National Institute for Health and Care Excellence

SEPSIS
Scope Consultation Table
04/04/14-02/05/14

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ID	Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
55	SH	College of Paramedics	1	3.2 a)	The screening tool devised for pre-hospital recognition and initial therapy in adults does allow a simple pathway for initial diagnosis. Whilst it is not designed for specificity, it will encourage clinicians to recognise a new infection with two or more SIRS criteria.	Thank you for your comment and further information. We will examine available tools within the guideline.
56	SH	College of Paramedics	2	3.2 c)	In pre-hospital care, a screening tool for adults has been developed to recognise the presence of sepsis in any setting and its subsequent initial treatment.	Thank you for the information. We will look at the evidence on screening tools during development.
57	SH	College of Paramedics	3	4.3.1 a)	Whilst many ambulance services are moving towards NEWS scores, it is important that there is recognition that screening tools are utilised as well as scoring tools, sometimes in tandem.	Thank you for the information.
58	SH	College of Paramedics	4	4.3.1 d)	There needs to be an indication that following the recognition of a person with sepsis in the pre-hospital arena, a prompt pre-alert by ambulance services into the hospital is pivotal in directing care of the patient towards senior specialists.	Thank you for this suggestion.
51	SH	Department of Health	1	General	It would be helpful if the scope of the guidelines included specific mention of the role of care bundles. In particular, the value of actions within each care bundle within given time periods, for example, "within 3 hours"; within 6 hours" etc.	Thank you for your comment. We will review the evidence for care bundles during development. We expect the output to be in a related format.
52	SH	Department of Health	2	4.1.1b	It would be useful to clarify whether coverage of children outside critical care are included.	Thank you for your comment. We can confirm that we will be including children. We have not specified groups because we do not want to omit anyone.
53	SH	Department of Health	3	4.3.1b	Diagnostic markers are an important area and the Technology Strategy Board will have a particular interest.	Thank you for this information. We agree the TSB may be interested in

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						some research recommendations.
54	SH	Department of Health	4	4.3.1cii	The text could be clarified here, because empiric antibiotic use is fairly standard practice for suspected sepsis.	Thank you for your comment. The wording of this section was not clear and we have amended this.
73	SH	Digital assessment service, NHS Choices	1	General	The Digital Assessment Service welcome the guidance andhave no comments to make as part of the consultation.	Thank you for your comments.
10	SH	Faculty of Intensive Care Medicine	1	3.1 (a)	These definitions are either outdated or plain wrong!	Thank you for your comment. Please response to the comment below.
11	SH	Faculty of Intensive Care Medicine	2	3.2 (a)	It is well recognized by the critical care community that the current definitions developed in 1992 are no longer fit for purpose. There are major issues with over-diagnosis and concerns over excess/inappropriate use of antibiotics. I am Co-Chair of a North American/European Sepsis Redefinitions Task Force organized by the (US) Society of Critical Care Medicine and the European Society of Critical Care Medicine that is due to report by early 2015. We are hoping, as part of the redefinitions, to generate an improved organ dysfunction scoring system that will improve the sensitivity and specificity of diagnosis. This will involve interrogation of very large patient databases (emergency dept/general ward/ICU) with subsequent validation against other databases (including UK populations).	Thank you for your comment and this information. We look forward to hearing more about this work.
12	SH	Faculty of Intensive Care Medicine	3	3.2 (a)	Again, errors here- eg sepsis does not necessarily have to involve two or more organ systems in terms of obvious dysfunction	Thank you - we have corrected this error.
13	SH	Faculty of Intensive Care Medicine	4	3.2 (b)	Again, errors and omissions. Young children are not particularly susceptible (unless they have other risk factors), except with certain types of infection eg influenza or meningococcus. The elderly are a much greater at-risk population – 13-fold increased risk in over 65s compared to under 65s (Martin GS et al. The effect of age on the development and outcome of adult sepsis. Crit Care Med. 2006;34:15–21).	Thank you for your comment. The text has been clarified.

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					Women following childbirth also does not represent a high-risk group – the RCOG (2011 Confidential Enquiry) reported that between 2006-8 there were 29 deaths from sepsis yet approx. 2m births would have occurred in this timespan. Clearly, maternal sepsis should be identified and treated promptly, though this is a relatively rare problem.	
14	SH	Faculty of Intensive Care Medicine	5	4.1.1.(b)	See point 4 above re: pregnant women.	Thank you for your comment. We have amended the scope accordingly.
15	SH	Faculty of Intensive Care Medicine	6	4.3.1 (a)	Though not at liberty to divulge the revised sepsis definitions (see point 2), the current definition of 'sepsis' can include someone with a bad cold. Such patients do not need hospital admission, let alone antibiotics. More emphasis needs to be placed on the early recognition of new onset organ dysfunction, and to consider whether infection is the underlying cause. Scoring systems are generally flawed in that they do not take into account coexisting morbidities that affect many (? the majority) of patients with severe sepsis, nor age (e.g. normal blood pressure varies ++). Alas, none have been properly validated and specificity, in particular, is not great for any of them.	Thank you we agree to the importance of recognising the early organ dysfunction. The evidence review will examine existing scoring systems and their potential use.
16	SH	Faculty of Intensive Care Medicine	7	4.3.1(b)	None of the list given are specific for sepsis. All current clinical and laboratory markers of 'sepsis' are not particularly specific. Any cause of an exaggerated inflammatory response (e.g. reaction to blood transfusion, drug reaction, response to surgery) can generate a virtually identical clinical and biochemical picture as sepsis.	Thank you for your comment; this is one of the questions the GDG will likely consider.
17	SH	Faculty of Intensive Care Medicine	8	4.3.1 (b)	It's lactate – not lactic acid. Why haemoglobin? Liver function tests are more valid (for cholecystitis/cholangitis)	Thank you for your comment. We have changed the wording to lactate. Haemoglobin is included because of occurrence of DIC. The inclusion of these tests and other options such as liver function tests will be discussed with the GDG.

