NICE National Institute for Health and Care Excellence

Sepsis

Consultation on draft guideline
Stakeholder comments table

11/01/2016 – 22/02/2016

Stakeholder	Document	Page No	Line No	Comments Please insert each new comment in a new row	Developer's response Please respond to each comment
Abbott Molecular	Full	25	26	Blood culture seems to be described throughout the guideline document as the only means of pathogen detection and/or identification. A number of non-culture dependent technologies including molecular testing are available within the NHS. They are CE-marked and used for determining the presence of blood pathogens. *Suggested wording (in bold):* 'Carry out a venous blood test for the following: **Pathogen detection and identification, including** blood culture {…}' This comment also applies to: Page 25, line 26 Page 26, line 36 Page 28, line 10 Page 29, line 13 Page 30, line 27 Page 31, line 34 Page 195, line 33 Page 197, line 4 Page 198, line 18	Thank you for your comment. The guideline did not include non-culture dependent technologies for pathogen ection/identification. The NICE Diagnostics Assessment programme, which is cross-referred to in the 'linking evidence to recommendations' section in the full guideline, has assessed these (DG20). The findings of the assessment showed that there was not enough evidence to recommend these technologies.

				Page 199, line 20 Page 200, line 33 Page 202, line 4 Pages 349-351, recommendations and link to evidence Pages 403-404 Pages 435-437	
Abbott Molecular	Full	510	Trade-off between clinical benefits and harms	It may be worthwhile noting that in addition to blood culture, other non-culture dependent technologies including molecular tests could potentially help for identification of organisms. <u>*Suggested wording (in bold):*</u> It is widely accepted that taking blood cultures is beneficial for identification of organisms causing systemic infection. **In addition, there are methods including rapid molecular diagnostics which may be beneficial for the identification of organisms causing systemic infections. These could complement the current standard of care and potentially provide an opportunity for earlier intervention, especially in circumstances where antibiotic treatment has been initiated prior to specimen collection for culture which increases the likelihood of false negative detection and identification. Accurate and timely pathogen identification** is beneficial in ensuring appropriate antibiotics are used and particularly enabling de-escalation from	Thank you for your comment. The guideline has not looked at new ways of diagnosing infection or identifying causative organisms. These were not included when the guideline was scoped. The diagnostic assessment programme at NICE considers new technologies and has examined biomarkers and molecular testing in sepsis and agreed there is insufficient evidence to recommend these currently.

				broad spectrum to narrow spectrum antimicrobials. There are no anticipated harms from taking blood cultures.	
Abbott Molecular	Full	511	Economic considerations	*Suggested wording (in bold):* Identifying the source of the infection which has led to sepsis, and doing this in a timely way, will allow tailoring of treatment such as antibiotics which is likely to impact upon the patient's outcome. Resources likely to be involved in diagnosing the infection may include clinical assessment, blood cultures, urine samples, and imaging. The method used to diagnose the infection can very much depend upon the Finding the source of infection type of infection itself. Therefore although blood cultures tend to be the gold standard in identifying systemic organisms causing infection, other interventions may need to be used including molecular diagnostic methods. The GDG noted that blood cultures are a relatively inexpensive test in the context of the total cost of care of people with sepsis/suspected sepsis. The cost increases for positive blood cultures that require additional laboratory time and analysis. The GDG considered that the costs or resources involved in diagnosing the cause of the sepsis was likely to be outweighed by the benefit that diagnosis could bring in terms of appropriate treatment. Severe sepsis can be very expensive to treat, particularly because patients are generally in ICU where	Thank you for your comment. The guideline has not looked at new ways of diagnosing infection or identifying causative organisms. These were not included when the guideline was scoped. The diagnostic assessment programme at NICE considers new technologies and has examined biomarkers and molecular testing in sepsis and agreed there is insufficient evidence to recommend these currently.

				continuous monitoring can take place. It is also associated with a high mortality rate. There is therefore a benefit to early identification **(including molecular methods)** of the cause of the sepsis in terms of downstream savings and also a likely clinical benefit to appropriate treatment taking place as soon as possible before deterioration occurs. **Management of this critically-ill patient population and rapid tailored intervention could benefit from faster diagnostic solutions.** From one of the other questions within this guideline, patients suspected of sepsis will have already been administered early broad spectrum antibiotics, as taking cultures should not delay the administration of antimicrobials. However the fast turnaround of analysis of blood cultures will allow treatment to be more tailored to the underlying cause of the sepsis which is likely to have a positive impact on the outcome of the patient. **Emerging direct-from-specimen diagnostic solutions may improve rates of pathogen identification in cases where prior antibiotic administration results in false negative cultures.** The GDG made recommendations of good practice for diagnosing sepsis based on their own clinical experiences. If blood cultures are taken these should be done to a high standard i.e. taking adequate samples.	

Abbott Molecular	Full	511	Other considerations	*(p511-512)* *Suggested wording (in bold):* The GDG used epidemiology of causes of sepsis and their clinical experience and knowledge of clinical tests to inform these recommendations. Blood cultures are recommended as one of the tests to be done when people at high risk or high to moderate risk of severe illness of death are initially assessed. Blood cultures are used to identify the organism causing infection. It is current good practice is to take blood culture samples when possible and blood cultures are considered the gold standard when assessing other methods of identifying organisms that cause systemic infection such as **molecular methods and** DNA sequencing. Taking the cultures should not delay antimicrobial administration Yield increases with increased number of cultures taken (up to 3 or 4 samples), with the biggest difference in yield occurring between 1 and 2 samples. The GDG considered it important to emphasise that yield can be improved by ensuring valid samples are taken i.e. ensuring bottles are adequately filled and stored appropriately. **Further, the culture could be negative due to prior antibiotic treatment. Therefore, clinicians could consider using molecular methods for pathogen identification.**	Thank you for your comment. The guideline has not looked at new ways of diagnosing infection or identifying causative organisms. These were not included when the guideline was scoped. The diagnostic assessment programme at NICE considers new technologies and has examined biomarkers and molecular testing in sepsis and agreed there is insufficient evidence to recommend these currently.
Abbott Molecular	Full	512	La	Typo: ‘contracinidcation’	Thank you for your comment. We have proofread the

			st se nt en ce	*Suggested wording:* contraindication	document and corrected typos and spelling errors.
Abbott Molecular	Sh ort	26	9	Blood culture seems to be described throughout the guideline document as the only means of pathogen detection and/or identification. A number of non-culture dependent technologies including molecular testing are available within the NHS. They are CE-marked and used for determining the presence of blood pathogens. *Suggested wording (in bold):* 'Carry out a venous blood test for the following: **Pathogen detection and identification, including** blood culture {…}' This comment also applies to: Page 28, line 10 Page 30, line 22 Page 32, line 16 Page 34, line 23 Page 36, line 21	Thank you for your comment. The guideline did not include non-culture dependent technologies for pathogen detection/identification. The NICE Diagnostics Assessment programme has assessed these (DG20). This is discussed in section 14.2 of this guideline.
Alder Hey Children's NHS Foundation Trust	Full	Ge ner al		On algorithms it is unclear how many risk factors count i.e. one or 2 etc. (the notes sections have this but it is unclear on the bit people will use.) Suggesting a review by "paeds st4 or above" should be an example of paediatric experience not a prescription. A+E doctors,	Thank you for your comment. We have altered the algorithms to make the number of criteria clear. The wording about senior clinical decision maker has been altered to indicate that people of equivalent experience are

				staff grades, anaesthetists etc. may be well suited. High risk under 5 algorithm suggests “call critical care” before consultant, rather than after and I can find no definition of critical care. This could be local paeds HDU, local adult HDU/ICU, paeds transfer team, tertiary HDU/PICU depending on local patterns and hence own consultant should be first as gatekeeper. I understand the premise is not to delay but significant numbers of these cases stay in DGH HDU areas without burdening tertiary calls. Calling tertiary services also adds delays in communications that the clinician should be using to treat the patient whilst their consultant comes to review/refer	appropriate to see these patients. The wording of the recommendation has been altered to remove the inclusion of admission to critical care. The GDG agree that different services may provide critical care input and have clarified this in the recommendation. The GDG however considered that while the consultant needs to be involved they may not have the required expertise for people who are at highest risk and critical care expertise is required for these people.
Alder Hey Children’s NHS Foundation Trust	Full	General		In the flow diagram considering the hospital setting, and on the left hand side (severe sepsis) I think there should be some mention of source control (draining abscesses, removing infected lines). This could be in the box that I have already mentioned which starts with ‘Arrange immediate review by…’ or 2 boxes below it (two of which start with give iv fluids)	Thank you for your comment. The importance of source control is recognised in the recommendations. The algorithms are not intended to include all aspects of care but to highlight early immediate steps. On review the GDG agreed that adding source control to the algorithm made it less easy to read.
Alder Hey Children’s NHS Foundation Trust	Full	13		(p13 and 30) There are a collection of typos… ‘youg people’ page 13, ‘parentral antibiotics’ page 30	Thank you for your comment. We have proofread the document and corrected typos and spelling errors.
Alder Hey Children’s	Full	14		Page 14 flow diagram named ‘managing	Thank you for your comment. This is already included in the

NHS Foundation Trust				adults and children and young people…in acute hospital setting' coming down the left hand side, 4th box down which starts with 'Arrange immediate review by…' there's a comment 'venous blood for blood culture crp…' I'd add in a blood glucose as some (5% at a guess) will be hypoglycaemic, maybe more in younger children. You'll probably get a glucose level if doing lactate or blood gas, but you might not.	recommendation for children and young people. The algorthim does not contain all detail in the recommendations to aid clarity of presentation.
Alder Hey Children's NHS Foundation Trust	Full	16		(p16 and 18) And the need for a blood glucose determination is even more true for children 5-11 and (page 16) and even truer (!) for children under 5 (flow diagram on page 18). There are even some references on this I am sure but I don't have any to hand	Thank you for your comment. Assessment of blood glucose is already included in the pathway for children under 12 years.
Alder Hey Children's NHS Foundation Trust	Full	33	34	98. For children younger than 3 months, an additional antibiotic active against listeria (for 34 example, ampicillin or amoxicillin) should be given. This advice is outdated – cover for Listeria only needed in infants under 1 month – see Okike et al – Arch Dis Child. 2015 May; 100(5):423-5	Thank you for your comment. This recommendation is from the Fever in Under 5s guideline. We will pass this information on to the NICE surveillance team.
Alere Ltd.	Full	348	Table 105	Table 105, the **GP Point of Care** Column states that testing for Blood gas:pH, bicarbonates,lactate, glucose, Na, K, is not available, but possible. This is incorrect. The Alere EPOC Blood Analysis System is a point of care system that can deliver all these test results from a single drop of	Thank you for your comment. The costs from the table were from the clinical experts on the guideline development group. Where 'NA' is written in the table this does not imply that such a test does not exist, but that the experiences of the guideline development group were that they do not use those devices or they are not commonly used. Therefore the costs in the table are a

				blood and provide results in 30 seconds. The cost of one test card to complete all of these analyses in one test is £5. The EPOC reader cost is £7000 (however on a per patient basis the cost of the reader would be small)l.	snapshot of the experience of a small group of people from their hospitals and are not intended to be nationally representative. It has been clarified in a footnote in the table however that such point of care devices can exist.
Alere Ltd.	Full	348	Table 105	Table 105, the **GP Point of Care** Column states that testing for Lactate is not available, but possible. This is incorrect. The Alere EPOC Blood Analysis System is a point of care system that can deliver these test results from a single drop of blood and provide results in 30 seconds. The cost of one test card to complete a lactate test (will also simultaneously run blood gas:pH, bicarbonates,glucose, Na, K and creatinine at no additional cost) is £5.	Thank you for your comment. The costs from the table were from the clinical experts on the guideline development group. Where 'NA' is written in the table this does not imply that such a test does not exist, but that the experiences of the guideline development group were that they do not use those devices or they are not commonly used. Therefore the costs in the table are a snapshot of the experience of a small group of people from their hospitals and are not intended to be nationally representative. It has been clarified in a footnote in the table however that such point of care devices can exist.
Alere Ltd.	Full	348	Table 105	Table 105, the **GP Point of Care** Column states that testing for CRP s not available, but possible. This is incorrect. The Alere Afinion is a point of care system that can deliver these test results from a single drop of blood and provide results in 4 minutes. The cost of one CRP test is £4. The cost of the Afinion Analyser is £2000 (however on a per patient basis the cost of the machine would be small).	Thank you for your comment. The costs from the table were from the clinical experts on the guideline development group. Where 'NA' is written in the table this does not imply that such a test does not exist, but that the experiences of the guideline development group were that they do not use those devices or they are not commonly used. Therefore the costs in the table are a snapshot of the experience of a small group of people from their hospitals and are not intended to be nationally representative. It has been clarified in a footnote in the table however that such point of care devices can exist.

