The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) quickly drew the attention of virologists, epidemiologists, and infectious disease experts after its identification in Wuhan (China) in December 2019. The speed with which the virus was spreading and the imminent challenge to global health as the pathogen of coronavirus disease 2019 (COVID-19) were evident even before the World Health Organization declared the outbreak a pandemic in March 2020. The novelty of both the virus and the disease meant that very little information was initially available to guide decisions about treating and preventing illness. As the pandemic spread, there was an unprecedented push by investigators around the world to rapidly plan, conduct, and publish the results of clinical studies to provide such information. Effectively managing the subsequent explosion in evidence required consideration of two factors. Firstly, a process was needed to rapidly incorporate evidence into guidelines to ensure that recommendations remained up to date. Secondly, a single voice providing consistent advice to clinicians, rather than potentially conflicting advice from multiple bodies, was needed. The Australian National COVID-19 Clinical Evidence Taskforce (https://covid19evidence.net.au), originally comprising 32 organisations representing health care workers caring for people with COVID-19, was established to achieve these goals in Australia.

In this article, we describe the recommendations for treating non-pregnant adults with COVID-19 in Australia, as current on 1 August 2022 (version 61.0). Previous Taskforce publications have included recommendations specific for children and adolescents, for women who are pregnant or have recently given birth, and for older people and people requiring palliative care. Updated recommendations. As a result, a guideline can be updated and published within days of the publication of the findings of a major study, considerably more rapid than for a traditional guideline. We have previously published details of the methods used by the Taskforce.

**Methods**

In view of the unprecedented global research volume and the rapidly evolving evidence base, the Taskforce adopted a living approach to guideline development. Living guidelines enable rapid identification and translation of research findings into recommendations, ensuring that advice reflects current knowledge. Prior to the COVID-19 pandemic, Australian Living Evidence Consortium members had developed and continuously improved the methods of evidence-based living guideline production, and the ability to use the knowledge and systems developed during this process has been crucial to the success of the Taskforce.

The Taskforce uses a two-stage, high throughput process to ensure rapid updating of recommendations as new evidence becomes available, while maintaining scientific rigour and transparency. We use efficient methods for identifying, analysing, and reviewing evidence, then apply a streamlined process for developing, approving, and publishing new and updated recommendations. As a result, a guideline can be updated and published within days of the publication of the findings of a major study, considerably more rapid than for a traditional guideline. We have previously published details of the methods used by the Taskforce.

**Strength of recommendations**

The Taskforce uses the Grading of Recommendations Assessment, Development and Evaluation (GRADE) framework to determine the strength and direction of its recommendations. We primarily base recommendations regarding medications on the findings of randomised controlled trials, but data from observational studies are occasionally considered. Following analysis of the evidence, the relevant Taskforce expert panel develops a strong or conditional recommendation for or against an intervention, based on the balance of benefits and harms, certainty of evidence, and other considerations, including resource use, equity, and acceptability. The importance of each

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outcome is ranked and the threshold required to reach clinical significance defined. Certainty of evidence is determined for each outcome as high, moderate, low, or very low by applying a set of established criteria, including risk of bias, inconsistency, indirectness, imprecision, and publication bias. If sufficient high quality evidence is not available, the panel may develop a consensus recommendation based on expert opinion. Alternatively, insufficient evidence for determining the benefits and harms of a treatment may lead to an “only in research” recommendation; that is, the treatment should not be used outside randomised trials with appropriate ethics approval.

Definition of disease severity

Definitions of disease severity in people with COVID-19 have not always been consistent across trials. Further, trial publications frequently do not use the terms “mild”, “moderate”, “severe”, and “critical” to define the included patient group, instead providing clinical data such as respiratory rate, blood oxygen saturation, and presence of lung infiltrates. An important task for the Taskforce was to develop a consensus recommendation for defining levels of disease severity for adults (Supporting Information, table 1).

Recommendations

Disease-modifying treatments

The paucity of direct evidence initially available to the Taskforce is exemplified by the single consensus recommendation regarding therapeutic agents for COVID-19 in version 1.0 of the guideline (3 April 2020): “For patients with COVID-19 illness, only administer antiviral medications or other disease-modifying treatments in April 2020): “For patients with COVID-19 illness, only administer antiviral medications or other disease-modifying treatments in those with severe disease: Baricitinib (four studies, 1332 participants 16,17,19,20 ). As a result, the conditional recommendation for the use of remdesivir was retained for patients who are hospitalised and require supplemental oxygen but not ventilation (six studies, 6904 participants 15,25 ), but the Taskforce recommends against its use in patients who are hospitalised and require ventilation (four studies, 1332 participants 15,25,35,26 ).

Subsequently, three immunomodulators have been reported to reduce mortality risk in patients who require supplemental oxygen, and the Taskforce conditionally recommends their use in these patients. Tocilizumab (eleven studies, 7221 participants 21-31 ) and sarilumab (seven studies, 3668 participants 32-38 ), are monoclonal antibodies against the interleukin-6 receptor; baricitinib (four studies, 10815 participants 39-42 ) is a Janus kinase (JAK) inhibitor.