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18	SH	Faculty of Intensive Care Medicine	9	4.3.1 (b)	Again, factually incorrect statement – a normal white count does not mean an overwhelmed immune response.	Thank you. We are not implying that a normal white cell count inevitably means an overwhelmed immune response and consider eh wording accurate.
19	SH	Faculty of Intensive Care Medicine	10	4.3.1 c (iii)	Clearly, delay is generally not a good idea for treating severe sepsis but not so valid for 'sepsis' (see point 6 above) There is no good evidence to support the rationale that treatment within a 'golden hour' makes any difference to outcomes. Oxygen is only appropriate for correcting hypoxaemia and acid-base balance does not need to be corrected per se. Treating the underlying cause (e.g. hypovolaemia will often improve lactate etc… . Specifically targetting acid-base balance (e.g. with bicarbonate) is voodoo.	Thank you. We will consider these issues during guideline development,
20	SH	Faculty of Intensive Care Medicine	11	4.3.1 c	'Early treatment with vasopressors in people with sepsis' – I hope not! I think you mean vasopressor treatment for patients with shock who have not first responded to appropriate fluid resuscitation. Vasopressor agents are harmful in themselves.	Thank you for alerting us to this error. We have altered the wording.
21	SH	Faculty of Intensive Care Medicine	12	4.3.1. c	The treatment of sepsis is not a medical emergency. See point 6 above re: a bad cold. I think you mean what is currently called 'severe sepsis'. Inotropes should not be considered as soon as severe sepsis is suspected. Same applies as for Point 11 above.	Thank you for your comment, the guideline is focused on the early recognition and early management of sepsis and severe sepsis, and appropriate early interventions, to prevent severe sepsis. The definitions of sepsis and their use for all settings will be discussed by the GDG
22	SH	Faculty of Intensive Care Medicine	13	4.3.1.f	Lactate not lactic acid. Urine output, conscious level, pain, pulse oximetry need to be added	Thank you. The list is not exhaustive and we have clarified this.
23	SH	Faculty of Intensive Care Medicine	14	4.4b	Do you mean 'progression to severe sepsis'? Problem with outcomes is that comorbidities often dictate outcomes, length of stay etc.. and not the infection/sepsis/severe sepsis. For instance, a patient with bad COPD who gets a pneumonia may end up on a ventilator and	Thank you- we have altered this to progression to severe sepsis.

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					not be weaned off the machine despite recovering from the pneumonia/sepsis. Also, sepsis is often the final nail in the coffin of a terminally ill patient, eg. with advanced cancer or severe end-stage liver disease.	
97	SH	Group B Strep Support	1	General	GBSS welcomes the development of a guideline for the recognition, diagnosis and management of severe sepsis. Speedy recognition and treatment, coupled with appropriate management will improve outcomes.	Thank you for your comment.
98	SH	Group B Strep Support	2	4.3.1 g on page 9	There should also be info & support for the patient with sepsis	Thank you. We have added this.
99	SH	Group B Strep Support	3	4.3.2 ii on page 10	Although earlier the scope states that no groups are excluded (point 4.1.2), managing sepsis in neonates is excluded. It is not clear whether recognising/diagnosing is still included – we believe it should be. Please clarify.	Thank you. We have clarified what is included in the guideline.
100	SH	Group B Strep Support	4	4.3.2 v on page 11	Although earlier the scope states that no groups are excluded (point 4.1.2), here it states that premature/preterm neonates are excluded. 1. What difference is the scope trying to capture using the terms premature neonates and preterm neonates? It seems unclear 2. CG149 does not cover identifying sepsis, only highlighting risk factors/clinical signs of infection in neonates. I think the recognition & diagnosis of sepsis aspects should be included, so these 'key clinical areas' should be included in (ii) above.	Thank you. The wording included in the draft scope was an error. We have removed these terms
59	SH	ICUsteps	1	3.2.a	'Struggle' to identify – this term gives the wrong impression. Early stages of sepsis seems like mild flu and can be easily missed, especially if the medic is not aware or thinking of the possibility of sepsis – so they are not 'struggling' to identify it! It	Thank you for your comment. We have changed the wording in the scope.

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					should also be mentioned that sepsis can progress very quickly from mild to a serious illness so if it is not spotted early, patients can quickly become critically ill.	
60	SH	ICUsteps	2	3.2.a	When it says 'current definitions' does it mean the clinical signs for identifying sepsis? This needs to be worded more clearly.	Thank you for your comment. We have clarified the wording.
61	SH	ICUsteps	3	3.2.c	'All healthcare professionals' – could clarify that this means primary care (GPs; 111 service; pharmacies; Ambulance services; community midwives), not just hospital based staff, because that is where sepsis is easily missed.	Thank you we agree. We do intend that this refers to everybody in your list. We would prefer not to provide a list as this is more likely to miss individual healthcare professional groups.
62	SH	ICUsteps	4	4.1.1.b	Perhaps pregnant women **and** those who have just given birth.	Thank you for your comment. We have amended the scope accordingly.
63	SH	ICUsteps	5	4.3.1 a	Could 'red flags' also include identifying those in higher risk groups for getting sepsis (such as immune compromised people, those just had surgery, etc)?	Thank you. We will look at this during development.
65	SH	ICUsteps	7	4.4	I wasn't quite sure what the 'main outcomes' related to in the context of the protocol. I think a line of explanation below the heading is needed.	Thank you for your comment. 'Main outcomes' relates to the important factors to consider when making recommendations. This is a standardised NICE template and we will ask the editor to consider whether further explanation is needed under this heading.
80	SH	Infection Prevention Society	1	4.3 f) Early monitoring of people with	We would like to see this guidance clarify whether or not urinary catheterisation is always necessary to accurately monitor urine output in the patient with sepsis, i.e. hourly measurement via catheter may not always be required. Feedback from medical colleagues is that it may be	Thank you. It is unlikely that we will be able to offer specific recommendations to cover all such situations and these decisions are more likely to rely on clinical judgement about the accuracy of