Alere Ltd.	Full	348	Table 105	Table 105, the **Ambulance Point of Care** Column states that testing for Blood gas:pH, bicarbonates,lactate, glucose, Na, K, is not available. This is incorrect. The Alere EPOC Blood Analysis System is a point of care system that can deliver all these test results from a single drop of blood and provide results in 30 seconds. The cost of one test card to complete all of these analyses in one test is £5.	Thank you for your comment. The costs from the table were from the clinical experts on the guideline development group. Where 'NA' is written in the table this does not imply that such a test does not exist, but that the experiences of the guideline development group were that they do not use those devices or they are not commonly used. Therefore the costs in the table are a snapshot of the experience of a small group of people from their hospitals and are not intended to be nationally representative. It has been clarified in a footnote in the table however that such point of care devices can exist.
Alere Ltd.	Full	348	Table 105	Table 105, the **Ambulance Point of Care** Column states that testing for Lactate is not available, but possible. This is incorrect. The Alere EPOC Blood Analysis System is a point of care system that can deliver the lactate test result from a single drop of blood and provide results in 30 seconds. The cost of one test card to complete a lactate (will also simultaneously run blood gas:pH, bicarbonates,glucose, Na, K and creatinine, at no additional cost) is £5.	Thank you for your comment. There is an example of the cost of a lactate test in the ambulance point of care column which was from a guideline development group member.
Alere Ltd.	Full	348	Table 105	Table 105, the **Ambulance Point of Care** Column states that testing for CRP s not available, but possible. This is incorrect. The Alere Afinion is a point of care system that can deliver these test results from a single drop of blood and provide results in 4 minutes. The cost of one CRP test is £4.	Thank you for your comment. The costs from the table were from the clinical experts on the guideline development group. Where 'NA' is written in the table this does not imply that such a test does not exist, but that the experiences of the guideline development group were that they do not use those devices or they are not commonly used. Therefore the costs in the table are a snapshot of the experience of a small group of people from their hospitals and are not intended to be nationally

					representative. It has been clarified in a footnote in the table however that such point of care devices can exist.
Alere Ltd.	Full	348	Table 105	Table 105, the **ED or Ward Point of Care** Column states that testing for Blood gas:pH, bicarbonates,lactate, glucose, Na, K, costs £11.70. The Alere EPOC Blood Analysis System is a point of care system that can deliver all these test results from a single drop of blood and provide results in 30 seconds. The cost of one test card to complete all of these analyses in one test is £5.	Thank you for your comment. The cost of £11.70 was from a guideline development group member and is the cost for a test using a blood gas analyser machine which would be different to a handheld point of care device.
Alere Ltd.	Full	348	Table 105	Table 105, the **ED or Ward Point of Care** Column states that testing for Lactate cost is similar to £11.70 quoted for the Blood gases etc. The Alere EPOC Blood Analysis System is a point of care system that can deliver the lactate test result from a single drop of blood and provide results in 30 seconds. The cost of one test card to complete a lactate (will also simultaneously run blood gas:pH, bicarbonates,glucose, Na, K and creatinine) at no additional cost) is £5.	Thank you for your comment. The cost of £11.70 was from a guideline development group member and is the cost for a test using a blood gas analyser machine which would be different to a handheld point of care device.
Alere Ltd.	Full	348	Table 105	Table 105, the **ED or Ward Point of Care** Column states that testing for CRP s not available, but possible. This is incorrect. The Alere Afinion is a point of care system that can deliver these test results from a single drop of blood and provide results in 4 minutes. The cost of one CRP test is £4.	Thank you for your comment. The costs from the table were from the clinical experts on the guideline development group. Where 'NA' is written in the table this does not imply that such a test does not exist, but that the experiences of the guideline development group were that they do not use those devices or they are not commonly used. Therefore the costs in the table are a

					snapshot of the experience of a small group of people from their hospitals and are not intended to be nationally representative. It has been clarified in a footnote in the table however that such point of care devices can exist.
Alere Ltd.	Full	348	Table 105	Table 105, the **GP Point of Care** Column states that Biochemical tests for electrolytes and creatinine, is not available. This is incorrect. The Alere EPOC Blood Analysis System is a point of care system that can deliver electrolytes and creatinine (as well as for Blood gas:pH, bicarbonates, lactate, glucose, Na, K) all from one single drop of blood and in one test card, in just 30 seconds. The cost of one test card to complete all of these analyses in one test is £5.	Thank you for your comment. The costs from the table were from the clinical experts on the guideline development group. Where 'NA' is written in the table this does not imply that such a test does not exist, but that the experiences of the guideline development group were that they do not use those devices or they are not commonly used. Therefore the costs in the table are a snapshot of the experience of a small group of people from their hospitals and are not intended to be nationally representative. It has been clarified in a footnote in the table however that such point of care devices can exist.
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Alere Ltd.	Full	348	Table 105	Table 105, the **ED or Ward Point of Care** Column states that Biochemical tests for electrolytes and creatinine, is not available. This is incorrect. The Alere EPOC Blood Analysis System is a point of care system that can deliver electrolytes and creatinine (as well as for Blood gas:pH, bicarbonates,lactate, glucose, Na, K) all from one single drop of blood and in one test card, in just 30 seconds. The cost of one test card to complete all of these analyses in test is £5.	Thank you for your comment. The costs from the table were from the clinical experts on the guideline development group. Where 'NA' is written in the table this does not imply that such a test does not exist, but that the experiences of the guideline development group were that they do not use those devices or they are not commonly used. Therefore the costs in the table are a snapshot of the experience of a small group of people from their hospitals and are not intended to be nationally representative. It has been clarified in a footnote in the table however that such point of care devices can exist.
Alere Ltd.	Full	366	Table 113	Table 113, the **ED or Ward Point of Care** Column states that Lactate test cost is £11.70. The Alere EPOC Blood Analysis System is a point of care system that can deliver the lactate test result from a single drop of blood and provide results in 30 seconds. The cost of one test card to complete a lactate (will also simultaneously run blood gas:pH, bicarbonates,glucose, Na, K and creatinine at no additional cost) is £5.	Thank you for your comment. The cost of £11.70 was from a guideline development group member and is the cost for a test using a blood gas analyser machine which would be different to a handheld point of care device.
All-Party Parliamentary Group on Sepsis	Full	General	General	The All-Parliamentary Group on Sepsis welcomes this draft guideline and the important step this takes towards wider awareness of sepsis and the importance of diagnosing and treating this condition appropriately.	Thank you for your comment.
All-Party Parliamentary Group on Sepsis	Full	Gener	Gene	The Group welcomes the focus on public and healthcare professional awareness.	Thank you for your comment.

		al	ral	The group believes that in order for any changes to be implemented there needs to be further awareness around sepsis, both in healthcare settings and in the wider public.	
All-Party Parliamentary Group on Sepsis	Full	General	General	The All-Parliamentary Group on Sepsis is concerned that there is no reference to 'Red Flag' sepsis which is something that the UK Sepsis Trust has been working around recently.	Thank you for your comment. The GDG acknowledges the importance of the work of the UK Sepsis Trust. 'Red flag' sepsis has a specific meaning in the context of UK Sepsis Trust tools. The GDG independently examined the evidence to consider choice of criteria and subsequent actions and have therefore labelled their criteria as high risk criteria rather than use a term already in use with specific meaning.
All-Party Parliamentary Group on Sepsis	Full	General	General	The All-Parliamentary Group on Sepsis would welcome a further focus on NEWS and using this to support recognition of sepsis in patients.	Thank you for your comment. The evidence available on use of NEWS was of low quality. Following review of the evidence the GDG preferred to cross refer to existing NICE guidance on Acute illness in adults in hospital (CG50). In that guideline there is a recommendation to consider use of scores when assessing people who might have sepsis in hospital settings and to use track and trigger systems for monitoring. We have included a research recommendation examining the use of scores such as NEWS in primary and community settings as we did not find evidence for their use.
All-Party Parliamentary Group on Sepsis	Full	General	General	The All-Party Parliamentary Group welcomes the recommended intervention programme identified within this draft guideline however we believe that this should be named, or at least referenced, as the Sepsis Six. According to the recent NCEPOD report 94% of hospitals use the Sepsis Six and we therefore believe that the Sepsis Six should be appropriately acknowledged within the NICE Guideline.	Thank you for your comment. The GDG acknowledges the importance of the work of the UK Sepsis Trust. The recommended interventions in the guideline were agreed by the GDG following a review of the evidence and differ slightly from the current Sepsis Six. The GDG preferred not to use a term already in use.
All-Party Parliamentary Group on Sepsis	Full	Gener	Gene	The All-Party Parliamentary Group on Sepsis is concerned that Section 14 on	Thank you for your comment. The GDG recognises the importance of blood cultures and we have added reference

		al	ral	Blood Cultures fails to include recommendations mentioned in Public Health England's UK Standards for Microbiology Investigations (SMI), guidance 2014 and EI National clinical guideline #6 - sepsis management published in November 2014 from the National Clinical Safety committee of the Department of Health Ireland. The recommendations around the minimal time from patient blood collection to incubation is not included in this guidance. By keeping a short time to incubation valuable time is saved and there is a shortening time to detection of microorganisms. Blood cultures should ideally be placed on the continuous monitoring blood culture machine 24 hours a day, as soon as possible after collection and within a maximum of 4hr. This means that a patient can be diagnosed appropriately and often moved from broad spectrum antibiotics to specific treatment more quickly. The SMI Guideline also recommends that in the majority of cases two blood culture sets should be used for most patients. A second or third set taken from a different site not only increases yield but also allows recognition of contamination. We are concerned that the number of blood culture bottles recommended in Sepsis Management National Clinical Guideline No. 6 from NCEC Ireland have not been	to the standards you outline to the 'linking evidence to recommendations' section in the Full guideline. Specific detail about filling of blood culture bottles is too detailed for inclusion in the guideline recommendations. We have added comment about this also to the training and education section of the Full guideline.

				stipulated in the NICE guidance draft which will reduce the effectiveness of blood cultures and lead to less positive results. There is also no recommendation regarding training in the need for adequate fill volume in blood culture bottles which is the most significant factor affecting the detection of organisms in bloodstream infection.	
All-Party Parliamentary Group on Sepsis	Full	General	General	We are concerned that no provision has been made in the guidance towards the implementation of sepsis guidance locally. Research suggests that there are several barriers to physicians adopting clinical guidance. In both Ireland and Germany national groups were set up to ensure implementation of recommendations. We would recommend the creation of a similar National Group that will support hospitals in the implementation of the NICE guidance to allow speedy and effective implementation of the guidance.	Thank you for your suggestions. NHS England have produced a cross –system action plan for improving outcomes for patients with sepsis which includes a number of initiatives which will build on these guidelines and subsequent quality standards.
All-Party Parliamentary Group on Sepsis	Full	38	10 - 11	The All-Parliamentary Group on Sepsis welcomes the call for a national registry on sepsis and supports this.	Thank you for your comment. The research recommendation has been changed to reflect the NICE process for research recommendations. The GDG agreed to recommend that an epidemiological study on the presentation and management of sepsis in England be conducted.
Association of Healthcare Organisations (AIHO)	General	General	General	The guidance is excellent, and in line with what was excepted from the NCEPOD presentation. The only comments would be that it should be made clear that it builds on “Sepsis 6” which is generally what everybody has been using.	Thank you for your comment. The guideline recommendations were developed independently following review of the evidence. It is inevitable that they overlap with the Sepsis 6 but were not developed with them in mind.
Association of Healthcare	Gener	Gener	Gene	There are some very good flow charts within it that will be very useful in practice	Thank you for your comment.

Organisations (AIHO)	al	al	ral		
Association of Healthcare Organisations (AIHO)	General	General	General	Some of the algorithms are not user friendly	Thank you for your comment. We have edited the algorithms to improve presentation.
Association of Paediatric Emergency Medicine (APEM)	Short	1		1.1 While it is important we recognise sepsis should there be at some point in this document a clear balance in some cases between sepsis recognition and treatment and antimicrobial stewardship, overtreatment and mis-diagnosis. Especially in children there is a real risk that services will become overloaded and increase patient harm if SEPSIS protocols are adequately utilised.	Thank you for your comment. The GDG considered the balance between sepsis recognition and treatment and antimicrobial stewardship throughout guideline development. Antibiotics within one hour are only recommended in those at highest risk because of this concern. Following stakeholder comment the recommendations have been changed to increase emphasis on clinical assessment and consideration of other diagnoses.
Association of Paediatric Emergency Medicine (APEM)	Short	1		Even in the short guidance I think that definitions need to be present. There is still confusion over sepsis, septicaemia, SIRS, red flag sepsis for both the public and health care professionals. *I note this has been included at the end but this should be brought to the beginning*	Thank you for your comment. We have added information to the short guideline and the Full guideline about definitions of sepsis. The 'context' section following the recommendations is NICE format.
Association of Paediatric Emergency Medicine (APEM)	Short	1		The diagrams contain far too much text and detail to be useful. While I understand they are probably illustrative the amount of information contained is likely to get lost.	Thank you for your comment. We have worked to improve the layout and wording of the algorithms.
Association of Paediatric Emergency Medicine (APEM)	Short	3	17	"*Consider using an early warning score in hospital settings*" would probably be more correct has consider using a 'scoring system or bespoke proforma". There is no evidence early warning scores are effective outside of ward environments.	Thank you for your comment. 'Consider' is used to indicate the lack of evidence for early warning scores and the recommendation is to use a structured assessment.
Association of Paediatric Emergency Medicine (APEM)	Short	4	17	*Ask the person, parent or carer about frequency of urination in the past 18 hours* - what is the rational for 18 hours. This will	Thank you for your comment. This recommendation has been amended following stakeholder comment.

