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RAPID RECOMMENDATIONS

Oxygen therapy for acutely ill medical patients: a clinical practice guideline

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This *BMJ* Rapid Recommendation article is one of a series that provides clinicians with trustworthy recommendations for potentially practice changing evidence. *BMJ* Rapid Recommendations represent a collaborative effort between the MAGIC group (http://magicproject.org/) and *The BMJ*. A summary is offered here and the full version including decision aids is on the MAGICapp (https://app.magicapp.org), for all devices in multilayered formats. Those reading and using these recommendations should consider individual patient circumstances, and their values and preferences and may want to use consultation decision aids in MAGICapp to facilitate shared decision making with patients. We encourage adaptation and contextualisation of our recommendations to local or other contexts. Those considering use or adaptation of content may go to MAGICapp to link or extract its content or contact *The BMJ* for permission to reuse content in this article. Series adviser Rafael Perera-Salazar.

What is the best way to use oxygen therapy for patients with an acute medical illness? A systematic review published in the *Lancet* in April 2018 found that supplemental oxygen in inpatients with normal oxygen saturation increases mortality.[1] Its authors concluded that oxygen should be administered conservatively, but they did not make specific recommendations on how to do it. An international expert panel used that review to inform this guideline. It aims to promptly and transparently translate potentially practice-changing evidence to usable recommendations for clinicians and patients.[2] The panel used the GRADE framework and following standards for trustworthy guidelines.[3]

The panel asked;

- In acutely ill patients, when should oxygen therapy be started? (What is the lower limit of peripheral capillary oxygen saturation (SpO_2)?)
- In acutely ill patients receiving oxygen therapy, how much oxygen should be given? (What is the upper limit of SpO_2?)

The panel makes a strong recommendation for maintaining an oxygen saturation of no more than 96% in acutely ill medical patients (upper limit). The panel did not make a recommendation on when to start (the lower limit) for all medical patients because there was not enough evidence. Instead, the panel suggests that patients with acute stroke or myocardial infarction and a SpO_2 ≥90% not receive supplemental oxygen (a weak recommendation if SpO_2 is 90-92% and a strong recommendation if 93-100%). Box 1 shows the article and evidence linked to this Rapid Recommendation. The infographic provides an overview of the key absolute benefits and harms, as well as the quality of evidence that informed each of the recommendations.

The panel was confident that the recommendation against letting oxygen saturation rise above 96% applies to almost all patients in hospital with a medical problem. The recommendation also applies to pre-hospital care. The evidence may apply to surgical and obstetric patients, but the panel did not review the evidence on postoperative healing and infections and therefore decided not to comment on these patients. Similarly, the panel did not review the evidence on oxygen therapy in neonates and infants.

WHAT YOU NEED TO KNOW

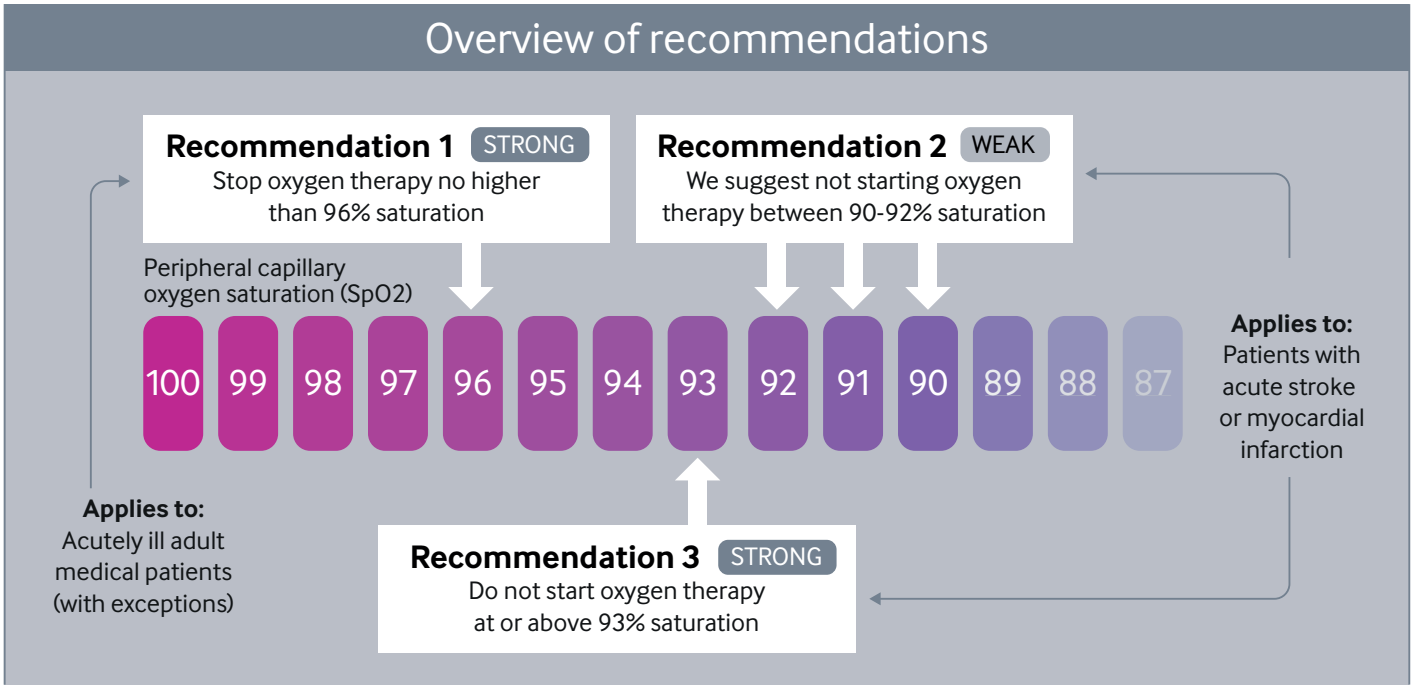
- It is a longstanding cultural norm to provide supplemental oxygen to sick patients regardless of their blood oxygen saturation
- A recent systematic review and meta-analysis has shown that too much supplemental oxygen increases mortality for medical patients in hospital
- For patients receiving oxygen therapy, aim for peripheral capillary oxygen saturation (SpO_2) of ≤96% (strong recommendation)
- For patients with acute myocardial infarction or stroke, do not initiate oxygen therapy in patients with SpO_2 ≥90% (for ≥93% strong recommendation, for 90-92% weak recommendation)
- A target SpO_2 range of 90-94% seems reasonable for most patients and 88-92% for patients at risk of hypercapnic respiratory failure; use the minimum amount of oxygen necessary

