NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

SCOPE

1 Guideline title

Sepsis: the recognition, diagnosis and management of severe sepsis

1.1 Short title

Sepsis

2 The remit

The Department of Health has asked NICE: 'to produce a guideline on Sepsis: the recognition, diagnosis and management of severe sepsis'.

3 Need for the guideline

3.1 Epidemiology

a) Sepsis is a clinical syndrome caused by the body's immune and coagulation systems being switched on by the presence of an infection (bacteria, viruses or fungi). Severe sepsis is defined as organ dysfunction or tissue hypoperfusion (decreased blood flow) in addition to sepsis, usually requiring a stay in an intensive care unit (ICU). Septic shock is a life-threatening condition that is characterised by low blood pressure despite adequate fluid replacement in addition to organ dysfunction and sepsis. The UK Sepsis Trust estimates that 37,000 people die from sepsis in the UK every year.

b) According to the Parliamentary and Health Service Ombudsman Annual Report (2013), the most common causes of severe sepsis in adults are pneumonia, bowel perforation, urinary infection and

severe skin infection. That report, based on example cases in children and adults, recommended that guidelines were needed to support the recognition and management of severe sepsis, particularly in its early stages, and they should cover areas such as initial recognition, timely use of antibiotics and fluid resuscitation.

3.2 Current practice

a) It can be difficult to identify cases of sepsis that need urgent treatment to prevent progression to severe sepsis. The current definitions of sepsis and severe sepsis were established in critical care and paediatric critical care to define whether people were eligible to join clinical trials. These definitions are used in International Critical Care guidelines and provide a framework for current intensive care management, but because sepsis is a variable syndrome affecting 1 or more organ systems, the existing critical care definitions and guidelines do not translate simply into diagnostic pathways for initial diagnosis and management.

b) Current standard practice varies according to the clinical experience of the physician or practitioner making the initial assessment, and the facilities immediately available. In secondary care, sepsis can present to any speciality involved in direct clinical care. Groups that are particularly at risk of missed diagnosis of sepsis are infants and young children, people who are immunocompromised for any reason (including those being treated for cancer), people who have recently had surgery, people with indwelling medical lines or devices and women following childbirth. These subgroups all have specific physiological factors that can lead to a missed or delayed diagnosis of sepsis.

c) Treatment involves immediate recognition, resuscitation, early treatment with antibiotics and continual monitoring and reassessment. Although many current guidelines include the assessment and management of sepsis in specific subgroups within their remit, most do not provide guidance for all healthcare

professionals in any situation to assess whether sepsis is present, and to guide initial assessment and treatment.

d) This guideline will provide recommendations for recognising sepsis and instituting treatment to prevent development of severe sepsis and septic shock in any person in any clinical environment, linking to other relevant existing NICE guidance. This guideline will not replicate the existing International Guidelines for Management of Severe Sepsis and Septic Shock: 2012, which cover the critical care management of sepsis in children or adults.

4 The guideline

The guideline development process is described in detail on the NICE website (see section 6, 'Further information').

This scope defines what the guideline will (and will not) examine, and what the guideline developers will consider. The scope is based on the referral from the Department of Health.

The areas that will be addressed by the guideline are described in the following sections.

4.1 Population

4.1.1 Groups that will be covered

a)

Group	Rationale
• All populations will be included.	This guideline will include all populations. There are a number of different NICE guidelines that may cover aspects of recognition and management of sepsis and severe sepsis in subgroups of the population. We will cross-reference existing guidance when it makes sepsis-specific recommendations.

b) The following subgroups have been identified:

Group	Rationale
• Pregnant women • People at higher risk of infection.	People may be at higher risk of sepsis when they have other medical conditions. This includes immunodeficiency from various causes, for example, treatment for cancer, people with indwelling catheters or devices and people who have recently had surgery.

4.1.2 Groups that will not be covered

a) There are currently no groups that are excluded.

4.2 Setting

a) All healthcare settings.

4.3 Management

4.3.1 Key issues that will be covered

(a) Recognition and early assessment of sepsis and severe sepsis: clinical signs and symptoms.

Key clinical areas	Rationale
• Clinical risk assessment, including history and examination. • 'Red flags' for early identification of sepsis and severe sepsis. • Scoring tools.	Recognition of people at risk of severe sepsis allows appropriate treatment to be started quickly and this is likely to improve outcomes. Evidence indicates that delayed recognition of sepsis and severe sepsis is common. Initial assessment in primary and community settings and on hospital wards consists of evaluating physical signs and symptoms. Scoring systems may be used to predict which people are likely to develop severe sepsis and/or to help make a diagnosis in people with sepsis or severe sepsis.

a) Value of blood markers for predicting and detecting sepsis and severe sepsis.

