic review and meta-analysis. *BMC Geriatr* 2021;21(1):321.
24. Xie J, Wang Q, Xu Y, Zhang T, Chen L, Zuo X, Liu J, Huang L, Zhan P, Lv T, Song Y. Clinical characteristics, laboratory abnormalities and CT findings of COVID-19 patients and risk factors of severe disease: a systematic review and meta-analysis. *Ann Palliat Med* 2021;10(2):1928-49.
25. Grant MC, Geoghegan L, Arbyn M, Mohammed Z, McGuinness L, Clarke EL, Wade RG. The prevalence of symptoms in 24,410 adults infected by the novel coronavirus (SARS-CoV-2; COVID-19): A systematic review and meta-analysis of 148 studies from 9 countries. *PLoS One* 2020;15(6):e0234765.
26. Mansourian M, Ghandi Y, Habibi D, Mehrabi S. COVID-19 infection in children: A systematic review and meta-analysis of clinical features and laboratory findings. *Arch Pediatr* 2021;28(3):242-48.
27. Toba N, Gupta S, Ali AY, ElSaban M, Khamis AH, Ho SB, Popatia R. COVID-19 under 19: A meta-analysis. *Pediatr Pulmonol* 2021;56(6):1332-41.
28. Qi K, Zeng W, Ye M, Zheng L, Song C, Hu S, Duan C, Wei Y, Peng J, Zhang W, Xu J. Clinical, laboratory, and imaging features of pediatric COVID-19: A systematic review and meta-analysis. *Medicine (Baltimore)* 2021;100(15):e25230.
29. Struyf T, Deeks JJ, Dinnes J, Takwoingi Y, Davenport C, Leeflang MM, Spijker R, Hooft L, Emperador D, Dittrich S, Domen J, Horn SRA, Van den Bruel A. Signs and symptoms to determine if a patient presenting in primary care or hospital outpatient settings has COVID-19 disease. *Cochrane Database Syst Rev* 2020;7(7):Cd013665.
30. NSW Health Pathology. Testing during COVID-19 disease. Clinical update: clinical pathology recommended for COVID positive patients 2021. Available from: https://www.pathology.health.nsw.gov.au/covid-19-info/covid-19-testing-information accessed November 29 2021.

31. Australian Government Department of Health TGA. COVID-19 point-of-care tests 2021. Available from: https://www.tga.gov.au/covid-19-point-care-tests accessed 22 March 2022.
32. Public Health Laboratory Network - Communicable Diseases Network Australia. Joint Statement on SARS-CoV-2 Rapid Antigen Tests 2022. Available from: https://www.health.gov.au/sites/default/files/documents/2022/02/phln-and-cdna-joint-statement-on-sars-cov-2-rapid-antigen-tests.pdf accessed March 22 2022.
33. Public Health Laboratory Network. PHLN statement on using saliva as a respiratory specimen for SARS-CoV-2 testing 7 June 2021. Available from: https://www.health.gov.au/sites/default/files/documents/2021/06/phln-statement-on-using-saliva-as-a-respiratory-specimen-for-sars-cov-2-testing.pdf accessed 22 March 2022.
34. Public Health Laboratory Network. PHLN guidance on laboratory testing for SARS-CoV-2 (the virus that causes COVID-19) 2022. Available from: https://www.health.gov.au/sites/default/files/documents/2021/11/phln-guidance-on-laboratory-testing-for-sars-cov-2-the-virus-that-causes-covid-19_0.pdf accessed March 22 2022.
35. Au WY, Cheung PPH. Diagnostic performances of common nucleic acid tests for SARS-CoV-2 in hospitals and clinics: a systematic review and meta-analysis. *Lancet Microbe*;2(12):e704-e14. doi: 10.1016/S2666-5247(21)00214-7
36. Tsang NNY, So HC, Ng KY, Cowling BJ, Leung GM, Ip DKM. Diagnostic performance of different sampling approaches for SARS-CoV-2 RT-PCR testing: a systematic review and meta-analysis. *Lancet Infect Dis* 2021;21(9):1233-45.
37. Riccò M, Ranzieri S, Peruzzi S, Valente M, Marchesi F, Balzarini F, Bragazzi NL, Signorelli C. RT-qPCR assays based on saliva rather than on nasopharyngeal swabs are possible but should be interpreted with caution: results from a systematic review and meta-analysis. *Acta Biomed* 2020;91(3):e2020025.
38. Mohammadi A, Esmaeilzadeh E, Li Y, Bosch RJ, Li JZ. SARS-CoV-2 detection in different respiratory sites: A systematic review and meta-analysis. *EBioMedicine* 2020;59:102903.
39. Böger B, Fachi MM, Vilhena RO, Cobre AF, Tonin FS, Pontarolo R. Systematic review with meta-analysis of the accuracy of diagnostic tests for COVID-19. *Am J Infect Control* 2021;49(1):21-29.
40. Bwire GM, Majigo MV, Njiro BJ, Mawazo A. Detection profile of SARS-CoV-2 using RT-PCR in different types of clinical specimens: A systematic review and meta-analysis. *J Med Virol* 2021;93(2):719-25.
41. Public Health Laboratory Network. Testing Framework for COVID-19 in Australia, February 2021. Available from: https://www.health.gov.au/sites/default/files/documents/2021/06/coronavirus-covid-19-testing-framework-for-covid-19-in-australia.pdf accessed November 23 2021.
42. Australian Government Department of Health. Coronavirus Disease 2019 (COVID-19): CDNA National Guidelines for Public Health Units (Version 6.7) 2022. Available from: https://www1.health.gov.au/internet/main/publishing.nsf/Content/7A8654A8CB144F5FCA2584F8001F91E2/$File/COVID-19-SoNG%20v6.7.pdf accessed March 30 2022.
43. Public Health Laboratory Network. Public Health Laboratory Network Guidance on Nucleic Acid Test Result Interpretation for SARS-CoV-2. 1.2 ed, 2020:7.
44. Centers for Disease Control and Prevention. Test for Past Infection 2021. Available from: https://www.cdc.gov/coronavirus/2019-ncov/testing/serology-overview.html accessed November 16 2021.
45. Centers for Disease Control and Prevention. Interim Guidelines for COVID-19 Antibody Testing 2022. Available from: https://www.cdc.gov/coronavirus/2019-ncov/lab/resources/antibody-tests-guidelines.html accessed March 22 2022.
46. Australian Government Department of Health TGA. COVID-19 testing in Australia - information for health professionals 2021. Available from:

https://www.tga.gov.au/covid-19-testing-australia-information-health-professionals accessed March 22 2022.
47. Abbasi J. Point-of-Care SARS-CoV-2 Variant Diagnostic in Development. *Jama* 2021;326(10):901. doi: 10.1001/jama.2021.15116
48. Centers for Disease Control and Prevention. Guidance for SARS-CoV-2 Point-of-Care and Rapid Testing 2021. Available from: https://www.cdc.gov/coronavirus/2019-ncov/lab/point-of-care-testing.html accessed Novemeber 16 2021.
49. Australian Government Department of Health TGA. COVID-19 test kits included in the ARTG for legal supply in Australia 2021. Available from: https://www.tga.gov.au/covid-19-test-kits-included-artg-legal-supply-australia accessed November 16 2021.
50. National Pathology Accreditation Advisory Council. National Pathology Accreditation Advisory Council (NPAAC) Guidance for Point of Care Testing 2021. Available from: https://www.safetyandquality.gov.au/sites/default/files/2021-08/guidance_point_of_care_testing_covid-19.pdf accessed November 16 2021.
51. Australian Government Department of Health TGA. COVID-19 Rapid Antigen Point of Care Testing: Guidance for implementation and checklist for businesses 2021. Available from: https://www.tga.gov.au/sites/default/files/covid-19-rapid-antigen-tests-guidance-and-checklist-businesses.pdf accessed November 16 2021.
52. Brümmer LE, Katzenschlager S, Gaeddert M, Erdmann C, Schmitz S, Bota M, Grilli M, Larmann J, Weigand MA, Pollock NR, Macé A, Carmona S, Ongarello S, Sacks JA, Denkinger CM. Accuracy of novel antigen rapid diagnostics for SARS-CoV-2: A living systematic review and meta-analysis. *PLoS Med* 2021;18(8):e1003735.
53. Muhi S, Tayler N, Hoang T, Ballard SA, Graham M, Rojek A, Kwong JC, Trubiano JA, Smibert O, Drewett G, James F, Gardiner E, Chea S, Isles N, Sait M, Pasricha S, Taiaroa G, McAuley J, Williams E, Gibney KB, Stinear TP, Bond K, Lewin SR, Putland M, Howden BP, Williamson DA. Multi-site assessment of rapid, point-of-care antigen testing for the diagnosis of SARS-CoV-2 infection in a low-prevalence setting: A validation and implementation study. *Lancet Reg Health – West Pac* 2021;9 doi: 10.1016/j.lanwpc.2021.100115
54. World Health Organisation (WHO). Target product profiles for priority diagnostics to support response to the COVID-19 pandemic 2020. Available from: https://cdn.who.int/media/docs/default-source/blue-print/who-rd-blueprint-diagnostics-tpp-final-v1-0-28-09-jc-ppc-final-cmp92616a80172344e4be0edf315b582021.pdf?sfvrsn=e3747f20_1&download=true accessed March 30 2022.
55. World Health Organisation (WHO). Antigen-detection in the diagnosis of SARS-CoV-2 infection 2021. Available from: https://www.who.int/publications/i/item/antigen-detection-in-the-diagnosis-of-sars-cov-2infection-using-rapid-immunoassays accessed November 16 2021.
56. The Royal College of Pathologists of Australasia. Position Statement: COVID-19 Antigen and Point of Care Testing 2021. Available from: https://www.rcpa.edu.au/Library/College-Policies/Position-Statements/COVID-19-Antigen-and-Point-of-Care-Testing accessed March 22 2022.
57. Centers for Disease Control and Prevention. Nucleic Acid Amplification Tests (NAATs) 2021. Available from: https://www.cdc.gov/coronavirus/2019-ncov/lab/naats.html accessed November 16 2021.
58. NSW Government COVID-19 Critical Intelligence Unit. Living Evidence: rapid testing 2021. Available from: https://aci.health.nsw.gov.au/covid-19/critical-intelligence-unit/living-evidence-rapid-testing accessed November 16 2021.
59. Ulhaq ZS, Soraya GV. The diagnostic accuracy of seven commercial molecular in vitro SARS-CoV-2 detection tests: a rapid meta-analysis. *Expert Rev Mol Diagn* 2021;21(7):733-40.
60. Dinnes J, Deeks JJ, Berhane S, Taylor M, Adriano A, Davenport C, Dittrich S, Emperador D, Takwoingi Y, Cunningham J, Beese S, Domen J, Dretzke J, Ferrante

