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POSITION PAPERS

Clinical care of pregnant and postpartum women with COVID-19: Living recommendations from the National COVID-19 Clinical Evidence Taskforce

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To date, 18 living recommendations for the clinical care of pregnant and postpartum women with COVID-19 have been issued by the National COVID-19 Clinical Evidence Taskforce. This includes recommendations on mode of birth, delayed umbilical cord clamping, skin-to-skin contact, breastfeeding, rooming-in, antenatal corticosteroids, angiotensin-converting enzyme inhibitors, disease-modifying treatments (including dexamethasone, remdesivir and hydroxychloroquine), venous thromboembolism prophylaxis and advanced respiratory support interventions (prone positioning and extracorporeal membrane oxygenation). Through continuous evidence surveillance, these living recommendations are updated in near real-time to ensure clinicians in Australia have reliable, evidence-based guidelines for clinical decision-making. Please visit https://covid19evidence.net.au/ for the latest recommendation updates.

KEYWORDS
Australia, COVID-19, guidelines, perinatal care, pregnancy

INTRODUCTION

The first cases of novel coronavirus SARS-CoV-2 infection were reported in December 2019 in Wuhan, China.[1] Novel coronavirus disease 2019 (COVID-19) was declared a global pandemic by the World Health Organization on 11 March 2020, and as of 17 September 2020, there have been over 3068 million confirmed cases and more than 954 000 deaths globally.[2] In Australia, there have been 26 942 confirmed cases and 854 deaths.[3] COVID-19 commonly presents with fever and respiratory symptoms including cough and shortness of breath; other symptoms (such as myalgia, sore throat, fatigue, diarrhoea and anosmia) are less common.[4] An estimated 15% of infected individuals will develop severe disease (requiring oxygen support) and 5% will progress to critical disease.[4] Critical COVID-19 disease is characterised by respiratory failure, acute respiratory distress syndrome (ARDS), thromboembolism, sepsis, shock or multiorgan failure. After recovery from acute illness, some individuals may experience longer-term sequelae, particularly respiratory complications.[5]

Experience from previous pandemics (H1N1) and coronavirus outbreaks (SARS and MERS) raised concerns that pregnant women may be particularly vulnerable to more severe COVID-19 disease.[6,7] While current data are limited, pregnant and recently pregnant women with COVID-19 are less likely to experience fever and myalgia, compared with non-pregnant women of reproductive age.[8] However, they have higher rates of intensive care unit admission or invasive ventilation, and their babies are more likely to be born preterm or require neonatal unit admission.[8] Epidemiological data from the Latin American region suggest maternal deaths may be increasing due to COVID-19.[9] Vertical transmission appears possible although probably rare.[10,11]

In response to the COVID-19 pandemic, state, national and international organisations rapidly developed clinical guidelines on how best to care for pregnant and postpartum women with COVID-19.[12] Ideally, clinical guidelines are developed using systematic reviews of available evidence to address pre-specified questions, with expert panels formulating recommendations based on this evidence. However, many such recommendations become outdated as new evidence emerges.[13,14] This is a particular challenge in the COVID-19 context, where the volume of COVID-19-related literature is increasing dramatically.[15] Living guideline methodologies were developed to meet such challenges.[16] In living guidelines, digital technologies and continuous evidence surveillance are used to continually update systematic reviews and recommendations, so as to reflect the latest available evidence.[17] This approach has been used successfully in stroke, diabetes, maternal health and other topics.[18–20]

The National COVID-19 Clinical Evidence Taskforce was established in March 2020 to produce living recommendations on the clinical care of people with COVID-19 in Australia.[21] As of 17 September 2020, the Taskforce has published 72 recommendations on disease severity, disease-modifying treatments, chemoprophylaxis, respiratory support, venous thromboembolism (VTE) prophylaxis, and use of therapies for pre-existing conditions, as well as specific recommendations on the care of women, neonates, children, adolescents, older people and people in palliative care with COVID-19. The aim of this article is to describe the Taskforce recommendations for the care of pregnant and postpartum women with COVID-19.