1 Drug treatments recommended for use in people with severe or critical coronavirus disease 2019 (COVID-19) (ie, who require supplemental oxygen)∧

| Drug treatment             | Category            | Recommendation                                                                 |
|----------------------------|---------------------|--------------------------------------------------------------------------------|
| Corticosteroids (systemic) | Recommended         | Use intravenous or oral dexamethasone for up to ten days (or another acceptable regimen) in adults who require supplemental oxygen (including mechanically ventilated patients). |
|                            | Conditional recommendation against | Do not routinely use dexamethasone (or other systemic corticosteroid) to treat COVID-19 in adults who do not require supplemental oxygen. |
| Remdesivir                 | Conditional recommendation | Consider using remdesivir in adults who require supplemental oxygen but not non-invasive or invasive ventilation. |
|                            | Not recommended      | Do not use remdesivir in adults hospitalised with COVID-19 who require non-invasive or invasive ventilation. |
| Tocilizumab                | Conditional recommendation | Consider using tocilizumab in adults who require supplemental oxygen, particularly when there is evidence of systemic inflammation. |
| Sarilumab                  | Conditional recommendation | Consider using sarilumab in adults who require high-flow oxygen, non-invasive ventilation, or invasive mechanical ventilation. |
| Baricitinib                | Conditional recommendation | Consider using baricitinib in adults hospitalised with COVID-19 who require supplemental oxygen. |
| Casirivimab/imdevimab      | Conditional recommendation | Consider using casirivimab/imdevimab in SARS-CoV-2 antibody-seronegative adults hospitalised with moderate to critical COVID-19. |
|                            | Not recommended      | Do not use casirivimab/imdevimab in SARS-CoV-2 antibody-seropositive adults hospitalised with moderate to critical COVID-19. |

SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2. * Status: 1 August 2022. For full recommendations, see Supporting Information, table 2.
In addition, two studies reported a benefit from casirivimab/imdevimab (Ronapreve; monoclonal antibodies against the SARS-CoV-2 spike protein) in adult inpatients seronegative for SARS-CoV-2 antibodies (3673 patients), but not in patients seropositive at baseline (7202 patients).

Adults who do not require supplemental oxygen

Prior to 26 August 2021, there were no treatment options for preventing disease progression in people with mild COVID-19 (ie, those who do not require supplemental oxygen). Almost eighteen months after the inception of the Taskforce and 64 recommendations regarding 57 different treatments, sotrovimab (Xevudy) received the first conditional recommendation, for use in people with mild COVID-19 at high risk of disease progression (one study, 1057 participants). The following month, we published a conditional recommendation for the use of inhaled budesonide in people with mild COVID-19 and one or more risk factors for disease progression. The Taskforce subsequently considered budesonide and ciclesonide sufficiently similar to justify pooling trial data, resulting in a single consensus recommendation for both inhaled corticosteroids (five studies, 2668 participants).

At the beginning of 2022, the Taskforce published several additional recommendations regarding treatments for people with mild COVID-19 and one or more risk factors for disease progression. Facilitated by early access to confidential Therapeutic Goods Administration clinical study reports, the Taskforce conditionally recommended casirivimab/imdevimab (Ronapreve; three studies, 5063 participants), the antiviral agents molnupiravir (Lagevrio; one study, 1433 participants) and nirmatrelvir/ritonavir (Paxlovid; one study, 2246 participants), and the anti-spike monoclonal antibodies regdanvimab (Regkirona; two studies, 1629 participants) and tixagevimab/cilgavimab (Evusheld; one study, 903 participants). More recently, findings of a clinically significant reduction in the hospitalisation of people with mild illness treated with the antiviral agent remdesivir (Veklury) have been published (one study, 562 participants).

The inclusion and exclusion criteria of the cited studies were similar. With few exceptions, each included adult outpatients who were not vaccinated against SARS-CoV-2 and had one or more risk factors for disease progression. In addition, most studies included only small numbers of immunosuppressed patients. Most of our conditional recommendations are therefore accompanied by a consensus recommendation specific to people considered most likely to benefit from treatment but for whom there is little or no direct evidence available, such as immunocompromised people and people partially vaccinated against SARS-CoV-2 and considered to be at high risk of progression because of their age and risk factors.

Treatments that are not recommended (“do not use”)

The Taskforce has recommended against several treatments and treatment combinations that are either ineffective (neither benefit nor harm the patient) or actively harm the patient (Box 3). The earlier “only in research” recommendation for hydroxychloroquine, based on the unclear findings of seven trials (1081 participants), was revised to “do not use” following publication of the findings of the RECOVERY trial on 15 July 2020, which added data for a further 4716 participants. Findings from an additional fourteen studies support the conclusion that hydroxychloroquine provides no benefit for patients with COVID-19 but increases the incidence of adverse events.

Recommendations against several other treatments have subsequently been made, primarily on the basis of the findings of the RECOVERY trial: convalescent plasma (fifteen studies, 16122 participants), lopinavir/ritonavir (nine studies, 9389 participants), colchicine (eight studies, 17782 participants), azithromycin (eight studies, 10728 participants), and aspirin (one study, 14892 participants). The recommendation against interferon β-1a was primarily based on the findings of the SOLIDARITY trial (four studies, 4646 participants); that against ivmectin was based on the findings of nineteen studies (3869 participants). Recommendations against two dual treatments (hydroxychloroquine/azithromycin, interferon β-1a/lopinavir/ritonavir) were made because of limited direct evidence for both the absence of a synergistic effect and for the components having little or no effect as stand-alone treatments.

Treatments for which there is insufficient evidence of efficacy (“only in research”)

The largest group of recommendations in the Taskforce guideline comprises “only in research” recommendations for treatments for which there is insufficient evidence for determining safety and effectiveness (Box 3). Although preliminary evidence for a beneficial effect in COVID-19 is available for many of these treatments, further evidence is needed to determine whether the reported findings are reliable indicators of their effectiveness in real-world practice.

Chemoprophylaxis

Three treatments have been reviewed for their ability to prevent SARS-CoV-2 infection and to improve patient outcomes when used for pre- or post-exposure prophylaxis (Box 4). No benefit for averting laboratory-confirmed COVID-19 was found for hydroxychloroquine, used either prior to (three studies, 1884 participants) or after exposure to people infected with SARS-CoV-2 (two studies, 3135 participants); its use is therefore not recommended. Casirivimab/imdevimab (Ronapreve) is conditionally recommended for post-exposure prophylaxis, based on one report of a significant reduction in symptomatic and confirmed infections (one study, 1505 participants). More recently, the Taskforce has given a highly specific consensus recommendation for considering tixagevimab/cilgavimab (Evusheld) for pre-exposure prophylaxis in people who are severely immunocompromised (one study, 5197 participants).