di Ruffano L, Harris IM, Price MJ, Taylor-Phillips S, Hooft L, Leeflang MM, McInnes MD, Spijker R, Van den Bruel A. Rapid, point-of-care antigen and molecular-based tests for diagnosis of SARS-CoV-2 infection. *Cochrane Database Syst Rev* 2021;3(3):Cd013705.
61. Graham M, Ballard SA, Pasricha S, Lin B, Hoang T, Stinear T, Druce J, Catton M, Sherry N, Williamson D, Howden BP. Use of emerging testing technologies and approaches for SARS-CoV-2: review of literature and global experience in an Australian context. *Pathology* 2021;53(6):689-99. doi: 10.1016/j.pathol.2021.08.001
62. NSW Health. Rapid PCR testing for SARS-CoV-2 on GeneXperts: Clinician factsheet 28 July 2021. Available from: https://www.health.nsw.gov.au/Infectious/covid-19/communities-of-practice/Pages/guide-rapid-prc-testing.aspx accessed December 6 2021.
63. Queensland Health. Aboriginal and Torres Strait Islander COVID-19 Point-of-Care Testing Program Guideline 2020. Available from: https://www.health.qld.gov.au/__data/assets/pdf_file/0018/1010835/Aboriginal-and-Torres-Strait-Islander-COVID-19-Point-of-Care-Testing-Program-Guideline.pdf accessed November 23 2021.
64. Brischetto A, Robson J. Testing for COVID-19. *Aust Prescr* 2020;43(6):204-08. doi: 10.18773/austprescr.2020.067
65. Australian Government Department of Health TGA. Post-market evaluation of serology-based point of care tests 2021. Available from: https://www.tga.gov.au/post-market-evaluation-serology-based-point-care-tests accessed November 16 2021.
66. Public Health Laboratory Network. Public Health Laboratory Network Statement on Point-of-Care Serology Testing for SARS-CoV-2 (the virus that causes COVID-19) 2020. Available from: https://www.health.gov.au/sites/default/files/documents/2020/03/phln-statement-on-point-of-care-serology-testing-for-sars-cov-2-the-virus-that-causes-covid-19.pdf accessed November 16 2021.
67. The Royal College of Pathologists of Australasia. COVID19 IgG/IgM Rapid POCT Tests 2020. Available from: https://www.rcpa.edu.au/Library/College-Policies/Position-Statements/COVID19-IgG-IgM-RAPID-POCT-TESTS accessed November 16 2021.
68. Australian Government Department of Health TGA. COVID-19 serology point-of-care tests 2022. Available from: https://www.tga.gov.au/covid-19-serology-point-care-tests accessed March 22 2022.
69. US Department of Health and Human Services; Food and Drug Administration; Center for Devices and Radiological Health; Office of Product Evaluation and Quality. Policy for Evaluating Impact of Viral Mutations on COVID-19 Tests: Guidance for Test Developers and Food and Drug Administration Staff 2021. Available from: https://www.fda.gov/media/146171/download accessed September 21 2021.
70. Communicable Diseases Genomics Network. Varients of concern 2021. Available from: https://www.cdgn.org.au/variants-of-concern accessed September 21 2021.
71. Australian Government Department of Health Therapeutic Goods Administration. The ability of COVID-19 tests to detect emerging genetic variants of SARS-CoV-2 2021. Available from: https://www.tga.gov.au/ability-covid-19-tests-detect-emerging-genetic-variants-sars-cov-2 accessed September 21 2021.
72. Osterman A, Badell I, Basara E, Stern M, Kriesel F, Eletreby M, Öztan GN, Huber M, Autenrieth H, Knabe R, Späth PM, Muenchhoff M, Graf A, Krebs S, Blum H, Durner J, Czibere L, Dächert C, Kaderali L, Baldauf HM, Keppler OT. Impaired detection of omicron by SARS-CoV-2 rapid antigen tests. *Med Microbiol Immunol* 2022:1-13. doi: 10.1007/s00430-022-00730-z
73. Jüni P, Baert, S., Corbeil, A., Johnstone, J., Patel, S.N., Bobos, P., Allen, U., Barrett, K.A., Barrett, L.L., Bodmer, N.S., Born, K.N., Bourns, L., Evans, G.A., Hopkins, J., Manuel, D.G., Morris, A.M. Razak, F., Sander, B., Science, Steiner, R., Tepper, J., Thampi N, McGeer, A. Use of Rapid Antigen Tests during the Omicron Wave: Science Briefs of the Ontario COVID-19 Science Advisory Table, 2022.