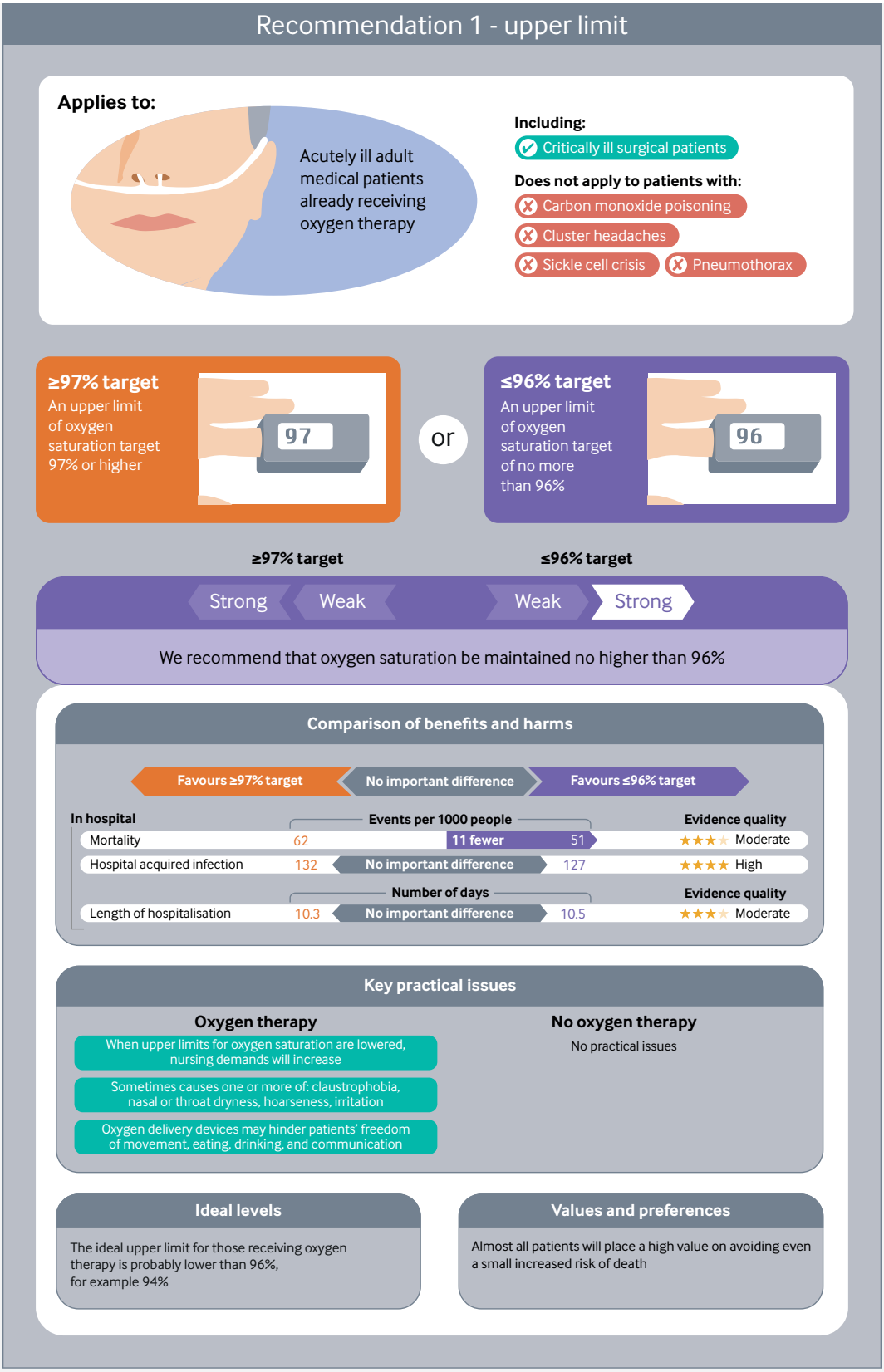
Current practice

Supplemental oxygen therapy is widely used in hospitals: 25% or more of patients who visit the emergency department receive oxygen.[4] Clinicians often give oxygen to many patients presenting with stroke without hypoxaemia, and to almost all patients presenting with myocardial infarction.[5] Until recently, many healthcare professionals believed that oxygen had little or no harm

Box 1 | Linked resources in this *BMJ* Rapid Recommendations cluster

- Siemieniuk RAC, Chu DK, Kim LH-Y, et al. Oxygen therapy for acutely ill medical patients: a clinical practice guideline. *BMJ* 2018;363:k4169
  - Summary of the results from the Rapid Recommendation process
- Chu DK, Kim LH, Young PJ, et al. Mortality and morbidity in acutely ill adults treated with liberal versus conservative oxygen therapy (IOTA): a systematic review and meta-analysis. *Lancet* 2018;391:1693-705.
  - Review and meta-analysis of all available randomised trials that assessed oxygen therapy for acute illnesses
- MAGICapp (https://app.magicapp.org/public/guideline/jxQ7OL)
  - Expanded version of the results with multilayered recommendations, evidence summaries, and decision aids for use on all devices





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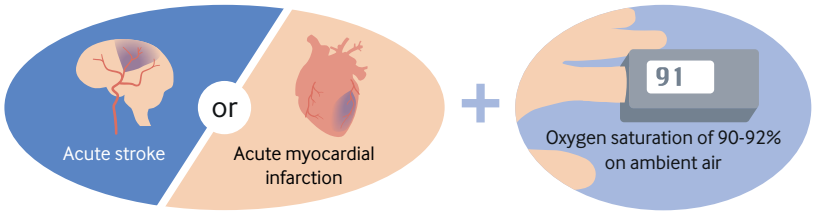
Recommendation 2 - lower limit (90-92%)

Applies to people with:



Oxygen therapy
Provision of supplemental oxygen

or

No oxygen therapy
No provision of supplemental oxygen

Oxygen therapy		No oxygen therapy	
