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CLINICAL PRACTICE GUIDELINES

Thoracic Society of Australia and New Zealand oxygen guidelines for acute oxygen use in adults: 'Swimming between the flags'*

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ABSTRACT

The purpose of the Thoracic Society of Australia and New Zealand guidelines is to provide simple, practical evidence-based recommendations for the acute use of oxygen in adults in clinical practice. The intended users are all health professionals responsible for the administration and/or monitoring of oxygen therapy in the management of acute medical patients in the community and hospital settings (excluding perioperative and intensive care patients), those responsible for the training of such health professionals, and both public and private health care organizations that deliver oxygen therapy.

Key words: adult, guideline, hyperoxia, hypoxia, oxygen, oxygen inhalation therapy.

Abbreviations: ABG, arterial blood gas; BTS, British Thoracic Society; COPD, chronic obstructive pulmonary disease; FiO_2, fraction of inspired oxygen; HDU, high dependency unit; ICU, intensive care unit; NIV, non-invasive ventilation; $PaCO_2$, arterial partial pressure of carbon dioxide; PaO_2, arterial partial pressure of oxygen; PCO_2, partial pressure of carbon dioxide; SaO_2, arterial oxygen saturation (measured by arterial blood gas); SpO_2, arterial oxygen saturation (measured by pulse oximeter); TSANZ, Thoracic Society of Australia and New Zealand.

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INTRODUCTION

Systematic review

The 2008 and draft 2015 British Thoracic Society (BTS) Guidelines for Emergency Oxygen Use in Adult Patients[1,2] were reviewed, including all references in these documents, which were evaluated in their entirety, together with additional references and texts where relevant. A systematic review was not performed for the purpose of developing this guideline. The BTS commissioned the Centre for Reviews and Dissemination and Centre for Health Economics at the University of York, UK, to undertake bespoke literature searches, using defined search strategies (appendix 14 in http://www.brit-thoracic.org.uk). While the Thoracic Society of Australia and New Zealand (TSANZ) Oxygen Guideline recommendations are similar to the BTS 2015 Oxygen Guidelines, there are a number of key differences including the general target oxygen saturation range (92–96% vs 94–98%) and the algorithms for emergency use of oxygen including greater emphasis on titration of oxygen administered via nasal cannulae. In contrast to the BTS 2015 Oxygen Guidelines, an extensive list of references is not provided, but rather reference is made to key reviews, studies and guidelines where appropriate. Readers are referred to the 2015 BTS guidelines for the more comprehensive detail that it provides.

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Table 1 Grades of recommendations

Grade of recommendation	Description
A	Body of evidence can be trusted to guide practice
B	Body of evidence can be trusted to guide practice in most situations
C	Body of evidence provides some support for recommendation(s) but care should be taken in its application
D	Body of evidence is weak and recommendation must be applied with caution

Source: National Health and Medical Research Council.

Grading
Grades of recommendation (Table 1) relate to the Australian National Health and Medical Research Council grading system based on level of evidence, consistency of that evidence, clinical impact, generalizability and applicability.[3] For a full explanation of the recommendation grades, please go to https://www.nhmrc.gov.au/_files_nhmrc/file/guidelines/developers/nhmrc_levels_grades_evidence_120423.pdf

Guideline Development Group
This group included representatives from a range of professions and disciplines relevant to the scope of the guidelines.

Peer review
The draft guidelines were peer-reviewed by the Australasian College for Emergency Medicine, the Australian and New Zealand College of Anaesthetists, the Australian College of Nursing Ltd, the Cardiac Society of Australia and New Zealand, the Australian and New Zealand Intensive Care Society, the Australian Physiotherapy Association, the Council of Ambulance Authorities Inc. and the Internal Medicine Society of Australia and New Zealand.

Presentation
The guidelines are presented in the format of key concepts, the recommendations with grades of evidence and practice points, and the background evidence on which the recommendations are based. Key recommendations are summarized in Table 2.

Dissemination plan
The guidelines will be sent to medical and nursing directors of hospitals, primary care organizations and ambulance services, and the deans of medical, physiotherapy and nursing schools in Australia and New Zealand.

Implementation
The implementation of these guidelines by organizations will require communication, education and training strategies, and an audit system for monitoring compliance within a designated timeframe.

Expiry date
2019.

CONCEPTS

1 Oxygen should be considered as a drug that is prescribed and administered for specific indications, with a documented target oxygen saturation range and with regular monitoring of the patient's response.
2 Oxygen is prescribed for the relief of hypoxaemia, not breathlessness.
3 Hypoxaemia is both a marker of risk of a poor outcome due to the severity of the underlying disease(s) that has caused hypoxaemia, and an independent risk factor of poor outcome.
4 There are risks associated with both hypoxaemia and hyperoxaemia, which underlie the importance of prescribing oxygen only if required, and to within a target oxygen saturation range.
5 The 'swimming between the flags' concept of titrating oxygen therapy, to within a specific target oxygen saturation range applies to a wide range of clinical situations, in addition to exacerbations of chronic obstructive pulmonary disease (COPD).
6 The variable accuracy of pulse oximetry in the estimation of arterial oxygen saturation (SaO_2) represents the major limitation in its use to guide the titration of oxygen therapy.
7 The use of high concentration oxygen in a breathless patient in an attempt to protect against hypoxaemia in the event of a subsequent deterioration has the potential to cause delay in recognizing clinical deterioration and reduce the time available to initiate additional treatment.
8 If a patient who requires a high fraction of inspired oxygen (FiO_2) to maintain adequate oxygen saturations deteriorates, there is limited opportunity to increase FiO_2 to avoid life-threatening hypoxaemia. For this reason, patients who need high FiO_2 should receive senior clinician review and transfer to an area where there are appropriate numbers of competent staff able to provide more intensive monitoring and therapy.

RECOMMENDATIONS

Assessment
1 Pulse oximetry should be available in all clinical situations in which oxygen is used.[4] **[Grade C]**
Practice point: There is variable accuracy of pulse oximetry to predict SaO_2 in acutely ill patients, with SaO_2 measurements by pulse oximeter (SpO_2) both over and underestimating SaO_2, with wide limits of agreement.[4–9] The accuracy of SpO_2 may worsen with increasingly severe hypoxaemia.[8,9] Clinicians need to