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				sepsis.	reasonable to suggest that catheter should be used in those with sepsis and AKI, or even with sepsis and AKI and urine collection is not possible. The Nice guidance: Acutely ill patients in hospital: Recognition of and response to acute illness in adults in hospital: states (section 1.6) states *In specific clinical circumstances, additional monitoring should be considered; for example:* *hourly urine output* In addition, though perhaps beyond the scope of this document, some guidance for staff as to when such monitoring may be stepped down would be useful, particularly with regards to timely removal of a urethral catheter.	monitoring e.g. without a catheter.
81	SH	Infection Prevention Society	2	General	There is only one mention of infection control' and it says (gloves, gowns) in brackets (section 4.3.2 page 11) Given the trinity statement that was issued by a number of organisations, including IPS and Sepsis UK, noting the importance of not just sepsis management but infection prevention and antimicrobial stewardship, we would like to comment that this document does not cover all the important aspects related to sepsis management for these vulnerable patients. While we note that AMR stewardship might not be within the remit, evidence based infection prevention measures must feature throughout to both support the prevention of sepsis but more importantly to ensure secondary HAI are not an issue for these patients, during procedures, etc. This is particularly important for the tests being carried out on these patients when PPE and appropriate application of hand hygiene must be emphasised (details	Thank you for your comment. Prevention is outside the scope of the guideline. There is already a NICE Infection Prevention and Control guideline.

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					including with the Government commissioned EPIC3 guidance recently published in JHI).	
74	SH	MRSA Action UK	1	4.3.1(g)	We welcome this guideline and the inclusion of information and support for patients and carers, and would like to see more poster campaigns in surgeries and care facilities and user friendly online information on relevant websites ie NICE, NHS Choices, SEPSIS Trust and other trusted websites.	Thank you for your comment. The NICE implementation team will be involved with implementing the guideline once it has been developed.
75	SH	MRSA Action UK	2	4.3.2 (iv)	We believe some basic guidance and reference to infection prevention and control measures should be included to promote the prevention of sepsis and this should be included in the scope.	Thank you. NICE have produced guidance on infection prevention and control and we will cross-refer to this.
101	SH	Paediatric Intensive Care Society	1	3.1.a	This guideline intends to be relevant across all age groups. My personal experience is that, unless there is specific reference to children, the eventual output of such guidance tends to be adult-centric. Therefore this introductory section might reference the number of children with sepsis who die in the UK each year.	Thank you we agree with your comment. The figures quoted include deaths of children. The proposed GDG will consist of equal number of professionals who look after children as look after adults.
102	SH	Paediatric Intensive Care Society	2	3.1.b	As above. I believe this reference to the 'commonest cause of severe sepsis being UTIs, bowel perforation, and severe skin infection' references the adult experience. Whilst it is true that in neonates, bowel perforation and severe skin infection are important contributory factors, in children pneumonia and primary bacteremia are the commonest cause of severe sepsis in immune-competent children in high income countries.	Thank you we agree. We have clarified that these are examples of causes in adults.
103	SH	Paediatric Intensive Care Society	3	3.2.d	Whilst it is stated that this guideline will apply to 'any person in any clinical environment', in 4.3.2.ii listed exclusion criteria are children with sepsis in neonatal, paediatric and adult ICU. At the outset, the guideline might more accurately be stated to apply to 'all health care professionals in primary and secondary care, excepting intensive care'	Thank you. The guideline will not cover management of sepsis in intensive care but aspects of recognition of sepsis may be relevant to those settings. We have altered the wording in 3.2.d.to clarify this.
104	SH	Paediatric Intensive Care	4	4.1.1.a	As above. "..excepting infants and children with sepsis managed in intensive care'	Thank you for your comment. We include diagnosis, but not management of infants and children

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		Society				with sepsis. We have changed the wording in the scope to clarify this.
105	SH	Paediatric Intensive Care Society	5	4.1.2.a	As above. Not strictly accurate.	Thank you for your comment. No groups are excluded from recognition and assessment and early management pathways.
106	SH	Paediatric Intensive Care Society	6	4.3.1.b	The NICE traffic light system for the feverish child reviews, in some detail, the evidence for and against pro-calcitonin (PCT), and seem to eventually adopt a fairly neutral position. It is noted that PCT will not be covered in this guidance as it informs a separate diagnostic assessment program. However, is this sensible? Firstly, important new research may have been published since the 2012/13 guidance. Secondly, 'near-point' testing in the community may more readily lend itself to a PCT assay. Thirdly, will the intended NICE diagnostic assay program be specific to children? On a separate point, the stakeholder wonders whether there is any value in including additional diagnostic tests: urinary pneumococcal antigen and B-glucan serology in immune suppressed children (to inform 4.3.1.c.ii)?	Thank you for your comment. We recognise the difficulties when different aspects of the same pathway are examined in different parts of the NICE programme. The Diagnostic Assessment review is proceeding at the same time as the guideline which will allow liaison between these and appropriate cross –referral. The list is not exhaustive. However the emphasis of the guideline is on early recognition and diagnosis of sepsis and the GDG will decide details required regarding tests for causes of sepsis.
107	SH	Paediatric Intensive Care Society	7	4.3.1.d	It is presumed that the Surviving Sepsis treatment bundles (*and it's supporting evidence base will inform these deliberations*)	Thank you.
108	SH	Paediatric Intensive Care Society	8	4.3.1.f	**Heart rate variability** is oft quoted as a sensitive marker for incipient sepsis, and there is an increasing array of electronic algorithms to allow bedside testing for this phenomena.	Thank you for this information
109	SH	Paediatric Intensive Care Society	9	4.3.1.g	This is a vital area in children. The term 'safety netting' applies to parents sent home from a secondary care setting with the correct information to allow them to make informed choices.	Thank you for your comment.