				be a difficult question to ask parents. Why not 24 hours which the parents/carers are likely to have a better understanding of.	
Association of Paediatric Emergency Medicine (APEM)	Short	4	24	Should be High, Moderate and Low – high to moderate is confusing	Thank you for your comment. The GDG preferred the term moderate to high to emphasise that some people within this group are at risk of significant morbidity or death.
Association of Paediatric Emergency Medicine (APEM)	Short	7	5	1.3.3 – and burns (risk of TSS)	Thank you for your comment. Breeches of skin are included in risk factors and the GDG considered that this covered burns.
Association of Paediatric Emergency Medicine (APEM)	Short	8	3	While I feel the term " *not responding to social cue*s" wasn't brilliant it seems odd to have different wording on the sepsis chart compared to the feverish illness one.	Thank you for your comment. In the case of children under 5 where we have adapted the risk stratification tool from the Fever in under 5s guideline (NICE guideline CG160) we do use the term 'not responding to social cues'. The GDG did not consider this wording was appropriate for older children and adults.
Association of Paediatric Emergency Medicine (APEM)	Short	8	3	Practically this is not a useful way of highlighting risk of RR. While I understand the CDG must follow evidence at the same time the NHS is not paper lite, in fact in many places it is still completely paper based. The values for the HR and RR while be very difficult to enforce without e-systems. This will lead to poor implementation. I do think the GDG need to consider the implications of this.	Thank you for your comment. The GDG considered this at length but were also concerned about having ranges that were inappropriate and risked over treatment. Following stakeholder comment the ranges have been simplified and presentation improved.
Association of Paediatric Emergency Medicine (APEM)	Short	11		Flushed – is there really evidence flushed is an independent predictor of sepsis? I am not sure that 'flushed' made it to the NICE fever guideline so not sure how it could be different for sepsis?	Thank you for your comment. We have adapted the risk stratification tool from the Fever in under 5s guideline (NICE guideline CG160).
Association of Paediatric Emergency Medicine (APEM)	Short	12	16	1.3.8 – assessment of feeding should be added	Thank you for your comment. The GDG reviewed this and agreed not to include feeding. Feeding difficulties has also been removed from the risk stratification criteria. The GDG

					agreed that feeding difficulties can be common in children who are unwell but were not a specific indication of children who might have sepsis. The inclusion of feeding difficulties in the draft guideline increased the risk of children being included in a sepsis pathway unnecessarily.
Association of Paediatric Emergency Medicine (APEM)	Short	13	26	1.3.9 – assessment of feeding should be added	Thank you for your comment. The GDG reviewed this and agreed not to include feeding. Feeding difficulties has also been removed from the risk stratification criteria. The GDG agreed that feeding difficulties can be common in children who are unwell but were not a specific indication of children who might have sepsis. The inclusion of feeding difficulties in the draft guideline increased the risk of children being included in a sepsis pathway unnecessarily.
Association of Paediatric Emergency Medicine (APEM)	Short	14	16	1.3.14 – children with diagnoses other than cancer and on immunosuppressive drugs/systemic steroids should also be in this risk group	Thank you for your comment. The list is not meant to be exhaustive and cannot include all possible examples.
Association of Paediatric Emergency Medicine (APEM)	Short	15	8	1.3.17 – recognise that if BP starts rising in unwell children, that this can be a sign of shock	Thank you for your comment. The GDG reviewed this recommendation following your comment. They considered that it was difficult to make more detailed recommendations about BP in children because of the paucity of data and preferred to emphasise that BP may appear normal in children with shock as this may be more useful information in early stages.
Association of Paediatric Emergency Medicine (APEM)	Short	23	15	1.5.23 – many children in this age group with a fever with focus - tonsillitis, otitis media, UTIs etc - will easily score 2 or more in the moderate risk group, necessitating blood tests. This will increase workload and impact on patient flow in the ED. Will the Guideline take this into account? I note that the GDG itself states: “The GDG considered that the evidence indicated that blood tests had poor	Thank you for your comment. The wording of recommendations has been changed to consider if someone might have sepsis and to include appropriate emphasis on clinical judgement to ensure people are not treated as suspected sepsis inappropriately.

				performance overall for diagnosis or prognosis." (page 352 of Full Guidleline). While WBC and CRP are useful in decision making, there are many children with a focus for their fever who do not need these tests – simply a period of observation.	
Association of Paediatric Emergency Medicine (APEM)	Short	23	25	Is there really the evidence to justify a defining treatment decision on a lactate alone, particularly given the low quality evidence and the statement on p.370 that it has a poor sensitivity and serious consequences could arise if used to decide if a patient should be treated? I think much greater consideration should be given to the clinical picture in terms of treatment and fluids. Using lactate alone seems to take clinical decision making out of the equation.	Thank you for your comment. The recommendations do not use lactate alone to decide on treatment. All those with high risk criteria have clinical assessment with a senior clinical decision maker, antibiotics and discussion with consultant. Lactate is used when considering fluids and critical care referral. For people with 2 or more moderate to high risk criteria a raised lactate suggests that they should be treated as high risk.
Association of Paediatric Emergency Medicine (APEM)	Short	27	8	1.5.38 – many infants 2-3 months presenting with bronchiolitis have a mild fever (<38.5°C) and we do not start antibiotics, or even perform blood tests	Thank you for your comment. The wording of recommendations has been changed and additional recommendations have been added to clarify that the intention is to consider if someone might have sepsis and to include appropriate emphasis on clinical judgement to ensure people are not treated as suspected sepsis inappropriately. The recommendation in the under 5 years group uses bronchiolitis as a specific example of an alternative diagnosis.

Association of Paediatric Emergency Medicine (APEM)	Short	27	18	1.5.39 - many children in this age group with a fever with focus - tonsillitis, otitis media, UTIs etc - will easily score 2 or more in the moderate risk group, necessitating blood tests. This will increase workload and impact on patient flow in the ED. Will the Guideline take this into account? I note that the GDG itself states: "The GDG considered that the evidence indicated that blood tests had poor performance overall for diagnosis or prognosis." (page 352 of Full Guideline). While WBC and CRP are useful in decision making, there are many children with a focus for their fever who do not need these tests – simply a period of observation.	Thank you for your comment. The wording of recommendations has been changed to consider if someone might have sepsis and to include appropriate emphasis on clinical judgement to ensure people are not treated as suspected sepsis inappropriately.
Association of Paediatric Emergency Medicine (APEM)	Short	34	16	1.10 – worth drafting short patient info leaflet explaining sepsis to go with published guideline	Thank you for your comment. NICE produce a document called Information for Patients which will accompany the guideline.
Becton Dickinson (BD)	Full	General	General	BD welcomes this draft guideline and the wider awareness around sepsis that this will bring.	Thank you for your comment.
Becton Dickinson (BD)	Full	General	General	BD is concerned that Section 14 on Blood Cultures fails to include recommendations mentioned in Public Health England's UK Standards for Microbiology Investigations (SMI), guidance 2014 and EI National clinical guideline #6 - sepsis management published in November 2014 from the National Clinical Safety committee of the Department of Health Ireland.	Thank you for your comment. The GDG recognises the importance of blood cultures and we have added reference to the standards you outline to the 'linking evidence to recommendations' section in section 14 of the Full guideline.
Becton Dickinson (BD)	Full	Gener	Gene	BD believes that blood cultures are a vital part of the sepsis pathway. Without a quick,	Thank you for your comment. The GDG agrees that blood culture is an important part of the pathway and have

		al	ral	accurate diagnosis patients will be kept on broad spectrum antibiotics for longer, sometimes not treated correctly and miss out on appropriate diagnosis. BD believes that the challenge of rapid reliable processing of blood cultures in order to optimise outcomes for patients, including reducing length of stay, while providing procedural opportunities to improve antimicrobial stewardship and facilitate seven day working remains and is an issue that needs to be given further profile.	included blood cultures where this will aid decision-making and management. Methods and equipment for taking and processing blood culture were not prioritised by stakeholders for inclusion in the scope of this guideline.
Becton Dickinson (BD)	Full	General	General	The pre-analytical stage from collection to loading represents an important area of potential missed opportunity in terms of minimising the time to diagnosis which BD believes should be addressed in the Guideline. The time to load is dependent on many factors *(Bacteriology B 37 Issue no: 8 Issue date: 04.11.14 Page: 18 of 51 UK Standards for Microbiology Investigations Issued by the Standards Unit, Public Health England)*: 1. The location of the laboratory in relation to the ward (onsite/offsite) 2. External transportation arrangements (frequency, out of hours service) 3. Internal transfer arrangements (frequency, availability of pneumatic tube transport, out of hours service) 4. Level of laboratory out of hours	Thank you for your comment. The GDG recognises the importance of blood cultures and we have added detail from the standards you outline to the 'linking evidence to recommendations' section in the Full guideline. Specific detail about blood culture incubation was not prioritised for inclusion when the guideline was scoped and is too detailed for inclusion in the guideline recommendations.

				service provision (out of hours loading frequency) The SMI guidelines state that "Blood cultures should ideally be placed on the continuous monitoring blood culture machine 24 hours a day, as soon as possible after collection and within a maximum of 4hr. Consider new developments/advances in current technology which decrease the collection to loading time and time to positivity". Hospital factors above lead to this often not being possible *(Ronnberg C, Mildh M, Ullberg M, Ozenci V. Transport time for blood culture bottles: underlying factors and its consequences. Diagn Microbiol Infect Dis 2013; 76:286-90).* Newer more portable technology exists that allows blood cultures to be incubated in instruments sited in critical areas like Intensive Care with these instruments linked directly to the Hospital IT system and main laboratory. This allows immediate incubation from collection, saving valuable time and shortening time to detection of microorganisms. BD would advise the inclusion of the consideration of the siting of blood culture incubation as close to possible to the patient within key areas of the hospital, for example in A&E, Intensive care, Paediatrics, and BD believe this should be mentioned within the guideline.	
Becton Dickinson (BD)	Full	Ge	Ge	For the majority of patients, two blood	Thank you for your comment. The GDG recognises the

		neral	neral	culture sets are recommended by the SMI guidelines. A second or third set taken from a different site not only increases yield but also allows recognition of contamination *(Washington JA, Ilstrup DM. Blood cultures: issues and controversies. Rev Infect Dis 1986; 8:792-802.).* At least two sets of blood cultures (both aerobic and anaerobic bottles) should be obtained before antimicrobial therapy with at least one drawn percutaneously and one drawn through each vascular access device, unless the device was recently (<48 hrs) inserted. *(EI National clinical guideline #6 - sepsis management published in November 2014 from the National Clinical Safety committee of the Department of Health Ireland. P36.)* BD is concerned that the number of blood culture bottles recommended in Sepsis Management National Clinical Guideline No. 6 from NCEC Ireland have not been stipulated in the NICE guidance draft which will reduce the effectiveness of blood cultures and lead to less positive results. BD are keen to ensure that these recommendations are included within the guideline to ensure that the blood culture process is as effective as possible.	importance of blood cultures and we have added reference to the standards you outline to the 'linking evidence to recommendations' section in the Full guideline. Specific detail about where samples should be drawn from and the number of bottles is too detailed for inclusion in the guideline recommendations.
Becton Dickinson (BD)	Full	General	General	Blood culture volume is the most significant factor affecting the detection of organisms in bloodstream infection. There is a direct relationship between blood volume and yield, with approximately a 3% increase in	Thank you for your comment. The GDG recognises the importance of blood cultures and we have added reference to national standards you outline to the 'linking evidence to recommendations' section in section 14 of the Full guideline. Specific detail about filling of blood culture bottles is too

				yield per mL of blood cultured. False negatives may occur if inadequate blood culture volumes are submitted *(Connell TG, Rele M, Cowley D, Buttery JP, Curtis N. How reliable is a negative blood culture result? Volume of blood submitted for culture in routine practice in a children's hospital. Pediatrics 2007; 119:891-6).* The number of organisms present in adult bacteraemia is frequently low, often <1 x 103 colony forming units per litre (cfu/L) *(Mermel LA, Maki DG. Detection of bacteremia in adults: consequences of culturing an inadequate volume of blood. Ann Intern Med 1993; 119:270-2.).* For adult patients it is recommended that 20-30mL of blood be cultured per set *(Patel R, Vetter EA, Harmsen WS, Schleck CD, Fadel HJ, Cockerill FR, III. Optimized pathogen detection with 30- compared to 20-milliliter blood culture draws. J Clin Microbiol 2011; 49:4047-51.).* There is no recommendation regarding training of healthcare professionals, especially junior doctors, in the need for adequate fill volume in blood culture bottles and BD believes that this is essential to ensuring blood culture results are accurate.	detailed for inclusion in the guideline recommendations but we have added reference to this in the training and education section of the Full guideline in section 16.
Becton Dickinson (BD)	Full	General	General	At the time of blood culture sampling 28-63% of patients are in the process of receiving antimicrobial treatment which may have reduced organism recovery, significantly increasing the likelihood of a false negative result. Medium containing	Thank you for this information. The GDG recognises the increased likelihood of false negative results when antimicrobial treatment has already been started. Recommendations have been worded specifically to emphasize the importance of taking blood cultures before initiating antimicrobial treatment. Microbiological and

				antibiotic inactivating resins have been developed to overcome the effect of antimicrobials *(Flayhart D, Borek AP, Wakefield T, Dick J, Carroll KC. Comparison of BACTEC PLUS blood culture media to BacT/Alert FA blood culture media for detection of bacterial pathogens in samples containing therapeutic levels of antibiotics. J Clin Microbiol 2007; 45:816-21; Miller NS, Rogan D, Orr BL, Whitney D. Comparison of BD Bactec Plus blood culture media to VersaTREK Redox blood culture media for detection of bacterial pathogens in simulated adult blood cultures containing therapeutic concentrations of antibiotics. J Clin Microbiol 2011; 49:1624-7).* BD would recommend the inclusion of this stipulation in the guidance.	biochemical technologies and methods are however outside the scope and remit of this guideline.
Becton Dickinson (BD)	Full	General	General	BD are concerned that no provision has been made in the guidance towards the implementation of guidance locally. Research suggests that there are several barriers to physicians adopting clinical guidance *(Michael D. Cabana, MD, MPH, Cynthia S. Rand, PhD, Neil R. Powe, MD, MPH, MBA, Albert W. Wu, MD, MPH, Modena H. Wilson, MD, MPH, Paul-Andre´ C. Abboud, MD, Haya R. Rubin, MD, PhD Why Don't Physicians Follow Clinical Practice Guidelines? 1458 JAMA, October 20, 1999—Vol 282, No. 15, 1460-1461.)* In Germany, a Centre for Sepsis Control, centrally funded by the ministry of science	Thank you for your suggestions. NHS England have produced a cross –system action plan for improving outcomes for patients with sepsis which includes a number of initiatives which will build on these guidelines and subsequent quality standards.