Respiratory support

As the major complication of COVID-19 pneumonia is respiratory deterioration, one of the Taskforce focuses has been developing recommendations regarding the safety and effectiveness of various methods of respiratory support. Unlike the use of therapeutic agents, limited direct and high quality evidence has been available to inform these recommendations.

Based on the best available evidence (primarily systematic reviews and observational data) and expert clinical judgement, the Taskforce Hospital and Acute Care Panel formulated eleven recommendations regarding supplemental oxygen — continuous positive airway pressure and high-flow nasal oxygen therapy, non-invasive ventilation, invasive ventilation and extracorporeal membrane oxygenation — and the use of additional therapies,
### 2 Drug treatments recommended for use in people with mild coronavirus disease 2019 (COVID-19) (ie, who do not require supplemental oxygen)*

| Treatment                  | Category                | Recommendation                                                                                                                                 |
|----------------------------|-------------------------|---------------------------------------------------------------------------------------------------------------------------------------------|
| Casirivimab/Imdevimab      | Conditional recommendation | • Consider casirivimab/imdevimab within seven days of symptom onset for adults who do not require supplemental oxygen and have one or more risk factors for disease progression.  
- When infection with Omicron BA.1, BA.2, BA.4 or BA.5 is confirmed or likely, use of casirivimab/imdevimab should only be considered if other treatments are not suitable or available. |
| Corticosteroids (inhaled) | Conditional recommendation | • Consider inhaled corticosteroids (budesonide or ciclesonide) within 14 days of symptom onset for adults who do not require supplemental oxygen and have one or more risk factors for disease progression. |
| Molnupiravir (Lagevrio)   | Consensus recommendation | • Consider molnupiravir within five days of symptom onset for unvaccinated adults who do not require supplemental oxygen and have one or more risk factors for disease progression if other treatments (such as remdesivir or nirmatrelvir/ritonavir) are not suitable or available.  
- Within this group, decisions about the appropriateness of molnupiravir treatment should be based on the individual's risk of severe disease, including their age, presence of multiple risk factors, and vaccination status (including number of doses and time since last dose or most recent SARS-CoV-2 infection). |
| Nirmatrelvir/Ritonavir (Paxlovid) | Conditional recommendation | • Consider nirmatrelvir/ritonavir within five days of symptom onset in unvaccinated adults who do not require supplemental oxygen and are immunocompromised, or who are at particularly high risk of severe disease because of advanced age and multiple risk factors.  
- Within this group, decisions about the appropriateness of nirmatrelvir/ritonavir treatment should be based on the individual's risk of severe disease, including their age, presence of multiple risk factors, and vaccination status (including number of doses and time since last dose or most recent SARS-CoV-2 infection).  
- When infection with Omicron BA.1, BA.2, BA.4 or BA.5 is confirmed or likely, nirmatrelvir/ritonavir should only be considered if other treatments are not suitable or available. |
| Regdanvimab (Regkirona)   | Conditional recommendation | • Consider regdanvimab within seven days of symptom onset for unvaccinated adults who do not require supplemental oxygen and have one or more risk factors for disease progression.  
- Within this group, decisions about the appropriateness of regdanvimab treatment should be based on the individual's risk of severe disease, including their age, presence of multiple risk factors, SARS-CoV-2 vaccination status, and time since vaccination.  
- When infection with Omicron BA.1, BA.2, BA.4 or BA.5 is confirmed or likely, regdanvimab should only be considered if other treatments are not suitable or available. |
| Remdesivir (Veklury)      | Conditional recommendation | • Consider remdesivir within seven days of symptom onset in unvaccinated adults who do not require supplemental oxygen and have one or more risk factors for disease progression.  
- Within this group, decisions about the appropriateness of remdesivir treatment should be based on the individual's risk of severe disease, including their age, presence of multiple risk factors, and vaccination status (including number of doses and time since last dose or most recent SARS-CoV-2 infection).  
- When infection with Omicron BA.1, BA.2, BA.4 or BA.5 is confirmed or likely, remdesivir should only be considered if other treatments are not suitable or available. |
| Sotrovimab (Xevudy)       | Conditional recommendation | • Consider sotrovimab within five days of symptom onset for unvaccinated adults who do not require supplemental oxygen and are immunocompromised, or are at particularly high risk of severe disease because of advanced age and multiple risk factors.  
- When infection with Omicron BA.1, BA.2, BA.4 or BA.5 is confirmed or likely, sotrovimab should only be considered if other treatments are not suitable or available. |
| Tixagevimab/Cilgavimab (Evusheld) | Conditional recommendation | • Consider tixagevimab/cilgavimab within five days of symptom onset for unvaccinated adults who do not require supplemental oxygen and who have one or more risk factors for disease progression.  
- Within this group, decisions about the appropriateness of tixagevimab/cilgavimab treatment should be based on the individual's risk of severe disease, including their age, presence of multiple risk factors, and vaccination status (including number of doses and time since last dose or most recent SARS-CoV-2 infection).  
- When infection with Omicron BA.1, BA.2, BA.4 or BA.5 is confirmed or likely, tixagevimab/cilgavimab should only be considered if other treatments are not suitable or available.  
- When infection with Omicron BA.2, BA.4 or BA.5 is confirmed or likely, use of tixagevimab/cilgavimab should only be considered when other treatments are not suitable or available. |
such as prone positioning and recruitment manoeuvres, positive end-expiratory pressure, and video laryngoscopy. Each of these recommendations includes the caveat that personal protective equipment be used and that these treatments not be provided in shared wards or hospital department cubicles, or during inter-hospital patient transfer and retrieval (Box 5).

