





COVID-19 rapid guideline: managing COVID-19

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Your responsibility

The recommendations in this guideline represent the view of NICE, arrived at after careful consideration of the evidence available. When exercising their judgement, professionals and practitioners are expected to take this guideline fully into account, alongside the individual needs, preferences and values of their patients or the people using their service. It is not mandatory to apply the recommendations, and the guideline does not override the responsibility to make decisions appropriate to the circumstances of the individual, in consultation with them and their families and carers or guardian.

All problems (adverse events) related to a medicine or medical device used for treatment or in a procedure should be reported to the Medicines and Healthcare products Regulatory Agency using the <u>Yellow Card Scheme</u>.

Local commissioners and providers of healthcare have a responsibility to enable the guideline to be applied when individual professionals and people using services wish to use it. They should do so in the context of local and national priorities for funding and developing services, and in light of their duties to have due regard to the need to eliminate unlawful discrimination, to advance equality of opportunity and to reduce health inequalities. Nothing in this guideline should be interpreted in a way that would be inconsistent with complying with those duties.

Commissioners and providers have a responsibility to promote an environmentally sustainable health and care system and should <u>assess and reduce the environmental</u> <u>impact of implementing NICE recommendations</u> wherever possible.

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This guideline replaces NG159, NG163, NG165, NG171, NG173, NG175, NG186, ES27, ES33, ES34, ES23, ES24, ES25 and ES26.

Overview

This guideline covers managing COVID-19 in babies, children, young people and adults in community and hospital settings. It includes recommendations on communication, assessment, therapeutics for COVID-19, non-invasive respiratory support, preventing and managing acute complications, and identifying and managing co-infections.

NICE has also produced <u>COVID-19</u> rapid guidelines on managing long-term effects of <u>COVID-19</u> ('long COVID') and <u>haematopoietic stem cell transplantation</u>.

1 Communication and shared decision making

1.1.1 Explain to people with COVID-19, their families, carers and close contacts that they should follow the <u>UK Heath Security Agency's guidance for people with</u> symptoms of a respiratory infection including COVID-19.

> The <u>Royal College of Obstetricians and Gynaecologists has produced information</u> on COVID-19 and pregnancy for pregnant women and their families. [23 March 2021]

- 1.1.2 Give people information in a way that they can use and understand, to help them take part in decisions about their care. Follow relevant national guidance on communication, providing information (including in different formats and languages) and shared decision making, for example, <u>NICE's guideline on patient</u> <u>experience in adult NHS services</u>. **[23 March 2021]**
- 1.1.3 Communicate with people with COVID-19, and their families and carers, and support their mental wellbeing to help alleviate any anxiety and fear they may have. Signpost to charities and support groups (including NHS Volunteer Responders), to <u>NHS every mind matters</u> and to <u>Royal College of Paediatrics and Child Health resources for parents and carers</u>. **[23 March 2021]**
- 1.1.4 For carers of people with COVID-19 (for example, carers of people with dementia and COVID-19), signpost to relevant support and resources, such as the <u>Alzheimer's Society's information on Dementia and coronavirus risk</u>. [23 March 2021, amended 23 January 2024 and 13 March 2024]

2 Assessment

2.1 In the community

Identifying severe COVID-19

- 2.1.1 Use the following signs and symptoms to help identify people with COVID-19 with the most severe illness:
 - severe shortness of breath at rest or difficulty breathing
 - reduced oxygen saturation levels measured by pulse oximetry (see recommendation 2.1.2 on pulse oximetry levels that indicate serious illness)
 - coughing up blood
 - blue lips or face
 - feeling cold and clammy with pale or mottled skin
 - collapse or fainting (syncope)
 - new confusion
 - becoming difficult to rouse
 - reduced urine output.

For signs and symptoms to help identify paediatric inflammatory multisystem syndrome (PIMS) temporally associated with COVID-19 (PIMS-TS), see the guidance on PIMS from the Royal College of Paediatrics and Child Health. [23 March 2021]

- 2.1.2 When pulse oximetry is available in primary and community care settings, to assess the severity of illness and detect early deterioration, use:
 - <u>NHS England's guide to pulse oximetry</u> in people 18 years and over with COVID-19

- oxygen saturation levels below 91% in room air at rest in children and young people (17 years and under) with COVID-19. [23 March 2021, amended 27 May 2021]
- 2.1.3 Be aware that some pulse oximeters can underestimate or overestimate oxygen saturation levels, especially if the saturation level is borderline. Overestimation has been reported in people with dark skin. For more information about this, see <u>NHS England's guide on how to look after yourself at home if you have COVID-19</u> or symptoms of COVID-19.

For information on pulse oximetry at home, see <u>NHS England's COVID oximetry</u> @home service. [23 March 2021, amended 27 May 2021]

2.1.4 For people with severe respiratory symptoms associated with COVID-19 (for example, suspected pneumonia) being managed in the community, see recommendation 5.3.14 on venous thromboembolism in hospital-led acute care in the community. [23 March 2021]

Assessing shortness of breath (dyspnoea) is important but may be difficult via remote consultation. Tools such as the <u>Medical Research Council's dyspnoea scale</u> or the <u>Centre for Evidence-Based Medicine's review of ways of assessing dyspnoea</u> (breathlessness) by telephone or video can be useful.

The <u>National Early Warning Score (NEWS) 2 tool</u> may be used in adults in addition to clinical judgement to assess a person's risk of deterioration. Note that use of NEWS2 is not advised in children or pregnant women. Although the NEWS2 tool is not validated for predicting the risk of clinical deterioration in prehospital settings, it may be a helpful adjunct to clinical judgement in adults. A face-to-face consultation should not be arranged solely to calculate a NEWS2 score.

Locally approved Paediatric Early Warning Scores (PEWS) should be used for children. When using early warning scores, ensure that readings are based on calibrated machines. Be aware that readings may be incomplete when doing remote consultations.

Care planning

- 2.1.5 Discuss with people with COVID-19, and their families and carers, the benefits and risks of hospital admission or other acute care delivery services (for example, virtual wards or hospital at home teams). **[23 March 2021]**
- 2.1.6 Explain that people with COVID-19 may deteriorate rapidly. Discuss future care preferences at the first assessment to give people who do not have existing advance care plans an opportunity to express their preferences. **[23 March 2021]**

For a short explanation of why the panel made these recommendations, see the rationale section on assessment in the community.

2.2 In hospital

- 2.2.1 When a person is admitted to hospital with COVID-19, ensure a holistic assessment is done, including discussion about their treatment expectations and care goals:
 - Document and assess the stability of underlying health conditions, involving relevant specialists as needed.
 - Use the Clinical Frailty Scale (CFS) when appropriate, available from the NHS Specialised Clinical Frailty Network, to assess baseline health and inform discussions on treatment expectations.
 - Use the CFS within an individualised assessment of frailty.
 - Do not use the CFS for younger people, people with stable long-term disabilities (for example, cerebral palsy), learning disabilities or autism. Make an individualised assessment of frailty in these people, using clinical assessment and alternative scoring methods.
 - Record the assessment and discussion in the person's medical records.

For assessment of paediatric inflammatory multisystem syndrome (PIMS), follow the guidance on PIMS from the Royal College of Paediatrics and Child

Health. [23 March 2021]

2.2.2 When making decisions about the care of children and young people under 18 years, people with learning disabilities or adults who lack mental capacity for health decision making, for example, people with advanced dementia, see <u>NICE's</u> <u>guideline on decision making and mental capacity</u>.

Ensure discussions on significant care interventions involve families and carers as appropriate, and local experts or advocates. **[23 March 2021]**

3 Management

3.1 In the community

Care planning

- 3.1.1 In the community, consider the risks and benefits of face-to-face and remote care for each person. Where the risks of face-to-face care outweigh the benefits, remote care can be optimised by:
 - offering telephone or video consultations (see <u>BMJ guidance on Covid-19: a</u> remote assessment in primary care for a useful guide, including a <u>visual</u> summary for remote consultation)
 - cutting non-essential face-to-face follow-up
 - using electronic prescriptions rather than paper
 - using different methods to deliver medicines to people, for example, pharmacy deliveries, postal services and NHS volunteers, or introducing drive-through pick-up points for medicines. **[23 March 2021]**
- 3.1.2 When possible, discuss the risks, benefits and possible likely outcomes of the treatment options with people with COVID-19, and their families and carers. Use decision support tools (where available). **[23 March 2021]**
- 3.1.3 Put treatment escalation plans in place in the community after sensitively discussing treatment expectations and care goals with people with COVID-19, and their families and carers. **[23 March 2021]**
- 3.1.4 People with COVID-19 may deteriorate rapidly. If it is agreed that the next step is:
 - a move to secondary care, ensure that they and their families understand how to access this with the urgency needed
 - other community-based support (whether virtual wards, hospital-at-home

services or palliative care), ensure that they and their families understand how to access these services, both in and out of hours. **[23 March 2021]**

Managing cough

- 3.1.5 Encourage people with cough to avoid lying on their backs, if possible, because this may make coughing less effective. **[23 March 2021]**
- 3.1.6 Be aware that older people or those with comorbidities, frailty, impaired immunity or a reduced ability to cough and clear secretions are more likely to develop severe pneumonia. This could lead to respiratory failure and death. **[23 March 2021]**
- 3.1.7 For guidance on managing acute cough, see <u>NICE's guideline on cough (acute):</u> antimicrobial prescribing. **[30 November 2023]**

Managing fever

- 3.1.8 Advise people with COVID-19 and fever to drink fluids regularly to avoid dehydration. Support their families and carers to help when appropriate.
 Communicate that fluid intake needs can be higher than usual because of fever.
 [23 March 2021]
- 3.1.9 Advise people to take paracetamol or ibuprofen if they have fever and other symptoms that antipyretics would help treat. Tell them to continue only while both the symptoms of fever and the other symptoms are present (see the <u>Central Alerting System: ibuprofen and coronavirus [COVID-19]</u> for further details of ibuprofen including dosage). **[23 March 2021]**

Managing breathlessness

3.1.10 Identify and treat reversible causes of breathlessness, for example, pulmonary oedema, pulmonary embolism, chronic obstructive pulmonary disorder and

asthma. **[23 March 2021]**

For further information on identifying and managing pulmonary embolism, see <u>NICE's guideline on venous thromboembolic diseases: diagnosis, management</u> and thrombophilia testing.

- 3.1.11 When significant medical pathology has been excluded or further investigation is inappropriate, the following may help to manage breathlessness as part of supportive care:
 - keeping the room cool
 - encouraging relaxation and breathing techniques, and changing body positioning
 - encouraging people who are self-isolating alone to improve air circulation by opening a window or door. [23 March 2021]
- 3.1.12 If hypoxia is the likely cause of breathlessness:
 - consider a trial of oxygen therapy
 - discuss with the person, their family or carer, possible transfer to and evaluation in secondary care. [23 March 2021]
- 3.1.13 Be aware that breathlessness with or without hypoxia often causes anxiety, which can then increase breathlessness further. **[23 March 2021]**

Managing anxiety, delirium and agitation

- 3.1.14 Assess reversible causes of delirium. See <u>NICE's guideline on delirium:</u> prevention, diagnosis and management in hospital and long-term care. [23 March 2021]
- 3.1.15 Address reversible causes of anxiety by:
 - exploring the person's concerns and anxieties

• explaining to people providing care how they can help. [23 March 2021]

Managing medicines

- 3.1.16 When supporting people with symptoms of COVID-19 who are having care in the community delivered by social care, follow <u>NICE's guideline on managing</u> <u>medicines for adults receiving social care in the community</u>. This includes processes for ordering and supplying medicines, and transporting, storing and disposing of medicines. **[23 March 2021]**
- 3.1.17 When prescribing, handling, administering and disposing of medicines in care homes and hospices, follow <u>NICE's guideline on managing medicines in care homes</u>. **[23 March 2021]**

3.2 In hospital

Deciding when to escalate treatment

For support with decision making, see:

- ethical guidance from the Royal College of Physicians
- <u>national guidance presented by the Faculty of Intensive Care Medicine, Intensive</u> <u>Care Society, Association of Anaesthetists and Royal College of Anaesthetists</u>
- <u>advice on decision making under pandemic conditions by the Intensive Care</u>
 <u>Society</u>
- advice on decision making and consent from General Medical Council.