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Table 2 Key recommendations

Key recommendations
1. Pulse oximetry should be available in all clinical situations in which oxygen is used. [GRADE C]
2. ABG measurements should be considered in the following situations: [GRADE C] • Critically ill patients with cardiorespiratory or metabolic dysfunction • In patients with an SpO_2 of <92% • Deteriorating SpO_2 requiring increased FiO_2 • Patients at risk of hypercapnia • Breathless patients in whom a reliable oximetry signal cannot be obtained.
3. Oxygen saturation measured by pulse oximetry should be considered a 'vital sign' and documented with other vital signs in patient assessment and management. [GRADE D]
4. An oxygen prescription should be documented in the patient records and drug chart. [GRADE D]
5. In COPD [GRADE B] and other conditions associated with chronic respiratory failure [GRADE C], oxygen should be administered if the SpO_2 is less than 88%, and titrated to a target SpO_2 range of 88–92%.
6. In other acute medical conditions, oxygen should be administered if the SpO_2 is less than 92%, and titrated to a target SpO_2 range of 92–96%. [GRADE C]
7. Patients who need an: • FiO_2 of ≥0.40 (such as ≥6 L/min via a simple face mask) to maintain an adequate SpO_2, should receive senior clinician review. [GRADE D] • FiO_2 of ≥0.50 (such as ≥8 L/min via a simple face mask) to maintain an adequate SpO_2, should be referred for ICU review. [GRADE D]
8. In COPD and other conditions associated with chronic respiratory failure the preferred method of bronchodilator administration is an air-driven nebulizer or metered dose inhaler +/– a spacer. [GRADE B]
9. For most patients standard nasal cannulae are the preferred method of oxygen delivery, with the flow rate varied to achieve the target oxygen saturation. [GRADE D]
10. In patients with hypercapnic respiratory failure (arterial pH of <7.35 and $PaCO_2$ of >45 mm Hg), NIV or invasive ventilation should be considered. [GRADE A] COPD patients with a pH of <7.26 managed with NIV require intensive monitoring with a low threshold for intubation.
11. It is recommended that patients receiving ventilatory support are located in an area, such as an HDU, ICU, a close observation unit or monitored bed unit, where there are adequate numbers of staff experienced in ventilatory support to provide an appropriate level of monitoring and titration of therapy. [GRADE D]

ABG, arterial blood gas; COPD, chronic obstructive pulmonary disease; FiO_2, fraction of inspired oxygen; HDU, high dependency unit; ICU, intensive care unit; NIV, non-invasive ventilation; $PaCO_2$, arterial partial pressure of carbon dioxide; SpO_2, arterial oxygen saturation measured by pulse oximeter.

be aware of the variable accuracy of SpO_2 in the utilization of pulse oximetry in clinical practice. An SpO_2 of ≥92% is a practical lower threshold to rule out hypoxaemia, defined as an SaO_2 of <90%[7] or an arterial partial pressure of oxygen (PaO_2) of <60 mm Hg (8 kPa).[5]

2 Arterial blood gas (ABG) measurement should be considered in the following situations. **[Grade C]**

- Critically ill patients with cardiorespiratory or metabolic dysfunction
- In patients with an SpO_2 of <92% in whom hypoxaemia may be present
- Deteriorating SpO_2 requiring increased FiO_2
- Patients at risk of hypercapnia
- Breathless patients in whom a reliable oximetry signal cannot be obtained.

Peripheral venous blood gas analysis is a less invasive test; however, it does not provide an accurate estimate of arterial partial pressure of carbon dioxide ($PaCO_2$) or PaO_2.[10] It does, however, provide rapid clinically important information to assess acutely unwell patients, including pH, lactate, glucose, haemoglobin, sodium and potassium. In addition it provides a venous PCO_2 which if less than 40 mm Hg, effectively rules out hypercapnia.[10]

Arterialized capillary earlobe or fingertip blood gas measurements represent an alternative if unable to obtain an ABG measurement, recognizing that while providing accurate information about $PaCO_2$ and pH, they variably underestimate PaO_2 measurements.[11,12] As a result, patient assessment can be based on pH and partial pressure of carbon dioxide (PCO_2) levels measured from earlobe or fingertip blood gases, together with SpO_2 by pulse oximetry.

Practice point: Hypoxaemia requires investigation and treatment of the underlying cause, and consideration of the contribution of hypoventilation, including measurement of $PaCO_2$ and pH.

Prescription

1 A specific oxygen prescription should be documented in the patient records and the drug chart.[13] **[Grade D]**

Practice point: The main requirement for an oxygen prescription is documentation of the target SpO_2 range.

In its most detailed form, the prescription could include the delivery system and interface, the target oxygen saturation range, the range of flow rates for each delivery system, and instruction as to SpO_2 and FiO_2 at which clinical review should be sought. Considerable space on the prescription form is needed to provide such detail.

Oxygen administration (see Fig. 1)

1 An SpO_2 target of 88–92% is recommended in exacerbations of COPD[14] **[Grade B]** and other conditions associated with chronic respiratory failure (such as obesity hypoventilation syndrome,[15] bronchiectasis, cystic fibrosis,[16] neuromuscular disease and chest wall deformities such as severe kyphoscoliosis). **[Grade C]**

Practice points: Where there is diagnostic uncertainty as to whether COPD is the primary cause of the exacerbation, it may be preferable to titrate oxygen therapy to the 88–92% SpO_2 target range.[14,17–19]

If the patient is breathing room air and has a saturation of ≥88%, then the initiation of oxygen is not routinely required and may result in oxygen saturations outside the target saturation range.

2 In the presence of hypoxaemia in other acute medical conditions, oxygen should be administered to achieve a target SpO_2 range of 92–96%.[20,21] **[Grade C]**

Practice point: If the patient is breathing room air and has a saturation of ≥92%, then the initiation of oxygen is not routinely required and may place the patient at risk of oxygen saturations outside the target saturation range.

3 A target of around 85% is recommended in patients previously exposed to bleomycin or in paraquat poisoning.[22–24] **[Grade C]**

4 Patients with carbon monoxide poisoning should receive normobaric hyperoxia or hyperbaric oxygen therapy.[25,26] **[Grade B]** Note that pulse oximetry is likely to be inaccurate in this setting.[4]

Practice point: In the immediate assessment of an acutely unwell patient, oxygen saturations should be measured by oximetry, pending the availability of blood gas results if required (See Assessment, Point 2).

a. In the presence of COPD or conditions associated with chronic respiratory failure:
   - If $SpO_2 \geq 88\%$, oxygen therapy is not initially required.
   - If $SpO_2 < 88\%$, oxygen can be administered at 1–2 L/min via nasal cannulae or 2–4 L/min via 24% or 28% Venturi mask, and titrated to achieve target SpO_2.
   - The avoidance of inappropriate high concentration oxygen therapy may be facilitated by the provision of a COPD oxygen alert card.[27]

b. In the absence of COPD or known chronic respiratory failure:
   - If $SpO_2 \geq 92\%$, oxygen therapy is not routinely required.
   - If SpO_2 is 85–91%, oxygen can be initially instituted at 2–4 L/min via nasal cannulae or other suitable oxygen delivery method, and titrated to achieve target SpO_2. In many situations, this range of oxygen saturations is unlikely to be associated with risk, although oxygen is commonly administered.
   - If $SpO_2 < 85\%$, oxygen can be initiated at 4 L/min via nasal cannulae, through a simple face mask at 5–10 L/min, a 100% non-rebreather reservoir mask at 15 L/min, or humidified high flow nasal cannulae ($FiO_2 > 0.35$). The choice of delivery system will depend on the SpO_2 level (higher FiO_2 will be required with greater reductions in SpO_2), and titrated to achieve the target SpO_2 as soon as practically possible.