METHODS

The living guidelines are being developed according to Australian National Health and Medical Research Council (NHMRC) standards, including the use of GRADE (Grading of Recommendations

Assessment, Development and Evaluation) methodology.[22] The Taskforce brings together over 220 clinical experts from across Australia to assess the latest evidence and keep recommendations up-to-date on a weekly basis. All outputs are overseen by a Steering Committee composed of representatives from 31 peak health professional bodies, including the Australian College of Midwives (ACM) and the Royal Australian and New Zealand College of Obstetricians and Gynaecologists (RANZCOG).[23] The Taskforce's remit is to focus on the clinical care of people with COVID-19, with other national agencies responsible for producing guidance on infection prevention, control and diagnosis. The Taskforce also produces clinical flowcharts to facilitate translation of living recommendations into clinical practice.[24] As these living recommendations are regularly updated with new evidence, we encourage clinicians to visit https://covid19evidence.net.au/ and freely subscribe to the weekly updates.

The Guidelines Leadership Group (GLG) oversees seven expert panels developing recommendations for primary, hospital and critical care settings. An evidence review team composed of experienced systematic reviewers and guideline methodologists identifies, appraises and synthesises evidence to inform the development of these recommendations. The Taskforce uses the MAGIC (Making GRADE the Irresistible Choice) digital platform for formulating and publishing recommendations.[25] The multi-disciplinary Pregnancy and Perinatal Care panel (one of seven panels) is composed to ensure diverse representation of setting, culture, geography and gender. It includes 13 experts from Aboriginal and Torres Strait Islander health, general practice, infectious diseases, midwifery, neonatology, obstetrics and gynaecology, obstetric anaesthesia, perinatal epidemiology, public health, and rural and remote medicine. Recommendations formulated by any panel are reviewed and approved by the GLG and the Steering Committee, prior to their publication.

Identification and formulation of clinical questions

We conducted a systematic mapping of available guidelines on the antenatal, intrapartum and postpartum care of women during the COVID-19 pandemic, identifying 81 guidelines from 48 organisations in Australia and internationally.[12] This mapping informed a prioritisation by panel members, who ranked a shortlist of clinical questions on the basis of: (1) interventions that are likely to impact on patient outcomes; (2) proportion of clinical population impacted; (3) extent of variation in current practice; and (4) likelihood of new evidence emerging. The panel also reviewed existing Taskforce recommendations on the clinical care of adults with COVID-19 to identify those clinical questions where adaptation was needed.

Literature searching, data collection and synthesis

An information specialist oversees the evidence surveillance process, which combines daily searches of COVID-19-related articles and preprints across broad topic areas (such as pregnancy and newborn care) with targeted searches for specific clinical questions as they are proposed by the expert panels.[26] The evidence review team uses Covidence,[27] a collaborative online software for managing and streamlining systematic reviews, for screening literature. Titles and abstracts are initially screened by two reviewers independently, with full texts of potentially eligible studies retrieved and also reviewed in duplicate. Disagreements are resolved through discussion or consultation with a third member of the evidence review team. Eligible articles are primary research (typically trials) or systematic reviews relating to the clinical questions of interest. Systematic reviews (particularly living systematic reviews that are kept up-to-date) of reasonable quality are the preferred evidence source. If required, a limited update may be used to integrate findings from more recent primary studies into an existing systematic review. Where no such systematic review exists, the evidence review team initiates a new systematic review. For some clinical questions where direct trial evidence is unlikely to be available for pregnant and postpartum women, lower quality evidence such as observational studies or studies from related topics (eg, studies of women with ARDS due to other causes) are considered.

Data on study characteristics and priority outcomes are extracted in duplicate using standardised data collection forms, with disagreements resolved through discussion or consulting a third reviewer.[27] Included studies are assessed using an appropriate quality assessment tool, such as AMSTAR 2 for systematic reviews and the Cochrane Risk of Bias 2.0 assessment tool for randomised trials.[28–30]

Developing and updating recommendations

Since 14 May 2020, the panel convened on a weekly basis to review the evidence, develop and update recommendations. Where necessary, assistance is sought from additional expert advisory groups (eg, haematology, critical care). The panel reviews evidence profiles on the benefits, harms and certainty of the evidence for priority questions, as well as considering the resource requirements, cost-effectiveness, feasibility, acceptability and equity of each intervention. This is done systematically using GRADE evidence to decision frameworks.[22] Recommendations are formulated in line with established Australian maternity care principles, including the need for evidence-based, person-centred care that is responsive to women's needs and preferences.[31] Recommendations are also reviewed by a separate Consumer Panel, co-convened by the Consumers Health Forum of Australia and the Taskforce. Ongoing literature surveillance is maintained for published recommendations. If relevant new studies become available, evidence profiles are updated and the recommendations may be revised.

RESULTS

The following recommendations are current as of 17 September 2020, with any subsequent updates freely available at https://

covid19evidence.net.au/. Classifications of disease severity used by the Taskforce are described in Table 1.