Tools such as the <u>BMJ's emergency care and resuscitation plans</u> may be useful when making decisions about a treatment plan.

3.2.1 Base decisions about escalating treatment within the hospital on the likelihood of

a person's recovery. Take into account their treatment expectations, goals of care and the likelihood that they will recover to an outcome that is acceptable to them. [23 March 2021]

- 3.2.2 Ensure healthcare professionals have access to resources to support discussions about treatment plans (see, for example, <u>decision making for escalation of</u> <u>treatment and referring for critical care support</u>, and an <u>example decision support</u> <u>form</u>). **[23 March 2021]**
- 3.2.3 Discuss treatment escalation with a multidisciplinary team of medical and allied health professional colleagues (such as from critical care, respiratory medicine, geriatric medicine and palliative care) when there is uncertainty about treatment escalation decisions. **[23 March 2021]**
- 3.2.4 Document referral to and advice from critical care services and respiratory support units in a standard format. When telephone advice from critical care or respiratory support units is appropriate, this should still be documented in a standard format (see an <u>example referral form</u>). **[23 March 2021]**

Escalating and de-escalating treatment

- 3.2.5 Before escalating respiratory or other organ support, identify agreed treatment goals with the person (if possible), and their family and carers, or an independent mental capacity advocate (if appropriate). Start all advanced respiratory support or organ support with a clear plan of how it will address the diagnosis and lead to agreed treatment goals (outcomes). Ensure this includes management plans for when there is further deterioration or no response to treatment. **[23 March 2021, amended 2 September 2021]**
- 3.2.6 Do not continue respiratory or other organ support if it is considered that it will no longer result in the desired overall goals (outcomes). Record the decision and the discussion with the person (if possible), and their family and carers, or an independent mental capacity advocate (if appropriate). [23 March 2021, amended 2 September 2021]

Delivering services in critical care and respiratory support units

- 3.2.7 Trusts should review:
 - their strategy on management for people who are deteriorating and
 - use of the track-and-trigger system (NEWS2 has been endorsed by NHS England).

See <u>NICE's guideline on acutely ill adults in hospital for recommendations on</u> identifying patients whose clinical condition is deteriorating or is at risk of deterioration and the <u>Royal College of Physician's information on the place of</u> <u>NEWS2 in managing patients with COVID-19</u>. [23 March 2021, amended 2 September 2021]

Non-invasive respiratory support

For further information on treating respiratory failure secondary to COVID-19, the British Thoracic Society and Intensive Care Society have produced information on management of acute respiratory hypoxaemia associated with COVID-19.

For management of clinical deterioration of COVID-19 in pregnancy, see the <u>Royal</u> <u>College of Obstetricians and Gynaecologists information on management of</u> <u>coronavirus infection in pregnancy</u>.

For more information on respiratory support in children with COVID-19, see the <u>Royal</u> <u>College of Paediatrics and Child Health National guidance for the management of</u> <u>children in hospital with viral respiratory tract infections (2023)</u>.

Early treatment escalation planning for non-invasive respiratory support

3.2.8 For information on deciding when to escalate and de-escalate treatment for people who need <u>non-invasive respiratory support</u>, see the <u>section on deciding</u> when to escalate treatment and the <u>section on escalating and de-escalating</u> treatment. Also, consider factors such as:

- how much supplemental oxygen is needed to reach target oxygen saturation
- the person's overall clinical trajectory
- the person's effort of breathing (inspiratory effort and respiratory rate)
- how well the person has tolerated treatments so far
- treatment preferences after discussion with the person, and their family and carers (when appropriate). [2 September 2021]
- 3.2.9 Optimise pharmacological and non-pharmacological management strategies in people who need non-invasive respiratory support. [2 September 2021, amended 10 March 2022]
- 3.2.10 Consider awake prone positioning for people in hospital with COVID-19 who are not intubated and have higher oxygen needs. Discuss this with the person to reach a shared decision on whether to try the position. **[10 March 2023]**
- 3.2.11 When trying awake prone positioning, factors to consider may include:
 - whether the person has any contraindications to prone positioning (for example, communication difficulties that affect their ability to try the position, respiratory distress, potential need for invasive ventilation, untreated pneumothorax, or recent abdominal, thoracic, facial, pelvic or spinal injury)
 - availability of support from healthcare professionals with skills and experience in prone positioning
 - allowing a suitable duration to measure response to prone positioning (for example, by monitoring oxygen saturation, need for supplemental oxygen, respiratory rate, sensation of breathlessness)
 - ensuring regular review and continuous monitoring (for example, oxygen saturation level)
 - how well the person can tolerate prone positioning and the importance of breaks

 stopping prone positioning if it causes excessive discomfort (including pressure damage, or pins and needles or numbness in the upper limbs), or there is worsening hypoxia or excessive breathlessness.

The Intensive Care Society has produced information on conscious prone positioning for people with COVID-19.

Follow relevant national guidance on communication, providing information (including in different formats and languages) and shared decision making, for example, <u>NICE's guideline on shared decision making</u>. **[10 March 2023]**

For a short explanation of why the panel made these recommendations, see the rationale section on early escalation treatment planning for non-invasive respiratory support.

Full details of the evidence and the panel's discussion are in:

- evidence review G: prone positioning
- <u>evidence review H: respiratory support strategies</u>.

Delivering non-invasive respiratory support

3.2.12 Do not routinely offer <u>high-flow nasal oxygen (HFNO)</u> as the main form of respiratory support for people with COVID-19 and respiratory failure in whom escalation to <u>invasive mechanical ventilation</u> would be appropriate. **[10 March 2023]**

See recommendation 3.2.16 on when to consider HFNO.

- 3.2.13 Consider <u>continuous positive airway pressure (CPAP)</u> for people with COVID-19 when they have hypoxaemia that is not responding to supplemental oxygen with a fraction of inspired oxygen of 0.4 (40%) or more **and either:**
 - escalation to invasive mechanical ventilation would be an option but it is not

immediately needed or

• it is agreed that respiratory support should not be escalated beyond CPAP.

In June 2021, the <u>Medicines and Healthcare products Regulatory Agency</u> (MHRA) issued a National Patient Safety Alert for Philips ventilator, CPAP and <u>bilevel positive airway pressure devices</u> because of a potential for harm from inhaled particles and volatile organic compounds. This applies to all devices manufactured before 26 April 2021. [2 September 2021, amended 10 March 2022]

- 3.2.14 For people with COVID-19 having CPAP, ensure:
 - there is access to critical care providers for advice, review and prompt escalation of treatment if needed
 - regular review by an appropriate senior clinician (such as every 12 hours) and more frequent review if needed, in line with the <u>British Thoracic Society</u> <u>guidance on respiratory support units</u> and the <u>Faculty of Intensive Care</u> <u>Medicine guidelines on the provision of intensive care services</u>
 - regular assessment and management of symptoms alongside non-invasive respiratory support. [2 September 2021, amended 10 March 2022]
- 3.2.15 Staff caring for people with COVID-19 having CPAP should have appropriate skills and competencies and provide appropriate monitoring. For further information on standards of care and provision of services, see the <u>Faculty of Intensive Care</u> <u>Medicine and Intensive Care Society guidelines on the provision of intensive care</u> <u>services</u>, the <u>British Thoracic Society and Intensive Care Society guidance on</u> <u>development and implementation of respiratory support units</u> and the <u>Paediatric</u> <u>Intensive Care Society guidance on the management of critically ill children</u>. [2 <u>September 2021, amended 10 March 2022]</u>
- 3.2.16 Consider using HFNO for people when:
 - they cannot tolerate CPAP but need humidified oxygen at high-flow rates
 - maximal conventional oxygen is not maintaining their target oxygen saturations and:

- they do not need immediate invasive mechanical ventilation or escalation to invasive mechanical ventilation is not suitable **and**
- CPAP is not suitable
- they need:
 - a break from CPAP (such as at mealtimes, for skin and pressure area relief, or for mouth care)
 - humidified oxygen or nebulisers (or both)
 - weaning from CPAP. [2 September 2021, amended 10 March 2022]

For a short explanation of why the panel made these recommendations, see the rationale section on delivering non-invasive respiratory support.

Full details of the evidence and the panel's discussion are in:

- evidence review G: prone positioning
- evidence review H: respiratory support strategies.

4 Therapeutics for COVID-19

4.1 Antivirals

Nirmatrelvir and ritonavir

There is a funding variation in place for nirmatrelvir plus ritonavir until 1 June 2025. See <u>NICE's technology appraisal guidance on nirmatrelvir plus ritonavir, sotrovimab</u> <u>and tocilizumab</u>.

- 4.1.1 Nirmatrelvir plus ritonavir is recommended as an option for treating COVID-19 in adults, only if they:
 - do not need supplemental oxygen for COVID-19 and
 - have any of the following:
 - an increased risk for progression to severe COVID-19, as defined in section 5 of NICE's technology appraisal guidance on nirmatrelvir plus ritonavir, sotrovimab and tocilizumab
 - age 70 years and over
 - a body mass index (BMI) of 35 kg/m² or more
 - diabetes
 - heart failure.

This recommendation is from <u>NICE's technology appraisal guidance on</u> <u>nirmatrelvir plus ritonavir, sotrovimab and tocilizumab</u>. **[13 April 2022, amended 29 March 2023 and 13 March 2024]**

For a short explanation of why we made this recommendation, see the <u>rationale</u> <u>section on nirmatrelvir and ritonavir</u>.

Remdesivir

- 4.1.2 Remdesivir is recommended as an option for treating COVID-19 in hospitals in:
 - adults, only if they have a high risk of serious illness (risk factors as defined in section 5 of NICE's technology appraisal guidance on nirmatrelvir plus ritonavir, sotrovimab and tocilizumab for treating COVID-19)
 - babies, children and young people, only if they:
 - are aged 4 weeks to 17 years and weigh at least 3 kg, and:
 - \diamondsuit have pneumonia, and
 - \diamond need supplemental oxygen, or
 - weigh at least 40 kg, and have a high risk of serious illness (risk factors as defined in section 5 of NICE's technology appraisal guidance on nirmatrelvir plus ritonavir, sotrovimab and tocilizumab for treating COVID-19).

Remdesivir is only recommended if the company provides it according to the commercial arrangement (see <u>section 2 of NICE's technology</u> <u>appraisal guidance on remdesivir and tixagevimab plus cilgavimab for</u> <u>treating COVID-19</u>).

This recommendation is from <u>NICE's technology appraisal guidance on</u> remdesivir and tixagevimab plus cilgavimab. **[23 March 2021, amended 29 March 2023 and 8 May 2024]**

For a short explanation of why we made this recommendation, see the <u>rationale</u> <u>section on remdesivir</u>.

Molnupiravir

- 4.1.3 Consider a 5-day course of molnupiravir for adults with COVID-19 who:
 - do not need supplemental oxygen for COVID-19 and

- are within 5 days of symptom onset **and**
- are thought to be at high risk of progression to severe COVID-19. (<u>NHS</u> <u>England's Interim Clinical Commissioning Policy on remdesivir and</u> <u>molnupiravir</u> provides a list of people prioritised for treatment with antivirals.)