Strong	Weak	Weak	Strong

We suggest not providing oxygen therapy

Comparison of benefits and harms - patients with stroke

Favours oxygen therapy | No important difference | Favours no oxygen therapy

	Events per 1000 people			Evidence quality
In hospital				
Mortality	87	18 fewer	69	★★☆☆ Low
3-6 months				
Functionally dependent	560	No important difference	549	★★☆☆ Low
Severe disability	270	No important difference	270	★★☆☆ Low

Comparison of benefits and harms - patients with myocardial infarction

Favours oxygen therapy | No important difference | Favours no oxygen therapy

	Events per 1000 people			Evidence quality
In hospital				
Mortality	55	No important difference	49	★★☆☆ Low
Chest pain requiring antianginal	215	No important difference	211	★★☆☆ Low
6 months				
Coronary revascularisation	106	34 fewer	72	★★☆☆ Low
6 months to 1 year				
Recurrent myocardial infarction	62	11 fewer	51	★★★☆ Moderate

Key practical issues

Oxygen therapy
- Sometimes causes one or more of: claustrophobia, nasal or throat dryness, hoarseness, irritation
- Oxygen delivery devices may hinder patients' freedom of movement, eating, drinking, and communication

No oxygen therapy
No practical issues

Ideal levels

The ideal oxygen saturation at which to start oxygen therapy is uncertain, but is probably 90% or lower

Values and preferences

Wearing a mask or nasal prongs can be uncomfortable. However, aside from terminally ill patients, almost all patients are likely to accept this discomfort for even a small reduction in chance of death