Pregnancy and perinatal care of women with COVID-19

Seven recommendations on mode of birth, delayed umbilical cord clamping, skin-to-skin contact, breastfeeding, rooming-in, antenatal corticosteroids and angiotensin-converting enzyme (ACE)-inhibitors support continuing with the provision of usual care, although the need for masks and hand hygiene when mothers are caring and feeding their babies, is emphasised (Table 2).

While systematic reviews on the risks of vertical transmission by mode of birth, rooming-in status and different infant feeding approaches have been published, only very low certainty evidence (predominantly case reports and case series) is currently available.[32,33] Additional evidence is available from a US multi-centre cohort study of 106 neonates born to mothers who were positive for COVID-19.[34] In this study, mode of birth, skin-to-skin contact and breastfeeding were managed as per usual care, although maternal use of surgical masks, hand hygiene and breast cleansing were encouraged. Newborns roomed-in with mothers, except for 17 newborns who were separated at parental request or due to medical complications. Newborns were tested by nasopharyngeal polymerase chain reaction at 12–24 h (n = 106), 5–7 days (n = 79) and 14 days (n = 72) of life, with all newborns testing negative at all timepoints. While the possibility of vertical transmission cannot be excluded based on this evidence, this must be weighed against the known, substantial benefits of these interventions.[35–42]

No direct evidence was identified on delayed cord clamping in women with COVID-19, or on antenatal corticosteroids or use of ACE inhibitors for postpartum women with hypertension requiring drug treatment. Hence, these recommendations are aligned with current Australian pregnancy and perinatal care guidance on use of these interventions.[43–45]

Use of disease-modifying treatments in women with COVID-19

Corticosteroids

Evidence on corticosteroids compared with standard care for COVID-19 in adults comes from eight randomised trials (over 5700 patients), including the multi-centre RECOVERY trial that evaluated dexamethasone against usual care in 2104 patients.[46,47] Pregnant women were specifically excluded from all trials, except for RECOVERY (six pregnant women enrolled) and REMAP-CAP (the number of pregnant women enrolled has not been reported).[47,48] Corticosteroids reduce mortality for adult patients with severe or critical COVID-19 (relative risk (RR) 0.86 95% Ci 0.77–0.97), and probably also reduce the need for mechanical ventilation or death, and time to discharge from hospital. However, in patients who do not require oxygen, corticosteroids may increase mortality (RR 1.27 95% CI 1.00–1.61). Considering these benefits and the likely acceptability of the intervention, using dexamethasone 6 mg

TABLE 1 Classification of COVID-19 disease severity†

Mild illness	Adults not presenting any clinical features suggestive of moderate or severe disease or a complicated course of illness. Characteristics: • no symptoms • or mild upper respiratory tract symptoms • or cough, new myalgia or asthenia without new shortness of breath or a reduction in oxygen saturation
Moderate illness	Stable adult patient presenting with respiratory and/or systemic symptoms or signs. Able to maintain oxygen saturation above 92% (or above 90% for patients with chronic lung disease) with up to 4 L/min oxygen via nasal prongs. Characteristics: • prostration, severe asthenia, fever> 38°C or persistent cough • clinical or radiological signs of lung involvement • no clinical or laboratory indicators of clinical severity or respiratory impairment
Severe illness	Adult patients meeting any of the following criteria: • respiratory rate ≥ 30 breaths/min • oxygen saturation ≤ 92% at a rest state • arterial partial pressure of oxygen (PaO2)/ inspired oxygen fraction (FiO2) ≤300
Critical illness	Adult patient meeting any of the following criteria: Respiratory failure 1. Occurrence of severe respiratory failure (PaO2/FiO2 < 200), respiratory distress or acute respiratory distress syndrome (ARDS). This includes patients deteriorating despite advanced forms of respiratory support (noninvasive ventilation, high-flow nasal oxygen) OR patients requiring mechanical ventilation. OR other signs of significant deterioration • hypotension or shock • impairment of consciousness • other organ failure

†Recommendations were current at the time of writing. Please visit The National COVID-19 Clinical Evidence Taskforce (https://covid19evidence.net.au/) for the latest updates to the recommendations.