				& headed by Professor Konrad Reinhardt was set up to support hospitals in the implementation of national Sepsis guidelines. This intervention took the form of staff from the Centre for Sepsis Control going into hospitals to support both implementation actions and reflect performance metrics. The subsequent Medusa trial ("medical education for sepsis source control and antibiotics" - 44 hospitals and 5000 patients) to check time to diagnosis and the administration of first antimicrobial therapy and to check compliance regarding blood cultures found significantly more blood cultured drawn in intervention group compared to other group. In Ireland a national steering committee was set up by the Minister for Health & Dr Vida Hamilton MB, FCARCSI, FJFICMI was appointed as the National Clinical Lead Sepsis with a remit to aid hospitals implement guidelines from the Sepsis Management National Clinical Guideline No. 6. Key actions of the Steering committee were 1. Provided sepsis education talk during grand rounds during existing educational times. 2. Met with senior people in each hospital - CEO, Clinical Director and Director Of Nursing to outline the scale of problem and create a local action plan that included a local Sepsis Committee with	

				strong leadership from the hospital Clinical Director. Again, implementation of guidance has been far speedier and more effective in the intervention hospitals than those outside these actions. BD would recommend the creation of a similar National group that will support hospitals in the implementation of the NICE guidance to allow speedy and effective implementation of the guidance.	
Becton Dickinson (BD)	Full	511 - 512	44 - 51 ; 1-5	BD welcomes the inclusion of these points regarding gold standard blood cultures, the importance of yield and the importance of adequately filling and storing bottles. However BD feels that these points are not given appropriate profile by being listed under 'other considerations' and fear that they may be overlooked in this position. We would welcome these recommendations being specified as the minimum standard and including the further emphasis highlighted in the below points.	Thank you for your comment. We have added more detail about blood cultures to this section. However further information in the recommendations about the minimum standards for blood cultures would be too detailed information in this guideline.
British Association of Critical Care Nurse	Short	34	1.10.4 Line26	Should it not be made clearer that organisations should provide written information	Thank you for your comment. The recommendations in this guideline should be used in conjunction with other NICE guidance, for example the Patient Experience guideline, where communication is covered in more detail.
British Association of Critical Care Nurses	Full	General	General	Appears to be a fully comprehensive document	Thank you for your comment.
British Association of Critical Care Nurses	General	General	General	Thank you for the opportunity to comment on the draft of this clinical guideline.	Thank you for your comment.

British Association of Critical Care Nurses	Short	General	General	Appears to be a fully comprehensive document	Thank you for your comment.
British Association of Critical Care Nurses	Short	General	General	Page numbering is not correct especially on the pages with the algorithms which then makes remaining page numbers wrong	Thank you for your comment. We have proofread the document and corrected typos and spelling errors.
British Association of Critical Care Nurses	Short	Short	General	We accept that all information in the algorithms is important but it does make the algorithm difficult to follow and to read due to amount of information present in all the algorithms	Thank you for your comment. We have worked to improve the layout and wording of the algorithms.
British Association of Critical Care Nurses	Short	General	General	It is a bit confusing that at time you are talking about …"adult and children and young people aged 12 and older…" and yet at others your are making clear distinctions about the ages e.g. under fluids section on Page 31 you talk about people aged over and under 16	Thank you for your comment. We have used this terminology as per NICE convention. We adapted recommendations from the IV fluid therapy in children guideline (NG29), which covers children and young people under 16. We have not changed the age cut-off for these recommendations as per NICE convention.
British Association of Critical Care Nurses	Short	General	General	The term "…adult and children and young people aged 12 and older…" is rather cumbersome. Can it not be simplified to all people aged over 12 years	Thank you for your comment. We have used this terminology as per NICE convention.
British Association of Critical Care Nurses	Short	3	1. 2. 1 Line 19	For adults should you not be specially saying use the National Early Warning Score	'Consider' is used to indicate the lack of evidence for early warning scores. The GDG recognise that NEWS is commonly used but there was inadequate evidence to recommend this.
British Association of Critical Care Nurses	Short	4	General	(p4-6)We like the stratification of high risk, moderate to high risk and low risk	Thank you for your comment.
British Association of Critical Care Nurses	Short	17	Line	Should it not be "carry out venous blood TESTS…"	Thank you for your comment. The document has been proofread and typos and spelling errors have been

			8		amended.
British Association of Critical Care Nurses	Short	20	Line 9	Should it not be “carry out venous blood TESTS…”	Thank you for your comment. The document has been proofread and typos and spelling errors have been amended.
British Association of Critical Care Nurses	Short	32	Line 15	Who decides if patients are at risk of hypercapnic respiratory failure - are you trying to say those patients with known COPD	Thank you for your comment. COPD is a common cause of hypercapnic respiratory failure but is not the only cause.
British Association of Critical Care Nurses	Short	35	1.10.7 Lines 13 to 15	This needs to be more explicit	Thank you for your comment. Following stakeholder comments the GDG reviewed the recommendation but considered they could not make it more explicit.
British Association of Critical Care Nurses	Short	36	General	(p36-37)It would be useful to define what “regular appropriate training is” – should this perhaps be annually	Thank you for your comment. The GDG agree that annual training appropriate to setting would be ideal. NICE guidelines do not have a remit to make recommendations for education authorities and/or competencies for professional groups.
British Association of Critical Care Nurses	Short	36	1.10.11 Lines 8 to 9	Organisations should provide written information	Thank you for your comment. The recommendations in this guideline should be used in conjunction with other NICE guidance, for example the Patient Experience guideline, where communication is covered in more detail.
British Association of Critical Care Nurses	Short	38	27	This UK sepsis registry should be mandatory	Thank you for your comment.
British Infection Association	Full	Gener	Gene	We are concerned that this document has come out before the international	Thank you for your comment. The GDG have reviewed the new definitions and the recommendations in light of these.

		al	ral	definitions of sepsis have been released as this could change some of the management algorithms	This has not resulted in change to management algorithms. We have added information on how the guideline fits with new international definitions in chapter 6.
British Infection Association	Full	General	General	This document could be made easier to read by having a general section and then dividing into sections for adults, children/neonates and pregnant women	Thank you for your comment. The Full guideline reports the evidence reviews and how the recommendations were developed from these. Each evidence review included people in all age groups and the Full guideline is therefore organised by review rather than by age. The recommendations in the short guideline are organised by age, as are the algorithms to improve clarity.
British Infection Association	Full	General	General	The recommendation of venous blood gas is concerning as it is often inaccurate. The evidence presented does not recommend one over the other. Arterial blood gases may be preferable.	Thank you for your comment. The GDG recognised that arterial blood gases can be difficult to take and did not want to delay assessment and treatment by stipulating that arterial blood gas should be taken.
British Infection Association	Full	General	General	The recommendation for a broad spectrum antimicrobial is concerning given the challenges of antimicrobial stewardship. It also appears to contradict the NHS guidance on appropriate antibiotic use in their sepsis action plan. In one Trust, the Sepsis Six® has been used for over 6 years, advocating tailored antibiotics for likely source of infection and a regimen for sepsis of unknown origin which does not utilise a single agent broad spectrum antibiotic. They have seen their mortality rates from sepsis fall without an associated rise in antimicrobial resistance.	Thank you for your comment and this information. The GDG are very aware of the importance of antimicrobial stewardship. The recommendation for broad spectrum antimicrobial for adults (recommendation 1.7.7) does suggest use of antibiotic from agreed local formulary or national guidelines if there is no confirmed diagnosis. We have also added reference to the NICE guideline on Antimicrobial stewardship (NG15) to the recommendations. NG15 discusses appropriate review of antibiotics.
British Infection Association	Full	General	General	We feel that this guidance needs to be more aligned with both the critical care guidelines and the NHS England Sepsis Action Plan.	Thank you for your comment. The guideline covers recognition and early treatment of people with sepsis and does not deal with critical care of people with sepsis. When the guideline was scoped it was recognised that excellent critical care guidelines already exist and that attention to

					earlier parts of the patient pathway were what was required. The title of the guideline has been changed to clarify that the guideline deals with early management of sepsis. The development of this guideline and subsequent NICE quality standards are included in NHS England Sepsis Action Plan.
British Infection Association	Full	General		No detail on promoting MDT working – pharmacist – role of nursing team	Thank you for your comment. The guideline has concentrated on the early recognition and management of people with suspected sepsis. Recommendations have been made about appropriate escalation of care but the other aspects of service delivery such as MDT working were not prioritised when the guideline was scoped.
British Infection Association	Full	General		No detail promoting seeking travel or other exposure history in choosing anti-infective treatment	Thank you for your comment. Immediate broad spectrum antibiotics are specified only when people at high risk of morbidity or mortality from sepsis are being treated and there is no confirmed diagnosis. The recommendations indicate that clinical assessment of the patient is required and that local or national guidelines should be used to inform antibiotic choice. The GDG discussed whether to specify travel history and other issues when considering antibiotic choice and agreed that while important for continued antibiotic treatment they did not want to complicate the message for immediate antibiotics for those at highest risk. The GDG considered that travel or other significant issues concerning antibiotic choice should be highlighted by clinical assessment or antibiotic guidelines.
British Infection Association	Full	General		No detail advising seeking local anti-infective policy to guide choice of anti-infective	Thank you for your comment. Recommendation 1.7.7 states - For people aged 18 years and over who need an empirical intravenous antimicrobial for a suspected infection but who have no confirmed diagnosis, use an intravenous antimicrobial from the agreed local formulary and in line with local (where available) or national guidelines .

British Infection Association	Full	14	figure 2	We understand the importance of identifying sepsis rapidly and initiating appropriate therapy. The advice to treat as sepsis if any one of the high risk factors in the red box is identified will certainly result in overexposure of patients to unnecessary antibiotic if factors such as altered mental state or tachycardia are used as individual identifiers of sepsis. Using such factors in the overall assessment is sensible, but as isolated factors, would identify a large number of individuals without serious sepsis. Many old patients presenting to hospital are more confused than usual without requiring immediate broad spectrum antibiotic therapy. Cognisance of antimicrobial Stewardship should go hand in hand with the appropriate management of sepsis which is accurately identified. Use of algorithms like this without appropriate complementary training will result in overuse of antibiotics.	Thank you for your comment. The algorithms cannot include all possible caveats about assessment and treatment and are intended as a summary of guidance rather than a complete record of all recommendations. The recommendations do include caveats about criteria. The recommendations have been altered to emphasise that clinical judgement should be used to assess for other diagnoses and to assess appropriate management which may include deciding the sepsis pathway is not appropriate. We have also added reference to the NICE guideline on Antimicrobial stewardship (NG15) to the short guideline.
British Infection Association	Full	18		(p18-37) With a total of 130 main recommendations, it is quite hard to use this guideline in a meaningful way ‘on the job’ although the use of the flowcharts would hopefully permit better accessibility.	Thank you for your comment. The full list of recommendations will not be relevant to all clinical settings and it is expected that individual settings will require different formats of the guidance. Algorithms will be available for download from the NICE website.
British Infection Association	Full	20	11	We are concerned by the comment “consider” using an early warning score in hospitals, especially when national guidance is to use one	Thank you for your comment. The wording of recommendations reflects the strength of the evidence. It is NICE policy to use the word ‘consider’ for recommendations for which the evidence of benefit is less certain.
British Infection Association	Full	25	7-9	This recommendation will be challenging in practice because GPs cannot always see patients within 1 hour in the community.	Thank you for your response. The recommendation for GPs to see patients within 1 hour has been removed from the

				This is a particular challenge in intermediate care and residential and nursing facilities.	guideline.
British Infection Association	Full	25	22 - 23	Having a ST3/CT3 or above (ST4 in paediatrics) review is challenging, especially in the emergency department where there is often a shortage of middle grade staff.	Thank you for your comment. The GDG considered that this level of expertise or equivalent is required in emergency departments and altered the wording to indicate that healthcare professionals such as advanced practitioners who have equivalent expertise can also assess and manage adults in this patient group. For paediatrics ST4 or equivalent is required.
British Infection Association	Full	27	23 - 26	No timeframe given for the consultant to respond. This might be challenging in the emergency department due to other patients with critical conditions and staffing levels.	Thank you for your comment. This recommendation refers to clinician attendance and does not need to be a consultant. The GDG agreed not to define a time for consultant attendance as this would be too prescriptive.
British Infection Association	Full	27	26	To have a review a lactate might be important so rather than “perform blood tests if indicated” we recommend that at the very least an arterial blood gas is taken.	Thank you for your comment. These patients may have only one moderate to high risk criteria and the GDG did not think all require blood tests.
British Infection Association	Full	33	9-10	We feel clarification is required; is meeting a high risk criterion taken as the time that observations indicting this are taken or when a change in mental status is noted?	Thank you for your comment. The timing of meeting criteria has been clarified as when assessed in acute hospital setting.
British Infection Association	General	Layout of document		This set of guidelines, as some other NICE guidelines before, may seem to some, to be written for the purpose of avoiding scrutiny and external assessment. The full document is 577 pages, the “short version” a mere 50 pages but provides no evidence basis for the recommendation. There are examples of good, detailed, review articles on complex subjects, including sepsis, condensed in no more than 10 journal pages.	Thank you for your comment. The short guideline is intended to provide the recommendations without the evidence while the Full guideline and appendices include all the evidence, and therefore the evidence is freely available for external assessment (and forms part of the consultation documents which stakeholders have commented on). The Linking Evidence to Recommendations sections in each chapter provide an overview of the issues, including the evidence, which contributed to the recommendation.