Practice point: If oximetry is not available, or reliable SpO_2 cannot be determined and hypoxaemia is suspected, oxygen can be delivered at:

- 1–2 L/min via nasal cannulae or 2–4 L/min via 24% or 28% Venturi mask in patients with acute exacerba-

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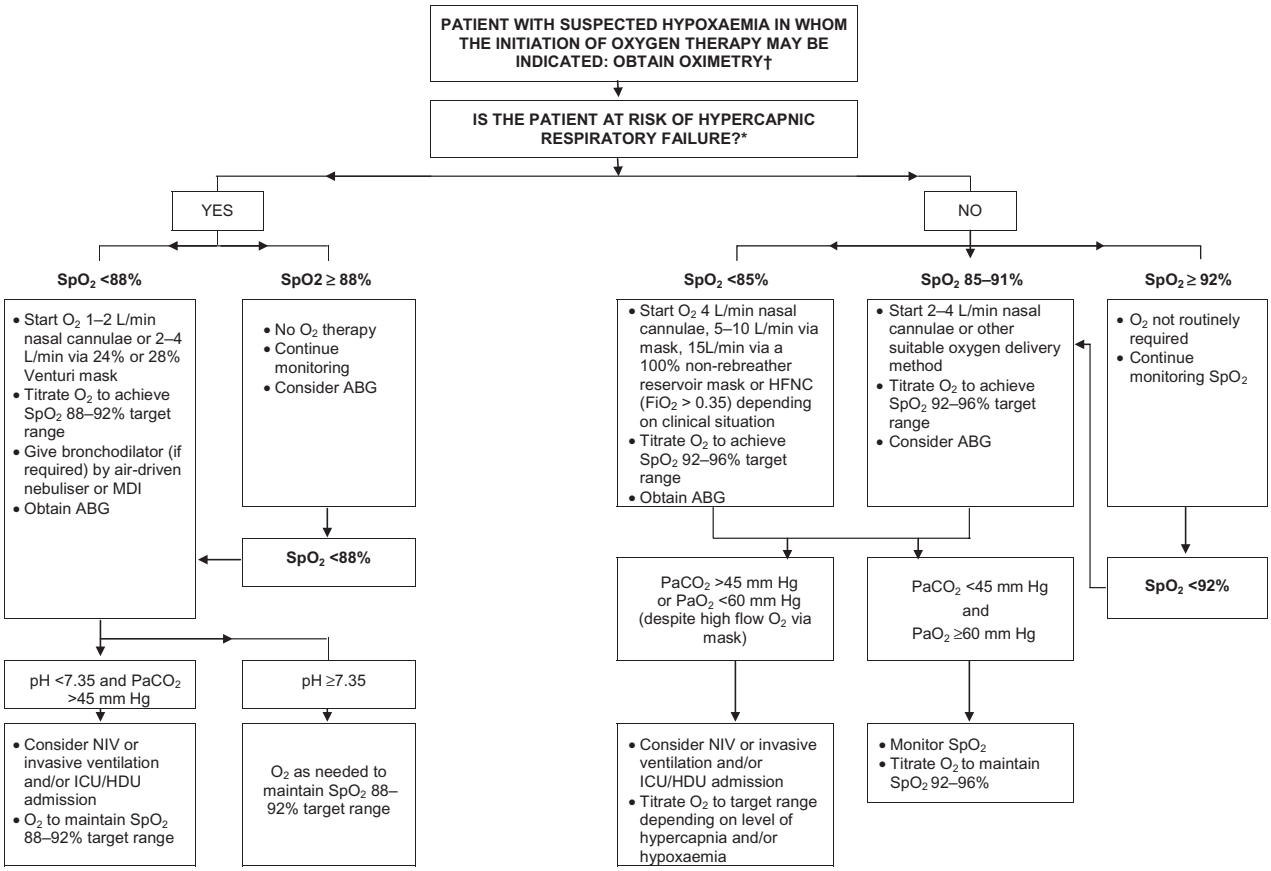

Figure 1 Treatment algorithm for oxygen therapy. Please refer to the text for full recommendations, references and evidence grading. *Such as COPD, obesity hypoventilation syndrome, chest wall deformities, cystic fibrosis, bronchiectasis or neuromuscular disease. †If oximetry is not available, or reliable oxygen saturations cannot be determined and hypoxaemia is suspected, oxygen can be delivered at:

○ 1–2 L/min via nasal cannulae or 2–4 L/min via 24% or 28% Venturi mask in patients with acute exacerbations of COPD or conditions known to be associated with chronic respiratory failure.*

○ 2–4 L/min oxygen via nasal cannulae in patients who are not critically ill and life-threatening hypoxaemia is not suspected.

○ 5–10 L/min via simple face mask, or 15 L/min through a 100% non-rebreather reservoir mask, or high flow nasal cannulae ($FiO_2 > 0.35$) in patients who are critically ill or in whom life-threatening hypoxaemia is suspected (e.g. post-cardiac arrest or resuscitation, shock, sepsis, near drowning, anaphylaxis, major head injury or in suspected carbon monoxide poisoning). NIV or invasive ventilation and transfer to HDU or ICU should also be considered in this situation.

ABG, arterial blood gas; COPD, chronic obstructive pulmonary disease; HDU, high dependency unit; HFNC, high flow nasal cannulae; ICU, intensive care unit; MDI, metered dose inhaler; NIV, non-invasive ventilation; O_2, oxygen; $PaCO_2$, arterial partial pressure of carbon dioxide; PaO_2, arterial partial pressure of oxygen; Sats, oxygen saturations; SpO_2, oxygen saturation determined by pulse oximetry.

tions of COPD or conditions known to be associated with chronic respiratory failure.

- 2–4 L/min oxygen via nasal cannulae in patients who are not critically ill and life-threatening hypoxaemia is not suspected.
- 5–10 L/min via simple face mask, 15 L/min through a 100% non-rebreather reservoir mask or high flow nasal cannulae ($FiO_2 > 0.35$) in patients in whom life-threatening hypoxaemia is suspected (see Fig. 1).

Monitoring

1 Monitoring of SpO_2 is a fundamental requirement for a target SpO_2 to be achieved.

2 An important component of monitoring is documentation of the delivery system and flow rate, in addition to documentation of the SpO_2.

Practice point: As hypoxaemia is a risk factor for poor clinical outcomes,[28] SpO_2 is a 'vital sign', to be considered together with other signs, including respiratory rate, which is a predictor of potentially serious clinical events.[29] **[Grade D]**

The New South Wales Standard Adult Observation Chart provides a practical example of the documentation of SpO_2 as one of the vital signs and a designated level for clinical review and rapid response. (http://nswhealth.moodle.com.au/DOH/DETECT/content/00_worry/when_to_worry_07.htm).