TABLE 2 Pregnancy and perinatal care recommendations for women with COVID-19†

Intervention	Recommendation and remarks
Mode of birth	For pregnant women with COVID-19, mode of birth should remain as per usual care *(conditional recommendation, very low certainty evidence)* • There is currently no evidence to indicate that caesarean section for women with COVID-19 reduces the risk of vertical transmission to the newborn. Mode of birth should continue as per usual care. Respiratory deterioration due to COVID-19 may prompt urgent delivery on an individual basis.
Delayed umbilical cord clamping	Delayed umbilical cord clamping is supported as part of standard care, independent of the presence of COVID-1 *(consensus recommendation)* • There is currently no evidence that delayed umbilical cord clamping affects the risk of vertical transmission of COVID-19.
Skin-to-skin contact	Early skin-to-skin contact after birth and during the postnatal period is supported, irrespective of the presence of COVID-19. However, parents with COVID-19 should use infection prevention and control measures (mask and hand hygiene) *(consensus recommendation)* • Early skin-to-skin contact refers to placing the naked baby prone on the parent's bare chest immediately after birth. • Skin-to-skin contact should be encouraged and continue as per usual practice in other postnatal and neonatal settings, such as neonatal intensive care unit and postnatal wards, providing infection prevention and control measures are maintained.
Breastfeeding	Breastfeeding is supported irrespective of the presence of COVID-19. However, women with COVID-19 who are breastfeeding should use infection prevention and control measures (mask and hand hygiene) while infectious *(conditional recommendation, very low certainty evidence)* • There is currently no evidence to indicate that breastfeeding increases the risk of vertical transmission to the newborn. As there are substantial known benefits for breastfeeding, women should be supported to initiate or continue breastfeeding. If the baby is being fed with expressed breastmilk or formula, these same infection prevention and control measures should be used.
Rooming-in	For women with COVID-19 who have given birth, support rooming-in of mother and newborn in the birth suite and on the postnatal ward when both mother and baby are well. However, women with COVID-19 should use infection prevention and control measures (mask and hand hygiene) *(conditional recommendation, very low certainty evidence)* • There is currently no evidence to indicate that a woman with a known COVID-19 infection should be separated from her newborn to prevent transmission. As there are substantial known benefits for keeping mother and newborn together postpartum, women should be supported to be with their newborn as per usual care. • Women with COVID-19 should be encouraged and supported in using good hand hygiene before and after handling their baby, and using a mask while in close contact with their baby. To the extent possible, these women should practice physical distancing when not feeding or caring for the baby.
Antenatal corticosteroids	The use of antenatal corticosteroids for women at risk of preterm birth is supported as part of standard care, independent of the presence of COVID-19 *(consensus recommendation)* • There are clear benefits to using antenatal corticosteroids for women at risk of preterm birth at less than 34 weeks gestation. There is currently no evidence to suggest that antenatal corticosteroids cause additional maternal or fetal harm in the setting of COVID-19 when used for this indication. They should therefore be given where indicated. • The Taskforce has separate recommendations regarding the use of dexamethasone as a disease-modifying treatment in pregnant or breastfeeding women for COVID-19. Women with COVID-19 who are on oxygen and receiving dexamethasone do not require additional doses of corticosteroids for fetal lung maturation.
ACE inhibitors for postpartum women with hypertension requiring drug treatment	In postpartum women with COVID-19 who have hypertension requiring treatment with ACE inhibitors, there is currently no evidence to deviate from usual care. These medications should be initiated or continued unless otherwise contraindicated *(consensus recommendation)* • ACE inhibitors are contraindicated in the antenatal period due to risk of fetal and neonatal harm.

†Recommendations were current at the time of writing. Please visit The National COVID-19 Clinical Evidence Taskforce (https://covid19evidence.net.au/) for the latest updates to the recommendations. ACE, angiotensin-converting enzyme

daily (IV or oral) for up to ten days is recommended in pregnant or breastfeeding women with COVID-19 who are receiving oxygen (Table 3). While the RECOVERY Trial specified that enrolled pregnant women receive oral prednisolone or intravenous hydrocortisone,[49] dexamethasone is preferred as it is used for other clinical indications in pregnancy.[50] Corticosteroids should not be used in women with COVID-19 who do not require oxygen, due to the lack of benefit and possible harms in this subgroup.