74. Islam N, Ebrahimzadeh S, Salameh JP, Kazi S, Fabiano N, Treanor L, Absi M, Hallgrimson Z, Leeflang MM, Hooft L, van der Pol CB, Prager R, Hare SS, Dennie C, Spijker R, Deeks JJ, Dinnes J, Jenniskens K, Korevaar DA, Cohen JF, Van den Bruel A, Takwoingi Y, van de Wijgert J, Damen JA, Wang J, McInnes MD. Thoracic imaging tests for the diagnosis of COVID-19. *Cochrane Database Syst Rev* 2021;3(3):Cd013639.
75. Adams HJA, Kwee TC, Yakar D, Hope MD, Kwee RM. Systematic Review and Meta-Analysis on the Value of Chest CT in the Diagnosis of Coronavirus Disease (COVID-19): Sol Scientiae, Illustra Nos. *AJR Am J Roentgenol* 2020;215(6):1342-50.
76. Bellini D, Panvini N, Carbone I, Rengo M, Wang CL, Mileto A. Diagnostic Yield of Computed Tomography for the Identification of Coronavirus Disease 2019 Using Repeated Reverse Transcriptase Polymerase Chain Reaction Testing or Confirmed True-Negative State as Reference Standard: Systematic Review and Meta-Analysis. *J Comput Assist Tomogr* 2020;44(6):812-20.
77. Duarte ML, Santos LRD, Contenças ACS, Iared W, Peccin MS, Atallah Á N. Reverse-transcriptase polymerase chain reaction versus chest computed tomography for detecting early symptoms of COVID-19. A diagnostic accuracy systematic review and meta-analysis. *Sao Paulo Med J* 2020;138(5):422-32.
78. Khatami F, Saatchi M, Zadeh SST, Aghamir ZS, Shabestari AN, Reis LO, Aghamir SMK. A meta-analysis of accuracy and sensitivity of chest CT and RT-PCR in COVID-19 diagnosis. *Sci Rep* 2020;10(1):22402.
79. Kim H, Hong H, Yoon SH. Diagnostic Performance of CT and Reverse Transcriptase Polymerase Chain Reaction for Coronavirus Disease 2019: A Meta-Analysis. *Radiology* 2020;296(3):E145-e55.
80. Mair MD, Hussain M, Siddiqui S, Das S, Baker A, Conboy P, Valsamakis T, Uddin J, Rea P. A systematic review and meta-analysis comparing the diagnostic accuracy of initial RT-PCR and CT scan in suspected COVID-19 patients. *Br J Radiol* 2021;94(1119):20201039.
81. Xu B, Xing Y, Peng J, Zheng Z, Tang W, Sun Y, Xu C, Peng F. Chest CT for detecting COVID-19: a systematic review and meta-analysis of diagnostic accuracy. *Eur Radiol* 2020;30(10):5720-27.
82. Centers for Disease Control and Prevention. Interim Guidance on Developing a COVID-19 Case Investigation & Contract Tracing Plan: Overview 2022. Available from: https://www.cdc.gov/coronavirus/2019-ncov/php/contact-tracing/contact-tracing-plan/appendix.html accessed January 17 2022.
83. Meena J, Yadav J, Saini L, Yadav A, Kumar J. Clinical Features and Outcome of SARS-CoV-2 Infection in Children: A Systematic Review and Meta-analysis. *Indian Pediatr* 2020;57(9):820-26.

Appendix A: Definitions of close contact

Communicable Diseases Network Australia (CDNA)

The definition of a close contact, previously reported in accordance with the Communicable Diseases Network Australia (CDNA), has since been updated. The *Coronavirus Disease 2019 (COVID-19) CDNA National Guidelines for Public Health Units* (Version 6.7, published 22 March 2022) containing the new definition is available here: https://www1.health.gov.au/internet/main/publishing.nsf/Content/7A8654A8CB144F5FCA2584F8001F91E2/$File/COVID-19-SoNG%20v6.7.pdf

Contacts have been delineated into close contact or other contact. A **close contact** is defined as a person who:

- 'A person who resides with or stays overnight in the same premises or has had more than 4 hours of cumulative contact with a COVID-19 case in a residential setting.* In exceptional circumstances or where a significant transmission event has occurred, PHUs may consider classifying additional persons as close contacts.
    - * A residential setting is a building or a part of a building where individuals: spend the night for sleeping; including a house, apartment, or other private dwelling, and share facilities for acts of daily living which have the potential to create exposure between co- residents.
    - Residential settings may include: aged care facilities, military residential settings, boarding schools, boarding houses, homeless shelters, and maritime vessels.'[42]

An **other contact** is defined as a person who:

- 'has been exposed to a COVID-19 case but does not meet the definition of a close contact.'

For the purposes of contact tracing, infectious periods are considered from 48 hours prior to the onset of symptoms for symptomatic cases or 48 hours prior to the initial positive test for asymptomatic cases, until the case is no longer considered infectious and meet the criteria for release from isolation. Release from isolation is dependent on an individual's vaccination and symptom status and varies between jurisdictions. Full details can be accessed in the CDNA National Guidelines (link above).[42]

Centers for Disease Control and Prevention (CDC)

The Centers for Disease Control and Prevention (CDC) also recently updated its definition of a close contact (January 4 2022) in their *Interim Guidance on Developing a COVID-19 Case Investigation & Contract Tracing Plan: Overview*. The new definition is available here: https://www.cdc.gov/coronavirus/2019-ncov/php/contact-tracing/contact-tracing-plan/appendix.html[82]

A **close contact** is defined through proximity and duration of exposure. Specifically, a close contact is a person who has been:

- within 6 feet (1.8 metres) of an infected person[r]
  for a cumulative duration of 15 minutes or more over a 24-hour period (for example, 3 separate exposures of 5 minutes, within 24 hours).