When assessing the person, take into account their likely response to any vaccinations already given, any comorbidities or risk factors, and whether their condition is deteriorating. **[23 March 2021, amended 29 March 2023]**

4.1.4 Do not offer molnupiravir to children and young people aged under 18, or pregnant women. **[23 March 2021, amended 29 March 2023]**

For a short explanation of why the panel made these recommendations, see the rationale section on molnupiravir.

Full details of the evidence and the panel's discussion are in <u>evidence review Q:</u> <u>Molnupiravir</u>.

4.2 Sotrovimab

- 4.2.1 Sotrovimab is recommended as an option for treating COVID-19 in adults and young people aged 12 years and over and weighing at least 40 kg, only if:
 - they do not need supplemental oxygen for COVID-19 and
 - they have an increased risk for progression to severe COVID-19, as defined in section 5 of NICE's technology appraisal guidance on nirmatrelvir plus ritonavir, sotrovimab and tocilizumab and
 - nirmatrelvir plus ritonavir is contraindicated or unsuitable.

Sotrovimab is only recommended if the company provides it according to the <u>commercial arrangement</u>.

This recommendation is from NICE's technology appraisal guidance on

nirmatrelvir plus ritonavir, sotrovimab and tocilizumab. [27 January 2022, amended 29 March 2023 and 13 March 2024]

For a short explanation of why we made this recommendation, see the <u>rationale</u> <u>section on sotrovimab</u>.

4.3 Corticosteroids

- 4.3.1 Offer dexamethasone, or either hydrocortisone or prednisolone when dexamethasone cannot be used or is unavailable, to people with COVID-19 who:
 - need supplemental oxygen to meet their prescribed oxygen saturation levels
 or
 - have a level of hypoxia that needs supplemental oxygen but who are unable to have or tolerate it.

Continue corticosteroids for up to 10 days unless there is a clear indication to stop early, which includes discharge from hospital or a hospital-supervised virtual COVID ward. **[8 April 2021]**

See box 1 on dosage information.

Box 1 Dosage information

Dosage in adults

Dexamethasone

- 6 mg orally once a day for 10 days (three 2 mg tablets or 15 ml of 2 mg/5 ml oral solution) or
- 6 mg intravenously once a day for 10 days (1.8 ml of 3.3 mg/ml ampoules [5.94 mg]).

For people able to swallow and in whom there are no significant concerns about enteral absorption, prescribe tablets. Only use intravenous administration when tablets or oral solutions are inappropriate or unavailable.

Suitable alternatives

Prednisolone: 40 mg orally once a day for 10 days.

Hydrocortisone: 50 mg intravenously every 8 hours for 10 days (0.5 ml of 100 mg/ml solution; powder for solution for injection or infusion is also available); this may be continued for up to 28 days for people with septic shock.

Dosage in pregnancy

Follow Royal College of Obstetrics and Gynaecology guidance.

Dosage for children with a greater than 44-week corrected gestational age

- **Dexamethasone:** 150 micrograms/kg (as a base) orally, nasogastrically or intravenously once a day for 10 days (max 6 mg).
- **Prednisolone:** 1 mg/kg orally, nasogastrically or intravenously once a day for 10 days (maximum 40 mg; doses can be rounded as per routine clinical practice).

Dosage for preterm babies with a corrected gestational age of less than 44 weeks

Seek specialist advice.

For more information on the management of children, follow the <u>Royal College of</u> <u>Paediatrics and Child Health National guidance for the management of children in</u> <u>hospital with viral respiratory tract infections (2023)</u>.

For people able to swallow and in whom there are no significant concerns about enteral absorption, prescribe tablets. Only use intravenous administration when tablets or oral solutions are inappropriate or unavailable.

4.3.2 Do not use corticosteroids to treat COVID-19 in people who do not need supplemental oxygen. (People who need corticosteroids for another medical reason should still have them.) **[8 April 2021, amended 20 April 2022]**

For a short explanation of why the panel made these recommendations, see the <u>rationale section on corticosteroids</u>.

Full details of the evidence and the panel's discussion are in <u>evidence review A:</u> <u>corticosteroids</u>.

4.4 Casirivimab and imdevimab – for people hospitalised because of COVID-19

4.4.1 This recommendation has been deleted because the conditional marketing authorisation for casirivimab plus imdevimab for treating COVID-19 was withdrawn. **[13 March 2024]**

4.5 Tocilizumab

- 4.5.1 Tocilizumab is recommended, within its marketing authorisation, as an option for treating COVID-19 in adults who:
 - are having systemic corticosteroids and
 - need supplemental oxygen or mechanical ventilation.

Tocilizumab is only recommended if the company provides it according to the <u>commercial arrangement</u>.

This recommendation is from <u>NICE's technology appraisal guidance on</u> <u>nirmatrelvir plus ritonavir, sotrovimab and tocilizumab</u>.

The <u>summary of product characteristics for tocilizumab</u> specifies that it should only be offered when there is no evidence of a bacterial or viral infection (other than SARS-CoV-2) that might be worsened by tocilizumab. It also states that the efficacy of tocilizumab has not been established in the treatment of COVID-19 in people who do not have elevated C-reactive protein levels. **[8 April 2021, amended 29 March 2023 and 13 March 2024]**

For a short explanation of why we made this recommendation, see the <u>rationale</u> <u>section on tocilizumab</u>.

4.6 Baricitinib

4.6.1 Consider baricitinib for people 2 years and over in hospital with COVID-19 who:

- need supplemental oxygen for COVID-19 and
- are having or have completed a course of corticosteroids such as dexamethasone, unless they cannot have corticosteroids **and**
- have no evidence of infection (other than SARS-CoV-2) that might be worsened by baricitinib.

In March 2023, this was an off-label use of baricitinib. See <u>NICE's information</u> <u>on prescribing medicines</u>.

Baricitinib may be considered in people who meet the above criteria, and who cannot have tocilizumab. When there is clinical deterioration despite treatment with tocilizumab, it may be appropriate to add baricitinib.

Baricitinib is contraindicated in pregnancy and breastfeeding. The <u>Royal</u> <u>College of Obstetricians and Gynaecologists has produced guidance on</u> <u>managing coronavirus infection in pregnancy</u>. **[6 May 2022, amended 29 March 2023]**

For a short explanation of why the panel made this recommendation, see the <u>rationale</u> <u>section on baricitinib</u>.

Full details of the evidence and the panel's discussion are in <u>evidence review L:</u> <u>baricitinib</u>.

4.7 Antibiotics

4.7.1 Do not use antibiotics for preventing or treating COVID-19 unless there is clinical suspicion of additional bacterial co-infection. See the <u>section on suspected or</u> <u>confirmed co-infection</u>. See also the <u>recommendations on azithromycin</u> and <u>doxycycline</u>. **[21 March 2021, amended 3 June 2021]**

4.8 Azithromycin

4.8.1 Do not use azithromycin to treat COVID-19. [3 June 2021]

For a short explanation of why the panel made this recommendation, see the <u>rationale</u> <u>section on azithromycin</u>.

Full details of the evidence and the panel's discussion are in <u>evidence review B:</u> <u>azithromycin</u>.

4.9 Budesonide (inhaled)

4.9.1 Only use budesonide to treat COVID-19 as part of a clinical trial. (People already on budesonide for conditions other than COVID-19 should continue treatment if

they test positive for COVID-19.) [3 November 2021]

For a short explanation of why the panel made this recommendation, see the <u>rationale</u> <u>section on budesonide</u>.

Full details of the evidence and the panel's discussion are in <u>evidence review E</u> inhaled <u>budesonide</u>.

4.10 Colchicine

4.10.1 Do not use colchicine to treat COVID-19. [27 May 2021, amended 1 December 2021]

For a short explanation of why the panel made this recommendation, see the <u>rationale</u> <u>section on colchicine</u>.

Full details of the evidence and the panel's discussion are in <u>evidence review F:</u> <u>colchicine</u>.

4.11 Doxycycline

4.11.1 Do not use doxycycline to treat COVID-19 in the community. [2 September 2021]

For a short explanation of why the panel made this recommendation, see the <u>rationale</u> <u>section on doxycycline</u>.

Full details of the evidence and the panel's discussion are in <u>evidence review C:</u> <u>doxycycline</u>.

4.12 Ivermectin

4.12.1 Do not use ivermectin to treat COVID-19 except as part of an ongoing clinical

trial. [22 November 2021, amended 15 June 2022]

For a short explanation of why the panel made this recommendation, see the <u>rationale</u> <u>section on ivermectin</u>.

Full details of the evidence and the panel's discussion are in <u>evidence review M:</u> <u>ivermectin</u>.

4.13 Tixagevimab plus cilgavimab

4.13.1 Tixagevimab plus cilgavimab is not recommended, within its marketing authorisation, for treating COVID-19 in adults who do not need supplemental oxygen and who have an increased risk of progression to severe COVID-19.

> This recommendation is from <u>NICE's technology appraisal guidance on remdesivir</u> and tixagevimab plus cilgavimab for treating COVID-19. [8 May 2024]

For a short explanation of why we made this recommendation, see the <u>rationale</u> <u>section on tixagevimab plus cilgavimab</u>.

4.14 Vitamin D

4.14.1 Do not use vitamin D to treat COVID-19 except as part of a clinical trial.

For existing UK guidance on taking vitamin D to maintain muscle and bone health, see <u>NHS advice on vitamin D</u>. **[14 July 2022]**

For a short explanation of why the panel made this recommendation, see the <u>rationale</u> <u>section on vitamin D</u>.

Full details of the evidence and the panel's discussion are in <u>evidence review N:</u> <u>vitamin D</u>.

5 Preventing and managing acute complications

5.1 Acute kidney injury (AKI)

Assessing and managing AKI

5.1.1 Be aware that in people with COVID-19, acute kidney injury (AKI):

- may be common, but prevalence is uncertain and depends on clinical setting (the <u>Intensive Care National Audit and Research Centre's report on COVID-19</u> <u>in critical care</u> provides information on people in critical care who need renal replacement therapy for AKI)
- is associated with an increased risk of dying
- can develop at any time (before, during or after hospital admission)
- may be caused by volume depletion (hypovolaemia), haemodynamic changes, viral infection leading directly to kidney tubular injury, thrombotic vascular processes, glomerular pathology or rhabdomyolysis
- may be associated with haematuria, proteinuria and abnormal serum electrolyte levels (both increased and decreased serum sodium and potassium). [23 March 2021]
- 5.1.2 Be aware that in people with COVID-19:
 - maintaining optimal fluid status (euvolaemia) is difficult but critical to reducing the incidence of AKI
 - treatments for COVID-19 may increase the risk of AKI
 - treatments for pre-existing conditions may increase the risk of AKI
 - fever and increased respiratory rate increase insensible fluid loss. [23 March 2021]

For information on assessing and managing acute kidney injury (AKI), see the <u>NICE</u> guideline on AKI: prevention, detection and management and the <u>NHS England AKI</u> algorithm.

For information on the management of acute life-threatening hyperkalaemia, see <u>NICE's technology appraisal guidance on patiromer</u> and <u>sodium zirconium</u> <u>cyclosilicate</u> for treating hyperkalaemia.

For information on using intravenous fluids, see <u>NICE's guidelines on intravenous fluid</u> <u>therapy in adults in hospital</u> and <u>intravenous fluid therapy in children and young</u> <u>people in hospital</u>.

For information on managing renal replacement therapy for adults who are critically unwell with COVID-19, see the <u>Renal Association's guidelines on renal replacement</u> <u>therapy for critically unwell adults</u>.