British Infection Association	Short	: High risk criteria in the algorithm		We do not recognise having just 1 of the high risk criteria as a good identifier of SEVERE SEPSIS: in particular “new altered mental state” which is quite common in the elderly with any infection even of mild severity. Again J Antimicrob Chemother 2011; 66 Suppl 2: ii11–ii23 seems to address this point in a simpler algorithm at identifying SEVERE SEPSIS.	Thank you for your comment. The term severe sepsis is no longer being used and sepsis is now suggested as the appropriate term. The GDG recognise the problem of confusion in older people and following stakeholder comment the recommendations have been altered to emphasise the importance of clinical judgement. However the evidence reviewed in the guideline and the new qSOFA score recently developed by the European Society of Intensive Care Medicine and the Society of Critical Care Medicine as the Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3) indicated that altered mental state is an important predictor of ICU stay and mortality. It is one of only 3 indicators in qSOFA score.
British Infection Association	Short	Algorithms + Page 1: sepsis definition		The definition is too vague “patients presenting with signs or symptoms that indicate infection” and is not conducive to a proper targeted application of these guidelines. Surely not all patients with “suspected infection” (a concept very difficult to define) have sepsis? The sepsis definition in Surviving the first hours in sepsis: getting the basics right (an intensivist’s perspective) published in J Antimicrob Chemother 2011; 66 Suppl 2: ii11–ii23 are clearer: sepsis consists of meeting the SIRS criteria + clinical suspicion of infection. It is very disappointing to read in the full document version (page 70) that no evidence review was conducted to find the most appropriate	Thank you for your comment. Establishing a definition for sepsis was not part of the remit of this guideline and as such an evidence review on this topic was not conducted. We have included information on the latest definitions in chapter 6 of the Full guideline. The new definitions no longer include the term SIRS.

				definition of sepsis: surely this should have been an important thing to do? Identification of a set of criteria with reasonably high sensitivity and specificity to identify patients with sepsis, or at least those with severe sepsis, should have been the starting point.	
British Infection Association	Short	17	1.5.1	The recommendation to give a "broad spectrum antimicrobi9al" even if just 1 high risk criterion is met, would encourage unnecessarily extensive use of broad spectrum antibiotics. Are we going to give meropenem to all the newly confused elderly patients with suspected infection? Even in genuinely SEVERE SEPSIS relatively narrow-spectrum is preferable when there is an organ-based diagnosis and/or culture results: e.g. daptomycin with exclusive gram-positive cover is fine for severe cellulitis. From what we can see, this recommendation to give broad spectrum antibiotics is not backed up by any evidence to demonstrate that broad spectrum antibiotics give better outcomes that narrower spectrum targeted onto the likely source and pathogens. The full version of the guidelines on page 407 says that: "No evidence review was carried out for choice of antimicrobial agents". Antibiotic stewardship must be considered in this regard.	Thank you for your comment. Following stakeholder comment the recommendations have been changed to put more emphasis on clinical judgement to consider alternative diagnosis. A recommendation has also been added to clarify that local antibiotic guidelines are appropriate if the likely source of sepsis is known.
British Infection Association	Short	38	crea tio	Having not provided a stringent definition of sepsis the document now suggests we should spend our day reporting the multiple	Thank you for your comment. The GDG agreed that the feasibility and costs of a registry should be assessed and anticipate that this would be part of any consideration of the

			n of a UK sepsis registry	cases of sepsis we see in every hospital every day. No evidence is provided that the creation of a sepsis registry is beneficial. The cost benefits of such a registry should be assessed first. At best the registry should be restricted to the most severe cases such as septic shock. We would like to propose to change the recommendation to: all hospitals should conduct an audit of septic shock patients using a defined national template and report their audit findings: at least 20 patients need to be audited. Achievement of low-level of compliance will require a re-audit. Such audit may have to be repeated at least once every 5 years.	setting up of a registry. However, the research recommendation has been changed to reflect the NICE process for research recommendations. The GDG agreed to recommend that an epidemiological study on the presentation and management of sepsis in England be conducted instead. This recognises the possibility that appropriate recording of sepsis will need to be addressed. Information about definitions of sepsis have been added to the Full guideline in chapter 6 and to the context section of the short guideline.
British Infection Association	Short	39	16 - 19	Analysis of the impact of this guidance on management of sepsis, including the identification of how frequently appropriate vs inappropriate prescribing has occurred would certainly be of value, though no doubt difficult to achieve.	Thank you for your comment.
British Society for Haematology	Full	General		Whilst we agree that the treatment of sepsis is an important area and one in which we all need to work to improve practice and outcomes, we do have concerns about this guidance in its current form. The scope of the guideline is very broad, we are concerned that the recognition of sepsis in neutropenic or potentially neutropenic paitents will be hindered rather than helped by these guidelines. There appears to be a degree of contradiction	Thank you for your comment. It was not the intention to hinder the care of people likely to have neutropenic sepsis. We have added additional recommendations and cross reference to make it clear that people with suspected neutropenic sepsis should be treated according to CG151.

				between this guideline and that in NICE CG 151: Prevention and management of neutropenic sepsis. In CG 151 there is a clear statement that the 'treatment of suspected neutropenic sepsis is an acute medical emergency- offer empiric antibiotic therapy immediately'. We are concerned that a febrile neutropenic or potentially neutropenic patient may not fit directly into the high risk arm and may be treated as being at moderate risk of sepsis, lactates will be awaited and the patient may end up on a pathway of clinical review rather than receiving antibiotics immediately. In our view this is a dangerous practice. The risk of sepsis in a patient with significant neutropenia is very much higher than that of the general population and the threshold for antibiotics needs to be very low. This was reflected in CG151 but not in the current sepsis draft. Given that NICE already has guidance on neutropenic sepsis it would seem reasonable to exclude neutropenic and potentially neutropenic patients from the guidance.	
British Society for Haematology	Full	General		The guidelines suggest use of arterial lactate as a key measure of the severity of sepsis. Whilst lactate is certainly a measure of severity, we can find no evidence to favour an arterial over a venous lactate. As a practical point, for patients who have had high intensity chemotherapy and subsequent severe thrombocytopenia (eg a leukaemia patient with platelets<10) it will	Thank you for your comment. The guideline does not suggest use of arterial lactate and recommends use of venous lactate for the reason you suggest. The GDG recognised the difficulties that can arise in taking arterial blood gases and considered that a venous sample is usually adequate and that the relative ease of collection outweighed concerns about accuracy.

				not be feasible or indeed in our view reasonable to undertake repeated arterial sampling. The bleeding risk would be high and the gain relatively low especially if CG 151 is followed and antibiotics are given immediately. We are concerned that attempts at arterial stabs may simply delay antibiotic delivery in this very vulnerable group.	
CC3N-Critical Care Networks	Full	General	General	The high risk markers for sepsis in hospital include observations that would not be unusual for patients already in ICU, and it would not necessarily be correct to leap in with a new antibiotic within one hour. Is it worth some sort of clarification that patients receiving ICU may have very deranged physiology the risk markers be both less sensitive and less specific. Also, with regards to pulse oximeters, the guidance says that pulse oximetry should be done in the community setting unless the equipment was not available or unless to do so would delay arranging hospital admission. It seems to me that the let out on basis of availability is losing a chance to drive cheap and available oximetry into the GP setting and so miss out on its benefits, and the second, comment about delaying - I cannot imagine any circumstance when to do an observation of O2 sats would delay admission. I would however fully accept that if a patient meets other criteria for immediate admission then the phone call can be made while doing the observation.	Thank you for your comment. Following stakeholder comment the GDG agree to exclude people already in intensive care settings to avoid inappropriate use of resources and antibiotics. The recommendation about access to pulse oximetry was included because GDG opinion was that this equipment may not always be available in all primary care settings. Respiratory rate is also part of the assessment and can give an indication of the respiratory function of a patient.

CC3N-Critical Care Networks	Full	General	General	With regard to the Critical Care aspect, there seems to be an automatic referral to Critical Care with expectation that CVC should be inserted and vasoactives commenced whenever the first lactate is above 4. There does not seem to be mention of assessment following IV fluid challenge. There is plenty of mention that sepsis is prevalent in those with multiple comorbidities, but no mention as to whether how beneficial escalation to critical care actually is in these circumstances. As it stands the guidance will overwhelm the referral capacity of most Critical Care Services.	Thank you for your comment. The recommendation is for referral and discussion with critical care experts and it is recognised that that discussion may include the need for re-assessment. Following stakeholder consultation the recommendations have been altered to clarify the need to consider alternative diagnoses and appropriate treatment. The GDG considered that appropriateness of treatment could be part of the senior clinical decision maker's assessment and part of the discussion with the consultant and is included in the Full guideline.
CC3N-Critical Care Networks	Short	13		Sepsis algorithm, green low risk criteria – Heart rate 10-15BPM, should this be respiratory rate rather than heart rate?	Thank you for your comment. This has been removed.
Department of Health	General	General		Thank you for the opportunity to comment on the draft for the above clinical guideline. I wish to confirm that the Department of Health has no substantive comments to make, regarding this consultation.	Thank you for your comment.
DH Advisory Committee on Antimicrobial Resistance and Healthcare associated infections	Full	11	general	There was only one microbiologist in the panel despite the importance of the subject to antimicrobial resistance	Thank you for your comment. NICE has developed guidance on anti-microbial stewardship which covers these issues in more detail. We have highlighted cross referral to this guidance.
DH Advisory Committee on Antimicrobial	Full	28	17	The 1 hour window is inference not evidence based. A 3 hour window is more	Thank you for your comment. The GDG considered that the evidence was adequate for people at highest risk. The one

Resistance and Healthcare associated infections				rational. Very early prescription before full examination may encourage unnecessarily broad spectrum agents to be used. Clearly there are exceptions such as meningococcal infection. On page 405 this lack of evidence is acknowledged	hour window refers only to people with suspected sepsis and high risk criteria. The section you refer to has been altered to reflect the evidence as the evidence statement on page 405 was previously incorrect. In addition, following stakeholder comments the wording of the recommendations has been altered to emphasise the importance of clinical assessment and judgement, including the consideration of diagnoses other than sepsis.
DH Advisory Committee on Antimicrobial Resistance and Healthcare associated infections	Full	30	34	As above	
DH Advisory Committee on Antimicrobial Resistance and Healthcare associated infections	Full	34	4	Many neonatal units use amikacin because of gentamicin resistance	Thank you for your comment and this information. The recommendation is from the NICE guideline on Neonatal infection. The GDG recognised that antibiotic recommendations must be used in light of local patterns of resistance.
DH Advisory Committee on Antimicrobial Resistance and Healthcare associated infections	Full	17	Figure 5	Slight concern that this figure implies that children <1 year with a respiratory rate of 59 bpm and oxygen saturation of 95% might be managed in primary care – this might be a little brave since this child might require oxygen in the very near future?	Thank you for your comment. It was a difficult balance deciding where the line should be drawn, however the guideline does not intend to replace clinician judgement. The risk factors are not intended to be rigid but to allow clinicians flexibility to use their own judgement about how a patient presents. The wording of the recommendations has been changed following consultation to emphasise the importance of clinical judgement.
DH Advisory Committee on Antimicrobial Resistance and Healthcare associated infections	Full	general	general	The Committee remains concerned regarding insufficient emphasis given to the principles of antimicrobial stewardship and the need for 48 hour review to stop treatment or step down to narrow spectrum antibiotics	Thank you for your comment. NICE has developed guidance on anti-microbial stewardship which covers these issues in detail. We have added additional cross referral to this guidance.

Dorset County Hospital Foundation Trust	Full	General		For ease of use this guideline would benefit from being split at least into adult and paediatric guidelines (albeit the paediatric guideline would have the inherent complexities of managing paediatric patients with their variability in signs/ symptoms and normal parameters).	Thank you for your comment. The Full guideline reports the evidence reviews and how the recommendations were developed from these. Each evidence review included people in all age groups and the Full guideline is therefore organised by review rather than by age. The recommendations in the short guideline are organised by age, as are the algorithms to improve clarity.
Dorset County Hospital Foundation Trust	Full	13	Algorithm 1	Be clear who is making this assessment for example 'algorithm for assemssment by pre-hospital professionals including ambulance personnel, pharmacists, advanced nurse practitioners' – or is this intended for patients to use this algorithm themselves	Thank you for your comment. The recommendations are organised by setting and are intended for healthcare professionals who are assessing patients.
Dorset County Hospital Foundation Trust	Full	13	Algorithm 1 Bottom yellow	Suggest a time frame in which to see the GP for assessment for example within 12 hours.	Thank you for your comment. The recommendations have been altered and the GDG decided not to put a time period but to leave this to judgement of the person doing the assessment.

			box		
Dorset County Hospital Foundation Trust	Full	13	Algorithm 1 Bottom left box	Suggest ambulance transfer to emergency department OR ADMISSIONS UNIT. Emergency departments are already overcrowded, it may be appropriate for patients to be referred to inpatient teams and go direct to admissions units where possible depending on local arrangements.	Thank you for your comment. The most appropriate place for a patient from either the high risk or moderate to high risk group could be the emergency department, or an acute admissions unit (such as a paediatric assessment unit) therefore the wording has been amended by the addition of a footnote to reflect this. The best location for an emergency may vary locally and should be somewhere with resuscitation facilities.
Dorset County Hospital Foundation Trust	Full	14	Algorithm 2 Box below high risk criteria	This recommendation may be challenging in practice to ensure all these patients are seen immediately by a senior clinician due to the high number of patients with abnormal observations on arrival to hospital, particularly in emergency departments. I believe NICE guidance should focus more on what needs to be done for example give IV antibiotics and fluids early and less on who should be delivering these simple therapies.	Thank you for your comment. The level of clinician has been indicated mainly for the high risk groups. Appropriate and timely senior input was identified by the Parliamentary and Health Services Ombudsman's report as a potential failing in management of people with severe sepsis. The GDG considered that the evidence available indicated that appropriate expertise was important to improve outcomes in people at high risk.
Dorset County Hospital Foundation Trust	Full	14	Algorit	Suggest ICU referral if initial fluid bolus does not improve lactate/ SBP to lactate <4 and SBP >90	Thank you for your comment. Following stakeholder comments the recommendations have been changed to clarify that referral may involve discussion only and the

			hm2 Box below red box lactate >4		‘admission to critical care’ part of the sentence has been removed.
Dorset County Hospital Foundation Trust	Full	14	Algorithm 2 First red box – high risk criteria	Question: Is this if these features have been present at any time (including pre-hospital phase) or only on arrival? This is a common dilemma in interpretation for emergency department teams.	Thank you for your comment. The recommendations have been altered to clarify that time starts on arrival in acute hospital settings if the patient is seen in an emergency care setting.