3 Patients who need an estimated FiO_2 of ≥0.40, such as ≥6 L/min via a simple face mask, to maintain an adequate SpO_2 should receive senior clinician review and may require transfer to a facility such as a high dependency unit (HDU), where there are appropriate numbers of competent staff able to provide more intensive monitoring and therapy. **[Grade D]**

4 Patients who need an estimated FiO_2 of ≥0.50, such as ≥8 L/min via a simple face mask, to maintain an adequate SpO_2, should receive intensive care unit (ICU) review and most will require ICU transfer. **[Grade D]**
Practice point: In patients whose oxygen saturations improve with oxygen therapy to above the target oxygen saturation range, their inspired oxygen therapy can be reduced or stopped. Oxygen saturation monitoring would continue to allow the detection of any subsequent deterioration of the underlying condition and the requirement to increase or resume oxygen therapy.
A reduction in SpO_2 while the FiO_2 is maintained, or increasing FiO_2 requirements to maintain SpO_2, should lead to a further assessment of the patient.

Delivery system

1 For most patients standard nasal cannulae are the preferred method of oxygen delivery, with the flow rate varied to achieve the target oxygen saturation. **[Grade D]**
2 The FiO_2 levels delivered by the different delivery systems may vary considerably between patients and be influenced by a number of factors, including respiratory rate and whether the patient's mouth is open or closed.[30–37] Approximate FiO_2 values delivered by different delivery systems are:

- Standard nasal cannulae can deliver an FiO_2 of 0.24–0.35 at an oxygen flow of 1–4 L/min
- Venturi masks can deliver an FiO_2 of 0.24–0.60
- High flow nasal cannulae can deliver an FiO_2 of 0.21–0.80
- A simple face mask can deliver an FiO_2 of 0.35–0.60 at an oxygen flow of 5–10 L/min
- A 100% non-rebreather reservoir mask at 15 L/min can deliver an FiO_2 of >0.60

3 For simple face masks, flow rates of <5 L/min should be avoided due to the potential risk of carbon dioxide rebreathing.[38,39] **[Grade C]**
4 Humidification of oxygen via high flow nasal cannulae may improve comfort and tolerance.[40,41]

Bronchodilator administration

1 In COPD and other conditions associated with chronic respiratory failure, if a bronchodilator is required, the preferred methods of administration are via an air-driven nebulizer or via a metered dose inhaler +/− a spacer, with supplementary nasal oxygen continued as required.[14,42] **[Grade B]**
Practice point: The administration of bronchodilator via an oxygen-driven nebulizer has the potential to cause an increase in $PaCO_2$.[43,44] It has been recommended that if an oxygen-driven nebulizer is used in a patient with an exacerbation of COPD, then its use is limited to 6 min.[1]
2 In asthma, if a bronchodilator is required, methods of delivery include an oxygen or air-driven nebulizer or metered dose inhaler +/− a spacer.[45]

Positioning

1 Fully conscious hypoxaemic patients should be allowed to position themselves according to their preference and comfort. **[Grade D]** In some, but not all patients, upright posture may result in improved oxygenation.[46–48]

Ventilatory support

1 In patients with hypercapnic respiratory failure, in whom an ABG measurement shows a pH of <7.35 and $PaCO_2$ of >45 mm Hg, non-invasive ventilation (NIV) or invasive ventilation should be considered.[49–53] **[Grade A]** COPD patients with a pH of <7.26 managed with NIV require more intensive monitoring with a low threshold for intubation.[52]
2 In patients in whom oxygen-induced hypercapnia is suspected, oxygen therapy should be titrated to maintain the 88–92% target oxygen saturation range and not be abruptly stopped due to the risk of profound rebound hypoxaemia.[54–56] **[Grade C]**
3 In patients with severe cardiogenic pulmonary oedema continuous positive airway pressure should be considered.[57] **[Grade A]**
4 NIV is not routinely recommended in acute hypoxaemic respiratory failure, as results from clinical trials and observational studies have provided mixed results for various patient groups[50,58–61]; however, there is some evidence of benefit in certain patients with immunosuppression.[50,59,61–63] **[Grade C]**
5 It is recommended that patients receiving ventilatory support are located in a ward area such as an HDU, ICU, a close observation unit or monitored bed unit, where there are adequate numbers of staff experienced in ventilatory support to provide an appropriate level of monitoring and titration of therapy.[49] **[Grade D]**

BACKGROUND EVIDENCE

1 Oxygen therapy does not relieve breathlessness in the absence of hypoxaemia. For example, there is no clinical benefit with short burst oxygen therapy in COPD patients with breathlessness,[64] or with the use of oxygen over room air via nasal cannulae for patients with COPD who do not have severe resting hypoxaemia.[65] Similarly, there is no additional symptomatic benefit in the use of oxygen over room air via nasal cannulae for refractory breathlessness in the palliative setting.[66]
In the absence of hypoxaemia, oxygen therapy is not indicated in the treatment of acute coronary syndrome or stroke, conditions associated with reversible ischaemia. In myocardial infarction, high concentration oxygen therapy is associated with greater infarct size, when compared with room air or titrated oxygen therapy if required to avoid hypoxaemia.[67,68] In stroke, routine administration of continuous or nocturnal oxygen therapy does not improve outcomes.[69,70]
2 Hypoxaemia is both a marker of risk of a poor outcome due to the severity of the underlying disease(s) that has caused hypoxaemia, and an independent risk factor of poor outcome.[28,71] The clinical impact depends on the underlying cause(s), the speed of onset and severity of hypoxaemia, the age of the

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patient and associated co-morbidities. It has been proposed that an PaO_2 of 50 mm Hg (6.6 kPa) can be considered as the safe lower limit of hypoxaemia in patients with COPD,[72] and that oxygen therapy that achieves an PaO_2 of at least 50 mm Hg would prevent immediate death from hypoxaemia.[73]

3 The potential risks due to hyperoxaemia with high concentration oxygen therapy include respiratory (increased $PaCO_2$, absorption atelectasis and direct pulmonary toxicity), cardiovascular (increased systemic vascular resistance and blood pressure, reduced coronary artery blood flow, reduced cardiac output), cerebrovascular (reduced cerebral blood flow) effects and increased reperfusion injury due to increased reactive oxygen species.[74–78]

4 The physiological response of an increase in $PaCO_2$ due to high concentration oxygen therapy has been demonstrated not only in stable and acute exacerbations of COPD,[72] but also in severe asthma,[20,79] community-acquired pneumonia[21] and obesity hypoventilation syndrome.[15] Proposed mechanisms for oxygen-induced hypercapnia include increased ventilation perfusion mismatch due to reduced hypoxic pulmonary vasoconstriction, reduced ventilatory drive, atelectasis and the Haldane effect, with the contribution of each likely to depend on the clinical situation.[1]

5 There is variable accuracy of pulse oximetry to predict SaO_2 in acutely ill patients, with SpO_2 measurements both over and under estimating SaO_2, with wide limits of agreement.[4–9] Clinicians need to be aware of the variable accuracy of SpO_2 in the utilization of pulse oximetry in clinical practice. Factors that might affect the accuracy of pulse oximetry include severe hypoxaemia, carboxyhaemoglobin and methaemoglobin levels, anaemia, dark skin, low perfusion, excessive ambient light and nail polish.[4,8,9]

6 The use of high flow oxygen in an attempt to protect against subsequent hypoxaemia in the event of deterioration has the potential to delay the recognition of such a deterioration.[80,81] This may provide a false reassurance that the patient is stable. There is likely to be no major change in vital signs[82] or a marked decrease in SpO_2 as assessed by pulse oximetry[83] until a potentially life-threatening situation has developed. At this stage there is limited opportunity to further increase the oxygen therapy while medical review and an intervention such as transfer to an HDU or ICU is undertaken.