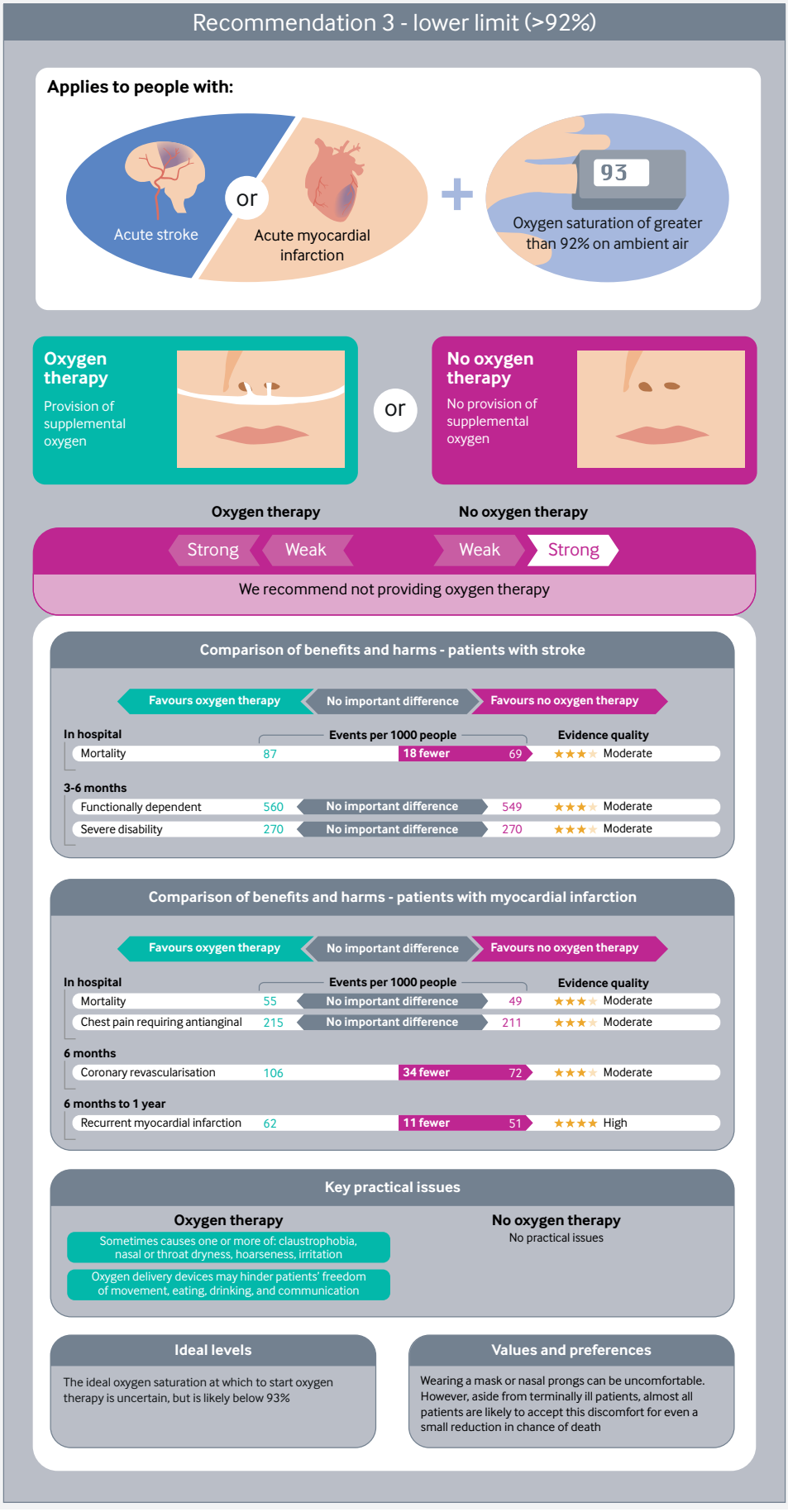


Table 1 | Current guidance on supplemental oxygen therapy

		Recommendations	
Organisation	Condition	Lower limit	Upper limit
AARC, 2002[8]	All patients in acute care facility	Provide oxygen if SaO_2 <90%	No upper limit
AHA/ASA, 2018[9]	Ischaemic stroke	Provide oxygen to maintain SaO_2 >94%	No upper limit
EAN, 2018[10]	Ischaemic stroke	Provide oxygen to maintain normoxia in patients with SaO_2 <95%. Routine use of O_2 is not recommended	None mentioned
AHA, 2013[11]	Myocardial infarction with ST elevation	Provide oxygen in patients with SaO_2 <90%, heart failure, or dyspnoea	No upper limit
ESC, 2017[12]	Myocardial infarction with ST elevation	Provide oxygen in patients with hypoxaemia (SaO_2 <90% or PaO_2 <60 mm Hg). Routine oxygen not recommended if SaO_2 ≥90%	No upper limit
ESC, 2015[13]	Myocardial infarction without ST elevation	Provide oxygen blood oxygen saturation <90% or respiratory distress.	No upper limit
BTS, 2017[14]	Acute medical conditions	Provide oxygen if SaO_2 <94% for most acutely ill patients; <88% for patients with hypercapnia	98% for most patients, 92% for patients with hypercapnia
TSANZ[15]	Acute medical conditions	Provide oxygen if SpO2 <92%	96% for most patients

AARC=American Association for Respiratory Care; AHA=American Heart Association; ASA=American Stroke Association; EAN=European Academy of Neurology; ESC=European Society of Cardiology; BTS=British Thoracic Society; TSANZ=Thoracic Society of Australia and New Zealand.
SaO_2=oxygen saturation; PaO_2=partial pressure of oxygen; SpO_2=peripheral capillary oxygen saturation

for acutely ill adults. In addition to mortality, other difficulties caused by oxygen can include nasal or throat irritation and hampered mobility. Doctors first used oxygen for medical purposes in the 19th century,[6] and its use became routine in the early 20th century.[7] Modern guidelines vary in their advice on when to give oxygen for acute medical conditions and how much to give (see table 1).