Dorset County Hospital Foundation Trust	Full	15	Algorithm 3 Bottom left box	Suggest ambulance transfer to emergency department OR ADMISSIONS UNIT. Emergency departments are already overcrowded, it may be appropriate for patients to be referred to inpatient teams and go direct to admissions units where possible depending on local arrangements.	Thank you for your comment. The most appropriate place for a patient from either the high risk or moderate to high risk group could be the emergency department, or an acute admissions unit (such as a paediatric assessment unit) therefore the wording has been changed to reflect this. The best location for an emergency may vary locally and should be somewhere with resuscitation facilities.
Dorset County Hospital Foundation Trust	Full	16	Figure 4	I believe NICE guidance should focus more on what needs to be done for example give IV antibiotics and fluids early and less on who should be delivering these simple therapies. It may be appropriate for these children to be seen initially by ED personnel also.	Thank you for your comment. The level of clinician has been indicated for the high risk group which includes people with possible septic shock. Appropriate and timely senior input was identified by the Parliamentary and Health Services Ombudsman's report as a potential failing in management of people with Severe Sepsis. The GDG considered that the evidence available indicated that appropriate expertise was important to improve outcomes in people at high risk.
Dorset County Hospital Foundation Trust	Full	17	Figure 5 Bottom left box	Suggest ambulance transfer to emergency department OR ADMISSIONS UNIT. Emergency departments are already overcrowded, it may be appropriate for patients to be referred to inpatient teams and go direct to admissions units where possible depending on local arrangements.	Thank you for your comment. The most appropriate place for a patient from either the high risk or moderate to high risk group could be the emergency department, or an acute admissions unit (such as a paediatric assessment unit) therefore the wording has been changed to reflect this. The best location for an emergency may vary locally and should be somewhere with resuscitation facilities.
Dorset County Hospital Foundation Trust	Full	39	10	Diagnostic criteria for sepsis should be included in the guideline. Question: When does infection become sepsis? This will be a cornerstone in the	Thank you for your comment. New definitions of sepsis do not use terms from SIRS. A section on the new definitions has been added to the guideline in chapter 6. This guideline does not aim to define sepsis but to identify those people

				interpretation of these guidelines. Does it rely on traditional definitions of infection + SIRS criteria, with gradings of severe sepsis when there is organ involvement? The text later suggests not. Would suggest sepsis (v. simple infection) if any high risk criteria or >2 moderate risk criteria are met. Or will the international consensus definitions be inserted?	who require assessment and early treatment.
East Lancashire Hospitals NHS Trust	General	General		Current stratification of risk uses the terminology – SIRS, Sepsis, Severe Sepsis and Septic shock. These all have associated ICD 10 codes, which are used in mortality and morbidity figures. It is concerning that this guidance will not reflect these ICD 10 codes and therefore may influence mortality and morbidity figures which are nationally reported.	Thank you for your comment. This guideline does not aim to define sepsis or categorise patients based on previous or current sepsis definitions. Categories such as SIRS and Severe Sepsis are now considered unhelpful by sepsis experts. This guideline offers clinical trigger points that can help identify people at risk of developing sepsis and ensure that those people receive appropriate care.
East Lancashire Hospitals NHS Trust	General	General		No recommendations are made for a nationally agreed change to ICD 10 codes to reflect the draft guidance.	Thank you for your comment. The GDG made a research recommendation on the epidemiology of sepsis and acknowledge that before such a study is performed coding of sepsis may first need to be addressed. Recommending a national agreed change to ICD 10 codes is beyond the remit of this guideline.
Editor	General	General		Algorithms will need to be reworked before publication as the web viewer cannot handle landscape format	As discussed we are awaiting confirmation of this.
Editor	General	General		References to other guidelines need reformatting to correct style (can be done in post-colsultation edit)	Thank you. This has been done.
Editor	General	General		Need to clarify the difference between 'from' and 'adapted from' when used with recs from other guidance, as there are 4 instances where 'from' is used where the	Thank you. This has been done.

				recommendation is in fact adapted or vice versa. There are also referrals to IV fluid therapy for adults when it should be either IV fluid therapy for children, or to both IV fluid therapy for children and IV fluid therapy for adults. We've made a table of all the recs that mentioned that they are from or adapted from another guideline, and highlighted in yellow those for which there seem to be an issue. The table is attached. r	
Editor	General	General		It would be very useful if the GC could define what they mean by an 'acute hospital' in the guideline. We think this means a hospital with some sort of critical care or intensive care unit, but it could be ambiguous and it would be helpful to have it clarified.	Thank you. We have added this to glossary.
Editor	Short	13	16	Rec 1.1.6: In this rec there used to be a bullet point that read ` have a history of group B streptococcal infection`. Was this intentionally removed? (rec 1.1.6 is for women and rec 1.1.7 for babies still mentions group B streptococcal infection)	Yes this is correct – streptococcal B is relevant for babies and not for adults.
Editor	Short	17	2	Rec 1.3.2: …40% oxygen to maintain oxygen saturation more than 92%… should this read …40% or more… to be in line with the risk stratification tool?	Thank you for your comment, this has now been amended.
Editor	Short	20	2	Rec 1.3.5: word missing in first bullet - should it be 'mental state'?	Thank you for your comment, this has now been amended.
Editor	Short	28	7	Rec 1.4.1: Should this refer to tables 1-3 rather than just table 1?	Thank you for your comment, this has now been amended.
Editor	Short	29		General correction - all recs in section 1.5 use 'adults and children and young people'	Thank you for your comment, this has now been amended.

				instead of ‘adults, children and young people’ as elsewhere	
Editor	Short	29	21	Rec 1.5.2 (also applies to 1.5.17 & 1.5.32) units incomplete: ‘lactate over 4 mmol’ should read ‘4mmol/litre’	Thank you for your comment. The document has been proofread and typos and spelling errors have been amended.
Editor	Short	30	22	Rec 1.5.6 (also applies to 1.5.21 & 1.5.36) Glasgow Coma Scale, not Glasgow Coma Score	Thank you for your comment. The document has been proofread and typos and spelling errors have been amended.
Editor	Short	32	8	Rec 1.5.11 ‘who meet 2 moderate to high risk criteria’ should read ‘who meet 2 or more moderate to high risk criteria’ to be in line with other recs in the same section?	Thank you for your comment, this has now been amended.
Editor	Short	37	17	Rec 1.5.30 footnote – should this be ‘this should be…’ rather than ‘this could be…’?	Thank you for your comment, this has now been amended.
Faculty of Intensive Care Medicine and Intensive Care Society	Appendix L	139		In Appendix L p139, the 20% albumin trial of Caironi 2014 has been excluded due the “incorrect interventions”. However the trial of 20% albumin and 6% HES by Dolech 2009 has been included. Again trial inclusion consistency is required.	Thank you for pointing out this error. This study has now been included in the analysis. The inclusion of this study has not changed the overall results and thus the conclusions of the evidence review remain.
Faculty of Intensive Care Medicine and Intensive Care Society	Full	424	13	On p424 L13-14 it states “A multivariable analysis in one study indicated that patients receiving albumin had a higher chance of death at 28 days compared to those receiving saline.” Is this the SAFE study? As page 425 states “A follow-up paper (SAFE 2011) presented more detailed data on the severe sepsis subgroup. A multivariate analysis showed that albumin was independently associated with a decreased 28-day mortality.” Has p424 been written incorrectly?	Thank you for your comment. The multivariable analysis comparing albumin with saline is taken from the SAFE study. The study showed that people with severe sepsis receiving albumin had a lower chance of 28-day mortality compared to those receiving saline. This sentence has now been corrected in the evidence statement.
Faculty of Intensive Care Medicine and	Full	428	Para	On page 428 paragraph 2, the GDG excluded the 6S trial (Perner 2012) on the	Thank you for your comment. The 6S trial was excluded because the intervention had not started within 6 hours of

Intensive Care Society			2	grounds that the EMA have stated that HES is contraindicated in sepsis. However, the GDG have included the CHEST trial (Myburgh 2012) that used a similar HES that is also contraindicated in sepsis after the EMA ruling. Surely the inclusion/exclusion of trials should be consistent. As HES is potentially still available for other (non-sepsis) indications it would be appropriate for the GDG to recommend that HES not be used for sepsis.	diagnosis. This has now been made clearer in the relevant section.
Faculty of Intensive Care Medicine and Intensive Care Society	Full	493	8	We are disappointed to see that the GDG does not offer any recommendation about early goal directed therapy (page 493 line 8) despite this being the one area with the highest quality, direct evidence available. We understand the GDG concerns that any recommendation might be misunderstood but not to make a recommendation despite good evidence will not help everyday clinicians to improve their management of septic patients. Furthermore the PROMISE trial was conducted in 56 acute hospitals in the UK and to not use this high-quality evidence for directly relevant guidelines will be demoralising for clinicians and patients. Why conduct a trial or volunteer to be a trial patient if the evidence generated is not going to improve patient care! Possible recommendations could have been, “Protocolised early goal directed therapy does not need to be instituted for all sepsis patients but for high risk patients individual	Thank you for your comment. The guideline deals with recognition, assessment and early management of people with suspected sepsis and this is now clarified in the title. A review of EGDT was included to assess what could be learned about early management. The studies of EGDT deal with the first six hours and recruitment criteria for the trials were of people who had already received antibiotics and fluids. The priority in this guideline has been to ensure that people who need early antibiotics and fluids get them and are referred to those with critical care expertise who can provide the treatment described in the EGDT trials.

				patient goals should be set by experienced clinical teams".	
Faculty of Intensive Care Medicine and Intensive Care Society	General	General		We would first like to congratulate the NICE team on producing a high quality, very comprehensive, evidence based review. The GRADE evidence tables and background review material provides a very good resource for the critical care community. We are pleased that they acknowledge different levels of risk and different treatment strategies based on this risk stratification (summarised in Fig 2). However, we are aware that the new international sepsis definitions are due to be published this month and include risk stratification too. They have taken a different strategy to develop these risk levels but have identified similar clinical parameters (namely respiratory rate, hypotension, raised lactate levels and decreased level of consciousness). In order not to confuse clinicians it will be vital to ensure that the various trigger thresholds align so that uniform guidelines can be implemented in all hospitals.	Thank you for your comment. We have added a section on the new sepsis definitions and clinical parameters in chapter 6. The pathways included in this guideline use clinical parameters that have been identified through evidence reviews or consensus recommendations by the GDG.
Faculty of Intensive Care Medicine and Intensive Care Society	General	General		We think that a separation of the paediatric and adult guidelines would greatly simply the presentation of the information in the document. Currently there is significant replication in the sections and it is often difficult to find the relevant sections of adult v paediatric practice.	Thank you for your comment. We have tried to balance the need for completeness with reducing repetition, bearing in mind that some recommendations apply to all age groups. We have added some subheadings to the short version to emphasise the various age categories.
Faculty of Intensive	Ge	Ge		Treatment algorithms are very useful.	Thank you for your comment. The development of this

Care Medicine and Intensive Care Society	neral	neral		However there are also the sepsis six algorithms which have been widely adopted in adult practice. It would be helpful for a single, national algorithm to be proposed by the various organisations to avoid possible confusion and overlap. In particular the use of lactate as a treatment stratification tool is unproven and the single lactate threshold approach of the sepsis six bundles may be simpler to use in clinical practice.	guideline and subsequent NICE quality standards are included in NHS England Sepsis Action Plan which includes other national organisations working in this area. The evidence for the use of lactate as a stratification tool was of low quality and not sufficient to use it as a single threshold. It is not used in the recommendations as the main treatment stratification tool because of this. It is of note that it is also not included in qSOFA.
Faculty of Intensive Care Medicine and Intensive Care Society	General	General	Rec 45 and 50	The early & increased involvement of consultants and critical care in the high-risk sepsis cases is to be welcomed (recommendations 45 and 50). However, this is likely to have significant staffing implications in some hospitals and this is acknowledged in the economic evaluation. It will be important for managers and funders to make appropriate changes before these guidelines can be implemented. Also it should be recognised that parameters that might trigger a consultant review on a general ward for failure to improve (e.g. systolic blood pressure <90 mmHg after 1 hour of fluid resuscitation) may not require the same consultant review whilst in the intensive care unit.	Thank you for your comment and support. The GDG agreed it was important that consultants are involved early on and at key stages of decision making for the high risk group. This is initially recommended as a discussion which could be over the phone. The discussion does not have to be in person. The GDG considered that this group of patients are potentially very unwell and that it would be expected that the consultant would be aware that they are being treated under his/her care. The recommendation to attend is only if a patient with a high risk of mortality is not responding to treatment. Following stakeholder comments we have now excluded people already in intensive care from the guideline. We realise however that this may lead to an impact on implementation and resources, and the NICE resource impact and implementation team will consider your comment where relevant support activity is being planned.
FEAT – The Fiona Elizabeth Agnew Trust	Full	36	27	We have some concern regarding the information given at discharge whereby people will be told whether they're at	Thank you for your comment. The recommendation suggests that people who have had sepsis should be allowed to voice their concerns, and that one of these is that