Remdesivir

Four trials have compared remdesivir with standard care in hospitalised, non-pregnant adults with COVID-19.[51–54] As pregnant and breastfeeding women were excluded from these trials, there is no direct evidence on the impact of remdesivir for COVID-19 in these women, as well as a lack of safety data on its use in pregnancy.[55] In non-pregnant adults, remdesivir may decrease time to recovery

TABLE 3 Recommendations on use of disease-modifying treatments for pregnant or postpartum women with COVID-19†

Dexamethasone as treatment for COVID-19	1. Use dexamethasone 6 mg daily intravenously or orally for up to ten days in pregnant or breastfeeding women with COVID-19 who are receiving oxygen (including mechanically ventilated patients) *(strong recommendation, low certainty evidence)*. 2. Do not routinely use dexamethasone to treat COVID-19 in pregnant or breastfeeding women who do not require oxygen *(strong recommendation, low certainty evidence)*. • Antenatal corticosteroids should still be used for fetal lung maturation in pregnant women at risk of preterm birth who also have COVID-19. Dexamethasone should still be used for other evidence-based indications in pregnant and breastfeeding women who have COVID-19.
Remdesivir as treatment for COVID-19	Use of remdesivir for pregnant or breastfeeding women with COVID-19 outside of a trial setting should not be considered routinely *(conditional recommendation, very low certainty evidence)*. • As pregnant and breastfeeding women are often excluded from clinical trials, use of remdesivir in this population would be outside a clinical trial setting. Pregnant and breastfeeding women receiving remdesivir should nonetheless be enrolled in national COVID-19 registries. Currently, there is no direct evidence of the effects of remdesivir in pregnant and breastfeeding women. Information about the patients and the intervention (dosages, duration) in the trials used for this recommendation can be found in the Practical info tab. • Due to antagonism observed *in vitro*, concomitant use of remdesivir with chloroquine or hydroxychloroquine is not recommended.[90]
Hydroxychloroquine as treatment for COVID-19	Do not use hydroxychloroquine for the treatment of COVID-19 *(strong recommendation, moderate certainty evidence)*. • This recommendation applies to adults, children and adolescents, pregnant and breastfeeding women, older people living with frailty and those receiving palliative care. • Use of hydroxychloroquine may still be considered in the context of randomised trials with appropriate ethical approval, such as combination therapies that include hydroxychloroquine.
Hydroxychloroquine for post-exposure prophylaxis	For people exposed to individuals with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection, do not use hydroxychloroquine for post-exposure prophylaxis outside of randomised trials with appropriate ethical approval *(strong recommendation, low certainty evidence)*. Trials are needed in special populations, including children and adolescents, pregnant and breastfeeding women, older people living with frailty and those receiving palliative care. Until further evidence is available, do not use hydroxychloroquine for post-exposure prophylaxis in these populations unless they are eligible to be enrolled in trials.
Other disease-modifying treatments	For people with COVID-19, do not use the other disease-modifying treatments‡ outside of randomised trials with appropriate ethical approval *(strong recommendation, very low certainty evidence)*. • Trials are needed in special populations, including children and adolescents, pregnant and breastfeeding women, older people living with frailty and those receiving palliative care. Until further evidence is available, do not use in these populations unless they are eligible to be enrolled in trials.

†Recommendations were current at the time of writing. Please visit The National COVID-19 Clinical Evidence Taskforce (https://covid19evidence.net.au/) for the latest updates to the recommendations.
‡The treatments include: aprepitant, baloxavir marboxil, calcifediol, chloroquine, colchicine, convalescent plasma, darunavir-cobicistat, favipiravir, human mesenchymal stem cells, immunoglobulin plus methylprednisolone, interferon β-1a, interferon β-1b, interferon gamma, lopinavir-ritonavir, ruxolitinib, sofosbuvir-daclatasvir, telmisartan and umifenovir.

by a few days (hazards ratio (HR) 1.24, 95% CI 1.08–1.42) and time to improvement only slightly (HR 1.17, 95% CI 1.00–1.38). Its effect on mortality is uncertain, and it is currently unclear which regimen (five days or ten days) provides the most benefit. However, the panel noted that severity of disease is an important factor – for pregnant women with severe or critical COVID-19, the harm-to-benefit ratio may differ compared to pregnant women with mild or moderate disease. The Taskforce therefore made a conditional recommendation against the *routine* use of remdesivir in pregnant and breastfeeding women outside of a trial setting (Table 3).

Hydroxychloroquine for treatment or for post-exposure prophylaxis

There are currently 11 trials (over 6300 patients) comparing hydroxychloroquine with standard care in the treatment of patients with COVID-19.[56–66] In all trials, pregnant women were either excluded or their eligibility was not specified. Meta-analyses indicate that hydroxychloroquine is potentially harmful and no more effective than standard care, leading to a strong recommendation against its use for COVID-19 treatment (Table 3). Separately, hydroxychloroquine for post-exposure prophylaxis has been evaluated in two trials (3135 participants), both of which excluded pregnant and breastfeeding women; however, there is currently insufficient evidence to assess benefits.[67,68] The Taskforce recommends that hydroxychloroquine for post-exposure prophylaxis should not be used outside of randomised trials with appropriate ethical approval, emphasising that further trials (including in pregnant and breastfeeding women) are needed.