Follow-up

5.1.3 Monitor people with chronic kidney disease for at least 2 years after AKI, in line with <u>NICE's guideline on chronic kidney disease: assessment and management</u>.

See guidance on care after hospital discharge in the <u>Royal College of General</u> <u>Practitioners AKI toolkit</u>. **[23 March 2021]**

5.2 Acute myocardial injury

Diagnosing acute myocardial injury

- 5.2.1 For people in hospital with COVID-19 with signs or symptoms that suggest acute myocardial injury, measure high sensitivity troponin I (hs-cTnI) or T (hs-cTnT) and N-terminal pro B-type natriuretic peptide, and do an electrocardiogram (ECG).
 [23 March 2021]
- 5.2.2 Use the following test results to help inform a diagnosis:

- evolving ECG changes suggesting myocardial ischaemia
- an NT-proBNP level above 400 ng/litre
- high levels of hs-cTnl or hs-cTnT, particularly levels increasing over time.

Elevated troponin levels may reflect cardiac inflammatory response to severe COVID-19 rather than acute coronary syndrome. **[23 March 2021]**

Managing myocardial injury

- 5.2.3 For all people with COVID-19 and suspected or confirmed acute myocardial injury:
 - monitor in a setting where cardiac or respiratory deterioration can be rapidly identified
 - do continuous ECG monitoring
 - monitor blood pressure, heart rate and fluid balance. [23 March 2021]
- 5.2.4 For people with a clear diagnosis of myocardial injury:
 - seek specialist cardiology advice on treatment, further tests and imaging
 - follow local treatment protocols. [23 March 2021]
- 5.2.5 For people with a high clinical suspicion of myocardial injury, but without a clear diagnosis:
 - repeat high sensitivity troponin (hs-cTnl or hs-cTnT) measurements and ECG monitoring daily, because dynamic change may help to monitor the course of the illness and establish a clear diagnosis
 - seek specialist cardiology advice on further investigations such as transthoracic echocardiography and their frequency. **[23 March 2021]**

See also the management section for recommendations on care planning and recommendations on escalating and de-escalating treatment.

5.3 Venous thromboembolism (VTE) prophylaxis

In hospital

- 5.3.1 For young people and adults with COVID-19 that is being managed in hospital, assess the risk of bleeding as soon as possible after admission or by the time of the first consultant review. Use a risk assessment tool published by a national UK body, professional network or peer-reviewed journal. (The <u>Department of Health</u> <u>VTE risk assessment tool</u> is commonly used to develop treatment plans.) **[23 March 2021, amended 2 September 2021]**
- 5.3.2 Offer a <u>standard prophylactic dose</u> of a low molecular weight heparin (LMWH) as soon as possible, and within 14 hours of admission, to young people and adults with COVID-19 who need low-flow or high-flow supplemental oxygen, <u>continuous</u> <u>positive airway pressure (CPAP)</u>, <u>non-invasive ventilation (NIV)</u> or <u>invasive</u> <u>mechanical ventilation</u>, and who do not have an increased bleeding risk. **[2 September 2021]**
- 5.3.3 Continue management with a standard prophylactic dose of LMWH for a minimum of 7 days, including after discharge.

See recommendation 5.3.13 on LMWH self-administration. [2 September 2021]

5.3.4 Consider a <u>treatment dose</u> of an LMWH for young people and adults with COVID-19 who need low-flow supplemental oxygen and who do not have an increased bleeding risk.

In August 2021, using a treatment dose of a LMWH outside the treatment of confirmed VTE was an off-label use of parenteral anticoagulants. See <u>NICE's</u> <u>information on prescribing medicines</u>. **[2 September 2021]**

- 5.3.5 Continue management with a treatment dose of LMWH for 14 days or until discharge, whichever is sooner. Dose reduction may be needed to respond to any changes in a person's clinical circumstances. **[2 September 2021]**
- 5.3.6 Only offer an intermediate or treatment dose of an LMWH to young people and adults with COVID-19 who are receiving high-flow supplemental oxygen, CPAP,

NIV or invasive mechanical ventilation as part of a clinical trial. [2 September 2021]

For people with COVID-19 who do not need low-flow supplemental oxygen, follow the recommendations in <u>NICE's guideline on VTE in over 16s</u>.

- 5.3.7 Do not base prophylactic dosing of heparin on levels of D-dimer. [23 March 2021, amended 2 September 2021]
- 5.3.8 For people at extremes of body weight or with impaired renal function, consider adjusting the dose of LMWHs in line with the summary of product characteristics and locally agreed protocols. **[23 March 2021, amended 2 September 2021]**
- 5.3.9 For people who cannot have LMWHs, use fondaparinux sodium or unfractionated heparin (UFH).

In August 2021, LMWHs and fondaparinux sodium were off-label for people under 18 years. See <u>NICE's information on prescribing medicines</u>. **[23 March 2021, amended September 2021]**

- 5.3.10 For people who are already having anticoagulation treatment for another condition when admitted to hospital:
 - continue their current treatment dose of anticoagulant unless contraindicated by a change in clinical circumstances
 - consider switching to an LMWH if their current anticoagulant is not an LMWH and their clinical condition is deteriorating. [23 March 2021, amended September 2021]
- 5.3.11 If a person's clinical condition changes, assess the risk of VTE, reassess bleeding risk and review VTE prophylaxis. **[23 March 2021, amended September 2021]**
- 5.3.12 Organisations should collect and regularly review information on bleeding and other adverse events in people with COVID-19 having treatment or <u>intermediate</u> <u>doses</u> of LMWHs. **[23 March 2021, amended September 2021]**
- 5.3.13 Ensure that people who will be completing VTE prophylaxis after discharge are

able to use it correctly or have arrangements made for someone to help them. [23 March 2021, amended September 2021]

In hospital-led acute care in the community

5.3.14 For people with COVID-19 managed in <u>hospital-led acute care in the community</u> settings:

- assess the risks of VTE and bleeding
- consider pharmacological prophylaxis if the risk of VTE outweighs the risk of bleeding. [23 March 2021]

People with COVID-19 and additional risk factors

- 5.3.15 For women with COVID-19 who are pregnant or have given birth within the past 6 weeks, follow the <u>advice on VTE prevention in the Royal College of</u> <u>Obstetricians and Gynaecologists guidance on coronavirus (COVID-19) in</u> <u>pregnancy</u>. **[23 March 2021]**
- 5.3.16 For children with COVID-19 admitted into hospital, follow the advice on <u>COVID-19</u> guidance for management of children admitted to hospital in the Royal College of <u>Paediatrics and Child Health guidance</u>. **[23 March 2021]**

For a short explanation of why the panel made these recommendations, see the rationale section on prevention and management of venous thromboembolism (VTE) prophylaxis.

Full details of the evidence and the panel's discussion are in <u>evidence review D: VTE</u> prevention in COVID-19.

Information and support

5.3.17 Give people with COVID-19, and their families or carers if appropriate, information

about the benefits and risks of VTE prophylaxis.

See the <u>recommendations on giving information and planning for discharge in the</u> <u>NICE guideline on venous thromboembolism in over 16s</u>, including information on alternatives to heparin for people who have concerns about using animal products. **[23 March 2021]**

5.3.18 Offer people the opportunity to take part in ongoing clinical trials on COVID-19. [23 March 2021]

6 Identifying and managing co-infections

6.1 Managing viral or fungal pneumonia

Do not offer an antibiotic for preventing or treating pneumonia if SARS-CoV-2, another virus, or a fungal infection, is likely to be the cause.
 Antibiotics do not work on viruses, and inappropriate antibiotic use may reduce availability. Also, inappropriate use may lead to Clostridioides difficile infection and antimicrobial resistance, particularly with broad-spectrum antibiotics. [23 March 2021]

Evidence as of March 2021 suggests that bacterial co-infection occurs in less than about 8% of people with COVID-19, and could be as low as 0.1% in people in hospital with COVID-19. Viral and fungal co-infections occur at lower rates than bacterial co-infections.

Secondary infection or co-infection (bacterial, viral or fungal) is more likely the longer a person is in hospital and the more they are immunosuppressed (for example, because of certain types of treatment).

The type and number of secondary infections or co-infections will vary depending on the season and any restrictions in place (for example, lockdowns).

6.2 Other causes of pneumonia

Identifying other causes of pneumonia

- 6.2.1 To help identify other causes of pneumonia and to inform decision making about using antibiotics, consider the following tests:
 - a full blood count
 - chest imaging (X-ray, CT or ultrasound)

- respiratory and blood samples (for example, sputum or a tracheal aspirate sample, blood culture)
- urine samples for legionella and pneumococcal antigen testing
- throat, nasopharyngeal or sputum samples for respiratory viral (and atypical pathogen) polymerase chain reaction testing; for more information, see
 <u>Public Health England's COVID-19 guidance for sampling and for diagnostic
 laboratories</u>. [23 March 2021, amended 27 July 2022]

High C-reactive protein levels do not necessarily indicate whether pneumonia is due to bacteria or SARS-COV-2.

Low C-reactive protein level indicates that a secondary bacterial infection is less likely.

6.2.2 Do not use C-reactive protein to assess whether a person has a secondary bacterial infection if they have been having immunosuppressant treatment. [23 March 2021]

There is insufficient evidence to recommend routine procalcitonin testing to guide decisions about antibiotics. Centres already using procalcitonin tests are encouraged to participate in research and data collection.

Procalcitonin tests could be useful in identifying whether there is a bacterial infection. However, it is not clear whether they add benefit beyond what is suggested in recommendation 6.2.1 on tests to help differentiate between viral and bacterial pneumonia to guide decisions about antibiotics. The most appropriate threshold for procalcitonin is also uncertain.

Antibiotic treatment in the community

6.2.3 Do not offer an antibiotic for preventing secondary bacterial pneumonia in people with COVID-19. **[23 March 2021]**

6.2.4 If a person has suspected or confirmed secondary bacterial pneumonia, start antibiotic treatment as soon as possible. Take into account any different methods needed to deliver medicines during the COVID-19 pandemic (see recommendation 3.1.1 on minimising face-to-face contact).**[23 March 2021]**

For antibiotic choices to treat community-acquired pneumonia caused by a secondary bacterial infection, see the <u>recommendations on choice of antibiotic in</u> <u>NICE's guideline on pneumonia (community-acquired): antimicrobial prescribing</u>.

- 6.2.5 Advise people to seek medical help without delay if their symptoms do not improve as expected, or worsen rapidly or significantly, whether they are taking an antibiotic or not. **[23 March 2021]**
- 6.2.6 On reassessment, reconsider whether the person has signs and symptoms of more severe illness (see <u>recommendation 2.1.1 on signs and symptoms to help</u> <u>identify people with COVID-19 with the most severe illness</u>) and whether to refer them to hospital, other acute community support services or palliative care services. **[23 March 2021]**

Starting antibiotics in hospital

- 6.2.7 Start empirical antibiotics if there is clinical suspicion of a secondary bacterial infection in people with COVID-19. When a decision to start antibiotics has been made:
 - Start empirical antibiotic treatment as soon as possible after establishing a diagnosis of secondary bacterial pneumonia, and certainly within 4 hours.
 - Start treatment within 1 hour if the person has suspected sepsis and meets any of the high-risk criteria for this outlined in <u>NICE's guideline on sepsis</u>. [23 March 2021]

Choice of antibiotics in hospital

6.2.8 To guide decision making about antibiotics for secondary bacterial pneumonia in people with COVID-19, see <u>NICE's guideline on pneumonia (hospital-acquired):</u>

antimicrobial prescribing.