				greater risk of having a recurrence. Notwithstanding noted high risk groups (post-surgery, neutropaenia), does sufficient research or data exist to be able to provide meaningful information to those patients who were not previously in a high risk group? For example, individuals who have had recurrent Streptococcal infection. What standards will be put in place to ensure all such information is consistent at a national level?	sepsis might return. This was a finding from the review of evidence and is included so that healthcare professionals are alerted to it. The GDG recognise that responding to that concern in factual terms for each individual may be difficult and likely to depend on underlying risk factors. They considered however that the recognition of the concern remains important.
FEAT – The Fiona Elizabeth Agnew Trust	Full	525	10 - 22	We are concerned at the relative paucity of quality research in this area (impact and aftercare). We are concerned that the Guideline should actually recommend offering a follow up appointment at 2-6 months for ICU survivors of severe sepsis to discuss their experience, ongoing symptoms and to screen for symptoms of Post Traumatic Stress Disorder in both survivors and caregivers.	Thank you for your comment. The guideline did not look specifically at appropriate follow up for people who have been admitted to ICU. NICE has already developed guidance for Rehabilitation after critical illness. That guideline recommends review of rehabilitation needs 2–3 months after discharge from critical care. There will be a link to this guidance on the NICE website and we have added this detail to the Full guideline in section 15.5.
FEAT – The Fiona Elizabeth Agnew Trust	Full	526 - 529	All	See comment 2. The reference to CG83 on page 529 needs to be more strongly emphasised. We feel that that guideline and the sepsis guideline should be used by policymakers to encourage Intensive Care service providers to make moves to offering more consistent follow up on a national level and to end the current “postcode lottery.”	Thank you for your comment. Further linking between guidelines will be seen on the NICE Web page and on NICE pathways for this guideline.
FEAT – The Fiona Elizabeth Agnew Trust	Full	464	11 - 15	The paucity of evidence around inotropes/vasopressors in children does not mean there is not a case to be made for	Thank you for your comment. Integral to the pathway for children and young people is

				early initiation of inotropic agents in the Emergency Department for children with a 'cold shock' presentation, or for vasopressors in children with vasodilated shock; it simply represents the severe ethical, epidemiological and statistical difficulties of conducting high quality prospective research in this patient group. Common sense and sound physiological reasoning should prevail. We are concerned by the increasingly worrying signal from a body of research on the harm caused by high percentage fluid overload in critical illness and that not recommending early commencement of inotropic or vasopressor support may cause more children to be exposed to such harm. While accepting recent evidence regarding Early Goal Directed Therapy, the paradigm of sepsis resuscitation was completely altered by the early EGDT studies and the more recent studies were not able to compare against pre-EGDT "standard care". We are also concerned that this guideline does not make recommendations to follow current best practice that uses the expert-based guidance of the ACCM-PALS or Paediatric Sepsis Six algorithms, both of which recommend early initiation of peripheral vasoactive drugs. We are concerned that this guideline contradicts	involvement of healthcare professionals with appropriate training as well as early steps such as blood tests and antibiotics. For those children and young people who are at high risk discussion with a consultant is recommended and for those at highest risk referral or discussion with critical care is recommended expressly to consider use of inotropes. The GDG reviewed these recommendations following stakeholder comment and agreed that they do allow for the early initiation of inotropic agents using expert advice. We have amended the text in the Full guideline to clarify this. The recommendations in the guideline are informed by reviews of the evidence developed for this guideline and discussed by the GDG. The Sepsis Six algorithms are developed by the Sepsis Trust which has agreed to work with NICE in implementing these guidelines as part of the NHSE Sepsis action plan. The recommendations in the guideline cover recognition and early management of people with suspected sepsis and not more intensive aspects of care as recommended in ACCM-PALS. We have clarified that the guideline covers early management in the title. The fact that no recommendation is made is included in section 9.6 to ensure there is clarity about the GDG decision not to make a recommendation and this is explained in the remainder of the table. This is not repeated in the list of recommendations.

				some of the recommendations in these widely used paediatric practice algorithms on the basis of no new evidence. Thinking about human factors, we fear that 'no specific recommendation' in Section 9 may be interpreted as 'not recommended' and lead to decision paralysis and delay in treatment by clinicians dealing with children, with resultant adverse impacts upon this patient group. See: Brierley J, Carcillo JA, Choong K, Cornell T, DeCaen A, Deymann A et al. Clinical practice parameters for hemodynamic support of pediatric and neonatal septic shock: 2007 update from the American College of Critical Care Medicine. Crit Care Med 2009;**37**:666-688 Tong J, Plunkett A, Daniels R. The Paediatric Sepsis 6 Initiative, Arch Dis Child 2014; **99**:A93	
FEAT – The Fiona Elizabeth Agnew Trust	Full	464 - 465	All	See comment 4, above.	
FEAT – The Fiona	Full	14	Al	See comment 4, above.	

Elizabeth Agnew Trust			gorithm		
FEAT – The Fiona Elizabeth Agnew Trust	Full	16	Algorithm	See comment 4, above.	
FEAT – The Fiona Elizabeth Agnew Trust	Full	18	Algorithm	See comment 4, above.	
FEAT – The Fiona Elizabeth Agnew Trust	Full	38	10-11	We applaud the recommendation to set up a UK-wide sepsis registry that utilises the resources of the 4 National Health Services of the 4 nations of the UK. We are concerned that the guideline sets no timeline for the establishment of this Registry. We are concerned that the guideline makes no recommendation as to the structural and funding aspects of the proposed Registry.	Thank you for your comment. The research recommendations are developed by the GDG to highlight areas that they consider should be prioritised for funding and implementation. NICE works closely with funding bodies such as NIHR to highlight areas identified in guidelines for research but decisions about what is funded is outside our control. Please note that the research recommendation has been changed to reflect the NICE process for research recommendations. The GDG agreed to change the wording and recommend that an epidemiological study on the presentation and management of sepsis in England be conducted.
FEAT – The Fiona Elizabeth Agnew Trust	Full	38	ALL	We are concerned that the guideline makes no recommendation for future research into host-pathogen interactions, host immune genotyping, and other new potential means of identifying at-risk groups and potential targets for future point-of-care screening	Thank you for your comment. Research recommendations arise from areas reviewed within the guideline and the areas you mention were not included in the guideline scope. The GDG recognise that there are other important areas for research beyond those prioritised in the guideline.

				tests to identify those at greatest risk of fulminant sepsis.	
FEAT – The Fiona Elizabeth Agnew Trust	Short	General	General	Comments as above also apply to the relevant sections of the short guideline.	Thank you for your comment.
Group B Strep Support	General	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.	Thanks you for your comment and support of the guideline.
Group B Strep Support	General	General		There's a gap in the need to consider the importance of fetal tachycardia (and the need for fetal monitoring to detect it). In pregnant women, this should be both a trigger factor for initiating screening and a High Risk criterion, with as per the NICE Guideline for Intrapartum Care (CG190) recommendations for CTG monitoring, the 'non-reassuring' threshold of ≥161 BPM be used as a moderate risk criterion in this population, and the 'abnormal' threshold of >180 be used as a High Risk criterion.	Thank you for your comment. We have added the Intrapartum Care guideline to related guidance. This is currently being updated and the GDG therefore agreed it was inappropriate to add detail as the evidence will be reviewed in the update of the guideline and the recommendations may change.
Group B Strep Support	General	General		Uterine or adnexal tenderness should be included as a moderate to high risk criterion for pelvic infection	Thank you for your comment. The recommendations do not cover signs and symptoms of specific infection but seek to highlight when people should be assessed for sepsis.
Group B Strep Support	Short	2	21	What evidence is there that this is only relevant for 'spontaneous' rupture of membranes? Is there evidence and/or expert view that the length of time since artificial rupture of membranes is also a factor to take into account?	Thank you for your comment. We have removed 'spontaneous' from this section as we did not have evidence that this is only a risk in case of spontaneous rupture of membranes.
Group B Strep Support	Short	34	13	We would like to see the families and carers given details of who to contact with	Thank you for your comment. This is likely to vary according to location and therefore the GDG were not able to make

				any additional questions or concerns they may have.	recommendations about this.
Group B Strep Support	Short	35	9	Could this be expanded to include not only WHEN to get medical attention if their illness continues, but also where and how (when to contact the GP, when to access emergency care, etc)?	Thank you for your comment. The wording has been changed in line with your suggestion.
Group B Strep Support	Short	35	15	Could this be expanded to include not only WHEN to get medical attention if their illness continues, but also where and how (when to contact the GP, when to access emergency care, etc)?	Thank you for your comment. The wording has been changed in line with your suggestion.
Hampshire Hospitals NHS Foundation Trust Wessex Academic Health & Science Network Oxford Academic Health & Science Network	General			Is there anything on coding, data collection and definitions within the whole study? Without a means of measurement, traction for improvement will be difficult.	Thank you for your comment. The GDG has made a research recommendation on an epidemiological study on the presentation and management of sepsis in England. Such a study would provide population based statistics on the epidemiology of sepsis which are necessary to support evaluation of interventions, planning of services and service redesign.
Hampshire Hospitals NHS Foundation Trust Wessex Academic Health & Science Network Oxford Academic Health & Science Network	Short	1	General	The Algorithm is Hard to read and use as is, is the comment from my team. The definitions of sepsis need to be simple and usable. The complexity of this will make it hard to implement. The engineering of pathway design and forms is crucial.	Thank you for your comment. We have worked with the NICE editors to improve the algorithms.
Hampshire Hospitals NHS Foundation Trust Wessex Academic Health & Science Network	Short	1	General	Pragmatic application of the evidence into recommendations that are not counterproductive to current systems. We have a national early warning score that we run this risk of developing an additional and	Thank you for your comment. The recommendations are based on available evidence and GDG consensus. There is a lack of evidence for early warning scores outside hospital wards and a recommendation to use them in primary and community care is therefore not possible.

Oxford Academic Health & Science Network				different physiological scoring system to and we need to be mindful of the harm that would bring. Will these guidelines dovetail with the forthcoming NEWSDIG NEWS revisions, International surviving sepsis campaign guidance (Quick sofa) and the NHS programme board recommendations?	The GDG have reviewed the new international surviving sepsis definitions and consider the guideline is compatible with them. This is discussed in chapter 6 of the Full guideline. The development of this guideline and subsequent NICE quality standards are included in NHS England Sepsis Action Plan and the NHS programme board have been informed of the recommendations during development. We are not aware of NEWS revisions.
Hampshire Hospitals NHS Foundation Trust Wessex Academic Health & Science Network Oxford Academic Health & Science Network	Short	1	Adult hospital guidance	Would it be helpful to define what "infection" means for symptoms or signs in a validated way? E.g. cough/ SOB/pleurisy etc.	Thank you for your comment. The GDG did not think this was within the scope of the guideline.
Hampshire Hospitals NHS Foundation Trust Wessex Academic Health & Science Network Oxford Academic Health & Science Network	Short	1	Adult hospital guidance	The fact that any one high risk criteria is needed for the patient to be termed high risk needs to be clearly stated on the algorithm.	Thank you for your comment. This has been added to the algorithm.
Hampshire Hospitals NHS Foundation Trust Wessex Academic Health & Science	Short	1	Adult hospi	A single "red" score of BP, RR, Pulse would score 3 on most scoring systems, and give a lower aggregate than a moderate risk patient who might be sicker. The evidence	Thank you for your comment. The GDG recognised that individual parameters and scores are all associated with low quality evidence. There is a lack of evidence for scores outside hospital wards and a recommendation to use them in

Network Oxford Academic Health & Science Network			tal guida nce	from Jarvis et al. demonstrating this might be worth including. **Aggregate National Early Warning Score (NEWS) values are more important than high scores for a single vital signs parameter for discriminating the risk of adverse outcomes.** / Jarvis, Stuart; Kovacs, Caroline; Briggs, Jim; Meredith, Paul; Schmidt, Paul E; Featherstone, Peter I; Prytherch, David R; Smith, Gary B.In: Resuscitation, Vol. 87, 02.2015, p. 75-80.	primary and community care is therefore not possible. The guideline recognises that depending on setting scores may be used in assessment and monitoring. The study by Jarvis et al. (2015) was excluded from the evidence review because the intervention did not meet the criteria specified in the review protocol. The review only considered studies that reported outcomes for the use of early warning scores for monitoring. The study by Jarvis et al. (2015) however used NEWS to calculate risk of death and adverse outcomes.
Hampshire Hospitals NHS Foundation Trust Wessex Academic Health & Science Network Oxford Academic Health & Science Network	Short	1	Adult	Was current antibiotic treatment investigated, we consider this high risk clinically in masking septic presentations leaving “partially treated” patients” who might not trigger sepsis initially but who go onto to develop full septic presentations hours later.	Thank you for your comment. Current antibiotic treatment was not investigated. The GDG considered whether this group should be added to the ‘high risk’ criteria as a separate group but agreed that assessment would be the same as for other people presenting with infection.
Hampshire Hospitals NHS Foundation Trust Wessex Academic Health & Science Network Oxford Academic Health & Science Network	Short	1	Adult	If lactate >2 puts patients in high risk, why not consider this as a high risk patient in the presence of symptoms of infection My organisations and region are using NEWS to define sepsis currently across the whole care pathway, the definition of high, moderate and low risk is different from the terminology we use and might be confusing. We differentiate by Infection (low risk, NEWS <3), Sepsis (NEWS ≥3 + Red flag or Lactate>2 or NEWS ≥5) and Septic shock. By keeping everyone on side, it helps no	Thank you for your comment. The guideline is aims to stratify risk and direct more intensive treatment to those at highest risk. The evidence does not support use of lactate as a major discriminating factor and lactate > 2 plus signs of infection requires all people with infection to have a test which would not be a good use of resources. Current evidence does not support use of early warning scores in all settings.