Key clinical areas	Rationale
• Blood gas (arterial, venous or capillary). • Glucose.	Early identification of sepsis allows appropriate treatment to be started quickly. However, the

• Lactate. • Full blood count (haemoglobin, platelets, white cell count and differential). • Urea and electrolytes. • Clotting screen. • C-reactive protein (CRP).	use of markers of infection can be misleading in sepsis as apparently normal test results (such as for white cell count) may be associated with an overwhelmed immune response. Blood markers may be useful alone or in combination with other tests. Consideration will need to be given to the timing of tests and the feasibility of different tests in different settings.

b) Initial treatment for people with sepsis and with severe sepsis.

Key clinical issues	Rationale
(i) Intravenous fluids and electrolytes in early management of people with sepsis and with severe sepsis.	Sepsis can cause major systemic effects; severe sepsis with clinical shock is the worst of these. The products of the infecting organism (for example, endotoxin or exotoxin) cause the release and activation of inflammatory mediators which cause vasodilatation (the widening of blood vessels) and leakage from capillaries; this leads to people becoming hypovolemic (decreased blood volume). The initial choice of replacement fluid (that is, crystalloid, colloid or albumin), the timing of fluid treatment and the amount to be given will need to be considered. Note: NICE has developed guidelines on Intravenous fluid therapy in adults in hospital (CG174) and is developing guidance on Intravenous fluids therapy in children.
(ii) Empirical antimicrobial treatment strategies in early management of people with sepsis and severe sepsis.	It is not always possible to identify the cause of sepsis. Early use of antibiotics is part of the treatment for suspected meningococcal disease in all

	healthcare settings, and advice would be useful about how best to use antibiotics in suspected sepsis, due to any cause, in any setting (for example, pre-hospital treatment comparing immediate broad spectrum antibiotics to later targeted treatment). The incidence of different causes of sepsis in different populations and settings may be an important consideration.
(iii) Early treatment with oxygen and correcting the acid–base balance in people with sepsis and with severe sepsis.	There is increasing reference in the literature to optimal early treatment being within shorter time frames than the previous 'golden hour'. Correcting the acid–base balance and the delivery of oxygen may be appropriate once sepsis is suspected or has been diagnosed.

c) Escalating care for people with sepsis or with severe sepsis.

Key clinical issue	**Rationale**
• Timing of escalation of care in early management of sepsis. • Early treatment with inotropic agents in people with sepsis.	The care of a person with sepsis is a medical emergency and their care should be directed by senior specialists. The threshold

• Central venous access and arterial lines.	at which senior health professionals and/or critical care providers should be involved and central arterial or central venous access is needed will be considered. Inotropic drugs may be indicated for sepsis, and their use considered as soon as severe sepsis is suspected.

d) Identifying the source of infection.

Key clinical issues	**Rationale**
• The use of clinical symptoms and signs to identify the source of infection. • Tests, for example: - blood culture - lumbar puncture (clear contraindication criteria for lumbar puncture) - chest X-ray and other imaging.	Identifying the source of infection will allow treatment to be targeted in the management pathway. This may need appropriate healthcare staff (see 4.3.1.(d)) such as obstetricians and surgeons to be involved early on, depending on the clinical presentation. There may also be a need for prompt surgical treatment. Some investigations such as lumbar puncture may be contraindicated.

e) Early monitoring of people with sepsis.

Key clinical issue	**Rationale**
What parameters to continually assess, how often and by whom, for example: • heart rate • respiratory rate • blood pressure • blood gases • other blood markers, for example, lactate.	People with sepsis or suspected sepsis can deteriorate quickly, and appropriate monitoring can identify this deterioration and detect response to treatment.

f) Information and support for patients and carers.

Key clinical area	**Rationale**
Information and support.	Information and support is needed for: • people with sepsis or severe sepsis • people who are diagnosed as not having sepsis and are discharged from medical care • families and carers of people who have sepsis or severe sepsis • people who survive episodes of severe sepsis.

g) Training and education.

Key clinical area	Rationale
All healthcare providers.	Evidence indicates that sepsis is often not suspected or recognised. For some healthcare professionals the care of a person with severe sepsis will be an unusual event, but their suspicion of the diagnosis may be critical for that person.