Supportive recommendations
The Taskforce developed several supportive care recommendations. One focus has been the use of anticoagulants for venous thromboembolism prophylaxis in patients with COVID-19. The REMAP-CAP trial[^16] found that therapeutic
### 5 Respiratory support recommendations for patients with coronavirus disease 2019 (COVID-19)*

| Topic                                           | Category                  | Recommendation                                                                                           |
|-------------------------------------------------|---------------------------|-----------------------------------------------------------------------------------------------------------|
| Guiding principles of care                       | Consensus recommendation  | • For patients receiving respiratory support, use single and negative pressure rooms when possible; if unavailable, use single rooms or shared ward spaces with cohorting of patients with confirmed COVID-19. Ensure that precautions to reduce contact, droplet, and airborne transmission are observed. Health care workers should be fully vaccinated and wear fit-tested N95 masks. |
| Continuous positive airway pressure (CPAP)      | Conditional recommendation| • Consider CPAP for patients with hypoxaemic respiratory failure in whom oxygen saturation is not maintained within target range despite oxygen delivery by nasal prongs or mask. • CPAP therapy is preferred for patients with persistent hypoxaemia associated with COVID-19 (defined as requiring $F\text{O}_2 \geq 0.4$ to maintain oxygen saturation in target range). Adjust continuous positive airway pressure as required; most patients require pressures of 10–12 cmH₂O. Excessive pressure may increase risk of pneumothorax. Titrate oxygen to maintain saturation in the target range. Direct evidence for the value of bi-level positive pressure support is currently insufficient. • If CPAP is not available or not tolerated, consider high-flow nasal oxygen (HFNO), with the same safety parameters. • Monitor patients receiving CPAP or HFNO closely at all times; liaise with intensive care unit in case of deterioration. Do not delay endotracheal intubation and invasive mechanical ventilation of a patient whose condition deteriorates despite optimised, less invasive respiratory therapies. |
| Respiratory management of patients whose condition deteriorates | Consensus recommendation  | • Do not delay endotracheal intubation and mechanical ventilation in a patient whose condition deteriorates despite optimised, less invasive respiratory therapies. |
| Video laryngoscopy                               | Conditional recommendation| • In adults undergoing endotracheal intubation, prefer video laryngoscopy to direct laryngoscopy if trained operator is available. |
| Neurmuscular blockers                            | Conditional recommendation against| • For mechanically ventilated adults and moderate to severe acute respiratory distress syndrome, do not routinely use continuous infusions of neuromuscular blocking agents. |
| Positive end-expiratory pressure (PEEP)          | Consensus recommendation  | • For mechanically ventilated adults and moderate to severe acute respiratory distress syndrome, prefer higher PEEP strategy (PEEP > 10 cmH₂O) to lower PEEP strategy. • We do not expect to update this low priority recommendation in the near future, but will continue to review the published evidence. |
| Prone positioning                                | Consensus recommendation  | • For mechanically ventilated adults with hypoxaemia despite optimised ventilation, consider prone positioning for more than 12 hours a day. |
| Prone positioning and cardiopulmonary resuscitation (CPR) | Conditional recommendation | • For adults with respiratory symptoms receiving any form of supplemental oxygen therapy and not yet intubated, consider prone positioning for at least three hours a day, if tolerated, and closely monitor the patient. Prone positioning should not delay endotracheal intubation and mechanical ventilation in a patient whose condition deteriorates despite optimised less invasive respiratory therapies. |
| Prone positioning and cardiopulmonary resuscitation (CPR) | Consensus recommendation | • For patients in prone position who require CPR, return the patient to supine position and commence resuscitation, when safe and feasible. • If returning the patient to supine position is not safe and feasible, commence CPR in prone position. Once it is safe and feasible, return the patient to supine position and continue CPR. |
| Recruitment manoeuvres                           | Consensus recommendation  | • For mechanically ventilated adults with hypoxaemia despite optimised ventilation, consider recruitment manoeuvres, but not staircase or stepwise (incremental PEEP) recruitment manoeuvres. |
| Extracorporeal membrane oxygenation (ECMO)       | Conditional recommendation| • Consider early referral to an ECMO centre for mechanically ventilated adults who develop refractory respiratory failure despite optimised ventilation, including prone positioning and neuromuscular blockers. |

$F\text{O}_2 = \text{fraction of inspired oxygen.}$ * Status: 1 August 2022. For full recommendations, see Supporting Information, table 5.

Dose anticoagulation achieved a statistically significant greater reduction in blood clots than prophylactic dosing, but increased the risk of significant bleeding. Consequently, the Taskforce conditionally recommended against routinely offering therapeutic anticoagulation, instead supporting prophylactic dose anticoagulation in patients with moderate, severe, or critical COVID-19.

Another important consideration is whether to maintain or cease therapies for other diseases in patients with COVID-19. A systematic review of observational studies found no adverse effects of continued angiotensin-converting enzyme inhibitor or angiotensin II receptor blocker therapy in patients with COVID-19, and the Taskforce recommended these treatments be maintained. A further consensus recommendation supports maintaining steroid therapy for people with asthma or chronic obstructive pulmonary disease. Three linked consensus recommendations advise cessation of oral menopausal hormone therapy in women with severe or critical COVID-19, and consideration of cessation for women with mild or moderate COVID-19, because of the greater risk of venous thromboembolism in these patients.

Finally, the Taskforce has reviewed a large multicentre study of the timing of surgery after COVID-19. Given the reported increase in harms, the Taskforce conditionally recommended against elective surgery within eight weeks of recovery from acute COVID-19, and conditionally recommended multimodal pre-operative assessment of people who subsequently undergo surgery (Box 6).