Other disease-modifying treatments

The Taskforce has issued a further 19 recommendations on a wide range of disease-modifying treatments (Table 3), including:

TABLE 4 Venous thromboembolism (VTE) prophylaxis in pregnant and postpartum women†

Pregnant women in general are at an increased risk of venous thromboembolism (VTE). Hospitalised pregnant women with an acute infective illness (such as COVID-19) are at even greater risk of VTE. However, the exact duration of increased risk of VTE in association with COVID-19 infection is not yet established. All pregnant and postpartum women should undergo a documented assessment of risk factors for VTE on admission to hospital, if COVID-19 is diagnosed, if COVID-19 severity changes, and postpartum. The use of pharmacological prophylaxis in women should be accompanied by other measures to prevent VTE, such as anti-embolism stockings and sequential compression devices.

For pregnant or postpartum women who are admitted to hospital (for any indication) and who have COVID-19, use prophylactic doses of anticoagulants, preferably low-molecular weight heparin (LMWH: eg, enoxaparin 40 mg once daily or dalteparin 5000 IU once daily) unless there is a contraindication, such as risk for major bleeding or imminent birth.
Prophylactic anticoagulants should be continued for at least 14 days after discharge or until COVID-19-related morbidity (including immobility, dehydration and/or shortness of breath) has resolved *(consensus recommendation)*.

- Dosing of LMWH is dependent on pre-pregnancy body weight and current renal function.
- For women with early pregnancy body weight outside of 50-90 kg, consider adjusted LMWH dosing.
- There is limited evidence to guide the most appropriate dose in obese patients but standard dosing may be inadequate.

For pregnant women with severe or critical COVID-19, or where there are additional risk factors for VTE, consider using increased prophylactic dosing of anticoagulants, preferably LMWH (eg, enoxaparin 40 mg twice daily or dalteparin 5000 IU twice daily) unless there is a contraindication, such as risk for major bleeding or platelet count < 30 × 109/L. Prophylactic anticoagulants should be continued for at least four weeks after discharge or until COVID-19-related morbidity (including immobility, dehydration and/or shortness of breath) has resolved *(consensus recommendation)*.

- Dosing is dependent on pre-pregnancy body weight and current renal function. For women with early pregnancy body weight outside of 50-90 kg, consider adjusted LMWH dosing.
- There is limited evidence to guide the most appropriate dose in obese patients but standard dosing may be inadequate.
- Clinicians should refer to their local or jurisdictional guidance on additional VTE risk factors.
- In some situations, continuation of LMWH throughout the rest of pregnancy and postpartum may be required. Involvement of specialist obstetricians, obstetric medicine physicians, haematologists or other physicians with expertise in VTE in pregnant women would be warranted.

For pregnant or postpartum women who are self-isolating at home with mild COVID-19 and where additional risk factors for VTE are present, consider using prophylactic doses of anticoagulants, preferably LMWH (eg, enoxaparin 40 mg once daily or dalteparin 5000 IU once daily) unless there is a contraindication, such as risk for major bleeding or imminent birth. Prophylactic anticoagulants should be continued for at least 14 days or until COVID-19-related morbidity (including immobility, dehydration and/or shortness of breath) has resolved. For pregnant or postpartum women who are self-isolating at home with mild COVID-19 and who have no additional risk factors for VTE, routine pharmacological prophylaxis is not recommended *(consensus recommendation)*

- Dosing of LMWH is dependent on pre-pregnancy body weight and current renal function. For women with early pregnancy body weight outside of 50–90 kg, consider adjusted LMWH dosing.
- There is limited evidence to guide the most appropriate dose in obese patients but standard dosing may be inadequate.
- Clinicians should refer to their local or jurisdictional guidance on additional VTE risk factors.