Exceptions apply to K–12 students in the indoor classroom setting or a structured outdoor setting provided both the infected and exposed student correctly and consistently wore well-fitted masks throughout the entire exposure period. This does not apply to teachers, staff or other adults in an indoor school setting.[82]

[r] An infected person is considered one who is laboratory-confirmed or a clinical diagnosis.

Appendix B: Search strategy

No.	Reason	Query	Results (6 May 2020)	Results (27 Sep 2021)
1	COVID-19 pandemic	((((((("COVID-19" [tiab]) OR "SARS-CoV-2" [tiab]) OR "2019-nCoV" [tiab]) OR coronavirus [tiab]) OR "novel coronavirus" [tiab]) OR "corona virus" [tiab]) OR "severe acute respiratory syndrome coronavirus" [tiab]	19,687	183,700
2	Clinical presentation	((((((((((infecti* [tiab]) OR pathology [tiab]) OR pathological [tiab]) OR sign [tiab]) OR signs [tiab]) OR symptom [tiab]) OR symptoms [tiab]) OR symptomatic [tiab]) OR asymptomatic [tiab]) OR "clinical presentation" [tiab]) OR "clinical findings" [tiab]) OR pneumonia [tiab]	3,494,934	3,873,845
3	Point-of-care and serologic testing	((((((((((("Point-of-Care Testing"[Mesh]) OR (((point*of*care OR rapid OR bedside OR real*time OR near*patient OR fast OR prompt OR early) AND (test OR tests OR testing OR assay* OR PCR OR molecular OR diagnostic OR diagnosi* OR diagnostics OR diagnose* OR detection OR assessment* OR use*)))) OR ((Bedside AND (Computing OR Technology)))) OR ((“in field detection” OR POC OR POCT)))))) OR ((((((((((("Serologic Tests"[Mesh]) OR "Molecular Diagnostic Techniques"[Mesh]) OR ((“IgM” OR “IgG” OR “Ag”))) OR ((Immunoglobulin OR “antiviral immunoglobulin-G”))) OR ((Serologic* AND (test OR testing OR tests OR conversion* OR assay* OR analysis OR diagnostic OR diagnostics OR diagnosi* OR diagnose* OR screen*)))) OR ((Serology or seroconversion OR seroepidemiology OR serodiagnos* or seroprevalence*))) OR (((Antibod* AND (test OR tests OR testing OR serum OR detection* OR response*))))) OR ((Antigen OR antigeni* OR antigens*))) OR Immunoassa*) OR ((Molecular AND (diagnostic OR diagnostics OR diagnosi* OR diagnose*)))) OR Dynamic* profile))))	4,672,773	5,047,232
4	Diagnosis	((((((((((((("Diagnosis"[Mesh]) OR (("Diagnostic Techniques and Procedures"[Mesh]))) OR "Diagnostic Tests, Routine"[Mesh]) OR “Diagnostic Test Approval"[Mesh]) OR "Reagent Kits, Diagnostic"[Mesh]) OR "Predictive Value of Tests"[Mesh]) OR (("Sensitivity and Specificity"[Mesh]))) OR ((detect* OR laboratory OR evaluat* OR validat* OR clinical OR perform* OR sensitivity OR specificity OR area under the curve OR positive predictive value OR PPV OR negative predictive value OR NPV OR predictive value OR feasibility OR accuracy OR likelihood ratio OR false negative OR false positive OR Positive rate OR validation OR diagnostic odds ratio OR DOR OR valid*))) OR ((Diagnostic AND (value OR panel OR tool*)))) OR ((diagnosa* OR diagnosi* OR diagnose* OR diagnoss* OR diagnostic OR diagnostics))) OR (((Test OR tests OR testing) AND (infection OR virus OR disease OR diseases OR disease, OR antibod* OR blood OR nucleic acid or diagnostic OR diagnostics OR diagnosi* OR diagnose* OR diagnose*))))))	17,661,043	20,674,550
5	Computed	((((((((((("Radiography, Thoracic"[Mesh]) OR "Tomography, X-Ray Computed"[Mesh]) OR “Tomography, X-Ray”	664,529	127,375