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110	SH	Paediatric Intensive Care Society	10	4.3.1.h	The guideline group might compare UK training with primary care training schedules in other high-income countries. What evidence is there that 'extended training' pays divided in term so increase knowledge of the management of the sick child? What evidence is there that a GP with a special interest (GPSi) improves a generic skill set across a local CCG?	Thank you for these suggestions. The details of the questions will be agreed by the GDG.
111	SH	Paediatric Intensive Care Society	11	4.4	Might the guideline group consider any relevant Patient Reported Outcome Measures (PROMS), such as the beneficial sense of well being imparted through proper Parent Safety Netting	Thank you for this suggestion. We have added PROMS to the list of possible outcomes.
112	SH	Paediatric Intensive Care Society	12	GENERAL	Indirect experience suggests that properly managed 'health care systems' (the integration across primary and secondary health care) is probably more important than anything else in improving the patient pathway. The variety of health care models across Europe provides a good opportunity for comparative analysis of different approaches that supposedly deliver improved child mortality outcomes	Thank you for your comment. The guideline is not planning to examine service delivery issues. We recognise the importance of these but consideration of these issues is not possible within the timeframe available for this guideline. NICE is currently developing a guideline on Acute Medical Emergencies which will examine service delivery issues which we expect will cover some of these issues.
113	SH	Paediatric Intensive Care Society	13	GENERAL	The Personal, Social, and Health Education (PSHE) element of the school curriculum provides an opportunity for education young adults/parents of the importance of early recognition of severity of illness. NICE guidance that linked education with health outcomes would set an important precedent.	Thank you for your comment. The guideline is a clinical guideline directed to healthcare professionals and the NHS.
89	SH	Parliamentary and Health Service Ombudsman	1	General	The Parliamentary and Health Service Ombudsman investigates complaints that individuals have been treated unfairly or have received poor service from government departments and other public organisations and the NHS in England. Our role is to investigate without taking sides and make recommendations to put things right. Our service is free to use and completely independent. *Time to act: Severe sepsis: rapid diagnosis and treatment*	Thank you for the information and for taking the time to comment on the scope of the guideline.

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					saves lives (2013) highlights failures in NHS care and treatment to both diagnose and rapidly treat severe sepsis. Care failings occur mainly in the first few hours when rapid diagnosis and simple treatment can be critical to the chances of survival. We continue to receive frequent complaints where the clinical issue is poor management of severe sepsis. Our submission is supported by our casework and informed by the views of our clinical advisers. We hope that the following comments are helpful.	
90	SH	Parliamentary and Health Service Ombudsman	2	General	We have not identified anything in your draft which would better achieve equality objectives.	Thank you. The guideline will aim to ensure every patient in the UK is appropriately diagnosed and treated. The NICE process require us to consider equality issues at every stage of the guideline and we will consider whether specific recommendations need to be made for those with protected characteristics. These considerations are reported in the NICE Clinical Guideline Equality Impact Assessment forms.
91	SH	Parliamentary and Health Service Ombudsman	3	3.1 a	We question if it is necessary to include in your definition of severe sepsis the phrase "requiring a stay in an intensive care unit (ICU)". Our experience from complaints is that a frequent failing is delay or absence of intensive care involvement in patients who clearly meet the clinical definition of severe sepsis. It is worth emphasising that not all patients meeting the clinical definition always access ICU.	Thank you for your comment. The definition of severe sepsis relates to the presence of organ dysfunction rather than the stay in intensive care. We have altered the text to make this clear.
92	SH	Parliamentary and Health Service Ombudsman	4	4.3.1 a	We would strongly encourage NICE to make explicit that the assessment should include completion of an Early Warning Score (EWS). This should link to NICE CG50 *Acutely ill patients in hospital*, and be referenced in section 5.1.	Thank you for your comment; we will include evaluation of scoring systems and link to appropriate existing NICE guidelines.

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					Our complaints experience is that the physiological observations necessary to complete an EWS are not always recorded in primary care. This seems to be a missed opportunity to improve outcomes. We also find that the ambulance service does not often record patient temperature, which again appears to be a missed opportunity. A simple sepsis scoring system for ambulance staff could lead to 'low risk' earlier intravenous fluid administration.	
93	SH	Parliamentary and Health Service Ombudsman	5	4.3.1 c	We hope that you will find a suitable form of words to reconcile the need to start intravenous antibiotics as soon as possible, with the need to take blood cultures first (another frequent shortcoming in care). This links to Section 4.3.1 e.	Thank you.
94	SH	Parliamentary and Health Service Ombudsman	6	4.3.1 d	We strongly support the need for timely availability of senior clinical decision makers to support junior doctors in these challenging cases.	Thank you for your comment.
95	SH	Parliamentary and Health Service Ombudsman	7	4.3.1 e	It would be helpful if the important point about identifying source of infection could link to an additional point about timely surgical attention to identified localised sources. Complaints experience is that there are delays in timely surgical drainage of abscesses, and indeed, as in one of our cases in *Time to act*, of necrotising fasciitis.	Thank you for your comment. We have removed the word 'later' as your comment indicates that prompt specific treatment such as surgical treatment may be required. We have added to the rationale the importance of involvement of appropriate personnel both for assessment and early treatment.
96	SH	Parliamentary and Health Service Ombudsman	8	General	We would strongly welcome the concurrent development of a NICE quality standard on sepsis. A NICE quality standard will be critical to driving measurable improvements in this area. Examples of data collection which we believe would improve clinical performance would include time from arrival to starting intra-venous fluids, and time from arrival to administration of intra-venous antibiotics.	Thank you for your comment. We can confirm that Sepsis is on the list of topics that has been referred to NICE for development of Quality Standards. This would usually be developed following guideline development.
36	SH	Royal College of Midwives	1	General	The RCM considers the scope of this guideline to be appropriate and has no further comments at this point.	Thank you for your comment.