For postpartum women who have had COVID-19 during pregnancy, consider using at least 14 days of prophylactic dosing of anticoagulants, preferably LMWH (eg, enoxaparin 40 mg once daily or dalteparin 5000 IU once daily) unless there is a contraindication, such as risk for major bleeding. Increased duration of six weeks should be considered if severe or critical COVID-19 and/or additional risk factors for VTE are present *(consensus recommendation)*

- Dosing of LMWH is dependent on pre-pregnancy body weight and current renal function. For women with early pregnancy body weight outside of 50-90 kg, consider adjusted LMWH dosing.
- There is limited evidence to guide the most appropriate dose in obese patients but standard dosing may be inadequate.
- Clinicians should refer to their local or jurisdictional guidance on additional VTE risk factors.

†Recommendations were current at the time of writing. Please visit The National COVID-19 Clinical Evidence Taskforce (https://covid19evidence.net.au/) for the latest updates to the recommendations.

aprepitant, azithromycin, baloxavir marboxil, calcifediol, chloroquine, colchicine, convalescent plasma, darunavir-cobicistat, favipiravir, human mesenchymal stem cells, immunoglobulin plus methylprednisolone, interferon β-1a, interferon β-1b, interferon gamma, lopinavir-ritonavir, ruxolitinib, sofosbuvir-daclatasvir, telmisartan and umifenovir. These treatments have typically been evaluated in one or two trials with a small number of non-pregnant participants, resulting in low or very low certainty evidence from which no conclusions can be drawn. For some of these treatments (such as baloxavir marboxil or favipiravir), no pregnancy safety data are available, whereas others (such as azithromycin or lopinavir-ritonavir) have a well-described safety profile.[55] The Taskforce therefore recommends that these treatments should not be used outside of randomised trials, with emphasis that trials enrolling pregnant and breastfeeding women are needed.

Venous thromboembolism (VTE) prophylaxis

While COVID-19 infection appears to increase the risk of VTE, there is currently no direct evidence on the exact duration of this increased risk, or which prophylactic anticoagulant regimen is optimal.[69] The consensus recommendations (Table 4) were formulated based on a review of available international guidelines[69,70] and consultation with expert haematologists. Recognising that

TABLE 5 Respiratory support for pregnant and postpartum women with severe or critical COVID-19†

Prone positioning	1. For mechanically ventilated pregnant women with COVID-19 and hypoxaemia despite optimising ventilation, consider prone positioning for more than 12 h a day *(consensus recommendation)*. 2. For pregnant and postpartum women with COVID-19 and respiratory symptoms who are receiving any form of supplemental oxygen therapy and have not yet been intubated, consider prone positioning. When positioning a pregnant woman in prone, care should be taken to support the gravid uterus to reduce aorta-caval compression. Women who are deteriorating should be considered for early endotracheal intubation and invasive mechanical ventilation. Birth of the baby should be considered when it may enhance maternal resuscitation or be beneficial to the fetus *(consensus recommendation)*. • Current reports suggest prone ventilation in adult patients is effective in improving hypoxia associated with COVID-19. This should be done in the context of a hospital guideline that includes suitable personal protective equipment for staff, and that minimises the risk of adverse events, e.g. accidental extubation. • Proning of a pregnant woman should avoid abdominal compression and ensure a woman's hips and chest are supported. In the absence of specialised equipment, proning can be performed using pillows and blankets. • Proning can be challenging in late gestation and delivery of the baby may be warranted.
Extracorporeal membrane oxygenation (ECMO)	Consider referral to an ECMO centre for venovenous ECMO in mechanically ventilated pregnant women with COVID-19 and refractory respiratory failure (despite optimising ventilation, including proning). Delivery of the baby prior to ECMO to enhance maternal resuscitation should be considered on a case-by-case basis *(consensus recommendation)*. • Due to the resource-intensive nature of ECMO and the need for experienced centres, healthcare workers and infrastructure, ECMO should only be considered in selected pregnant women with COVID-19 and severe ARDS. • The decision on whether to use ECMO should be taken in consultation with the woman's family, as well as obstetric and intensive care specialists. Key considerations include gestational age, fetal viability, fetal well-being and the risks and benefits to mother and baby. • Early referral to an ECMO centre is preferred. • As pregnant and postpartum women may have haemostatic alterations, anticoagulation regimens may need to be modified appropriately.

†Recommendations were current at the time of writing. Please visit The National COVID-19 Clinical Evidence Taskforce (https://covid19evidence.net.au/) for the latest updates to the recommendations.

pregnancy and the postpartum period are inherently hypercoagulable states, the statement emphasises that all pregnant and postpartum women should be assessed for additional risk factors for VTE on admission to hospital, when COVID-19 is diagnosed, if COVID-19 severity changes, and postpartum.