HOW THIS RECOMMENDATION WAS CREATED

Our international panel included methodologists, a respiratory therapist/technician, a nurse, patient partners who have been hospitalised for an acute medical condition, pulmonologists, intensivists, internists, an anaesthesiologist, a cardiologist, emergency physicians, and a surgeon (see appendix 1 on bmj.com for details of panel members). They decided on the scope of the recommendation and the outcomes most important to patients. The panel identified three key patient-important outcomes: mortality, hospital acquired infections, and length of hospitalisation. For two specific populations for which there was substantial randomised evidence available, the panel noted additional key outcomes: for patients with stroke, disability; and for patients with acute myocardial infarction, recurrent myocardial infarction, revascularisation, and chest pain.

The panel met to discuss the evidence and formulate a recommendation. No member had financial conflicts of interest; intellectual and professional conflicts were minimised and are transparently described (appendix 2 on bmj.com). The panel followed the *BMJ* Rapid Recommendations procedures for creating a trustworthy recommendation,[2] including using the GRADE approach to critically appraise the evidence and create recommendations (appendix 3 on bmj.com).[3] The panel considered the benefits, as well as any harms and burdens, of oxygen therapy, the certainty (quality) of the evidence for each outcome, typical and expected variations in patient values and preferences, acceptability, and feasibility.[22] Within the GRADE framework, recommendations can be either strong or weak (also known as conditional), and for or against a specific course of action.[23]

The panel considered several key practical issues: psychological comfort from oxygen, discomfort (such as nasal irritation), and feasibility (such as impact on nursing resources). The panel was interested in knowing whether the impacts of oxygen were different in different medical conditions or study populations.

When to start oxygen—Peripheral capillary oxygen saturation (SpO_2) thresholds typically trigger the use of oxygen treatment. Thresholds range from SpO_2 <90% to <95% in guidelines. Recommendations for starting oxygen in specific groups vary: patients with stroke with SpO_2 <95%,[9] and, regardless of SpO_2, those experiencing an acute myocardial infarction who feel breathless, are offered oxygen.[11]

When to stop oxygen—Many guidelines do not say how much is too much. Healthcare workers may respond to this advice by keeping a buffer between a patient's SpO_2 and the lower limit (for example, by keeping the SpO_2 close to 100%). Some guidelines advocate targeting a SpO_2 range. Proposed limits range from 98% for most patients, to an upper limit of 92% for patients with risk of hypercapnic respiratory failure, such as patients with chronic obstructive pulmonary disease.[15]

The evidence

A recent systematic review and meta-analysis of randomised controlled trials of acutely ill adults quantified whether inpatients were at greater risk of death with liberal or conservative oxygen therapy.[1] Patients randomised to liberal oxygen therapy were more likely to die (risk ratio 1.21 (95% confidence interval 1.03 to 1.43)). The increase in mortality was highest in the trials with the greatest increase in SpO_2; this suggests a dose-response relation and strengthens the inference that excessive oxygen is a cause of death. The review included 25 randomised controlled trials. Figure 2 outlines key study and participant characteristics. This shows that the results apply to a wide variety of patient groups.

Upper limit of oxygen therapy

The panel had moderate certainty that oxygen increases mortality when the SpO_2 is above 96%. Providing supplemental oxygen above a SpO_2 of 96% probably increases mortality by around 1%. There is probably no difference in length of hospitalisation or risk of hospital acquired infections. Average (median) SpO_2 was 96% in participants randomised to none or limited oxygen therapy. The evidence was rated down from high to moderate certainty for indirectness (uncertain applicability) because the trials used varying SpO_2 thresholds, leaving some uncertainty regarding the value above which mortality increases.