No.	Reason	Query	Results (6 May 2020)	Results (27 Sep 2021)
	tomography imaging	[Mesh]) OR ((CT X*Ray* OR CT))) OR (((CT OR CAT OR chest OR lung or lungs or thoracic* OR thorax*) AND (Scan or screen* or imaging or film or radiograph* or radiogram or radiolog*)))) OR Compute* tomograph*) OR ((Cine-CT or "Cine CT"))) OR (((Thoracic* OR thorax* OR lung OR lungs OR Chest) AND CT))) OR (("Chest CT" AND (scan or imaging)))) OR ((X*ray* computed or x-ray compute*))) OR ((Compute* assist* tomograph* OR compute* axial tomograph*))) OR ((chest radiological imaging OR Roentgenolog* or roentgen ray*or roentgen OR Grenz Ray* or X*Radiation*))		
6	X-ray imaging	((((((("Radiography, Thoracic"[Mesh]) OR "Mass Chest X-Ray"[Mesh]) OR "X-Rays"[Mesh]) OR (((CXR OR CR OR x*ray* OR radiograph*)))) OR (((chest AND (film* OR radiograph*))))) OR ((((chest OR lung OR lungs OR thoracic* OR thorax*) AND (x*ray* OR radiograph* or radiogram* or radiolog*))))) OR (((Chest X-ray radiography OR chest radiological imaging OR thoracic radiology OR Roentgenolog* or roentgen ray*or roentgen OR Grenz Ray* or X*Radiation*)))	1,438,818	1,555,263
7	RT-PCR testing	((((((((((((((((((((((("Polymerase Chain Reaction"[Mesh]) OR "Reverse Transcriptase Polymerase Chain Reaction"[Mesh]) OR "Real-Time Polymerase Chain Reaction"[Mesh]) OR (((polymerase chain reaction) OR "PCR" OR "PCRs" OR ((Inverse OR Nested OR Anchored OR Kinetic) AND (Polymerase Chain Reaction)))))) OR ((reverse AND (transcriptase OR transcription) AND (PCR OR PCRs OR polymerase chain reaction)))) OR ((RT-PCR OR RT-PCR diagnostic panel OR RT-PCR assay* OR rRT-PCR OR qPCR OR qRT-PCR OR RT-qPCR OR mPCR OR WHO-PCR))) OR ((RT-PCR OR (RT-PCR diagnostic panel) OR (RT-PCR assay*) OR rRT-PCR OR qPCR OR qRT-PCR OR RT-qPCR OR mPCR OR WHO-PCR))) OR (((Real*Time AND (Polymerase Chain Reaction OR PCR OR PCRs OR RT-PCR))))) OR ((Real*time AND ((reverse AND (transcriptase OR transcription)) AND (PCR OR PCRs OR polymerase chain reaction))))) OR ((Real*time AND RT-PCR) OR ((reverse real*time) AND (PCR OR PCRs OR polymerase chain reaction)) OR ((real reverse AND (transcriptase OR transcription)) AND (PCR OR PCRs OR polymerase chain reaction)))) OR ((Quantitative Real*Time AND (Polymerase Chain Reaction OR PCR OR PCRs)))) OR ((((qualitative AND (real*time)) AND ((reverse AND (transcriptase OR transcription)) AND (PCR OR PCRs OR polymerase chain reaction)))))) OR ((Multiplex AND (PCR OR PCRs OR polymerase chain reaction)))) OR ((nucleic acid OR nucleic acid detection OR RNA))) OR (("Hologic Panther Fusion" OR "Hologic" OR "Hologic Panther" OR "DiaSorin Simplexa" OR "DiaSorin" OR "Roche Cobas 6800" OR "DiaSorin Simplexa COVID*19 Direct" OR "Cepheid Xpert Xpress SARS*CoV*2" OR "Cepheid Xpert Xpress" OR "QIAstat-Dx Respiratory SARS*CoV*2 Panel" OR "QIAstat-SARS" OR "QIAstat"))) OR (((lateral flow immunoassay) OR "LFIA"))) OR "LAMP assay" [Supplementary Concept]) OR ((((reverse AND (transcriptase OR transcription)) AND (loop*mediated isothermal amplification)) OR "RT-LAMP" OR (loop*mediated isothermal amplification) OR LAMP))) OR (((open reading frame 1ab) OR ORF1ab))) OR ((((magnetic chemiluminescence	2,724,819	2,947,444