### Discussion

From its inception in March 2020, the National COVID-19 Clinical Evidence Taskforce has implemented a robust process to continually maintain up-to-date recommendations for treating people with COVID-19. It involves daily searches for published evidence, rapid appraisal and analysis of study findings, and frequent meetings of clinical expert panels in which recommendations are developed and ratified. During its first two years, the guideline was updated 106 times, and
## 6 Additional supportive recommendations for managing adults with coronavirus disease 2019 (COVID-19)*

| Treatment                                      | Category                                    | Recommendation |
|------------------------------------------------|---------------------------------------------|----------------|
| Venous thrombo-embolism prophylaxis            | Conditional recommendation                   | Use prophylactic anticoagulant doses, preferably low molecular weight heparin (LMWH) (eg, enoxaparin 40 mg once daily or dalteparin 5000 IU once daily), in adults with moderate, severe, or critical COVID-19 unless contraindicated (eg, risk of major bleeding). If the estimated glomerular filtration rate is below 30 mL/min/1.73 m², unfractionated heparin or clearance-adjusted LMWH doses may be used (eg, enoxaparin 20 mg once daily). |
|                                               | Conditional recommendation against          | Do not routinely offer therapeutic anticoagulant doses to adults with moderate, severe, or critical COVID-19. There is no additional indication for therapeutic anticoagulant dosing for adults with severe or critical COVID-19 beyond current standard best practice. |

### Therapies for comorbid conditions

- **ACEIs/ARBs (hypertension)**
  - Recommended
  - In patients receiving ACEIs/ARBs, no evidence supports deviating from usual care; these medications should be continued unless contraindicated.

- **Steroids (asthma, COPD)**
  - Consensus recommendation
  - Use inhaled or oral steroids for managing co-existing asthma or COPD as usual for viral exacerbation of asthma or COPD. Do not use nebulisers.

- **Oestrogen-containing therapies**
  - Consensus recommendation
  - In women taking oral menopausal hormone therapy (MHT), manage these medications as usual. In women who stop or suspend oral MHT, review the indication for doing so and consider transitioning to a transdermal preparation. Manage transdermal MHT as usual.

- **Surgery following COVID-19 infection**
  - Conditional recommendation against
  - Do not routinely perform elective surgery within seven weeks of recovery from acute illness or following confirmed SARS-CoV-2 infection unless the risk of deferring surgery is considerable, such as disease progression or clinical priority. Very low risk or low risk procedures, such as endoscopy or skin incision, should be considered if warranted by clinical need.

- **Conditional recommendation**
  - For people undergoing elective surgery following confirmed SARS-CoV-2 infection, consider a multisystem pre-operative assessment in consultation with a unit familiar with the assessment of people recovering from COVID-19.

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*Status: 1 August 2022. For full recommendations, see Supporting Information, table 6.*

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its scope has increased from nine to 176 recommendations covering therapeutic treatment and respiratory support. The complete current version of the guideline, including specific recommendations for particular patient groups, clinical flowcharts, and decision support tools, is available at https://covid19evidence.net.au.

The work of the Taskforce will continue to evolve, particularly in areas such as the post-COVID-19 syndrome (“long COVID”), for which a treatment and care evidence base remains to be established. In addition, factors such as the vaccination status of trial participants, the paucity of direct evidence for the treatment of people infected with more recent SARS-CoV-2 variants, and laboratory findings regarding the activity of monoclonal antibodies against such variants, will be considered.

The ability to capture and assess new evidence quickly, facilitated by the committed work of the more than 250 volunteer members of the guideline panels, leadership group, steering committee, and other stakeholders, has shown that it is possible to maintain clear, up-to-date guidelines for a high priority area in which evidence is rapidly evolving, while speaking with a unified voice.

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1. World Health Organization. WHO Director General’s opening remarks at the media briefing on COVID-19. 11 March 2020. https://www.who.int/director-general/speeches/detail/who-director-general-s-opening-remarks-at-the-media-briefing-on-covid-19---11-march-2020 (viewed Aug 2022).
2. Fraile-Navarro D, Tendal B, Tingay D, et al. Clinical care of children and adolescents with COVID-19: recommendations from the National COVID-19 Clinical Evidence Taskforce. *Med J Aust* 2021; 216: 255-263. https://www.mja.com.au/journal/2021/216/5/clinical-care-child-ren-and-adolescents-covid-19-recommenda-tions-national-covid
3. Vogel J, Tendal B, Giles M, et al. Clinical care of pregnant and postpartum women with
COVID-19: living recommendations from the National COVID-19 Clinical Evidence Taskforce. Aust N Z J Obstet Gynaecol 2020; 60: 840-851.

Cheyne S, Lindley R, Smallwood N, et al. Care of older people and people requiring palliative care with COVID-19: guidance from the Australian National COVID-19 Clinical Evidence Taskforce. Med J Aust 2021; 216: 203-208. https://www.mja.com.au/journal/2022/216/care-older-people-and-people-requiring-palliative-care-COVID-19-guidance

Elliot J, Synnot A, Turner T, et al. Living Systematic Review Network. Living systematic reviews. 1. Introduction: the why, what, when and how. J Clin Epidem 2017; 9: 23-30.

Aki E, Meerpohl J, Elliot J, et al; Living Systematic Review Network. Living systematic reviews. 4. Living guideline recommendations. j Clin Epidem 2017; 9: 47-53.

White H, Tendal B, Elliot J, et al. Breathing life into Australian diabetes clinical guidelines. Med J Aust 2020; 212: 250-251. https://www.mja.com.au/journal/2022/212/breathing-life-australian-diabetes-clinical-guidelines

Elliott J, Lawrence R, Minx J, et al. Decision makers need constantly updated evidence synthesis. Nature 2021; 600: 383-385.