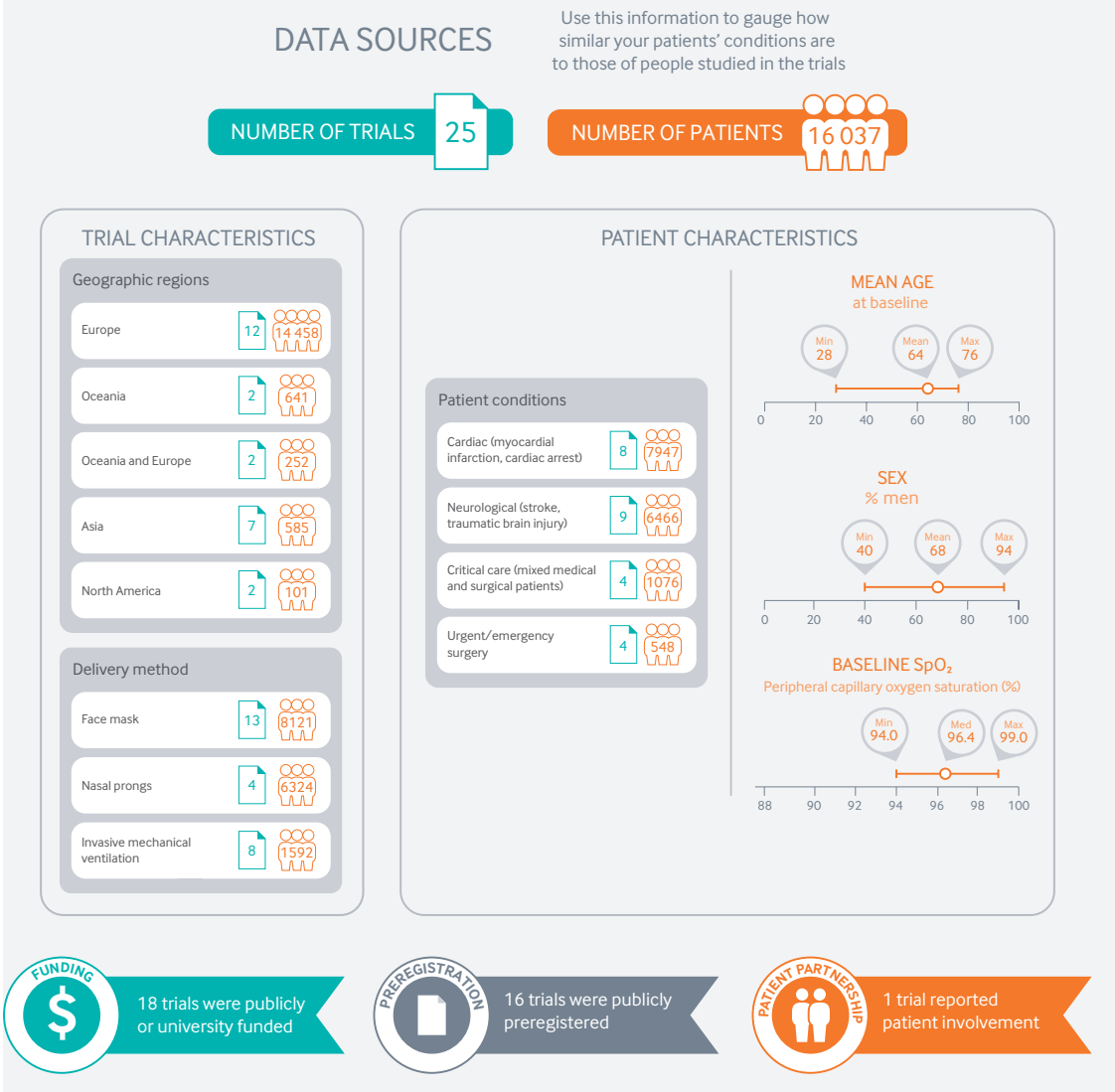


Fig 2| Characteristics of patients and trials included in systematic review of the use of oxygen therapy in acutely ill adults

Lower limit of oxygen therapy

The evidence regarding the lower limit comes from the patients who were included in the clinical trials with baseline SpO_2 over 90%. The evidence in patients with initially higher SpO_2 (>92%) is more certain because most patients in the trials had a baseline SpO_2 above 92%. For example, in the largest of eight trials of patients with stroke only 240 patients (3.1% of 7677 participants) had an initial SpO_2 of 90-93.9%.[16] For myocardial infarction, six trials enrolled 7898 patients: in the largest trial, 1062 patients (16.0%) had an initial SpO_2 ≤94%.[17] For all outcomes, the panel rated down the quality of the evidence for indirectness (uncertain applicability) in patients with a SpO_2 of 90-92%. Because trials informing the lower limit of when to start oxygen were restricted to patients with stroke and myocardial infarction, whether the evidence applies to patients without these conditions is uncertain.

The confidence intervals around the absolute effects in both stroke and myocardial infarction demonstrate that administering supplemental oxygen in patients with these conditions is unlikely to result in an important reduction in mortality. For stroke, supplemental oxygen probably does not reduce disability. In patients with acute myocardial infarction, supplemental oxygen probably does not reduce chest pain, recurrent myocardial infarction, or the need for a coronary revascularisation intervention.

Understanding the recommendations

The infographic summarises the benefits and harms of oxygen therapy.

Scope of recommendations

Our recommendations apply to critically ill or surgical patients with sepsis. They also apply to patients who are en route to hospital in an ambulance and to those who are hospitalised.