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66	SH	Royal College of Nursing	1	General	The Royal College of Nursing is a registered stakeholder for this guidance. The Royal College of Nursing was invited to comment on the draft scope for the clinical guideline for the recognition, diagnosis and management of Severe Sepsis**.** The document was circulated to RCN staff and the infection prevention and control nurses for their views. Find below comments received from the reviewers.	Thank you for your comments.
67	SH	Royal College of Nursing	2	General	The draft scope document is well written and reflects all the key areas for consideration.	Thank you for your comment.
68	SH	Royal College of Nursing	3	4.3.1 C) (ii)	Page 6 - Empirical antibacterial and antifungal treatment strategies: Regarding the wording '*It is not always possible to identify the cause of sepsis. Early use of antibiotics is part of the treatment for suspected meningococcal disease, and advice would be useful regarding when or whether to use early empirical treatment or when more delayed targeted treatment should be used'.* We are unsure why meningococcal disease has been specifically highlighted. The emphasis should be on the rapid administration of broad spectrum antibiotic therapy unless a specific focus or causative organism is known.	Thank you for your comment. The wording of this section was not clear and we have amended this.
69	SH	Royal College of Nursing	4	4.3.2 (IV)	*Infection control measures* should read ***Infection Prevention and Control measures***	Thank you. We have changed this.
70	SH	Royal College of Nursing	5	4.3.2 (IV)	Where *Gloves and gowns* is shown in brackets this should read as ***Personal Protective Equipment***	Thank you. We have changed this.
71	SH	Royal College of Nursing	6	General	A simple algorithm which could be used as a poster would be helpful to promote understanding	Thank you for your suggestion. We will work with the NICE editor and implementation team once the guideline is developed to present the recommendations in ways that are useful for health care professionals.

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72	SH	Royal College of Nursing	7	General	Referencing the Sepsis Trust as an organisation to which people can go for more information on the topic would be useful http://sepsistrust.org/	Thank you for your suggestion. NICE implementation team will work with interested organisations once the guideline is developed to identify appropriate resources.
24	SH	Royal College of Obstetricians and Gynaecologists	1	General	The RCOG welcomes the development of this guideline; please be aware that we have guidelines addressing bacterial sepsis in pregnancy, and bacterial sepsis in the puerperium. The evidence base which NICE usually uses ie RCTs/meta-analysis is likely to be lacking in many of the areas you will be addressing.	Thank you for this information.
25	SH	Royal College of Obstetricians and Gynaecologists	2	4.4b	One of the outcomes is 'progression to sepsis'. Is this incorrectly worded? I ask because the remit of the guideline is 'recognition, diagnosis and management of severe sepsis'….so the outcome 'progression to sepsis' can not correct (you are not addressing prevention of sepsis).	Thank you- we have altered this to progression to severe sepsis.
26	SH	Royal College of Obstetricians and Gynaecologists	3	3.1	The first sentence could be more explicit. As it stands it suggests that sepsis necessitates the 'presence of infection in the blood'. I suspect it should read as 'sepsis is a clinical syndrome caused by the body's systems in the blood being switched on by the presence of infection. Sepsis is defined as the presence (probable or documented) of infection together with systemic manifestations of infection. Severe sepsis is defined as sepsis plus sepsis-induced organ dysfunction or tissue hypoperfusion. – Society of Critical care Medicine	Thank you for your comment. We have removed 'In the blood'.
27	SH	Royal College of Obstetricians and Gynaecologists	4	3.1	In the second sentence, suggest adding in 'usually' as it implies that stay in ICU is a sine qua non of severe sepsis.	Thank you. We have added this.
28	SH	Royal College of Obstetricians	5	4.1.1 b)	Pregnant and recently pregnant women—as the subgroup to avoid missing post-partum/post-	Thank you for your comment; we have amended the scope

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		and Gynaecologists			miscarriage/post-abortion sepsis	accordingly.
29	SH	Royal College of Obstetricians and Gynaecologists	6	4.3.1 e)	Clinical examination to include pelvic examination with vaginal swabs, breast examination etc.	Thank you for these suggestions.
30	SH	Royal College of Obstetricians and Gynaecologists	7	4.3.1 A	The pregnant/postnatal woman has specific scoring tools, specific symptoms associated with GAS e.g. rash. Some of the 'red flags' relevant to a pregnant woman may also be very different to the non-pregnant population eg fetal tachycardia, temperature in labour and other labour identifying risk factors for post natal sepsis	Thank you for the information.
31	SH	Royal College of Obstetricians and Gynaecologists	8	4.3.1 C	Our antibiotic regime may be different for GAS/GBS sepsis	Thank you. We recognise that different regimens may be appropriate depending on a number of factors.
32	SH	Royal College of Obstetricians and Gynaecologists	9	4.3.1 D	Involvement of specialist care should include a mention of outreach/other local services for the ward patient as we all know this is the patient that is often missed whilst those on labour ward see the anaesthetist early and have level 2/3 care anyhow.	Thank you for suggestion. We are aware that patients already in hospital may be at particular risk of delayed recognition of sepsis and consider it likely that we will highlight the need to recognise this. NICE have already developed guidance on Acutely ill patient in hospital (CG50) and are currently developing an Acute Medical Emergencies guideline. We will cross- refer to these.
33	SH	Royal College of Obstetricians and Gynaecologists	10	4.3.1 E	There is should specifics to vaginal discharge and LVS. Breast examination to exclude abscess, mastitis	Thank you for these suggestions
34	SH	Royal College of Obstetricians and	11	4.3.1 F	Parameters used in pregnancy for these observations are different and should be used in conjunction with a scoring tool	Thank you we agree, the list is just an example, and we have clarified this.