No.	Reason	Query	Results (6 May 2020)	Results (27 Sep 2021)
		enzyme immunoassay) OR MCLIA)))) OR (((magnetic chemiluminescence enzyme immunoassay) OR MCLIA OR MCLA))) OR "Enzyme-Linked Immunosorbent Assay"[Mesh]) OR (((enzyme*linked immunosorbent assay*) OR ELISA))) OR "Luminescent Measurements"[Mesh]) OR (((chemiluminescence immunoassay) OR CLIA OR chemiluminescence))) OR spike protein) OR nucleocapsid protein		
8	Ultrasound imaging	(((((("Ultrasonography"[Mesh]) OR ((POCUS OR LU OR LUS OR US))) OR ((((Point*of*care OR bedside OR rapid OR real*time OR near*patient OR fast OR prompt OR early))) AND ((Ultrasound OR ultrasonography OR ultrasonic OR sonography OR sonographic)))) OR ((((Chest OR thoraci* OR thorax* OR lung or lungs))) AND ((Ultrasound OR ultrasonography OR ultrasonic OR sonography OR sonographic)))) OR ((((Chest OR thoraci* OR thorax* OR lung or lungs))) AND US)) OR ((((Point*of*care OR bedside OR rapid OR real*time OR near*patient OR fast OR prompt OR early))) AND ((Image OR imaging OR images)))) OR ((((Chest OR thoraci* OR thorax* OR lung or lungs))) AND ((Image OR imaging OR images)))) OR ((((Ultrasound OR ultrasonography OR ultrasonic OR sonography OR sonographic))) AND ((diagnosa* OR diagnosi* OR diagnose* OR diagnoss* OR diagnostic OR diagnostics)))	2,361,046	2,808,263
9	Treatments for COVID-19 in title	Ivermectin [TI] OR Stromectol [TI] OR Mectizan [TI] OR Eqvalan [TI] OR Ivomec [TI] OR "MK-933" [TI] OR "MK 933" [TI] OR MK933 [TI] OR Macrolide* [TI] OR "extracorporeal membrane oxygenation" [TI] OR ECMO [TI] OR "life support" [TI] OR Paracetamol [TI] OR Acetaminophen [TI] OR Antipyretic [TI] OR Amide* [TI] OR Ibuprofen [TI] OR NSAID [TI] OR Ibumetin [TI] OR Motrin [TI] OR Nuprin [TI] OR Rufen [TI] OR Salprofen [TI] OR Dolgit [TI] OR Brufen [TI] OR Phenylproprionate* [TI] OR "anti-inflammatory" [TI] OR "anti inflammatory" [TI] OR angiotensin [TI] OR "ACE-inhibitor*" [TI] OR "ACE inhibitor*" [TI] OR renin [TI] OR steroid* [TI] OR methylprednisolone [TI] OR tocilizumab [TI] OR atlizumab [TI] OR actemra [TI] OR roactemra [TI] OR heparin [TI] OR liquaemin heparin OR hydroxychloroquine [TI] OR oxychlorochin [TI] OR oxychloroquine [TI] OR hydroxychlorochin [TI] OR plaquenil [TI] OR sulfate [TI] OR quinolone* [TI] OR chloroquine [TI] OR chlorochin [TI] OR chingamin [TI] OR nivaquine [TI] OR khingamin [TI] OR aralen [TI] OR arequin [TI] OR arechine [TI] OR remdesivir [TI] OR alanine [TI] OR antiviral [TI] OR "anti-viral" [TI] OR "anti viral" [TI] OR vasodilator* [TI] OR corticosteroid* [TI] OR lipoic [TI] OR bevacizumab [TI] OR lopinavir [TI] OR protease [TI] OR pyrimidin* [TI] OR ritonavir [TI] OR cytochrome [TI] OR azole* [TI] OR interferon [TI] OR beta [TI] OR gamma [TI] OR "lopinavir-ritonavir" [TI] OR "lopinavir/ritonavir" [TI] OR azithromycin [TI] OR antibiotic* [TI] OR sumamed [TI] OR toraseptol [TI] OR vinzam [TI] OR Zithromax OR Azitrocin [TI] OR Ultreon [TI] OR oseltamivir [TI] OR interleukin [TI] OR lenzilumab [TI] OR monoclonal [TI]	1,115,209	1,183,389
10	Sensitivity string	2 OR 3 OR 4 OR 5 OR 6 OR 7 OR 8	19,561,598	22,835,144
11	Specifying for	1 AND 10	15,340	145,294

No.	Reason	Query	Results (6 May 2020)	Results (27 Sep 2021)
	COVID-19			
12	Eliminating treatments for COVID-19 in Title	11 NOT 9	14,178	136,574
13	Specifying to timeframe since WHO was alerted of COVID-19	Apply filter: Publication date from 31 Dec 2019	5,762	121,562
14	Specifying for humans	Apply filter: Humans, and results imported into EndNote	1,395	74,968
15	Systematic review filter	((((((((((((((((((((((((((((((((((Embase*[tiab]) OR Cinahl*[tiab]) OR systematic overview*[tiab]) OR methodological overview*[tiab]) OR methodologic overview*[tiab]) OR methodological review*[tiab]) OR methodologic review*[tiab]) OR quantitative review*[tiab]) OR quantitative overview*[tiab]) OR quantitative synthes*[tiab]) OR pooled analy*[tiab]) OR Cochrane[tiab]) OR Medline[tiab]) OR Pubmed[tiab]) OR Medlars[tiab]) OR handsearch*[tiab]) OR meta-regression*[tiab]) OR metaregression*[tiab]) OR data synthes*[tiab]) OR data extraction[tiab]) OR data abstraction*[tiab]) OR mantel haenszel[tiab]) OR peto[tiab]) OR der-simonian[tiab]) OR dersimonian[tiab]) OR fixed effect*[tiab]) OR "Cochrane Database Syst Rev"[Journal]) OR "health technology assessment winchester, england"[Journal]) OR "Evid Rep Technol Assess (Full Rep)"[Journal]) OR "Int J Technol Assess Health Care"[Journal]) OR "GMS Health Technol Assess"[Journal]) OR "Health Technol Assess (Rockv)"[Journal]) OR "Health Technol Assess Rep"[Journal])) OR ((((indirect treatment[tiab]) OR mixed-treatment[tiab])) AND comparison*[tiab])) OR ((((((((((((((((((((systematic[sb]) OR meta-analysis[pt]) OR meta-analysis as topic[mh]) OR meta-analysis[mh]) OR meta analy*[tw]) OR integrative review*[tiab]) OR integrative overview*[tiab]) OR research integration*[tiab]) OR research overview*[tiab]) OR collaborative review*[tiab]) OR collaborative overview*[tiab]) OR systematic review*[tiab]) OR technology assessment*[tiab]) OR technology overview*[tiab]) OR "Technology Assessment, Biomedical"[mh]) OR HTA[tiab]) OR HTAs[tiab]) OR comparative efficacy[tiab]) OR comparative effectiveness[tiab]) OR outcomes research[tiab]) OR indirect comparison*[tiab])	NA	517,819
16	Specifying for systematic reviews	14 AND 15	NA	3,821