Tendal B, Vogel J, McDonald S, et al; National COVID-19 Clinical Evidence Taskforce. Weekly updates of national living evidence-based guidelines: methods for the Australian living guidelines for care of people with COVID-19. J Clin Epidem 2021; 131: 11-21.

Schünemann H, Brozek J, Guyatt G, Oxman A, editors. GRADE handbook. Updated 2013. https://gdt.gradepro.org/app/handbook/handbook.html (viewed Aug 2022).

World Health Organization. Corticosteroids for COVID-19. Living Guidance. 2 Sept 2022. https://www.who.int/publications/item/WHO-2019-nCoV-corticosteroids-2020.1 (viewed Aug 2022).

WHO Solidarity Trial Consortium. Repurposed antiviral drugs for Covid-19: interim WHO Solidarity Trial results. N Engl J Med 2021; 384: 497-511.

Schandelmaier S, Briel M, Varadhan R, et al. Development of the Instrument to assess the Credibility of Effect Modification Analyses (ICEMAN) in randomized controlled trials and meta-analyses. CMAJ 2020; 192: E901-E906.

Mahajan L, Singh AP, Gifty. Clinical outcomes of remdesivir in patients with moderate to severe COVID-19: a prospective randomised study. Indian J Anaesth 2021; 65 (Suppl 1): S41-S46.

Wang Y, Zhang D, Du G, et al. Remdesivir in adults with severe COVID-19: a randomised, double-blind, placebo-controlled, multicentre trial. Lancet 2020; 395: 1569-1578.

Beigel JH, Tomashek KM, Dodd LE, et al. Remdesivir for the treatment of Covid-19: final report. N Engl J Med 2020; 383: 1813-1826.

Spinner CD, Gottlieb RL, Criner GJ et al. Effect of remdesivir vs standard care on clinical status at 11 days in patients with moderate COVID-19: a randomized clinical trial. JAMA 2020; 324: 1048-1057.

Ader F, Bouscambert-Duchamp M, Hites M, et al. Remdesivir plus standard care of versus standard of care alone for the treatment of patients admitted to hospital with COVID-19 (DioCoVeRy): a phase 3, randomised, controlled, open-label trial. Lancet Infect Dis 2021; 22: 209-221.

WHO Solidarity Trial Consortium. Remdesivir and three other drugs for hospitalised patients with COVID-19: final results of the WHO Solidarity randomised trial and updated meta-analyses. Lancet 2022; 399: 1941-1953.

Hermine O, Mariette X, Tharaux PL, et al. Effect of tocilizumab vs usual care in adults hospitalized with COVID-19 and moderate or severe pneumonia: a randomized controlled trial. JAMA Intern Med 2020; 181: 32-40.

Stone JH, Frigault MJ, Serling-Boyd NJ, et al. Efficacy of tocilizumab in patients hospitalized with Covid-19. N Engl J Med 2020; 383: 2333-2344.

Salvarani C, Dolci G, Massari M, et al. Effect of tocilizumab vs standard care on clinical worsening in patients hospitalized with COVID-19 pneumonia: a randomized clinical trial. JAMA Intern Med 2020; 181: 263-271.

Salama C, Han J, Yau L, et al. Tocilizumab in patients hospitalized with Covid-19 pneumonia. N Engl J Med 2020; 384: 20-30.

Veiga VC, Prats JAGG, Farias DCL, et al. Effect of tocilizumab on clinical outcomes at 15 days in patients with severe or critical coronavirus disease 2019: randomised controlled trial. BMJ 2021; 372: n84.

REMAP-CAP Investigators. Interleukin-6 receptor antagonists in critically ill patients with Covid-19. N Engl J Med 2021; 384: 1491-1502.

Rosas IO, Bräu N, Waters M, et al. Tocilizumab in hospitalized patients with severe Covid-19 pneumonia. N Engl J Med 2021; 384: 1503-1516.

Wang D, Fu B, Peng Z, et al. Tocilizumab in patients with moderate or severe COVID-19: a randomized, controlled, open-label, multicenter trial. Front Med 2021; 15: 486-494.

RECOVERY Collaborative Group. Tocilizumab in patients admitted to hospital with COVID-19 (RECOVERY): a randomised, controlled, open-label, platform trial. Lancet 2021; 397: 1637-1645.

Soin AS, Kumar K, Choudhary NS, et al. Tocilizumab plus standard care versus standard care in patients in India with moderate to severe COVID-19-associated cytokine release syndrome (CDVINTOC): an open-label, multicentre, randomised, controlled, phase 3 trial. Lancet Resp Med 2021; 9: 511-521.

Rosas IO, Diaz G, Gottlieb RL, et al. Tocilizumab and remdesivir in hospitalized patients with severe COVID-19 pneumonia: a randomized clinical trial. Intensive Care Med 2021; 47: 1258-1270.

REMAP-CAP Investigators. Effectiveness of tocilizumab, sarilumab, and anakinra for critically ill patients with COVID-19: the REMAP-CAP COVID-19 immune modulation therapy domain randomised clinical trial [preprint]. medRxiv 2021.06.18.21259133, version 2; 25 June 2021. https://doi.org/10.1101/2021.06.18.21259133 (Viewed Aug 2022).

Hermine O, Mariette X, Porcher R, et al. Effect of interleukin-6 receptor antagonists in critically ill adult patients with COVID-19 pneumonia: two randomised controlled trials of the CORIMUNO-19 Collaborative Group. Eur Respir J 2020; 62: 2102523.
48 Clemency BM, Varughese R, Gonzalez-Rojas Y, et al. Efficacy of inhaled ciclesonide for outpatient treatment of adolescents and adults with symptomatic COVID-19: a randomized clinical trial. JAMA Intern Med 2022; 182: 42-49.