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		Gynaecologists				
35	SH	Royal College of Obstetricians and Gynaecologists	12	4.3.1 H	Maternal sepsis should be part of skills drills and reviewed annually in these sessions	Thank you for your suggestion. Competencies for individual professionals and how these are maintained is outside the scope of a clinical guideline.
1	SH	Royal College of Paediatrics and Child Heath	1	3 - epidemiology	The epidemiology of severe sepsis and septic shock in children is not well known. The figures in this introduction of 37,000 deaths in a year are presumably related to adult epidemiology? There are some emerging data for epidemiology of sepsis in children which may be useful – in particular the SPROUT study has just finished collecting data and will be publishing soon. This is a very large international prevalence study of severe sepsis and septic shock in children in PICUs. In addition there are 2 papers by Watson, a decade apart, describing the prevalence of severe sepsis in children in the US. These may be useful references to describe the epidemiology in this section. Of note, the prevalence seems to be changing over time. The guideline would need to account for the fact that the epidemiology of sepsis is highly influenced by age – with much higher prevalence in the neonatal age group. Clinical presentation in the younger infants and neonates is also much more vague and non-specific than older children and adults, so I think that careful attention to the different manifestations across the age spectrum is required.	Thank you we agree, we will ensure the literature will be searched appropriately for all age groups.
2	SH	Royal College of Paediatrics and Child Heath	2	4	The Sepsis 6 initiative has inspired a Paediatric Sepsis 6 initiative – a simple tool to allow healthcare professionals (especially nursing staff) to recognise possible sepsis in	Thank you for the information. We will look at the evidence on screening tools during development.

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					children, and to prompt deliverers of healthcare to administer timely therapy. This is in use in a few centres in the UK, and although still in its infancy, may be worth mentioning in this guideline.	
3	SH	Royal College of Paediatrics and Child Heath	3	4b	What is the role of lactate in paediatric sepsis? This will need some careful review, as many children in ED will have a capillary lactate sample, which can be very difficult to interpret.	Thank you for your comment; we will review this during development.
4	SH	Royal College of Paediatrics and Child Heath	4	4cii	I fully support the idea of a guideline to promote early recognition and administration of treatment for sepsis (particularly timely antibiotics). The guideline needs to address the issue of the rising tide of antimicrobial resistance, and the need to be vigilant about duration and spectrum of antibiotic prescribing – i.e. the principles of antimicrobial stewardship. Any endeavour promoting the administration of antibiotics should address this issue, and provide guidance and pointers about how to exercise good stewardship.	Thank you for your comment. NICE are developing a specific guideline on Antimicrobial stewardship to which we will cross refer.
5	SH	Royal College of Paediatrics and Child Heath	5	4.11 b	Newborns and Children should be recognised as a separate subgroup due to the differences in management required. Differences in guidance of in-hospital vs out-of-hospital recognition and initial management of sepsis should be made clear, too. For example the early use of lactate…. See also the 3-hour and 6-hour bundle from the S*urviving Sepsis Campaign*	Thank you for these suggestions. We will consider these aspects of recognition and early treatment in the guideline.
6	SH	Royal College of Paediatrics and Child Heath	6	General	It would be important to align any documents and policies with the statements and recommendations from the *Surviving Sepsis Campaign* (http://www.survivingsepsis.org/About-SSC/Pages/default.aspx). The Surviving Sepsis Campaign is a joint collaboration of	Thank you for your comment. Recommendations will be made on the basis of cost and clinical effectiveness analysis.

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					the Society of Critical Care Medicine and the European Society of Intensive Care Medicine committed to reducing mortality from severe sepsis and septic shock worldwide.	
37	SH	Royal College Pathologists	1	3.1 a	Severe sepsis technically is defined as sepsis plus sepsis-induced with organ dysfunction or tissue hypoperfusion, which would often necessitate an intensive care unit stay but not always and many may not make it there so this should not be part of the definition.	Thank you. We have altered this sentence.
38	SH	Royal College Pathologists	2	3.1 a]	Need to add fungi to the line bacteria or viruses	Thank you. We have made this change.
39	SH	Royal College Pathologists	3	4.3.1 a p 5	As well as 'predicting' scoring systems may also be useful to monitor progress of sepsis and effects of therapy	Thank you your comment. We will examine parameters to use for early monitoring and these will include scores if appropriate.
40	SH	Royal College Pathologists	4	4.3.1.b Key clinical areas	should add albumin [prognostic] and liver function tests to the right hand column of the table	Thank you for your comment. The GDG will review the list. This list in the scope is an example.
41	SH	Royal College Pathologists	5	4.4.1.c ii [table p 6] Empirical antibacterial and antifungal strategies	Left hand column: should read 'empirical antibacterial, antifungal and antiviral strategies' since your sepsis definition incudes viral causes and should also include fungal causes. If viral causes and their treatment are outside this scope, then the original definition (3.1 a line 3) should specify this.	Thank you - we have changed this to 'anti-microbial'.
42	SH	Royal College Pathologists	6	.4.1.c ii [table p 6]	Early use of 'appropriate antimicrobials' would be better than 'antibiotics' if one is referring to viruses and fungal causes of sepsis	Thank you. We have changed the terminology of what we will include to 'anti-microbial' as you suggest.
43	SH	Royal College Pathologists	7	4.3.1.c ii [table p 7]	In sepsis for meningococcal disease there is no place for "delayed targeted treatment" and indeed in sepsis of any cause delay is not an option to consider. (Numerous papers and Cochran report assert delay in antimicrobials associated with adverse outcomes). Could better address perhaps the approach to deciding the nature of the empirical treatment.	Thank you for your comment. The wording of this section was not clear and we have amended this.
44	SH	Royal College Pathologists	8	4.3.1 c ii [table p 7][	Early empirical antibiotics is part of the therapy of any serious infection, and another classical example is necrotizing fasciitis	Thank you for your comment. The wording of this section was not clear and we have amended this..
45	SH	Royal College	9	4.3.1.e ii	Could add 'other samples for microbiological examination' [then	Thank you. The list is not intended