4.3.2 Issues that will not be covered

Key clinical areas	Rationale
(i) Procalcitonin.	Assessment commissioned from NICE Diagnostics Assessment Programme.
(ii) Managing sepsis in neonates, children and adults in the ICU.	This is a specialist area for which speciality guidelines already exist. Specialist treatments of conditions that result from sepsis and experimental interventions within the ICU will also be excluded. These may include: • blood products • corticosteroids • supportive therapies • treating sepsis caused by ventilator-associated

	pneumonia • neuromuscular blockade • renal replacement therapy • venous thromboembolism prophylaxis • pressure ulcers • glucose control • immunoglobulins.
(iii) Treatment and care of secondary effects on other organs.	Sepsis can lead to multisystem failure; however, managing this requires specialist ICU care, which we propose is excluded.
(iv) Preventing sepsis.	The guideline will not cover measures to prevent sepsis. This includes vaccination programmes; infection control and prevention measures; personal protective equipment; use of particular types of catheters/feeding tubes; preventing sepsis arising from, for example, mechanical ventilation or surgery; antibiotic prophylaxis to prevent infection; screening for pathogens in at-risk populations.

4.4 Main outcomes

a) Mortality.

b) Progression to severe sepsis.

c) Duration of hospital stay.

d) Duration of ICU stay.

e) Number of organs supported.

f) Change in physical signs and symptoms.

g) Adverse events.

h) Health-related quality of life (for example, as assessed by SF-12 or EQ-5D).

i) Psychological outcomes.

j) Outcomes indicating severity of long-term disability/rehabilitation needs.

k) Patient-reported outcome measures.

4.5 Economic aspects

Developers will take into account both clinical and cost effectiveness when making recommendations involving a choice between alternative interventions. A review of the economic evidence will be conducted and analyses will be carried out as appropriate. The preferred unit of effectiveness is the quality-adjusted life year (QALY), and the costs considered will usually be only from an NHS and personal social services (PSS) perspective. Further detail on the methods can be found in The guidelines manual.

4.6 Status

4.6.1 Scope

This is the final scope.

4.6.2 Timing

The development of the guideline will begin in July 2014.

5 Related NICE guidance

5.1 Published guidance

- Acute kidney injury. NICE clinical guideline CG169 (2013).
- Critical illness rehabilitation. NICE clinical guideline CG83 (2013).
- Intravenous fluid therapy in adults in hospital. NICE clinical guideline CG174 (2013).
- Feverish illness in children. NICE clinical guideline CG160 (2013).
- Patient experience in adult NHS services. NICE clinical guideline CG138 (2012).
- Antibiotics for early-onset neonatal infection. NICE clinical guideline CG149 (2012).
- Infection control. NICE clinical guideline CG139 (2012).
- Neutropenic sepsis. NICE clinical guideline CG151 (2012).
- Diabetic foot problems - inpatient management. NICE clinical guideline CG119 (2011).
- Bacterial meningitis and meningococcal septicaemia. NICE clinical guideline CG102 (2010).
- Chronic heart failure: Management of chronic heart failure in adults in primary and secondary care. NICE clinical guideline CG108 (2010).
- Venous thromboembolism - reducing the risk. NICE clinical guideline CG92 (2010).
- Diarrhoea and vomiting in children under 5. NICE clinical guideline CG84 (2009).
- Induction of labour. NICE clinical guideline CG70 (2008).
- Intrapartum care. NICE clinical guideline CG55 (2008) (update due for publication October 2014).
- Surgical site infection. NICE clinical guideline CG74 (2008).
- Acutely ill patients in hospital. NICE clinical guideline CG50 (2007).
- Urinary tract infection in children. NICE clinical guideline CG54 (2007).

- Nutrition support in adults. NICE clinical guideline CG32 (2006).
- Postnatal care. NICE clinical guideline CG37 (2006).

5.2 Guidance under development

NICE is currently developing the following related guidance (details available from the NICE website):

- Pneumonia. NICE clinical guideline. Publication expected December 2014.
- Intravenous fluids therapy in children. NICE clinical guideline. Publication expected October 2015.
- Antimicrobial stewardship guideline. NICE medicines practice guideline. Publication expected March 2015.
- Acute medical emergency guideline. NICE clinical guideline. Publication date to be confirmed.

6 Further information

Information on the guideline development process is provided in the following documents, available from the NICE website:

- How NICE clinical guidelines are developed: an overview for stakeholders the public and the NHS: 5th edition
- The guidelines manual.

Information on the progress of the guideline will also be available from the NICE website.