Appendix C: Full extraction for symptom prevalence

Table 14 Symptom prevalence in adults (highest to lowest)

Symptom	k	n	Prevalence (%)	95% CI
Fever[21]	156	15,921	78.8	76.2 to 81.3
Cough[21]	119	12,782	53.9	50.0 to 57.7
Malaise[21]	39	2,526	37.9	29.5 to 47.1
Fatigue[21]	99	13,680	32.2	28.0 to 36.6
Sputum production[25]	70	10,017	25	22 to 28
Hyposmia[25]	3	317	25	4 to 55
Expectoration[21]	61	8,748	24.2	21.0 to 27.8
Dyspnoea[25]	94	12,713	23	19 to 28
Myalgia[21]	78	10,728	21.3	18.1 to 24.9
Shortness of breath[21]	82	11,205	18.99	15.7 to 22.8
Chest tightness/distress[24]	25	3,632	18.7	12.5 to 25
Rigors[25]	17	2,834	18	13 to 22
Wheeze[25]	16	2,013	17	9 to 26
Chills/shivering[21]	28	4,430	15.7	12.3 to 19.7
Anorexia[21]	30	3,610	13.99	10.4 to 18.5
Sore throat[25]	78	11,721	12	10 to 14
Headache[21]	76	12,382	9.7	8.3 to 11.3
Diarrhoea[21]	94	12,149	9.5	7.8 to 11.5
Dizziness or confusion[21]	24	2,350	9.4	7.1 to 12.4
Chest pain[21]	32	3,512	9.0	6.2 to 13.1
Rhinorrhoea[21]	43	6,072	7.5	5.7 to 9.6
Nausea[21]	38	5,599	6.96	5.3 to 9.1
Nasal congestion[25]	10	2,584	5	3 to 7
Vomiting[21]	48	7,484	4.7	3.8 to 5.8
Abdominal pain[21]	23	3,350	4.5	3.3 to 6.2
Hypogeusia[25]	2	220	4	1 to 8
Conjunctivitis[25]	9	2,715	2	1 to 4
Haemoptysis[25]	21	4,698	2	1 to 2

Abbreviations
CI = confidence interval; **k** = number of studies; **n** = number of patients.
Notes
Symptoms not identified in the original guidance document are highlighted in grey.

Table 15 Symptom prevalence in children (≤18 years of age) (highest to lowest)

Symptom	k	n	Prevalence %	95% CI
Fever[22]	48	1,494	51	45 to 57
Cough[22]	45	1,435	41	35 to 47
Nasal congestion[22]	33	623	17	6 to 27
Sore throat[22]	38	1,040	16	7 to 25
Expectoration[27]	6	NR	15	9.2 to 23.6
Rhinorrhoea[22]	36	990	14	8 to 19
Myalgia or fatigue[22]	42	1,253	12	7 to 17
Tachycardia[22]	35	950	12	3 to 21
Headache[83]	6	546	10	1 to 19
Tachypnoea[22]	29	1,034	9	4 to 14
Diarrhoea[22]	42	1,250	8	6 to 11
Vomiting[22]	42	1,238	7	5 to 10
Dyspnoea[28]	21	1,284	7	2.3 to 13.5
Sputum production[26]	5	10	6	1 to 11
Abdominal pain[28]	12	1,047	3.6	1.7 to 6
Hyposmia/anosmia[27]	6	NR	3.5	1.4 to 8.1
Chest pain[22]	34	673	3	0 to 5
Hypoxemia[22]	33	623	3	1 to 4

Abbreviations
CI = confidence interval; **k** = number of studies; **n** = number of patients; **NR** = not reported.
Notes
Symptoms not identified in the original guidance document are highlighted in grey.

Table 16 Symptom prevalence in those aged ≥60 years (highest to lowest)

Symptom	k	n	Prevalence %	95% CI
Fever[23]	11	782	83	66-97
Cough[23]	11	782	60	50-70
Dry cough[23]	4	432	56	43-69
Dyspnoea[23]	11	782	42	16-67
Fatigue[23]	9	691	33	16-52
Anorexia[23]	3	470	31	1-67
Sputum production[23]	8	654	28	17-39
Chest pain/discomfort[23]	5	500	26	1-57
Diarrhoea[23]	6	575	18	2-39
Myalgia[23]	9	746	15	1-33
Gastrointestinal symptoms[23]	3	169	15	0-79
Abdominal pain[23]	4	219	11	2-22
Sore throat[23]	5	639	10	0-25
Headache[23]	7	714	9	0-24
Nausea & vomiting[23]	4	543	8	0-23

Abbreviations
CI = confidence interval; **k** = number of studies; **n** = number of patients.
Notes
Symptoms not identified in the original guidance document are highlighted in grey.