Prone positioning and extracorporeal membrane oxygenation (ECMO)

Internationally, there are few (and somewhat conflicting) guidelines on the use of prone positioning or ECMO in pregnant and postpartum women with COVID-19.[4,71–74] There is currently no primary evidence on their benefits and harms in these women, although it is known to be effective in some groups of adult patients with critical disease.[75,76] Recent reports describe their use in small numbers of pregnant women with critical COVID-19 disease.[77–80] The Taskforce recommends that prone positioning be considered in women receiving any form of supplemental oxygen therapy or mechanically ventilated women, although care should be taken to support the gravid uterus and reduce aorta-caval compression (Table 5). Referral to an ECMO centre for veno-venous ECMO can be considered for mechanically ventilated pregnant women, although this decision needs to consider gestational age, fetal viability, fetal well-being, and the risks and benefits to woman and baby. The Taskforce has issued separate recommendations on other respiratory support interventions that apply to adults (whether pregnant or non-pregnant), including the use of high-flow nasal oxygen therapy, noninvasive ventilation, respiratory management of the deteriorating patient, videolaryngoscopy, neuromuscular blockers, positive end-expiratory pressure and recruitment manoeuvres. These can be found on the Taskforce website.[21]

DISCUSSION

The treatment of COVID-19 is a rapidly expanding area of research, with an unprecedented global effort underway. However, with more than 53 000 COVID-19 articles in PubMed, as well as 2100 systematic review protocols and 1600 trial protocols registered online in less than eight months, it is increasingly difficult for clinicians to remain up-to-date on important developments.[15,21,81] There is also a growing recognition that a portion of the COVID-19 literature is of poor quality, further complicating its interpretation and application in clinical care.[82] The living guideline approach ensures that new, important evidence is rapidly translated into clinical recommendations, without compromising quality or rigour of guideline development. While living guidelines methods have been successfully applied to Australian guidelines on stroke and diabetes,[18,83] the approach of weekly updating used by this Taskforce is the most frequent of which we are aware. While resource-intensive, the collaborative effort of over 220 clinical experts nationwide, as well as support from commonwealth, state and territory governments and other funders, has shown this model to be highly feasible in the context of a global public health emergency.

A key finding from these recommendations is the lack of direct evidence specific to pregnant and breastfeeding women with COVID-19. Historically, women (and particularly pregnant and breastfeeding women) have been excluded from adult clinical trials, despite repeated calls from professional associations, regulatory agencies and researchers for their inclusion.[84–86] This trend has continued in the era of COVID-19, with pregnant and breastfeeding women excluded from large multi-centre trials of COVID-19 therapeutics.[87] Pastick et al. reported that in 1282 ongoing COVID-19 therapeutic clinical trials enrolling people of reproductive age, only 48 explicitly confirmed that pregnant and breastfeeding women could be enrolled.[88] Exclusion of pregnant women from COVID-19 trials creates uncertainty regarding safety and effectiveness of promising management strategies, and ultimately leads to reduced access to important treatments. Consequently, the Taskforce recommendations have considered whether available evidence from trials of non-pregnant adults can be generalised to pregnant and breastfeeding women.

These recommendations are intended to be used in conjunction with existing principles and guidelines on routine maternity care. However, living recommendations can require more dynamic approaches to implementation. Clinicians and other stakeholders need to be continually updated regarding new or revised recommendations, and clinical tools (such as flowcharts and algorithms) need to be regularly revised to align with updated recommendations. Since their launch, the Taskforce website has been visited over 180 000 times. We encourage hospital and clinical networks to sign up to the free weekly email updates, and update their jurisdictional guidance or local clinical protocols as necessary. While the scope of the living guidelines has thus far focused on clinical care of people with COVID-19, on 9 September 2020 the Commonwealth Government announced a new partnership between the Taskforce and the Infection Control Expert Group (ICEG) to apply the living guidelines model to selected infection prevention and control issues in Australian healthcare settings.[89]

CONCLUSION

Living guidelines are an innovative model than can accelerate the translation of new evidence into clinical practice. The National COVID-19 Clinical Evidence Taskforce has published 18 pregnancy and perinatal living recommendations, which will be updated as necessary in response to new, important evidence. We encourage clinicians in Australia's maternity services to freely subscribe to Taskforce updates (covid19evidence.net.au) to ensure they remain abreast of guideline updates.

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DATA SHARING AND DATA ACCESSIBILITY

All recommendations and evidence profiles are publicly available at https://covid19evidence.net.au/

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