We did not consider patients with uncomplicated surgery. There is a separate body of evidence, mostly in the elective surgical setting.[18] There is an unresolved debate about whether supplemental oxygen reduces the risk of

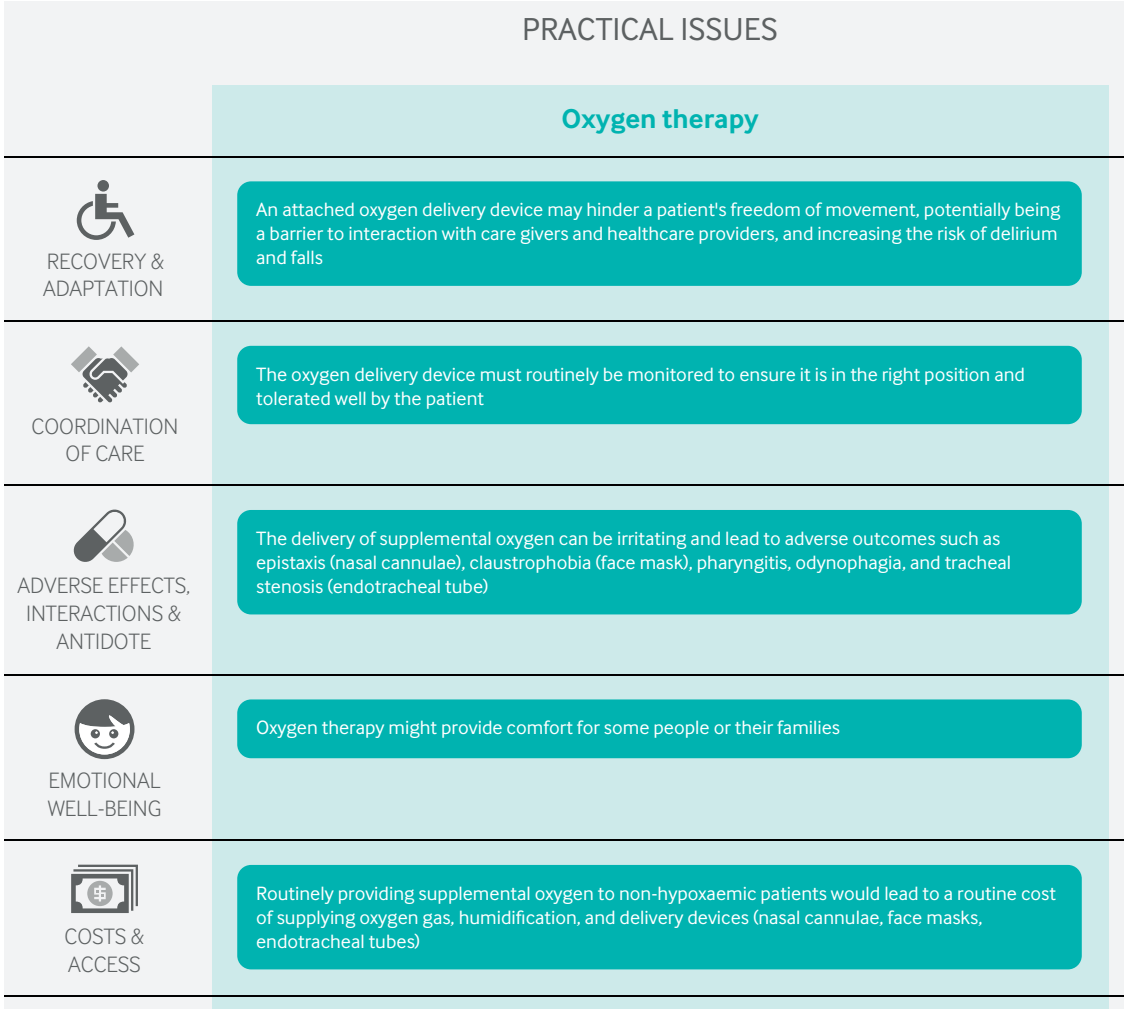


Fig 3| Practical issues about use of oxygen therapy for patients

surgical site infections. Our recommendations may not apply to young children (particularly neonates). There is a separate body of evidence and considerations such as necrotising enterocolitis and retinopathy of prematurity.[19]

Upper limit of oxygen therapy

- The panel makes a strong recommendation that, if supplemental oxygen is administered, clinicians ensure a maximum SpO_2 of 96%
  - This is because saturation above this level likely causes a small but important increased risk of death without plausible benefit. It is probable that the optimal upper SpO_2 limit is lower than 96%, but exactly how much lower is unknown. Patients randomised to more liberal oxygen therapy typically achieved a SpO_2 >96%. The data from the trials provide only limited support for any particular upper threshold, including the 96% chosen by the panel.

Lower limit of oxygen therapy

- For patients with myocardial infarction or stroke, the panel makes a strong recommendation against initiating supplemental oxygen when the initial SpO_2 is >92%
  - In patients with myocardial infarction or stroke, there are probably no benefits to initiating oxygen therapy when SpO_2 is >92%, and it may cause harm.
- The panel makes a weak recommendation against initiating oxygen in these patients with a SpO_2 of 90-92%
  - There may not be any benefits for patients with this lower SpO_2 (90-92%). Fewer patients with this SpO_2 range at baseline were included in the trials, so the panel had less certainty in the results. There is no evidence of benefit from supplemental oxygen initiated in patients with myocardial infarction and stroke whose SpO_2 is ≥90%, but there exists at least a modest risk of harm.

The panel did not issue recommendations for all patients or for other conditions because there were too few participants in the clinical trials who had a baseline SpO_2 <95%.