- 6.2.9 When choosing antibiotics, take account of:
 - local antimicrobial resistance data and
 - other factors such as their availability. [23 March 2021]
- 6.2.10 Give oral antibiotics if the person can take oral medicines and their condition is not severe enough to need intravenous antibiotics. **[23 March 2021]**
- 6.2.11 Consider seeking specialist advice on antibiotic treatment for people who:
 - are immunocompromised
 - have a history of infection with resistant organisms
 - have a history of repeated infective exacerbations of lung disease
 - are pregnant
 - are receiving advanced respiratory support or organ support. [23 March 2021]
- 6.2.12 Seek specialist advice if:
 - there is a suspicion that the person has an infection with multidrug-resistant bacteria and may need a different antibiotic or
 - there is clinical or microbiological evidence of infection and the person's condition does not improve as expected after 48 to 72 hours of antibiotic treatment. [23 March 2021]

Reviewing antibiotic treatment in hospital

6.2.13 Review all antibiotics at 24 to 48 hours, or as soon as test results are available. If appropriate, switch to a narrower-spectrum antibiotic, based on microbiological results. **[23 March 2021]**

6.2.14 For intravenous antibiotics, review within 48 hours and think about switching to oral antibiotics (in line with <u>NICE's guideline on pneumonia [hospital-acquired]:</u> <u>antimicrobial prescribing</u>)

Give antibiotics for 5 days, and then stop them unless there is a clear indication to continue (see <u>recommendation 6.2.12 on when to seek specialist advice</u>). [23 March 2021]

6.2.15 Reassess people if their symptoms do not improve as expected, or worsen rapidly or significantly. **[23 March 2021]**

6.3 COVID-19-associated pulmonary aspergillosis (CAPA)

For people who are critically ill and have, or have had, COVID-19 as part of their acute illness:

- COVID-19-associated pulmonary aspergillosis (CAPA) is a recognised cause of someone's condition not improving despite treatment (for example, antibiotic therapy, ventilatory support)
- there are no specific combinations of signs or symptoms for diagnosing CAPA
- the risk of having CAPA may increase with age and chronic lung disease.

Diagnosing CAPA

- 6.3.1 When deciding whether to suspect CAPA in someone who is critically ill and has, or has had, COVID-19 as part of their acute illness:
 - base your decisions on individual risk factors and the person's clinical condition
 - involve a multidisciplinary team, including infection specialists

• refer to local protocols on diagnosing and managing CAPA.

Local protocols for diagnosing and managing CAPA should be developed with a multidisciplinary team and based on knowledge of local prevalence. **[16 December 2021]**

- 6.3.2 Do not do diagnostic tests for CAPA if there is low clinical suspicion of the condition. **[16 December 2021]**
- 6.3.3 When investigating suspected CAPA:
 - use a range of tests to increase the likelihood of making a confident diagnosis
 - if possible, include bronchoalveolar lavage (BAL) as part of diagnostic testing, taking into account the risks of BAL in relation to the person's clinical condition
 - discuss the diagnostic testing strategy and final diagnosis with a multidisciplinary team that includes infection specialists. [16 December 2021]
- 6.3.4 Test for antifungal resistance if an Aspergillus isolate is cultured from a CAPA test sample. **[16 December 2021]**
- 6.3.5 Commissioners and local trusts should ensure that results of diagnostic tests for CAPA are available in a timeframe that informs and supports clinical decision making. **[16 December 2021]**
- 6.3.6 Monitor and report testing for, and diagnosis and management of, CAPA in line with local protocols.

Local protocols for diagnosing and managing CAPA should be developed with a multidisciplinary team and based on knowledge of local prevalence. [16 December 2021]

For a short explanation of why the panel made these recommendations, see the rationale section on diagnosing CAPA.

Full details of the evidence and the panel's discussion are in:

- evidence review I: CAPA risk factorssigns and symptoms
- evidence review J: CAPA diagnostics.

Treating CAPA

- 6.3.7 Only use antifungal treatments to treat CAPA if:
 - diagnostic investigations support a diagnosis of CAPA or
 - the results of diagnostic investigations are not available yet, but CAPA is suspected, and a multidisciplinary team or local protocols support starting treatment. [16 December 2021]
- 6.3.8 When considering antifungal treatment for CAPA:
 - discuss treatment options with a multidisciplinary team that includes infection specialists
 - follow local protocols that include best practice guidance on treating invasive aspergillosis. [16 December 2021]
- 6.3.9 For people having antifungal treatment for suspected CAPA, stop treatment if the results of investigations do not support a diagnosis of CAPA and a multidisciplinary team agrees. **[16 December 2021]**

For a short explanation of why the panel made these recommendations, see the rationale section on treating CAPA.

Full details of the evidence and the panel's discussion are in <u>evidence review K: CAPA</u> <u>– effectiveness and safety of treatments</u>.

7 Follow-up and rehabilitation

For follow-up and rehabilitation for people who have either ongoing symptomatic COVID-19 or post-COVID-19 syndrome, see <u>NICE's guideline on the long-term effects of COVID-19</u>.

Be aware of the UK Government's information on the COVID-19 vaccination programme.

8 Palliative care

- 8.1.1 For people who are nearing the end of their life, see NICE's guidelines on:
 - <u>Care of dying adults in the last days of life</u>: this includes recommendations on recognising when a person may be in the last days of life, communication and shared decision making.
 - End of life care for adults: service delivery: this includes recommendations for service providers on systems to help identify adults who may be at the end of their life, providing information and advanced care planning.
 - <u>Care and support of people growing older with learning disabilities</u>: this includes recommendations on accessing end of life care services, personcentred care, and involving families and support networks in end of life care planning.
 - End of life care for infants, children and young people with life-limiting conditions: planning and management: this includes recommendations on planning and managing end of life and palliative care for infants, children and young people (aged 0 to 17 years) with life-limiting conditions.

Terms used in the guideline

Continuous positive airway pressure (CPAP)

A type of non-invasive positive airway pressure that delivers a set pressure of airflow to the airways. This pressure is maintained throughout the respiratory cycle, both when the person is breathing in (inspiration) and breathing out (expiration). A CPAP device consists of a unit that generates airflow, which is delivered to the airway through a tight-fitting mask or other airtight interface.

High-flow nasal oxygen (HFNO)

Involves the delivery of warm and humidified oxygen (up to 70 litres per minute) through small nasal cannulae. The delivered gas flow is equal to or higher than the flow of air when the person is breathing in (inspiratory flow). This means that HFNO can deliver a higher and more stable concentration of inspired oxygen than conventional oxygen alone with nasal prongs. The higher flow also increases carbon dioxide washout in the upper airways and improves carbon dioxide clearance. Unlike CPAP, any positive pressure provided by HFNO is not measurable or sizeable.

Hospital-led acute care in the community

A setting in which people who would otherwise be admitted to hospital have acute medical care provided by members of the hospital team, often working with the person's GP team. They include hospital at home services and COVID-19 virtual wards.

Intermediate dose

Double the standard prophylactic dose of a low molecular weight heparin (LMWH) for medical patients.

Invasive mechanical ventilation

Any method of controlled ventilation delivered through a translaryngeal or tracheostomy

tube, or other methods as defined by the Intensive Care National Audit & Research Centre definition of 'advanced respiratory support'.

Low-flow supplemental oxygen

Oxygen delivered by a simple face mask or nasal canula at a flow rate usually up to 15 litres/min.

Non-invasive respiratory support

A broad umbrella term for different types of respiratory support given through external interfaces, and includes HFNO, CPAP and non-invasive ventilation (NIV). These are more intensive interventions than conventional oxygen therapy alone. The different types of support are not, however, interchangeable because they have differing effects on a person's respiratory and cardiac physiology. So, they typically have different indications for their use.

Non-invasive ventilation (NIV)

Refers to a mode of positive pressure ventilation that delivers airflow to the airways through a tight-fitting mask or other airtight interface. Airflow is delivered at variable pressures that are higher than when the person is breathing in (inspiratory pressure) and lower than when the person is breathing out (expiratory pressure). NIV differs from CPAP by providing additional inspiratory pressure assistance. Most devices have an option of adding positive expiratory airway pressure that can fulfil a similar role to CPAP by maintaining a positive pressure in the airways to aid lung recruitment (opening of the airways).

Standard prophylactic dose

The prophylactic dose of an LMWH, as listed in the medicine's summary of product characteristics, for medical patients.

Treatment dose

The licensed dose of anticoagulation used to treat confirmed venous thromboembolism

(VTE).

Recommendations for research

1 Vitamin D for treating COVID-19

What is the clinical effectiveness and safety of vitamin D for treating COVID-19 in children, young people and adults?

For a short explanation of why the committee made this recommendation for research, see the <u>rationale section on vitamin D</u>.

Full details of the evidence and the committee's discussion are in <u>evidence review N:</u> <u>vitamin D</u>.

2 Awake prone positioning

What is the effectiveness of awake body positioning in improving outcomes for people in hospital with COVID-19 who are not intubated and have higher oxygen needs?

For a short explanation of why the committee made this recommendation for research, see the <u>rationale section on early treatment escalation planning for non-invasive respiratory support</u>.

Full details of the evidence and the committee's discussion are in <u>evidence review G</u>: <u>prone positioning</u>.

3 Antifungal treatments for COVID-19-associated pulmonary aspergillosis (CAPA)

What are the clinical and cost effectiveness, and the safety, of specific antifungal treatments for treating suspected or confirmed CAPA, and the optimal treatment duration? When should treatment be started, stopped or modified?

For a short explanation of why the committee made this recommendation for research, see the <u>rationale section on treating CAPA</u>.

Full details of the evidence and the committee's discussion are in <u>evidence review K:</u> <u>CAPA – effectiveness and safety of treatments</u>.

4 Patient experience of CAPA diagnosis and management

What are the views, preferences and experiences of people with CAPA, and their families or carers, on: available tests for diagnosing CAPA and available treatments for CAPA?

For a short explanation of why the committee made this recommendation for research, see the <u>rationale section on treating CAPA</u>.

Full details of the evidence and the committee's discussion are in:

- evidence review J: CAPA diagnostics
- evidence review K: CAPA effectiveness and safety of treatments .

5 Diagnosing CAPA

In people with suspected CAPA, what are the most accurate tests for diagnosing the infection and when should they be done?

For a short explanation of why the committee made this recommendation for research, see the <u>rationale section on diagnosing CAPA</u>.

Full details of the evidence and the committee's discussion are in <u>evidence review J:</u> <u>CAPA – diagnostics</u>.

6 Outcomes for CAPA

What are the possible outcomes for people who are critically ill and have CAPA?

For a short explanation of why the committee made this recommendation for research, see the <u>rationale section on treating CAPA</u>.

Full details of the evidence and the committee's discussion are in <u>evidence review K:</u> <u>CAPA – effectiveness and safety of treatments</u>.

7 Risk factors for CAPA

What risk factors in people who are critically ill and have, or have had, COVID-19 as part of their acute illness are associated with developing CAPA?

For a short explanation of why the committee made this recommendation for research, see the <u>rationale section on diagnosing CAPA</u>.

Full details of the evidence and the committee's discussion are in <u>evidence review I:</u> <u>CAPA – risk factors and signs and symptoms</u>.

8 Budesonide for COVID-19

What is the clinical and cost effectiveness of budesonide for treating COVID-19 in the community in adults, young people and children?

For a short explanation of why the committee made this recommendation for research, see the <u>rationale section on budesonide (inhaled)</u>.

Full details of the evidence and the committee's discussion are in <u>evidence review E:</u> inhaled budesonide.

9 Multidisciplinary team agreed approach to continuous positive airway pressure (CPAP) weaning times

Does a multidisciplinary team agreed approach to weaning from CPAP improve weaning times and result in stopping CPAP for people with COVID-19 and acute respiratory failure?

For a short explanation of why the committee made this recommendation for research, see the <u>rationale section on delivering non-invasive respiratory support</u>.