49 Ezer N, Belga S, Daneman N, et al. Inhaled and intranasal ciclesonide for the treatment of COVID-19 in adult outpatients: CONTAIN phase II randomised controlled trial. BMJ 2021; 375 e068060.

50 Song JY, Yoon JG, Seo YB, et al. Ciclesonide inhaler treatment for mild to moderate COVID-19: a randomized, open-label, phase 2 trial. J Clin Med 2021; 10: 3456.

51 Weinreich DM, Sivapalasingam S, Norton T, et al. REGEN-COV antibody combination and outcomes in patients with Covid-19. N Engl J Med 2021; 385: e81.

52 O'Brien MP, Forleo-Neto E, Sarkar N, et al. Effect of subcutaneous casirivimab and imdevimab antibody combination vs placebo on development of symptomatic COVID-19 in early asymptomatic SARS-CoV-2 infection: a randomized clinical trial. JAMA 2022; 327: 432-441.

53 Jayk Bernal A, Gomes da Silva MM, Musungaije DB, et al. Molnupiravir for oral treatment of Covid-19 in nonhospitalized patients. N Engl J Med 2021; 386: 509-520.

54 Hammond J, Leister-Tebbe H, Gardner A, et al. Oral nirmatrelvir for high-risk, nonhospitalized adults with COVID-19. N Engl J Med 2022: 383: 1397-1408.

55 Eom J, Yoon M, Steineu-Cercel A. Efficacy and safety of CT-P59 plus standard of care: a phase 2/3 randomized, double-blind, placebo-controlled trial in patients with mild-to-moderate SARS-CoV-2 infection [preprint]. Research Square, 15 Mar 2021. https://doi.org/10.21203/rs.3.rs-296518/v1 (viewed Aug 2022).

56 Celltrion Inc (Incheon, South Korea). Protocol number CT-P59 3.2: day 28 clinical study report (part 2) [unpublished report].

57 Montgomery H, Hobbs FDR, Padilla F, et al. Efficacy and safety of intramuscular administration of tixagevimab-cilgavimab for early outpatient treatment of COVID-19 (TACKLE): a phase 3, randomised, double-blind, placebo-controlled trial. Lancet Resp Med 2022; S2213-2600:00180-1 [online ahead of print].

58 Gottlieb RL, Vaca CE, Paredes R, et al. Early remdesivir to prevent progression to severe COVID-19 in outpatients. N Engl J Med 2022; 386: 305-315.

59 Chen L, Zhang ZY, Fu JG. Efficacy and safety of chloroquine or hydroxychloroquine in moderate type of COVID-19: a prospective open-label randomized controlled study [preprint]. medRxiv 2020.06.19.20186093; 22 June 2020. https://doi.org/10.1101/2020.06.19.20186093 (viewed Aug 2022).

60 Chen CP, Lin YC, Chen TC, et al. A multicenter, randomized, open-label, controlled trial to evaluate the efficacy and tolerability of hydroxychloroquine and a retrospective study in adult patients with mild to moderate coronavirus disease 2019 (COVID-19). PLoS One 2020; 15: e0242763.

61 Chen J, Liu D, Liu L. [A pilot study of hydroxychloroquine in treatment of patients with moderate COVID-19]. Zhongguo Da Xue Xue Bao Yi Xue Ban 2020; 49: 215-219.

62 Chen Z, Hu J, Zhang Z, et al. Efficacy of hydroxychloroquine in patients with COVID-19: results of a randomized clinical trial [preprint]. medRxiv 2020.03.22.20047058; 10 Apr 2020. https://doi.org/10.1101/2020.03.22.20047058 (viewed Aug 2022).

63 Mitjà O, Corbacho-Monné M, Ulbas M, et al. Hydroxychloroquine for early treatment of adults with mild coronavirus disease 2019: a randomized, controlled trial. Clin Infect Dis 2020; 73: e4073-e4081.

64 Skipper CP, Pastick KA, Engen NW, et al. Hydroxychloroquine in nonhospitalized adults with early COVID-19: a randomized trial. Ann Intern Med 2020; 173: 623-631.

65 Tang W, Cao Z, Han M, et al. Hydroxychloroquine in patients with mainly mild to moderate coronavirus disease 2019: open label, randomized controlled trial. BMJ 2020; 369: m1849.

66 RECOVERY Collaborative Group. Effect of hydroxychloroquine in hospitalized patients with COVID-19. N Engl J Med 2020; 383: 2030-2040.

67 Johnston C, Brown ER, Stewart J, et al. Hydroxychloroquine with or without azithromycin for treatment of early SARS-CoV-2 infection among high-risk outpatient adults: a randomized clinical trial. EclinicalMedicine 2021; 33: 100773.

68 Reis G, Moreira Silva EADS, Medeiros Silva DC, et al. Effect of early treatment with hydroxychloroquine or lopinavir and ritonavir on risk of hospitalization among patients with COVID-19: the TOGETHER randomized clinical trial. Lancet 2021; 397: 1397-1408.

69 Beltran Gonzalez JL, González Gámez M, et al. Hydroxychloroquine for COVID-19 with hydroxychloroquine or lopinavir and lopinavir/ritonavir plus IFN-β-1a and hydroxychloroquine in hospitalized patients with COVID-19. Clin Microbiol Infect 2021; 27: 1826-1837.

70 Hernandez-Cardenas C, Thirion-Romerio I, Rodríguez-Llamazares S, et al. Hydroxychloroquine for the treatment of severe respiratory infection by COVID-19: a randomized controlled trial. PLos One 2021; 16: e0257238.