Similarly, if a patient who requires a high FiO_2 to maintain adequate SpO_2 deteriorates there is limited capacity to increase FiO_2 to avoid life-threatening hypoxaemia. For this reason it is recommended that patients who need an FiO_2 of ≥0.40, such as ≥6 Litres per minute via a simple face mask, to maintain an adequate SpO_2, should receive senior clinician review and may require transfer to a ward area, such as an HDU. Likewise, patients who need an FiO_2 ≥0.50, such as ≥8 L/min via a simple face mask, to maintain an adequate SpO_2, should receive ICU review as most will require ICU transfer.

7 Peripheral venous blood gas analysis is a less invasive test than an ABG; however, it does not provide an accurate estimate of $PaCO_2$ or PaO_2. It does, however, provide rapid clinically important information to assess acutely unwell patients, including pH, lactate, glucose, haemoglobin, sodium and potassium. In addition it provides a PCO_2 that, if less than 40 mm Hg, essentially rules out hypercapnia. A systematic review and meta-analysis has compared venous and ABG measurements.[10] The point estimate for the difference between $PaCO_2$ and venous PCO_2 was 4.1 mm Hg higher for the venous reading, but with wide 95% confidence limits from 10.7 mm Hg higher to 2.4 mm Hg lower. PaO_2 was higher than venous PO_2 by 36.9 mm Hg with a 95% confidence interval of 27.2–46.6 mm Hg. Arterial pH values were slightly higher than venous pH; 0.03 with a 95% confidence interval of 0.029–0.038.

8 A target SpO_2 range of 88–92% is recommended in the treatment of COPD and other conditions associated with chronic respiratory failure due to demonstration of:

- A greater than twofold reduction in mortality with pre-hospital oxygen therapy titrated to this target, compared with high concentration oxygen therapy in patients with an acute exacerbation of COPD.[14]
- An increase in $PaCO_2$ with 100% oxygen therapy in patients with chronic respiratory failure due to obesity hypoventilation syndrome.[15]

9 A general target SpO_2 range of 92–96% in acute medical conditions has been recommended, incorporating a lower range than that recommended in the BTS guidelines (94–98%). This lower target recognises that:

- An SpO_2 of ≥92% is a practical lower threshold to rule out hypoxaemia, defined as an SaO_2 of <90%[7] or an PaO_2 of <60 mm Hg (8 kPa).[5]
- There is no known risk of hypoxic tissue injury at an SaO_2 of 90%.
- Older healthy subjects have SaO_2 levels to this lower level of 90%.[84,85]
- Healthy subjects have a mean nadir SpO_2 of around 90% during sleep.[86]
- Subjects with sleep-disordered breathing commonly tolerate SpO_2 levels between 80% and 90% for prolonged periods.[86]
- Adults with co-morbidities tolerate SpO_2 levels between 80% and 90% during long distance travel.[87]
- Guidelines for acute coronary syndrome[88] and heart failure[89] recommend administration of oxygen if the SpO_2 is <93% and <90%, respectively.
- In adults with coronary artery disease, anaerobic metabolism indicative of myocardial ischaemia is observed in some patients with SaO_2 between 70% and 85%, suggesting a 'safe' lower limit of oxygen saturation of 90%.[90]
- There is an evidence base for titration of oxygen therapy to a target SpO_2 range of 93–95% in acute severe asthma,[20] and community-acquired pneumonia.[21]
- There is an evidence base for the safety of oxygen therapy to a target SpO_2 range of 88–92% in acute exacerbations of COPD.[14]

- This recommendation is likely to reduce excessive use of high concentration oxygen therapy.
- An upper level of 96% avoids the potential risks of hyperoxia and allows for patient improvement to be recognized earlier during monitoring, so that oxygen can be down-titrated.

10 A target SpO_2 range of 85% is recommended in patients with prior exposure to bleomycin or in paraquat poisoning due to the demonstration of:

- Potentiation of lung injury by oxygen[22,23]
- Lack of harm from hypoxaemia with saturations around 85% in these clinical situations[24]

11 The potential advantages of nasal cannulae as an initial method of delivering oxygen therapy are:

- Ability to give nebulized bronchodilator at the same time as oxygen is administered.
- Oxygen can be prescribed by variable flows to achieve a target saturation range rather than a fixed FiO_2, although oxygenation may be maintained better with a Venturi mask.[32]
- Comfort, ease of use and low cost.
- Less likely to be taken off to eat or speak, and less likely to fall off.
- No risk of rebreathing of carbon dioxide.

12 Humidified high flow nasal cannulae are an alternative to standard low flow nasal cannulae or high flow masks for oxygen delivery.[34,40,41,91–93] There are no published evidence-based guidelines for their clinical use in adults; however, currently, some centres recommend high flow nasal cannulae only in the emergency department, HDU or ICU. The potential advantages, demonstrated mostly from observational studies, of this delivery system include:

- Greater comfort and tolerance via delivery of warmed and humidified nasal oxygen, compared with delivery via a face mask.
- Better titration of FiO_2 across a wider range of FiO_2.
- Preservation of upper airways function, such as speech, swallowing and cough.

Potential disadvantages of high flow nasal cannualae include:

- Risk of complacency if a high FiO_2 requirement is not recognized to represent life-threatening illness requiring more than correction of hypoxaemia.
- Role in severe exacerbations of COPD and asthma has not been investigated.