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		Pathologists		[table p 8]	this would cover sputum, urine, wound drainage, pus and specimens for molecular tests, virology and mycological examination as appropriate].	to be exhaustive and will be specified more fully in the guideline
46	SH	Royal College Pathologists	10	4.3.1 f (Parameters to continually assess)	Should also include assessment of pain score (particularly important for assessment and diagnosis of necrotizing fasciitis) and change in colour or degree of spread of any rash (important particularly in streptococcal and meningococcal infection)	Thank you. This list is an example and we will discuss with the GDG other items to include such as pain.
47	SH	Royal College Pathologists	11	4. 3. 1 g	'People who are diagnosed as not having sepsis and are discharged from medical care' – not sure what this refers to exactly. There are several diseases/conditions that can present with sepsis-like illnesses, and this could be very difficult to cover since could be perhaps toxin related / drug reaction /metabolic and so on.	Thank you. We do not expect to cover detail required for all possible conditions but will review whether we can advise about general information.
48	SH	Royal College Pathologists	12	4.3.2. iv Preventing sepsis	Antibiotic prophylaxis to prevent infection e.g. before endoscopy – suggest remove the 'for example before endoscopy' since this is a poor example.	Thank you. We agree this was not a good example and have removed this.
49	SH	Royal College Pathologists	13	4.3.2. iv Preventing sepsis	'Screening for bacteria in at–risk patients' - Suggest change 'bacteria' to 'pathogens' since viruses and fungi can also cause infections and are included in the original definition.	Thank you. We have made this change.
50	SH	Royal College Pathologists	14	4.4 b progression to sepsis	Should this not read progression to 'severe sepsis' since by definition this GL applies to 'sepsis'?	Yes amended
82	SH	Society for Acute Medicine	1	4.3.1.a	Needs to be acknowledged that presentations of sepsis may be subtle, especially in the elderly. It also needs to reflect more recent research which shows that patients who develop sepsis while an inpatient often deteriorate in different ways from pts when first admitted ie. Pts who go on to die frequently are less physiologically deranged [Kellett, Resuscitation. 2013 Jan;84(1):13-20].	Thank you for your comment and further information.
83	SH	Society for Acute Medicine	2	4.3.1.a	It needs to be acknowledged that hospital acquired infections are fundamentally different from those that are community acquired. Patients present in different fashions – pts who go on to die are often less physiologically deranged [Kellett, Resuscitation. 2013 Jan;84(1):13-20]. Organisms and treatments are also fundamentally different.	Thank you for your comment and further information.

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84	SH	Society for Acute Medicine	3	4.3.1.b	Needs to be acknowledged that different markers perform differently at different time points – this fits with severe infection/sepsis being a dynamic and often progressive disease process.	Thank you for your comment and further information.
85	SH	Society for Acute Medicine	4	4.3.1.d	Needs to be explicitly acknowledged that higher levels of care are appropriate for a subset of patients with sepsis. Explicit decisions about ceilings of care will need to be made for many patients. It should also be made clear that patients receiving ward-only care should still receive appropriate therapies which still may often be life-saving.	Thank you we agree with your comment.
86	SH	Society for Acute Medicine	5	4.3.1.d	While early specialist care is important, the importance of timeliness in delivering early antibiotics and fluid resuscitation would suggest that early sepsis management should be part of the core skills of ALL hospital doctors.	Thank you we agree with your comment.
87	SH	Society for Acute Medicine	6	4.3.1.f	The National Early Warning Score (NEWS) was developed explicitly in response to previous work by NICE. It is the best performing early warning scoring system and this guidelines presents the opportunity to support its spread across the NHS [Smith, Resuscitation. 2013 Apr;84(4):465-70].	Thank you for this information.
88	SH	Society for Acute Medicine	7	General	Although the working group states that general physicians will be recruited, 95% of all acutely unwell medical patients are now cared for on Acute Medical Units for the first portion of their hospital stay. We would suggest that an Acute Physicians be included in the working party.	Thank you, we agree with your comment. The membership of the guideline development group will include intensive care, emergency care and general/acute physicians along with primary care to ensure that all aspects are taken into consideration
78	SH	Teleflex formerly Vidacare	1	4.3.1 C	In relation to the early administration of IV fluids in sepsis because the scope of the document is ambitious in incorporating all healthcare settings administration of fluids may prove challenging and require further clarification of modes of vascular access in order to achieve fluid administration. Often obtaining suitable vascular access can be the rate limiting step. If sepsis is to be perceived as a time critical intervention where treatment strategies are to be initiated in less than the previous "golden hour" it is likely that IV fluids and	Thank you. We agree on these important issues and expect these to be considered by the GDG during guideline development.