Values and preferences

The panel believes that almost all patients would value avoiding even a small increased risk of death with supplemental oxygen. Although the panel viewed nasal and throat irritation and a decrease in mobility from oxygen

Box 2 | Examples of conditions that might benefit from higher or lower oxygen saturation thresholds

Lower target (such as SpO_2 88-92%)

- Patients at risk of hypercapnic respiratory failure, for example:
  - Chronic obstructive pulmonary disease
  - Obesity hypoventilation
  - Neuromuscular respiratory diseases
  - Obstructive sleep apnoea
  - Decreased central respiratory drive (such as sedative overdose, stroke, encephalitis)

Higher target (such as SpO_2 approaching 100%)

- Carbon monoxide poisoning
- Cluster headaches
- Sickle cell crisis
- Pneumothorax

Table 2 | New evidence which has emerged after initial publication

Date	New evidence	Citation	Findings	Implications for recommendation(s)
There are currently no updates to the article.				

therapy as unimportant, they felt that most patients would not choose to endure even a minor inconvenience if there is probably no benefit.

Practical considerations

Figure 3 outlines the key practical issues about the use of oxygen therapy for patients.

A target SpO_2 range of 90-94% seems wide enough to allow for normal fluctuation, and is likely low enough to avoid harm.

Upper thresholds for SpO_2 in patients at risk of hypercapnic respiratory failure should be lower than for other patients (see box 2 for some common examples). Excessive oxygen could increase the risk of needing mechanical ventilation in these patients. Other existing evidence supports a target SpO_2 of about 88-92% in such patients.[20] Box 2 also shows a small number of acute illnesses with specific evidence to support more oxygen.

Shared decision making

The patient panellists said that oxygen therapy is often given to patients with insufficient discussion and explanation. Clearer information may reduce anxiety and improve patient satisfaction in patients where oxygen is needed.

Costs and resources

Patients are unlikely to view the modest cost of oxygen as excessive, particularly in settings where they do not directly pay for their care.

A target SpO_2 range (rather than a lower limit without an upper limit) will need closer monitoring by the healthcare team. Our recommendations do not consider healthcare payer considerations. We suggest a target SpO_2 range that is sufficiently wide that it does not require excessive attention (such as 90-94%). Some patients will have wider SpO_2 fluctuations and may therefore require a wider target range; these patients may also benefit from closer monitoring.

HOW PATIENTS WERE INVOLVED IN THE CREATION OF THIS ARTICLE

Three people with lived experience of acute medical conditions requiring hospitalisation were members of the panel. They identified and rated outcomes, and helped lead the discussion on values and preferences in a videoconference and email discussions before the full panel meetings. They noted that patients are often underinformed about the reason for and implications of supplemental oxygen therapy.

EDUCATION IN PRACTICE

- How do you use supplemental oxygen in medical patients?
- Based on this article, how do you think your practice might change? Is there anything that you would say to your patient or do differently?
- How might you share this information with your organisation or review local policies on oxygen targets?

Future research

There were no robust data comparing supplemental oxygen to no oxygen in patients with a SpO_2 <90%, so the impact of oxygen therapy in such patients is uncertain.

Addressing the following gaps in our knowledge may inform decision makers and future guideline recommendations:

- Does supplemental oxygen provide benefit to patients experiencing a stroke or myocardial infarction with a SpO_2 <92% (such as 85-92%)?
- Is supplemental oxygen harmful in patients with medical conditions other than stroke or myocardial infarction with a SpO_2 85-94%?

Possible mechanisms

The reasons why excessive supplemental oxygen increases mortality are uncertain. Excessive oxygen can lead to reduced cardiac output, vasoconstriction, inflammation, and oxidative stress.[21] In addition, excessive oxygen might lead to falsely reassuring SpO_2 values and make it difficult to recognise when a patient's condition worsens.

Updates to this article

Table 2 shows evidence that has emerged since the publication of this article. As new evidence is published, a group will assess the new evidence and make a judgment on to what extent it is expected to alter the recommendation.

Contributors: All panel members participated in the teleconferences or email discussions and met all authorship criteria.

Competing interests: All authors have completed the *BMJ* Rapid Recommendations interests disclosure form, and a detailed description of all disclosures is reported in appendix 2 on bmj.com. As with all *BMJ* Rapid Recommendations, the executive team and *The BMJ* judged that no panel member had any financial conflict of interest. Professional and academic interests are minimised as much as possible, while maintaining necessary expertise on the panel to make fully informed decisions. DK Chu, LH-Y Kim, and W Alhazzani co-authored the systematic review that formed the evidence base for this guideline. RAC Siemieniuk, T Agoritsas, PO Vandvik, L Lytvyn, and GH Guyatt are members of the GRADE Working Group: *BMJ* Rapid Recommendations adheres to GRADE methods.

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Transparency: RAC Siemieniuk affirms that the manuscript is an honest, accurate, and transparent account of the recommendation being reported; that no important aspects of the recommendation have been omitted; and that any discrepancies from the recommendation as planned (and, if relevant, registered) have been explained.

Provenance and peer review: Commissioned; externally peer reviewed

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