Full details of the evidence and the committee's discussion are in <u>evidence review H:</u> respiratory support strategies.

10 High-flow nasal oxygen (HFNO) for COVID-19 and respiratory failure

Is HFNO effective in reducing breathlessness compared with standard care or conventional oxygen therapy for people in hospital with COVID-19 and respiratory failure when it is agreed that treatment will not be escalated beyond non-invasive respiratory support or palliative care is needed?

For a short explanation of why the committee made this recommendation for research, see the rationale section on delivering non-invasive respiratory support.

Full details of the evidence and the committee's discussion are in <u>evidence review H:</u> respiratory support strategies.

11 Low molecular weight heparins (LMWHs) for venous thromboembolism (VTE) prophylaxis

What is the effectiveness and safety of a treatment dose with an LMWH compared with a standard prophylactic dose for VTE prophylaxis in young people under 18 years with COVID-19?

For a short explanation of why the committee made this recommendation for research, see the <u>rationale section on in-hospital prevention and management of venous thromboembolism (VTE) prophylaxis</u>.

Full details of the evidence and the committee's discussion are in <u>evidence review D:</u> <u>VTE prevention</u>.

12 Extended pharmacological VTE prophylaxis

What is the effectiveness and safety of extended pharmacological VTE prophylaxis for people who have been discharged after treatment for COVID-19?

For a short explanation of why the committee made this recommendation for research, see the <u>rationale section on in-hospital prevention and management of</u> <u>venous thromboembolism (VTE) prophylaxis</u>.

Full details of the evidence and the committee's discussion are in <u>evidence review D:</u> <u>VTE prevention</u>.

13 Standard- versus intermediate-dose VTE prophylaxis for COVID-19

What is the effectiveness and safety of standard-dose compared with intermediate-dose pharmacological VTE prophylaxis for people with COVID-19, with or without additional risk factors for VTE?

For a short explanation of why the committee made this recommendation for research, see the <u>rationale section on people with COVID-19 and additional risk</u> <u>factors</u>.

Full details of the evidence and the committee's discussion are in <u>evidence review D:</u> <u>VTE prevention</u>.

Rationales

Assessment in the community

Identifying severe COVID-19

Recommendation 2.1.2

This recommendation is based on the expert panel's consensus view. The panel agreed that using pulse oximetry to measure oxygen saturation threshold levels is appropriate for helping to identify people with acute COVID-19 in primary or community care, and to predict outcomes such as hospitalisation. NHS England has guidance on pulse oximetry in assessment in adults in the community. The panel agreed that it is appropriate to cross-refer to this guidance for adults but not for children. The panel's recommended oxygen saturation level for children and young people was based on their consensus view that oxygen saturation levels below 91% in room air at rest are appropriate to assess the severity of illness and detect early deterioration in this group.

Care planning

Recommendation 2.1.5

Some benefits and risks of hospital admission may be similar for all patients (for example, improved diagnostic tests and access to treatments, or better contact with families in the community), but others may be personal to the individual (such as loss of access to carers who can anticipate needs well in someone unable to communicate themselves, or risks of spreading COVID-19).

Return to recommendations

Management in hospital

Early treatment escalation planning for non-invasive respiratory support

Recommendation 3.2.9

Based on their experience, the panel concluded that to improve outcomes for patients, it was important to ensure that existing management is optimised for people who need escalation of respiratory support.

Recommendations 3.2.10 and 3.2.11

Evidence shows that, for people in hospital with COVID-19 who are not intubated and have higher oxygen needs, awake prone positioning reduces the need for intubation compared with standard care. There is no evidence showing that awake prone positioning improves other outcomes compared with standard care. Although evidence is limited and of low to very low certainty, the panel agreed that awake prone positioning may be beneficial for this population.

The panel noted that awake prone positioning may not be suitable for everyone, and some people may find it difficult or uncomfortable to be in a prone position. They emphasised the importance of involving the person in decisions to try awake prone positioning.

The panel agreed that more research is needed to guide treatment and made a <u>recommendation for research for trials done in the UK with a focus on patient-reported</u> <u>outcomes</u>.

Return to recommendations

Delivering non-invasive respiratory support

Recommendation 3.2.12

Evidence does not show that high-flow nasal oxygen (HFNO) has treatment benefits over conventional oxygen therapy for people in whom escalation to invasive mechanical ventilation would be appropriate. So, the panel agreed that it should not be used as the

preferred treatment option for this population.

The panel acknowledged that although HFNO should not be routinely offered as the main form of respiratory support, it may be considered in some situations.

Recommendation 3.2.13

Evidence from a clinical trial suggests that there may be some treatment benefits with continuous positive airway pressure (CPAP) for people who have hypoxaemia and when mechanical ventilation is not immediately needed. These benefits are mostly for intubation outcomes (including likelihood of needing tracheal intubation and IMV), but there are uncertainties in the evidence. In this clinical trial, hypoxaemia was defined as less than or equal to 94% using pulse oximetry.

Recommendation 3.2.14

Based on their experience, the panel agreed that it is important to closely review people with COVID-19 having CPAP. This is to ensure that CPAP is not used for longer than necessary and that treatment is escalated when needed.

Recommendation 3.2.16

Evidence showed no statistically significant benefits between HFNO compared with conventional oxygen. The panel acknowledged that although HFNO should not be the main form of respiratory support, it may be considered in some situations so made a recommendation for research on the use of HFNO where treatment would not be escalated beyond non-invasive respiratory support. The panel used their expertise to inform the recommendation on when to consider HFNO and proposed a recommendation for research to explore which treatment methods are effective for weaning people with COVID-19 from CPAP and the acceptability and safety of these methods.

Return to recommendations

Antivirals

Nirmatrelvir and ritonavir

Recommendation 4.1.1

Clinical evidence suggests that nirmatrelvir plus ritonavir is effective at treating mild COVID-19 compared with standard care. Nirmatrelvir plus ritonavir is recommended in these groups because the likely cost-effectiveness estimates are within what NICE considers an acceptable use of NHS resources. For evidence and information on how this decision was made, see <u>NICE's technology appraisal guidance on nirmatrelvir plus</u> ritonavir, sotrovimab and tocilizumab.

Return to recommendation

Remdesivir

Recommendation 4.1.2

For adults in hospital, remdesivir can improve how long adults needing low-flow supplemental oxygen live compared with standard care, but the evidence is highly uncertain. The cost-effectiveness estimates for remdesivir are only likely to be within what NICE considers an acceptable use of NHS resources for adults in hospital who have a high risk of serious illness. So, remdesivir is recommended for treating COVID-19 in this group.

There is limited clinical evidence comparing remdesivir with standard care for treating severe COVID-19 in babies, children and young people. So, the cost-effectiveness estimates are highly uncertain. But there are limited treatment options licensed for the groups covered, and the number who would have remdesivir is very small. So, remdesivir is recommended for treating COVID-19 in these groups.

For evidence and information on how this decision was made, see <u>NICE's technology</u> appraisal guidance on remdesivir and tixagevimab plus cilgavimab.

Return to recommendation

Molnupiravir

Recommendation 4.1.3

There is evidence from 2 randomised controlled trials that treatment with molnupiravir within 5 days of symptom onset reduces the risk of hospitalisation or death compared with placebo in adults who do not need supplemental oxygen and have at least 1 risk factor for development of severe COVID-19 disease. However, there is uncertainty about the generalisability of the evidence to current clinical practice because the trials only included people who were not vaccinated against COVID-19, and took place before the emergence of the Omicron (B.1.1.529) variant. Clinicians should refer to the <u>NHS England Interim</u> <u>Clinical Commissioning Policy for the most up-to-date information about people prioritised for treatment with antivirals</u>.

Recommendation 4.1.4

Two trials were included in the evidence, and both trials only included people aged 18 and above. Pregnant women were also excluded from the study population.

The summary of product characteristics states that molnupiravir is of low risk for mutagenicity or genotoxicity in adults. However, the safety and efficacy of molnupiravir has not been established in children and young people or pregnant women. Based on this, and the absence of these groups from the study populations, the panel concluded that there is no evidence on the efficacy and safety of molnupiravir for children and young people, or pregnant women, and so it cannot be recommended for them.

Return to recommendations

Sotrovimab

Recommendation 4.2.1

There is some evidence suggesting that sotrovimab is likely to be effective at treating mild COVID-19 compared with standard care. Its likely cost-effectiveness estimates are within what NICE considers an acceptable use of NHS resources for people in whom nirmatrelvir plus ritonavir is contraindicated or unsuitable. So, sotrovimab is recommended for this group. For evidence and information on how this decision was made, see <u>NICE's</u> technology appraisal guidance on nirmatrelvir plus ritonavir, sotrovimab and tocilizumab.

Return to recommendation

Corticosteroids

Recommendation 4.3.1

There is evidence to support using corticosteroids for people with COVID-19 who need supplemental oxygen, or who have a level of hypoxia that needs supplemental oxygen but who are unable to have or tolerate it. It is now established standard practice to offer dexamethasone. The growing evidence base, combined with its widespread availability, ease of administration and acceptable safety profile, supports its continued use. Hydrocortisone and prednisolone are suitable alternatives if dexamethasone cannot be used or is unavailable. The course duration recommended, for up to 10 days unless there is a clear indication to stop early, is based on that used in clinical trials. This includes being discharged from hospital or a hospital supervised virtual COVID ward. (Being on a hospital-supervised virtual COVID ward is not classed as being discharged from hospital.)

Recommendation 4.3.2

Evidence suggests that, in people with COVID-19 who do not need supplemental oxygen, corticosteroids may increase the risk of needing invasive mechanical ventilation and death at 28 days. The recommendation therefore cautions against using corticosteroids for people not on supplemental oxygen, unless there is another medical indication to do so.

Return to recommendations

Tocilizumab

Recommendation 4.5.1

Clinical evidence suggests that tocilizumab is effective at treating severe COVID-19 compared with standard care. Tocilizumab is recommended because the likely cost-effectiveness estimates are within what NICE considers an acceptable use of NHS resources. For evidence and information on how this decision was made, see <u>NICE's</u> technology appraisal guidance on nirmatrelvir plus ritonavir, sotrovimab and tocilizumab.

Return to recommendation

Baricitinib

Recommendation 4.6.1

There is evidence to support the use of baricitinib for moderate to severe COVID-19 in adults in hospital. It shows that baricitinib reduces mortality, duration of hospital stay and disease severity. Corticosteroids are part of standard treatment for COVID-19 in the UK, and there is evidence of an additional benefit when baricitinib is also used.

Baricitinib is not licensed for treating COVID-19. Off-label use of baricitinib for COVID-19 may be an option for adults who cannot have tocilizumab (for example, when tocilizumab is not available, the person cannot tolerate intravenous administration, or there are other important patient preferences or circumstances). The panel noted that, when there is clinical deterioration despite treatment with tocilizumab, it may be appropriate to also add baricitinib.

Based on the evidence supporting the use of baricitinib for moderate to severe COVID-19 in adults, the panel agreed that, in the event of severe or deteriorating illness, it could also be considered for children and young people 2 years and over. This is after careful clinical risk assessment and shared decision making that includes expert input from paediatricians and paediatric infectious disease specialists.

Return to recommendation

Azithromycin

Recommendation 4.8.1

The evidence suggests that azithromycin is no better than standard care at reducing risk of death in people in hospital with COVID-19. Limited evidence also suggests that azithromycin does not reduce the risk of hospitalisation or death in people with COVID-19 in the community. There is no evidence for azithromycin use for COVID-19 in children. The panel did not think there were reasons to expect different results in this group, so agreed that the recommendation applies to all age groups. They also noted the risk of antimicrobial resistance with azithromycin.