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					antibiotics may be required to be administered in a Pre hospital setting. Skill in obtaining vascular access in the Pre hospital setting may vary significantly and clear guidance should be provided in relation to difficult vascular access situations and how to manage these patients to ensure treatment timeframes are still achieved. If cross referencing to NICE guidance on Intravenous fluid therapy modes of administration are outside the scope of these documents again highlighting the need for clarification. If peripheral access cannot be gained within a set period consideration to utilise alternate methods of access should be considered. Intranasal could be considered for certain drugs or Intraosseous access for rapid vascular access and administration of fluids and IV antibiotics until the septic patient can reach an area where central access could be gained as per NICE recommendations for CVC insertion.	
79	SH	Teleflex formerly Vidacare	2	4.3.1 D	In relation to escalation of care and administration of vasopressors and insertion of central access and arterial lines, because the scope refers to all healthcare settings the initial management of the Septic Medical Emergency may occur in healthcare settings outside the Critical Care environment. Clear guidance should be provided on how to escalate a patient prior to arrival in hospital. In relation to vascular access a clear escalation protocol and timeframe in relation to difficult vascular access patients should be outlined perhaps similar to the RCUK guidance around management of Cardiac arrest "if peripheral access cannot be gained within 2 minutes then consider IO?" There are already clear NICE guidance around insertion of CVC, if the recommendations in this guidance cannot be achieved due to limitations in resource, clinical skill or environmental factors alternative modes of appropriate access should be identified. Intraosseous may offer a bridge to central vascular access for initial administration of fluids, antibiotics and vasopressors in septic emergencies until the patient can be	Thank you. We agree on these important issues and expect these to be considered by the GDG during guideline development.

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					moved to a Critical Care area where central access can be gained utilising maximal barrier precautions etc.	
7	SH	The Association of Anaesthetists of Great Britain & Ireland	1	General	Exclusion of potential additional biomarkers such as procalcitonin and possible other innervation markers will lead to a gap in the advice.	Thank you for your comment. The use of procalcitonin has been referred for assessment to the **NICE Diagnostics Assessment Programme**. The timelines for the two guidelines are similar and we will ensure appropriate cross-referral.
8	SH	The Association of Anaesthetists of Great Britain & Ireland	2	Section d 4.3.1d	The Level of care needs to be defined. - level 1,2,3 care. I don't think this crosses over into the ICM guidance. This is a relevant point in escalation of care.	Thank you for your comment. We will aim to ensure that escalation of care is described as clearly as possible. We are aware that terminology, such as levels of care, may differ in different parts of the healthcare system and we will use the expertise of the GDG and stakeholders to help us with this.
9	SH	The Association of Anaesthetists of Great Britain & Ireland	3	4.3.1 f	Early monitoring should include temp and SpO2. Need to refer to use of MEWS charts	Thank you. The GDG will review the evidence to inform the recommendations.
76	SH	Welsh Intensive Care Society	1	3.1 a)	This section needs to add in that sepsis may also be caused by fungal infection	Thank you. We have added fungi.
77	SH	Welsh Intensive Care Society	2	General	The scope of the consultation is wide-ranging and appropriate to the problem of sepsis. National guidance on the early recognition, diagnosis and management of sepsis is essential to reducing morbidity and mortality from sepsis. The Welsh Intensive Care Society looks forward to the development of this guideline as sepsis currently accounts for approximately one-third of all critical care expenditure and is responsible for more deaths than any major cancer other than lung cancer.	Thank you for your comments.

These organisations were approached but did not respond:

Barnsley Hospital NHS Foundation Trust
Bradford Teaching Hospitals NHS Foundation Trust
Brahms UK Limited-Thermo Fisher Scientific
British Kidney Patient Association
British Medical Journal
British Nuclear Cardiology Society
British Psychological Society
British Red Cross
Care Quality Commission (CQC)
Central Manchester University Hospitals NHS Foundation Trust
Cerner Ltd
Department of Health, Social Services and Public Safety - Northern Ireland
East and North Hertfordshire NHS Trust
Health & Social Care Information Centre
Health and Care Professions Council
Healthcare Improvement Scotland
Healthcare Quality Improvement Partnership
King's College Hospital NHS Foundation Trust
Medicines and Healthcare products Regulatory Agency
Meningitis Now
Meningitis Research Foundation
Ministry of Defence (MOD)
National Clinical Guideline Centre
National Collaborating Centre for Cancer
National Collaborating Centre for Mental Health
National Collaborating Centre for Women's and Children's Health
National Deaf Children's Society
National Institute for Health Research
National Outreach Forum
NHS Direct
NHS England
NHS Health at Work
NHS Sheffield CCG
Nottingham University Hospitals NHS Trust
PHE Alcohol and Drugs, Health & Wellbeing Directorate
Public Health England

Public Health Wales NHS Trust
Royal Brompton Hospital & Harefield NHS Trust
Royal College of Anaesthetists
Royal College of General Practitioners
Royal College of General Practitioners in Wales
Royal College of Physicians
Royal College of Physicians of Edinburgh
Royal College of Psychiatrists
Royal College of Radiologists
Royal College of Surgeons of England
Royal Pharmaceutical Society
Scottish Intercollegiate Guidelines Network
Sheffield Teaching Hospitals NHS Foundation Trust
Social Care Institute for Excellence
South East Coast Ambulance Service
South Tees Hospitals NHS Trust
Spectral Platforms, Inc.
St Mary's Hospital Isle of Wight NHS Trust
Stockport NHS Foundation Trust
The Association for Clinical Biochemistry & Laboratory Medicine
The Intensive Care Society
United Kingdom Sepsis Trust
University of Liverpool
Welsh Government