71 Li L, Zhang W, Hu YU, et al. Effect of convalescent plasma therapy on time to clinical improvement in patients with severe and life-threatening COVID-19: a randomized clinical trial. JAMA 2020; 324: 460-470.

72 Agarwal A, Mukherjee A, Kumar G, et al. Convalescent plasma in the management of moderate covid-19 in adults in India: open label phase II multicentre randomised controlled trial (PLACID Trial). BMJ 2020; 371: m3993.

73 Gharbarhan A, Jordans CC, GeurtsvanKessel C, et al. Effects of potent neutralizing antibodies from convalescent plasma in patients hospitalized for severe SARS-CoV-2 infection. Nat Commun 2021; 12: 3189.

74 AlQahtani M, Abdulrahman A, Almadani A, et al. Randomized controlled trial of convalescent plasma therapy against standard therapy in patients with severe COVID-19 disease. Sci Rep 2021; 11: 9927.

75 Simonovich VA, Burgos Pratx LD, Scibona P, et al. A randomized trial of convalescent plasma in Covid-19 severe pneumonia. N Engl J Med 2020; 383: 619-629.

76 Libster R, Pérez Marc G, Wapper D, et al. Early high-titer plasma therapy to prevent severe Covid-19 in older adults. N Engl J Med 2021; 384: 610-618.

77 Rasheed AM, Fatak DF, Hashim HA, et al. The therapeutic potential of convalescent plasma therapy on critically-ill COVID-19 patients residing in respiratory care units in hospitals in Baghdad, Iraq. Infect Dis Rep 2022; 14: 1-9927.

78 Bégin P, Callum J, Jamula E, et al. Convalescent plasma for hospitalized patients with COVID-19: an open-label, randomized controlled trial. Nat Med 2021; 27: 2012-2024.

79 Faghi F, Alharthy A, Abdulaziz S, et al. Therapeutic plasma exchange in patients with life-threatening COVID-19: a randomized controlled clinical trial. Int J Antimicrob Agents 2021; 57: 106334.

80 Körper S, Weiss M, Zickler D, et al. Results of the CAPSID randomized trial for high-dose convalescent plasma in severe COVID-19 patients. J Clin Invest 2021; 131: e152264.

81 Poulaizadeh M, Safdarian M, Eshghi P, et al. A randomized clinical trial evaluating the...
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135 Reis G, Silva EASM, Silva DCM, et al. Effect of early treatment with ivermectin among patients with Covid-19. N Eng J Med 2022; 386: 1721-1731.
136 de la Rocha C, Cid-Lopez M, Venegas-Lopez B. Ivermectin compared with placebo in the clinical evolution of Mexican patients with asymptomatic and mild COVID-19: a randomized clinical trial. Research Square; 23 May 2022. https://doi.org/10.21203/rs.3.rs-1640339/v1 (viewed Aug 2022).
137 George B, Moorthy M, Kulkarni U, et al. Single dose of ivermectin is not useful in patients with hematological disorders and COVID-19 illness: a phase II B open labelled randomized controlled trial. Indian J Hematol Blood Transfus 2022; doi: 10.1007/s12288-022-01546-w [online ahead of print].
138 Biber A, Harmelin G, Lev D, et al. The effect of ivermectin on the viral load and culture viability in early treatment of non-hospitalized patients with mild COVID-19: a double-blind, randomized placebo-controlled trial. Int J Infect Dis 2022; 122: 733-740.
139 Abella BS, Jollovsky EL, Biney BT, et al. Efficacy and safety of hydroxychloroquine vs placebo for pre-exposure SARS-CoV-2 prophylaxis among health care workers: a randomized clinical trial. JAMA Intern Med 2020; 181: 195-202.
140 Rajasingham R, Bangdiwala AS, Nicol MR, et al. Hydroxychloroquine as pre-exposure prophylaxis for COVID-19 in healthcare workers: a randomized trial. Clin Infect Dis 2020; 72: e835-e843.
141 Grau-Pujol B, Camprubi-Ferrer D, Martí-Soler H, et al. Pre-exposure prophylaxis with hydroxychloroquine for COVID-19: a double-blind, placebo-controlled randomized clinical trial. Trials 2021; 22: 808.
142 Boullware DR, Pullen MF, Bangdiwala AS, et al. A randomized trial of hydroxychloroquine as postexposure prophylaxis for Covid-19. N Eng J Med 2020; 383: 517-525.
143 Mitjà O, Corbacho-Monné M, Ubals M, et al. A cluster-randomized trial of hydroxychloroquine for prevention of Covid-19. N Eng J Med 2020; 384: 417-427.
144 O’Brien MP, Forleo-Neto E, Musser BJ, et al. Subcutaneous REGEN-COV antibody combination to prevent Covid-19. N Eng J Med 2021; 385: 1184-1195.
145 Levin MJ, Ustianovski A, De Wit S, et al. Intramuscular AZD7442 (toxagavimab-cilgavimab) for prevention of Covid-19. N Eng J Med 2022; 386: 2188-2200.
146 REMAP-CAP Investigators; ACTIV-4a Investigators; ATTACC Investigators. Therapeutic anticoagulation with heparin in critically ill patients with COVID-19. N Engl J Med 2021; 385: 777-789.
147 Lopes D, Macedo AV, de Barros E Silva P, et al. Effect of discontinuing vs continuing angiotensin-converting enzyme inhibitors and angiotensin II receptor blockers on days alive and out of the hospital in patients admitted with COVID-19: a randomized clinical trial. JAMA 2021; 325: 254-264.
148 COVIDSurg Collaborative; GlobalSurg Collaborative. Timing of surgery following SARS-CoV-2 infection: an international prospective cohort study. Anaesthesia 2021; 76: 731-735.

Supporting Information

Additional Supporting Information is included with the online version of this article.