Return to recommendation

Budesonide (inhaled)

Recommendation 4.9.1

Trial evidence suggests some benefit with inhaled budesonide in reducing how long it takes to recover from COVID-19. However, this evidence is limited because it comes from only 2 trials, 1 of which was very small and stopped early. Also, the population in the trials was mainly older people, which limits its generalisability to other age groups. The panel concluded that more research is needed to address these issues, and that inhaled budesonide should therefore only be used as part of a clinical trial. They also made a recommendation for research to address this.

Return to recommendation

Colchicine

Recommendation 4.10.1

The evidence from trials of colchicine to treat COVID-19 in adults, both in hospital and community settings, shows no beneficial effect on all-cause mortality or need for mechanical ventilation compared with standard care. It also shows no effect on duration of hospital stay or hospitalisation. The evidence also shows that colchicine causes statistically significantly more adverse events than standard care within 21 days of starting treatment in hospital or 30 days in the community. There is no evidence for children or young people. Therefore, colchicine should not be used to treat COVID-19 in people of any age.

Return to recommendation

Doxycycline

Recommendation 4.11.1

There is evidence from 1 trial in the community of doxycycline for COVID-19 in people 65 years and over and in people 50 years and over with comorbidities. The results suggest that, compared with standard care alone, doxycycline plus standard care does not reduce the risk of hospitalisation and death, admission to intensive care, the need for mechanical

ventilation or oxygen, or significant adverse events in these groups. The results also suggest that it does not improve symptoms or recovery.

There is no evidence for doxycycline use in the community for COVID-19 in people under 65 years or people under 50 years with comorbidities. But, it is unlikely that the results in these groups will differ, so the panel agreed that the recommendation applies to all age groups in the community. They also noted the risks of side effects and antimicrobial resistance with doxycycline. There was no evidence found for doxycycline use in hospital settings.

Return to recommendation

Ivermectin

Recommendation 4.12.1

Overall, there is a high degree of uncertainty about whether ivermectin is more effective than control (standard care, placebo or both) for managing COVID-19 in hospital or community settings. The panel raised concerns about the quality of the studies on ivermectin. They noted that most of the evidence is of low or very low certainty, with some that is of moderate certainty. The panel also noted the uncertainty about the overall safety and the possibility of rare serious adverse reactions with ivermectin. Because of the uncertainty in the evidence (including small sample sizes and issues with study quality), the panel agreed that ivermectin should only be used to treat COVID-19 in ongoing wellconducted clinical trials. The panel were aware of at least 1 ongoing trial, the results of which may improve the certainty of the evidence on the effectiveness of ivermectin for managing COVID-19.

Return to recommendation

Tixagevimab plus cilgavimab

Recommendation 4.13.1

Evidence suggests that it is highly uncertain that tixagevimab plus cilgavimab is effective against Omicron variants of COVID-19. Because of this, it is not possible to reliably estimate its cost effectiveness, so it is not recommended. For evidence and information on

how this decision was made, see <u>NICE's technology appraisal guidance on remdesivir and</u> <u>tixagevimab plus cilgavimab</u>.

Return to recommendation

Vitamin D

Recommendation 4.14.1

The panel agreed that the clinical-effectiveness evidence for vitamin D for treating COVID-19 is uncertain, but suggests that there is no clear evidence of benefit. The studies included diverse populations with different COVID-19 severity, and used varying dosages of vitamin D and definitions of standard care. This means the evidence may not be generalisable to the UK.

The panel noted that the daily doses used in the studies were far higher than the standard doses used to prevent or treat vitamin D deficiency in the UK. They also noted that there was limited evidence from the studies on the adverse effects of these doses of vitamin D. The panel pointed out the potential adverse effects of a vitamin D overdose, such as raised plasma and urine concentrations of calcium and phosphate, and nausea and vomiting (see the <u>BNF for more details on adverse effects</u>).

The panel highlighted that existing guidance recommends taking vitamin D to maintain muscle and bone health. They agreed that vitamin D is important and well established for this.

The panel agreed that, until there is more evidence on the effects of vitamin D for treating COVID-19, it should only be used for treating COVID-19 as part of a clinical trial. The panel noted that the study populations did not include pregnant women or older populations who may be at more risk of severe COVID-19 outcomes. They also did not include children and young people under 18 years. So, they agreed that more research is also needed in the area and made a recommendation for research on vitamin D for treating COVID-19.

Return to recommendation

Prevention and management of venous thromboembolism (VTE) prophylaxis

In hospital

Recommendation 5.3.1

The panel agreed that all people with COVID-19 have an increased risk of VTE. Initial risk assessment for these people (as soon as possible after admission or by the time of their first consultant review) should focus on identifying people whose bleeding risk contraindicates pharmacological VTE prophylaxis.

The panel agreed that a risk assessment tool published by a national UK body, professional body or peer-reviewed journal should be prioritised for use.

Recommendation 5.3.2 and 5.3.3

The panel agreed that a standard prophylactic dose of a low molecular weight heparin (LMWH) should be offered as soon as possible to manage the risk of VTE based on current standard practice. Following standard prophylactic dose administration on admission, a more detailed assessment should be done to see whether people should be offered a treatment dose or not.

The panel also noted that people who are discharged early (before 7 days) could be at risk of clots. They emphasised the importance of continuing treatment after discharge until 7 days has passed to ensure people have had a full dose of a LMWH. The treatment duration comes from <u>NICE's guideline on VTE in over 16s</u>. The panel also made a <u>recommendation for research on the effectiveness and safety of extended VTE prophylaxis after discharge from hospital</u>.

Recommendation 5.3.4 and 5.3.5

The panel agreed that some young people and adults with COVID-19 who need low-flow oxygen supplementation may benefit from a treatment dose of an LMWH. The evidence suggests that a treatment dose of an LMWH for adults with COVID-19 who are in hospital and needing low-flow oxygen supplementation may reduce the risk of death and need for organ support compared with a standard prophylactic dose. It also suggests an increased

risk in major bleeding compared with a standard prophylactic dose. Because of the fine balance of benefits and harms, the panel agreed that this decision should be carefully considered, and that this choice should be guided by bleeding risk, clinical judgement and local protocols.

The treatment duration in the largest included trial was 14 days or until discharge, whichever was sooner. The panel thought that the timeframe for treatment should reflect the trial evidence.

The panel noted an absence of evidence for anticoagulation in children. They recognised that younger children have different haematological physiology, meaning that VTE is less likely. However, their clinical experience suggested that, after puberty, people under 18 years are also at risk of VTE if admitted to hospital with COVID-19. For that reason, the panel included young people in the recommendations as well as adults and made a recommendation for research for this population.

Recommendation 5.3.6

Based on the lack of clear benefit with intermediate- or treatment-dose anticoagulation, the panel concluded that young people and adults with severe COVID-19 should be offered standard prophylactic-dose anticoagulation. They also concluded that intermediate- or treatment-dose VTE prophylaxis should only be used as part of a clinical trial.

The panel were aware of ongoing trials of LMWHs that use intermediate or treatment doses in this group of people, including REMAP-CAP. They agreed that intermediate- or treatment- dose LMWHs should only be used for VTE prophylaxis in this group as part of a clinical trial to support recruitment into these trials.

Recommendation 5.3.7

The panel agreed that D-dimer levels do not influence peoples' response to anticoagulation.

Recommendation 5.3.8

This recommendation was adapted from the original NICE rapid guideline on reducing the risk of VTE in over 16s with COVID-19 (now withdrawn) that considered intermediate

doses in this population. In its development, the panel indicated that dose adjustments may be needed for people at extremes of body weight and those with renal impairment. To ensure that everyone gets an appropriate dose, the panel included dose adjustment in their recommendation. They added that summary of product characteristics and local protocols should be used to guide decisions on dose adjustment.

Return to recommendation 5.3.8

Acute care in the community

Recommendation 5.3.14

There was no evidence to inform recommendations on reducing the risk of VTE in people with COVID-19 pneumonia managed in hospital-led acute care in the community settings with input from hospital clinicians, such as 'hospital-at-home' services or COVID-19 'virtual wards'. People whose condition is managed in these settings have an increased risk of VTE that is similar to that of people having management in hospital. The panel therefore included a recommendation to consider pharmacological VTE prophylaxis for these people to ensure that they have the same care as those admitted to hospital.

The panel also made a <u>recommendation for research on extending pharmacological VTE</u> <u>prophylaxis after discharge</u> in people who have had treatment for COVID-19 pneumonia.

Return to recommendation

Additional risk factors

Recommendations 5.3.15 and 5.3.16

The panel noted the lack of evidence on pharmacological VTE prophylaxis for people with COVID-19 and additional risk factors. They agreed that VTE risk in women with COVID-19 who are pregnant or have given birth in the past 6 weeks should be managed in line with advice on COVID-19 in pregnancy published by the Royal College of Obstetricians and Gynaecologists.

There was no evidence on pharmacological VTE prophylaxis for specific groups with additional risk factors for VTE, including people who are having treatment with sex hormones, have or have previously had cancer, are having renal replacement therapy or extracorporeal membrane oxygenation, have a clotting condition or history of VTE, or have obesity (body mass index 30 kg/m² or higher). The panel made a <u>recommendation for</u> <u>research on standard-dose compared with intermediate-dose pharmacological VTE</u> <u>prophylaxis</u> in people with COVID-19 who have additional risk factors for VTE.

Return to recommendations

Diagnosing and treating COVID-19-associated pulmonary aspergillosis (CAPA)

Diagnosing CAPA

Recommendation 6.3.1

The panel agreed that the evidence was not strong enough to recommend specific factors that increase the risk of CAPA so the panel made a <u>recommendation for research to</u> <u>identify risk factors associated with developing CAPA</u>. They noted the importance of multidisciplinary decision making and using local protocols when deciding whether to suspect CAPA.

Recommendation 6.3.2

Because the incidence of CAPA is low, there is a lack of evidence on how to diagnose the condition. Also, there are no specific combinations of signs and symptoms for diagnosing it. The panel concluded that the likelihood of CAPA should be considered when deciding whether to do diagnostic tests.

Recommendation 6.3.3

There is a lack of evidence on diagnosing CAPA, including on what diagnostic tests to use, how frequently to test and the diagnostic value of the different investigations so the panel made a <u>recommendation for research to identify the most accurate testing for CAPA</u>. The panel noted that using a range of tests, including bronchoalveolar lavage (BAL), follows current best practice recommended in a <u>taskforce report by Verweij et al. (2021) on</u> <u>diagnosing and managing CAPA</u>.

Because BAL is an invasive procedure, it is important that any benefits or harms are

considered before using it to investigate CAPA. The panel noted that BAL may not always be suitable or feasible and made a <u>recommendation for research on people's views and</u> <u>experiences on available testing for CAPA</u>. They agreed that other tests could be used instead of BAL, such as serological assays, non-bronchoscopic lavage or endotracheal aspirates.

Recommendation 6.3.4

In clinical practice, microbiological investigations can be used to assess antifungal resistance of isolates cultured from test samples. The panel noted the importance of testing for azole resistance to support clinical management decisions and ensure that suitable antifungal treatments are used. They agreed that treatment can be started before test results are confirmed, but should be reviewed when test results are available.

See the <u>British Society for Medical Mycology's guidance on therapeutic drug monitoring of</u> <u>antifungal agents</u>.

Recommendation 6.3.5

The panel noted that results of laboratory tests, in particular fungal antigen tests, are needed to diagnose CAPA. They also noted that if test results are not timely, there could be a delay in treatment, or people could have treatments that they do not need. They highlighted the importance of having test results available in an appropriate timeframe to support clinical decision making and to improve people's outcomes.