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REFERENCES

1 O'Driscoll BR, Howard LS, Davison AG, on behalf of the British Thoracic Society. BTS guideline for emergency oxygen use in adult patients. *Thorax* 2008; **63**: vi1–68.
2 O'Driscoll BR, Earis J, Howard LS, Mak V, on behalf of the British Thoracic Society. BTS guideline for emergency oxygen use in adult patients. *Thorax* 2015 (in press).
3 National Health and Medical Research Council. NHMRC additional levels of evidence and grades for recommendations for developers of guidelines. 2009. [Accessed Nov 2014.] Available from URL: https://www.nhmrc.gov.au/_files_nhmrc/file/guidelines/developers/nhmrc_levels_grades_evidence_120423.pdf
4 Pretto JJ, Roebuck T, Beckert L, Hamilton G. Clinical use of pulse oximetry: official guidelines from the Thoracic Society of Australia and New Zealand. *Respirology* 2014; **19**: 38–46.
5 Kelly AM, McAlpine R, Kyle E. How accurate are pulse oximeters in patients with acute exacerbations of chronic obstructive airways disease? *Respir. Med.* 2001; **95**: 336–40.
6 Perkins GD, McAuley DF, Giles S, Routledge H, Gao F. Do changes in pulse oximeter oxygen saturation predict equivalent changes in arterial oxygen saturation? *Crit. Care* 2003; **7**: R67.
7 Lee WW, Mayberry K, Crapo R, Jensen RL. The accuracy of pulse oximetry in the emergency department. *Am. J. Emerg. Med.* 2000; **18**: 427–31.
8 Wilson BJ, Cowan HJ, Lord JA, Zuege DJ, Zygun DA. The accuracy of pulse oximetry in emergency department patients with severe sepsis and septic shock: a retrospective cohort study. *BMC Emerg. Med.* 2010; **10**: 9.
9 Modica R, Rizzo A. Accuracy and response time of a portable pulse oximeter. The Pulsox-7 with a finger probe. *Respiration* 1991; **58**: 155–7.
10 Byrne AL, Bennett M, Chatterji R, Symons R, Pace NL, Thomas PS. Peripheral venous and arterial blood gas analysis in adults: are they comparable? A systematic review and meta-analysis. *Respirology* 2014; **19**: 168–75.
11 Murphy R, Thethy S, Raby S, Beckley J, Terrace J, Fiddler C, Craig M, Robertson C. Capillary blood gases in acute exacerbations of COPD. *Respir. Med.* 2006; **100**: 682–6.
12 Zavorsky GS, Cao J, Mayo NE, Gabbay R, Murias JM. Arterial versus capillary blood gases: a meta-analysis. *Respir. Physiol. Neurobiol.* 2007; **155**: 268–79.
13 Dodd ME, Kellet F, Davis A, Simpson JC, Webb AK, Haworth CS, Niven RM. Audit of oxygen prescribing before and after the introduction of a prescription chart. *BMJ* 2000; **321**: 864–5.
14 Austin MA, Wills KE, Blizzard L, Walters EH, Wood-Baker R. Effect of high flow oxygen on mortality in chronic obstructive pulmonary disease patients in prehospital setting: randomised controlled trial. *BMJ* 2010; **341**: c5462.
15 Wijesinghe M, Williams M, Perrin K, Weatherall M, Beasley R. The effect of supplemental oxygen on hypercapnia in subjects with obesity-associated hypoventilation: a randomized, crossover, clinical study. *Chest* 2011; **139**: 1018–24.
16 Gozal D. Nocturnal ventilatory support in patients with cystic fibrosis: comparison with supplemental oxygen. *Eur. Respir. J.* 1997; **10**: 1999–2003.
17 Denniston AK, O'Brien C, Stableforth D. The use of oxygen in acute exacerbations of chronic obstructive pulmonary disease: a prospective audit of pre-hospital and hospital emergency management. *Clin. Med.* 2002; **2**: 449–51.
18 Hale KE, Gavin C, O'Driscoll BR. Audit of oxygen use in emergency ambulances and in a hospital emergency department. *Emerg. Med. J.* 2008; **25**: 773–6.
19 Pilcher J, Weatherall M, Perrin K, Beasley R. Oxygen therapy in acute exacerbations of COPD. *Expert Rev. Respir. Med.* 2015; **9**: 287–93.
20 Perrin K, Wijesinghe M, Healy B, Wadsworth K, Bowditch R, Bibby S, Baker T, Weatherall M, Beasley R. Randomised controlled trial of high concentration versus titrated oxygen therapy in severe exacerbations of asthma. *Thorax* 2011; **66**: 937–41.
21 Wijesinghe M, Perrin K, Healy B, Weatherall M, Beasley R. Randomized controlled trial of high concentration oxygen in suspected community-acquired pneumonia. *J. R. Soc. Med.* 2011; **105**: 208–16.
22 Cersosimo RJ, Matthews SJ, Hong WK. Bleomycin pneumonitis potentiated by oxygen administration. *Drug Intell. Clin. Pharm.* 1985; **19**: 921–3.