Recommendation 6.3.6

There is a lack of evidence on the tests used to diagnose CAPA and on treatments for CAPA in people who are critically ill and have, or have had, COVID-19 as part of their acute illness. So, the panel agreed that local protocols should be developed to collect more information on the current prevalence of CAPA and practices for diagnosing and managing the condition.

Return to recommendations

Treating CAPA

Recommendation 6.3.7

The panel noted that there are risks with antifungal treatments for CAPA, including antifungal resistance and adverse effects. They agreed that treatment should only be started if investigations support a diagnosis of CAPA, or a multidisciplinary team agrees to start treatment.

Recommendation 6.3.8

The panel noted the lack of evidence on treatments for CAPA and decided to make a <u>recommendation for research on antifungal treatments for CAPA</u>. They agreed that treatment decisions, including on when to start treatment, should be guided by advice from infection specialists, and in line with local protocols and best practice guidelines. The panel noted that the evidence provided limited insights on the benefits or harms of antifungals so made a <u>recommendation for research on the outcomes for people with CAPA</u>. The panel also made a <u>recommendation for research on people's views and experiences on treatments for CAPA</u>.

For information on monitoring antifungal treatments, see the <u>British Society for Medical</u> <u>Mycology's guidance on therapeutic drug monitoring of antifungal agents</u>.

The panel noted the importance of national antifungal stewardship guidance, such as NICE's guideline on antimicrobial stewardship

Recommendation 6.3.9

The panel noted the importance of good antifungal stewardship for reducing the risk of adverse effects and antifungal resistance, particularly when treatment is started before diagnosis is confirmed. They wanted to ensure that antifungal treatment would be stopped when investigations do not support a diagnosis of CAPA. However, the panel were aware that interpreting diagnostic test results and confirming a diagnosis of CAPA can be challenging. So, they recommended a multidisciplinary approach when deciding whether to stop treatment.

Return to recommendations

Context

In response to the COVID-19 pandemic, NICE produced multiple rapid guidelines to support the health and social care system. We know that having different products can make it difficult for people trying to find guidance, so we have brought together NICE's published recommendations on managing COVID-19 into this single guideline. We hope users will find the content easier to find and use.

Many of the recommendations made early in the pandemic were based on the consensus of the guideline expert panels, so supporting information is limited. We have reviewed all content, using topic expert input and more recent evidence, and updated the recommendations where needed.

We aim to update these recommendations frequently in line with new evidence and will produce new recommendations where gaps are identified. We search and sift the evidence weekly to produce living recommendations that reflect the latest best available evidence.

We have developed this guideline using our <u>methods and processes for guidelines</u> <u>developed during health and social care emergencies</u>. For more details of the methods and processes used for this guideline, including details of the expert advisory panel members, see the <u>methods and processes section</u>.

Finding more information and expert advisory panel details

To find NICE guidance on related topics, including guidance in development, see the <u>NICE</u> topic page on COVID-19.

For full details of the evidence and the expert advisory panel's discussions, see the <u>evidence reviews</u>. You can also find information about <u>how the guideline was developed</u>, including details of the committee.

NICE has produced <u>tools and resources to help you put this guideline into practice</u>. For general help and advice on putting our guidelines into practice, see <u>resources to help you</u> <u>put NICE guidance into practice</u>.

Update information

8 May 2024

We updated the guidance on <u>remdesivir</u> and added a new recommendation on <u>tixagevimab plus cilgavimab</u> in line with <u>NICE's technology appraisal guidance on</u> <u>remdesivir and tixagevimab plus cilgavimab for treating COVID-19</u>.

13 March 2024

We updated the recommendation on nirmatrelvir plus ritonavir to include additional groups eligible for treatment (people with diabetes, obesity or heart failure, or people aged 70 years or older). We have included a link to the funding variation as set out in NICE's technology appraisal guidance on nirmatrelvir plus ritonavir, sotrovimab and tocilizumab.

We removed the recommendation on casirivimab plus imdevimab because the conditional marketing authorisation for casirivimab plus imdevimab for treating COVID-19 was withdrawn.

We clarified the wording of recommendation 1.1.4 by removing reference to isolation.

25 January 2024

We made editorial changes to ensure recommendations reflect the current context for COVID-19, including updating recommendation 1.1.4 to reflect that isolation is no longer mandatory. We transferred the guideline recommendations, evidence reviews and supporting information from the MAGICapp platform to the NICE website, changing the presentation.

30 November 2023

We replaced 2 recommendations on managing acute cough with a link to the <u>NICE</u> guideline on cough (acute): antimicrobial prescribing.

We removed the recommendation to consider benzodiazepine for managing anxiety or agitation because health system support for people with COVID-19 has changed significantly since the guideline was developed.

We removed the recommendations on medicines for end of life care because these are covered by the <u>NICE guidelines on care of dying adults in the last days of life</u>, <u>end of life</u> <u>care for adults: service delivery</u> and <u>care and support of people growing older with</u> <u>learning disabilities</u>, which are already linked from this guideline.

22 June 2023

We updated the recommendations on <u>nirmatrelvir plus ritonavir</u> and <u>sotrovimab</u> to link to <u>section 5 of NICE's technology appraisal guidance on casirivimab plus imdevimab,</u> <u>nirmatrelvir plus ritonavir, sotrovimab and tocilizumab</u>. The linked section provides supporting information on risk factors for progression to severe COVID-19 provided by the independent advisory group commissioned by the Department of Health and Social Care.

29 March 2023

We updated the <u>recommendations on casirivimab plus imdevimab for people in hospital</u> <u>because of COVID-19</u>, <u>nirmatrelvir plus ritonavir</u> and <u>tocilizumab</u>. We replaced the recommendations on neutralising monoclonal antibodies for people not in hospital with a <u>recommendation on sotrovimab</u>. The clinical and cost effectiveness of these therapeutics was reviewed through the <u>NICE multiple technology process</u>. For more information, see <u>NICE's technology appraisal guidance on casirivimab plus imdevimab, nirmatrelvir plus</u> <u>ritonavir, sotrovimab and tocilizumab</u>.

We replaced 2 <u>recommendations on baricitinib</u> with 1 updated recommendation to clarify how it should be used. We updated <u>recommendations on remdesivir</u> to account for an extension to the marketing authorisation to include the paediatric population.

We removed the recommendation on sarilumab, which was for off-label use of sarilumab because it is not licensed for use in COVID-19. This recommendation has been superseded by NICE's technology appraisal guidance on casirivimab plus imdevimab, nirmatrelvir plus ritonavir, sotrovimab and tocilizumab for people with COVID-19, which recommends tocilizumab.

14 July 2022

We updated recommendations on using remdesivir in hospital, and added a recommendation on vitamin D for treating COVID-19.

15 June 2022

We updated the recommendation on ivermectin.

19 May 2022

We replaced 2 recommendations about advice to give to people with COVID-19 with a single recommendation linking to the UK Health Security Agency's guidance for people with symptoms of a respiratory infection including COVID-19, which now provides this information. We deleted the recommendation for people with pre-existing advanced comorbidities because finding out if whether they have advance care plans or advance decisions to refuse treatment, is part of routine care. We also added a link to the UK Government's information on the COVID-19 vaccination programme to the section on discharge, follow-up and rehabilitation.

6 May 2022

We added new recommendations on baricitinib.

13 April 2022

We added a new recommendation on nirmatrelvir and ritonavir (Paxlovid) for people at high risk of progression to severe COVID-19.

30 March 2022

We updated existing recommendations on <u>casirivimab and imdevimab – for people</u> hospitalised because of COVID-19.

10 March 2022

We added a new recommendation on awake prone positioning and updated existing recommendations on non-invasive respiratory support.

23 February 2022

We added <u>recommendations on molnupiravir</u> and <u>remdesivir</u> for people with COVID-19 who do not need supplemental oxygen.

27 January 2022

We added recommendations on neutralising monoclonal antibodies for people with COVID-19 who are not in hospital.

16 December 2021

We added new <u>recommendations on COVID-19-associated pulmonary aspergillosis</u>. We revised our statement about the Omicron variant in the <u>recommendation on casirivimab</u> <u>and imdevimab</u>.

14 December 2021

We added a statement to the recommendation on casirivimab and imdevimab about the Omicron variant.

1 December 2021

We updated existing recommendations on colchicine.

22 November 2021

We added a new recommendation on ivermectin.

3 November 2021

We added a new recommendation on inhaled budesonide and updated the recommendations on casirivimab and imdevimab, clarifying that these recommendations apply to people who are hospitalised because of COVID-19.

27 October 2021

We updated existing recommendations on tocilizumab and sarilumab.

4 October 2021

We added new recommendations on casirivimab and imdevimab. We have also updated our supporting evidence on the use of heparins with the peer-reviewed REMAP-CAP trial results. This update does not change our current recommendations.

2 September 2021

We added new recommendations on non-invasive respiratory support and doxycycline, and updated existing recommendations on heparins.

10 August 2021

We corrected an error in the dosage information on corticosteroids. The dose of prednisolone for children with a greater than 44-week corrected gestational age is 1 mg/kg.

We made minor changes to:

- clarify that NHS England's Interim Clinical Commissioning Policy on remdesivir for patients hospitalised with COVID-19 was updated in June 2021 to include eligibility criteria for people who are significantly immunocompromised
- update hyperlinks in the recommendations on communication and shared decision making.

3 June 2021

We added new recommendations on azithromycin to treat COVID-19.

27 May 2021

We added new recommendations on colchicine to treat COVID-19 and updated existing recommendations on remdesivir for COVID-19 pneumonia.

We made a minor change to our recommendation on using pulse oximetry to identify people with severe COVID-19 in primary and community care settings to clarify that the NHS England guide should be followed for adults.

8 April 2021

We added recommendations for using corticosteroids, tocilizumab and sarilumab to treat COVID-19 (including the evidence and rationale for making the recommendations).

This updates and replaces our COVID-19 rapid evidence summaries on:

- remdesivir for treating hospitalised patients with suspected or confirmed COVID-19 (ES27, published 5 June 2020)
- tocilizumab for COVID-19 (ES33, published 15 January 2021, last updated 24 February 2021)
- sarilumab for COVID-19 (ES34, published 20 January 2021).

23 March 2021

This guideline updates and replaces our COVID-19 rapid guidelines on:

- critical care in adults (NG159, published 20 March 2020, last updated 12 February 2021)
- managing symptoms (including at the end of life) in the community (NG163, published 03 April 2020, last updated 13 October 2020)
- managing suspected or confirmed pneumonia in adults in the community (NG165, published 03 April 2020, last updated 23 April 2020)
- acute myocardial injury (NG171, published 23 April 2020)
- antibiotics for pneumonia in adults in hospital (NG173, published 01 May 2020, last updated 09 October 2020)
- acute kidney injury in hospital (NG175, published 06 May 2020)
- reducing the risk of venous thromboembolism in over 16s with COVID-19 (NG186, published 20 November 2020).

The guideline includes new recommendations on the use of therapeutics for people with COVID-19.

Minor changes since publication

11 July 2023: We updated links to the new NHS interim policy in the recommendations on remdesivir and molnupiravir.

22 June 2023: We updated hyperlinks to other sources in the recommendations on

nirmatrelvir and ritonavir, and sotrovimab.

06 April 2023: We updated hyperlinks to other sources in the recommendations on nirmatrelvir and ritonavir, and sotrovimab.

27 July 2022: We amended <u>section 6.2</u> to clarify that it covers tests for identifying other causes of pneumonia as well as bacterial.

22 July 2021: We added a cross-reference to the Renal Association's guidelines on renal replacement therapy for critically unwell adults for information on managing renal replacement therapy for adults who are critically unwell with COVID-19.

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