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23 Bismuth C, Garnier R, Dally S, Fournier PE, Scherrmann JM. Prognosis and treatment of paraquat poisoning: a review of 28 cases. *J. Toxicol. Clin. Toxicol.* 1982; **19**: 461–74.
24 Fairshter RD, Rosen SM, Smith WR, Glauser FL, McRae DM, Wilson AF. Paraquat poisoning: new aspects of therapy. *Q. J. Med.* 1976; **45**: 551–65.
25 Weaver LK. Clinical practice. Carbon monoxide poisoning. *N. Engl. J. Med.* 2009; **360**: 1217–25.
26 Buckley NA, Juurlink DN, Isbister G, Bennett MH, Lavonas EJ. Hyperbaric oxygen for carbon monoxide poisoning. *Cochrane Database Syst. Rev.* 2011; **4**: 1–39.
27 Gooptu B, Ward L, Ansari SO, Eraut CD, Law D, Davison AG. Oxygen alert cards and controlled oxygen: preventing emergency admissions at risk of hypercapnic acidosis receiving high inspired oxygen concentrations in ambulances and A&E departments. *Emerg. Med. J.* 2006; **23**: 636–8.
28 Bowton DL, Scuderi PE, Haponik EF. The incidence and effect on outcome of hypoxemia in hospitalized medical patients. *Am. J. Med.* 1994; **97**: 38–46.
29 Cretikos MA, Bellomo R, Hillman K, Chen J, Finfer S, Flabouris A. Respiratory rate: the neglected vital sign. *Med. J. Aust.* 2008; **188**: 657–9.
30 Marino P, Sutin K. *The ICU Book*. Lippincott Williams & Wilkins, Philadelphia, PA, 2007.
31 Waldau T, Larsen VH, Bonde J. Evaluation of five oxygen delivery devices in spontaneously breathing subjects by oxygraphy. *Anaesthesia* 1998; **53**: 256–63.
32 Bazuaye EA, Stone TN, Corris PA, Gibson GJ. Variability of inspired oxygen concentration with nasal cannulas. *Thorax* 1992; **47**: 609–11.
33 Boumphrey SM, Morris EA, Kinsella SM. 100% inspired oxygen from a Hudson mask—a realistic goal? *Resuscitation* 2003; **57**: 69–72.
34 Wettstein RB, Shelledy DC, Peters JI. Delivered oxygen concentrations using low-flow and high-flow nasal cannulas. *Respir. Care* 2005; **50**: 604–9.
35 Jeffrey AA, Warren PM. Should we judge a mask by its cover? *Thorax* 1992; **47**: 543–6.
36 Garcia JA, Gardner D, Vines D, Shelledy DC, Wettstein R, Peters J. The oxygen concentrations delivered by different oxygen therapy systems. *Chest* 2005; **128**: 389S-b.
37 Walls R, Murphy M. *Manual of Emergency Airway Management*. Lippincott Williams & Wilkins, Philadelphia, PA, 2012.
38 Jensen AG, Johnson A, Sandstedt S. Rebreathing during oxygen treatment with face mask. The effect of oxygen flow rates on ventilation. *Acta Anaesthesiol. Scand.* 1991; **35**: 289–92.
39 Bethune DW, Collis JM. The evaluation of oxygen masks. A mechanical method. *Anaesthesia* 1967; **22**: 43–54.
40 Gotera C, Diaz Lobato S, Pinto T, Winck JC. Clinical evidence on high flow oxygen therapy and active humidification in adults. *Rev. Port. Pneumol.* 2013; **19**: 217–27.
41 Ward JJ. High-flow oxygen administration by nasal cannula for adult and perinatal patients. *Respir. Care* 2013; **58**: 98–122.
42 Brocklebank D, Ram F, Wright J, Barry P, Cates C, Davies L, Douglas G, Muers M, Smith D, White J. Comparison of the effectiveness of inhaler devices in asthma and chronic obstructive airways disease: a systematic review of the literature. *Health Technol. Assess.* 2001; **5**: 1–149.
43 Gunawardena KA, Patel B, Campbell IA, MacDonald JB, Smith AP. Oxygen as a driving gas for nebulisers: safe or dangerous? *Br. Med. J. (Clin. Res. Ed)* 1984; **288**: 272–4.
44 Edwards L, Perrin K, Williams M, Weatherall M, Beasley R. Randomised controlled crossover trial of the effect on PtCO2 of oxygen-driven versus air-driven nebulisers in severe chronic obstructive pulmonary disease. *Emerg. Med. J.* 2011; **29**: 894–8.
45 Cates CJ, Welsh EJ, Rowe BH. Holding chambers (spacers) versus nebulisers for beta-agonist treatment of acute asthma. *Cochrane Database Syst. Rev.* 2013; **9**: 1–123.
46 Hardie JA, Morkve O, Ellingsen I. Effect of body position on arterial oxygen tension in the elderly. *Respiration* 2002; **69**: 123–8.
47 Tyson SF, Nightingale P. The effects of position on oxygen saturation in acute stroke: a systematic review. *Clin. Rehabil.* 2004; **18**: 863–71.
48 Cheng T. Platypnea-orthodeoxia syndrome: etiology, differential diagnosis, and management. *Catheter. Cardiovasc. Interv.* 1999; **47**: 64–6.
49 National Clinical Guideline Centre. Chronic obstructive pulmonary disease: management of chronic obstructive pulmonary disease in adults in primary and secondary care. London: National Clinical Guideline Centre. 2010. [Accessed Feb 2015.] Available from URL: http://guidance.nice.org.uk/CG101/Guidance/pdf/English
50 Nava S, Hill N. Non-invasive ventilation in acute respiratory failure. *Lancet* 2009; **374**: 250–9.
51 British Thoracic Society Standards of Care Committee. Non-invasive ventilation in acute respiratory failure. *Thorax* 2002; **57**: 192–211.
52 Royal College of Physicians, British Thoracic Society, Intensive Care Society. Chronic obstructive pulmonary disease: non-invasive ventilation with bi-phasic positive airways pressure in management of patients with acute type 2 respiratory failure. Concise Guidance to Good Practice series, No 11. London: RCP, 2008. [Accessed Feb 2015.] http://www.rcplondon.ac.uk/sites/default/files/concise-niv-in-copd-2008.pdf
53 New South Wales Agency for Clinical Innovation. Non-invasive ventilation for adult patients with acute respiratory failure. 2013. [Accessed Aug 2015.] http://www.aci.health.nsw.gov.au/networks/intensive-care/clinicians/ic-manual/niv-guidelines
54 Kane B, Turkington PM, Howard LS, Davison AG, Gibson GJ, O'Driscoll BR. Rebound hypoxaemia after administration of oxygen in an acute exacerbation of chronic obstructive pulmonary disease. *BMJ* 2011; **342**: d1557.
55 Rudolf M, Turner JA, Harrison BD, Riordan JF, Saunders KB. Changes in arterial blood gases during and after a period of oxygen breathing in patients with chronic hypercapnic respiratory failure and in patients with asthma. *Clin. Sci. (Lond.)* 1979; **57**: 389–96.
56 Campbell EJ. Respiratory failure: the relation between oxygen concentrations of inspired air and arterial blood. *Lancet* 1960; **2**: 10–11.
57 Vital FMR, Ladeira MT, Atallah AN. Non-invasive positive pressure ventilation (CPAP or bilevel NPPV) for cardiogenic pulmonary oedema. *Cochrane Database Syst. Rev.* 2013; **5**: 1–201.
58 Murad A, Li PZ, Dial S, Shahin J. The role of noninvasive positive pressure ventilation in community-acquired pneumonia. *J. Crit. Care* 2015; **30**: 49–54.
59 Keenan S, Sinuff T, Burns K, Muscedere J, Kutsogiannis J, Mehta S, Cook D, Ayas N, Adhikari N, Hand L *et al.* Clinical practice guidelines for the use of noninvasive positive-pressure ventilation and noninvasive continuous positive airway pressure in the acute care setting. *CMAJ* 2011; **183**: E195–214.
60 Lim WS, Baudouin SV, George RC, Hill AT, Jamieson C, Le Jeune I, Macfarlane JT, Read RC, Roberts HJ, Levy ML *et al.* BTS guidelines for the management of community acquired pneumonia in adults: update 2009. *Thorax* 2009; **64**: iii1–55.
61 AlYami MA, AlAhmari MD, Alotaibi H, AlRabeeah S, AlBalawi I, Mubasher M. Evaluation of efficacy of non-invasive ventilation in non-COPD and non-trauma patients with acute hypoxemic respiratory failure: a systematic review and meta-analysis. *Ann. Thorac. Med.* 2015; **10**: 16–24.
62 Antonelli M, Conti G, Bufi M, Costa MG, Lappa A, Rocco M, Gasparetto A, Meduri GU. Noninvasive ventilation for treatment of acute respiratory failure in patients undergoing solid organ transplantation: a randomized trial. *JAMA* 2000; **283**: 235–41.
63 Hilbert G, Gruson D, Vargas F, Valentino R, Gbikpi-Benissan G, Dupon M, Reiffers J, Cardinaud JP. Noninvasive ventilation in immunosuppressed patients with pulmonary infiltrates, fever, and acute respiratory failure. *N. Engl. J. Med.* 2001; **344**: 481–7.

64 O'Neill B, Mahon JM, Bradley J. Short-burst oxygen therapy in chronic obstructive pulmonary disease. *Respir. Med.* 2006; **100**: 1129–38.
65 Moore RP, Berlowitz DJ, Denehy L, Pretto JJ, Brazzale DJ, Sharpe K, Jackson B, McDonald CF. A randomised trial of domiciliary, ambulatory oxygen in patients with COPD and dyspnoea but without resting hypoxaemia. *Thorax* 2011; **66**: 32–7.
66 Abernethy AP, McDonald CF, Frith PA, Clark K, Herndon JE, Marcello J, Young IH, Bull J, Wilcock A, Booth S *et al*. Effect of palliative oxygen versus room air in relief of breathlessness in patients with refractory dyspnoea: a double-blind, randomised controlled trial. *Lancet* 2010; **376**: 784–93.
67 Stub D, Smith K, Bernard S, Nehme Z, Stepehnson M, Bray J, Cameron P, Barger B, Ellims AH, Taylor A *et al*. Air versus oxygen in ST-segment elevation myocardial infarction. *Circulation* 2015; **131**: 2143–50. doi: 10.1161/CIRCULATIONAHA.114.014494.
68 Rawles JM, Kenmure AC. Controlled trial of oxygen in uncomplicated myocardial infarction. *Br. Med. J.* 1976; **1**: 1121–3.
69 Ronning OM, Guldvog B. Should stroke victims routinely receive supplemental oxygen? A quasi-randomized controlled trial. *Stroke* 1999; **30**: 2033–7.
70 Roffe C, Nevattee T, Buttery A. Stroke oxygen study: a multicentre, prospective, randomised, open, blinded-endpoint study to assess whether routine oxygen treatment in the first 72 hours after a stroke improves long-term outcome. 2014. [Accessed Dec 2014.] http://www.so2s.co.uk/
71 Cameron L, Pilcher J, Weatherall M, Beasley R, Perrin K. The risk of serious adverse outcomes associated with hypoxaemia and hyperoxaemia in acute exacerbations of COPD. *Postgrad. Med. J.* 2012; **88**: 684–9.
72 Murphy R, Driscoll P, O'Driscoll R. Emergency oxygen therapy for the COPD patient. *Emerg. Med. J.* 2001; **18**: 333–9.
73 Hutchison DC, Flenley DC, Donald KW. Controlled oxygen therapy in respiratory failure. *Br. Med. J.* 1964; **2**: 1159–66.
74 Thomson AJ, Webb DJ, Maxwell SR, Grant IS. Oxygen therapy in acute medical care. *BMJ* 2002; **324**: 1406–7.
75 Sjoberg F, Singer M. The medical use of oxygen: a time for critical reappraisal. *J. Intern. Med.* 2013; **274**: 505–28.
76 Beasley R, McNaughton A, Robinson G. New look at the oxyhaemoglobin dissociation curve. *Lancet* 2006; **367**: 1124–6.
77 McHugh G, Freebairn R. Optimal oxygen therapy in the critically ill patient with respiratory failure. *Curr. Resp. Med. Rev.* 2010; **6**: 229–237.
78 Ridler N, Plumb J, Grocott M. Oxygen therapy in critical illness: friend or foe? A review of oxygen therapy in selected acute illnesses. *J. Intensive Care Soc.* 2014; **15**: 190–8.
79 Rodrigo GJ, Rodriquez Verde M, Peregalli V, Rodrigo C. Effects of short-term 28% and 100% oxygen on PaCO2 and peak expiratory flow rate in acute asthma: a randomized trial. *Chest* 2003; **124**: 1312–17.
80 Downs JB, Smith RA. Increased inspired oxygen concentration may delay diagnosis and treatment of significant deterioration in pulmonary function. *Crit. Care Med.* 1999; **27**: 2844–6.
81 Beasley R, Aldington S, Robinson G. Is it time to change the approach to oxygen therapy in the breathless patient? *Thorax* 2007; **62**: 840–1.
82 Thrush DN, Downs JB, Hodges M, Smith RA. Does significant arterial hypoxemia alter vital signs? *J. Clin. Anesth.* 1997; **9**: 355–7.
83 Fu ES, Downs JB, Schweiger JW, Miguel RV, Smith RA. Supplemental oxygen impairs detection of hypoventilation by pulse oximetry. *Chest* 2004; **126**: 1552–8.
84 Crapo RO, Jensen RL, Hegewald M, Tashkin DP. Arterial blood gas reference values for sea level and an altitude of 1,400 meters. *Am. J. Respir. Crit. Care Med.* 1999; **160**: 1525–31.
85 Hardie JA, Vollmer WM, Buist AS, Ellingsen I, Morkve O. Reference values for arterial blood gases in the elderly. *Chest* 2004; **125**: 2053–60.
86 Gries RE, Brooks LJ. Normal oxyhemoglobin saturation during sleep. How low does it go? *Chest* 1996; **110**: 1489–92.
87 Akero A, Christensen CC, Edvardsen A, Skjonsberg OH. Hypoxaemia in chronic obstructive pulmonary disease patients during a commercial flight. *Eur. Respir. J.* 2005; **25**: 725–30.
88 Chew DP, Aroney CN, Aylward PE, Kelly AM, White HD, Tideman PA, Waddell J, Azadi L, Wilson AJ, Ruta LA. 2011 Addendum to the National Heart Foundation of Australia/Cardiac Society of Australia and New Zealand Guidelines for the management of acute coronary syndromes (ACS) 2006. *Heart Lung Circ.* 2011; **20**: 487–502.
89 McMurray JJV, Adamopoulos S, Anker SD, Auricchio A, Bohm M, Dickstein K, Falk V, Filippatos G, Fonseca C, Gomez-Sanchez MA *et al*. ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure 2012. The Task Force for the Diagnosis and Treatment of Acute and Chronic Heart Failure 2012 of the European Society of Cardiology: developed in collaboration with the Heard Failure Association (HFA) of the ESC. *Eur. Heart J.* 2012; **33**: 1798–847.
90 Neill WA. Effects of arterial hypoxemia and hyperoxia on oxygen availability for myocardial metabolism. Patients with and without coronary heart disease. *Am. J. Cardiol.* 1969; **24**: 166–71.
91 Ricard JD. High flow nasal oxygen in acute respiratory failure. *Minerva Anestesiol.* 2012; **78**: 836–41.
92 Groves N, Tobin A. High flow nasal oxygen generates positive airway pressure in adult volunteers. *Aust. Crit. Care* 2007; **20**: 126–31.
93 Frat JP, Thille AW, Mercat A, Girault C, Ragot S, Perbet S, Prat G, Boulain T, Morawiec E, Cottereau A *et al*. High-flow oxygen through nasal cannula in acute hypoxemic respiratory failure. *N. Engl. J. Med.* 2015; **372**: 2185–96. doi: 10.1056/NEJMoa1503326.