				one.	
Hampshire Hospitals NHS Foundation Trust Wessex Academic Health & Science Network Oxford Academic Health & Science Network	Short	1.13	11	Usual behaviour comment- impairment of function either physical or cognitive	Thank you for this comment.
Hampshire Hospitals NHS Foundation Trust Wessex Academic Health & Science Network Oxford Academic Health & Science Network	Short	1.15		Antibiotics in the community masking sepsis on presentation to the hospital	Thank you for your comment. The GDG recognise this potential issue but did not consider it a significant enough issue to include in the list of factors to consider. It is recognised that these are not exhaustive and clinical judgement is always required.
Hampshire Hospitals NHS Foundation Trust Wessex Academic Health & Science Network Oxford Academic Health & Science Network	Short	1.21	2	We need to be encouraging the adoption of a **single** physiological scoring system in all environments, and really putting the final nail in the coffin of local variation.	Thank you for your comment. The GDG agree that this would be ideal but is beyond the scope of this guideline.
Hampshire Hospitals NHS Foundation Trust Wessex Academic Health & Science Network Oxford Academic Health & Science Network	Short	1.24		Was capillary refill considered in adults? Some tactile physical assessment of tissue perfusion is useful. Cap refill was considered to be the most useful physical sign in sepsis by WHO.	Thank you for your comment. Capillary refill time was not specifically considered in adults. The GDG recognise that tactile physical assessment of tissue perfusion is useful but that this was unlikely to override other physiological assessment.
Hampshire Hospitals	Sh	1.5	9	1 or two sets of blood cultures- we	Thank you for your comment. Specific detail about blood

NHS Foundation Trust Wessex Academic Health & Science Network Oxford Academic Health & Science Network	ort	1		advocate two.	cultures was not included in the scope of the guideline and we have added reference to national standards for taking of blood cultures to chapter 14 of the Full guideline.
Hampshire Hospitals NHS Foundation Trust Wessex Academic Health & Science Network Oxford Academic Health & Science Network	Short	1.67		The adult medical take starts at 16, why are we differentiating “children” at 18. This will cause confusion.	Thank you for your comment. The GDG report that this varies throughout the country and 18 years was an appropriate cut off for adults.
Hampshire Hospitals NHS Foundation Trust Wessex Academic Health & Science Network Oxford Academic Health & Science Network	Short	1.71		The 500ml/15 min fluid bolus recommendation needs to be within the algorithim	Thank you for your comment and this suggestion. We have worked with the NICE editors to improve the algorithms and have added this detail to the over 18 algorthim.
Health and Social Care Information Centre	Appendix A	7	General	It is stated ‘This guideline will provide recommendations for recognising sepsis and instituting treatment to provide development of severe sepsis and septic shock in any clinical environment, linking to other existing NICE guidance.’ However, as stated in the above point, clinical assessment via the NHS 111 or 999 setting is not considered. The NHS 111 service handles over a	Thank you for your comment. The guideline development group (GDG) aimed to identify symptoms and signs that help in diagnosis of sepsis or are indicators of poor outcome. The risk criteria chosen are those for which there is most evidence. The GDG recognise the challenge of remote assessment and triage and considered that this problem is also relevant to general practitioners doing triage and general practice out-of-hours services. The GDG recognise that more subtle signs may not be useful for remote triage however they did not think it

				million calls a month which utilise the NHS Pathways clinical decision tool, and there are 6 ambulance trusts which also utilise the NHS Pathways tool. It is our experience that remote triage guidance is essential in ensuring reproducibility, ensuring appropriate high risk and moderate to high risk symptoms and taken into account appropriately with the appropriate outcome for such patients. However, considering the challenges of telephone triage it is also our experience that more subtle symptoms or certain signs such as assessing reduced urine output, capillary refill time, identification of cold peripheries and leg pain may well be of limited value as part of remote triage assessment, especially when undertaken by trained non clinicians (call handlers). Within NHS Pathways, we have been liaising very closely with the following organisations and senior figures notably the Sepsis Trust further refine the remote identification of Sepsis in adults and children. As such, we are requesting further consideration of high and moderate to high risk features to be considered within the context of remote clinical assessment by trained call handlers and NHS Pathways would be willing to share our experiences	appropriate to change the criteria listed. They do recognise that different services have to consider how they perform triage and that different services may implement triage in different ways. Following stakeholder comments, additional recommendations have been added which emphasise risk factors and disorders of behaviour, breathing and circulation as important factors to consider when deciding if someone needs a face to face assessment. The GDG considered they could not define these further.

				to the NICE shared learning database.	
Health and Social Care Information Centre	Full	192	General	We are concerned that this recommendation is based for people presenting with sepsis outside an acute hospital setting, but are also outside an appropriate primary care setting as a referral to primary care (via a GP or doctor) within the aforementioned time frames of 1 hour for moderate to high risk cases. It is therefore possible that such patients are presenting to either the NHS 111 or 999 services, along with other open access services such a Minor Injury Units. However, there is no specific recommendation for remote triage guidance within the document as has been in previous NICE guidance documents, albeit in reference to a health care professional.	Thank you for your comment. Following stakeholder comment recommendations have been changed and reference to remote triage is now included.
Healthcare Infection Society (HIS)	Full	Section 18.4		This guideline will lead to gross over-prescription of unnecessary antimicrobials to patients who do not need them. This is a threat to antimicrobial resistance and is counterintuitive to the initiative to improve antimicrobial stewardship.	Thank you for your comment. The GDG sought to find a balance between appropriate use of antibiotics and targeting people with suspected sepsis at highest risk of mortality. The guideline aims to empower healthcare staff to make a diagnosis based on assessment and clinical judgement but also to lead to a cultural change where people think about sepsis. The risk factors highlighted in the guideline, and recommended approach following identification of those, is not intended to be a management pathway that replaces clinical judgement, but a tool to encourage clinicians to be

					able to place patients on a pathway should they have concerns that a patient might have sepsis. Following stakeholder comments the importance of clinical judgement has been highlighted to emphasise the importance of considering alternative diagnoses and this should also protect against overuse of antibiotics.
Healthcare Infection Society (HIS)	Full	405	General	Section on trade-off between clinical benefits and harms. This statement is not necessarily true “An individual is unlikely to suffer harm from receiving an antibiotic they do not need” All antibiotics and particularly broad spectrum ones have deleterious effects on the normal gut microbiota, this effect can be pervading and long lived (even after a single dose). There are several studies in the literature demonstrating this: Buffie et al. Profound alterations of intestinal microbiota following a single dose of clindamycin results in sustained susceptibility to Clostridium difficile induced colitis. Infect Immun 2012 80:62-73 Arat et al. Microbiome changes in healthy volunteers treated with GSK1322322, a novel antibiotic targeting bacterial peptide deformylase. Antimicrob Agents Chemother 2015 59:1182-92 Rashid et al. Ecological effect of ceftaroline-avibactam on the normal human intestinal microbiota. Antimicrob Agents Chemother. 2015 59:4505-9. It is accepted that the underlying cause of	Thank you for your comment. This sentence was an error and has been removed.

				Clostridium difficile infection is an abnormal gut microbiota, thus it is reasonable to assume (and demonstrated by the study by Buffie et al., above) that even patients who have been administered a single dose of antibiotic are at increased risk of CDI. There are also the as yet not fully elucidated detrimental effects of altering the gut microbiome by administering antimicrobials such as on glucose metabolism etc (Mikkelsen et al PLoS One 2015 e0142352) Given that CDI is seen as a healthcare infection of significant priority in the UK, and that there is a significant attributable mortality and excess healthcare costs associated with managing these cases, it would be important that this is acknowledges and recognised rather than claiming a single dose of antibiotic is unlikely to cause harem to an individual patient.	
Healthcare Infection Society (HIS)	Full	511	15 - 20	Blood cultures are part of the sepsis six. However, the mere taking of the specimen is often perceived as the endpoint in itself. A survey of blood culture practice across the UK (national, regional and teaching hospital) showed it to be in a poor state incurring significant avoidable delays (Royal College of Pathologists Bulletin July 2015 171, 194-196) . Additionally, there is inequality of practice between	Thank you for this information. Reference to the UK Standards for Microbiology Investigations has been added to the guideline and is discussed in the narrative in chapter 14.

				organisations and also within organisations depending on time of day, weekends and bank holidays. Blood cultures are collected from the sickest patients in a hospital from infection perspective but also from a much larger group of patients who have the potential to become the most unwell if not managed appropriately. Blood cultures allow correction of deficits in initial antibiotic therapy, permit stepdown to narrower spectrum agents thus promoting good antimicrobial stewardship, provide evidence to suggest the source of infection and in the case of neonates a negative blood culture at thirty-six hours providing the baby is well allowing early cessation of antibiotic therapy. The quicker results are available the likelihood the greater the impact in either preventing sepsis or in its management. The significant variation in performance uncovered in a national survey of blood culture practice was part of the spur for the Standards Unit at Public Health England to update SM1 B37– Investigation of Blood Cultures in 2013, recommending microbiology departments audit their blood culture pathway. In recognition of the clinical importance of blood cultures it also became the first Standard of Microbiology Investigation (SMI) to set time standards for processing. In Eire, following a number of high profile deaths investigated by the	

				coroner which found pathology wanting in terms of turnaround times, the Irish National Accreditation Board looked for blood culture standards to implement. Not having their own they have adopted and enforced the UK blood culture standard. Unfortunately, the UK standard is not enforced and the current state of blood culture practice (we have audit data to support this) still leaves much to be desired. The nice guidelines provide a unique and powerful opportunity to try and improve blood culture practice through supporting the Standard for Microbiology Investigation B 37. Failure of laboratories to optimise the blood culture pathway will impinge on both hospital costs, patient outcomes and antibiotic stewardship.	
Hywel Dda University Health Board	Full	General		Capital C for Consultant	Thank you for your comment. The grammar and spelling used throughout the guideline is in line with our NICE style guide.
Hywel Dda University Health Board	Full	General		There is no mention of venous lactate. In the absence of an arterial sample, a venous lactate is equivalent	Thank you for your comment. The guideline specifically recommends venous lactate as arterial lactate may be difficult to take and as you indicate they may be equivalent.
Hywel Dda University Health Board	Full	General		The tables of evidence early in the document, “Assessment and Risk” break up the flow of words, so that the sense of what is being said is lost. Can all evidence be added at the end of the document, separately from the text.	Thank you for your comment. The chapter is in the standard format for a Full guideline.
Hywel Dda University Health Board	Full	13		Under Low Risk category of algorithm, figures 1 and 2:	Thank you for your comment. This has been removed.

				?”baseline heart rate is 10-15 beats per minute” does not read well.	
Hywel Dda University Health Board	Full	13		1.1 above algorithm spelling mistake above the algorithm: young, not youg	Thank you for your comment. We have proofread the document and corrected typos and spelling errors.
Hywel Dda University Health Board	Full	13		(pages 13, 14, 15, 16, 17, 18) Algorithms are unreadable, even at 125% on screen (which is the largest practical size on a normal sized screen): can they be simplified?	Thank you for your comment. The algorithms have been altered. Following stakeholder comments it has been agreed to separate the algorithms from the recommendations. This will improve readability and the algorithms will be available for download from the NICE website.
Hywel Dda University Health Board	Full	34	99	CG149 scope is limited to early-onset neonatal infection, which is not reflected in this document. CG149 also advises that if meningitis is suspected the choice should be iv amoxicillin and cefotaxime	Thank you for your comment. The recommendation has been altered to reflect this.
Hywel Dda University Health Board	Full	34	100	‘Community-acquired’ is not defined. Presumably amoxicillin / ampicillin is given as well (as p33 line 98)	Thank you for your comment. The GDG considered community acquired to be self- explanatory.
Hywel Dda University Health Board	Full	510	3	(line 3 under table): Spelling error: Thorough, not Thorought	Thank you for your comment. We have proofread the document and corrected typos and spelling errors.
Hywel Dda University Health Board	Full	511	22	It should be considered to add using ANTT (Aseptic Non-Touch Technique) when taking blood cultures using a high standard. i.e: If blood cultures are taken these should be done to a high standard ie taking adequate samples and using ANTT (Aseptic Non-Touch Technique) to avoid the risk of contamination of cultures.	Thank you for this information. Specific techniques for taking blood cultures are not within the remit and scope of this guideline. Reference to the UK Standards for Microbiology Investigations has been added to the guideline and are discussed in the narrative in chapter 14.
Hywel Dda University Health Board	Full	511	35	May need rewording: The strength of most of these recommendations is consider, (?) reflecting... Or place the word “consider” in inverted	Thank you for your comment. We have re-worded this section to clarify the meaning.

				commas?	
Hywel Dda University Health Board	Full	511	49	It is current good practice is (?) to take..... Need to remove 'is'. Insert space between full stop and 'It... '	Thank you for your comment. We have proofread the document and corrected typos and spelling errors.
Hywel Dda University Health Board	Full	512	18	The GDG discussed whether they could recommend choice of imaging further investigate... ? should read ..further investigations...	Thank you for your comment. We have proofread the document and corrected typos and spelling errors.
Hywel Dda University Health Board	Full	530	3	Capital O for Ombudsman	Thank you for your comment. We have proofread the document and corrected typos and spelling errors.
Integrated Care 24 Ltd	Short	General	General	The discriminators for the age groups is welcome	Thank you for your comment.
Integrated Care 24 Ltd	Short	3	Algorithms	(p3,6,8) Pyrexia as a discriminator is only specified for under 5's. Does this mean that fever should be discounted in other age groups? Perhaps an explanatory note (on the algorithm) would be helpful as the majority would put significance on the presence of fever.	Thank you for your comment. The aim of the guideline is to ensure healthcare professionals think about sepsis when a patient presents with possible infection. The risk criteria are designed not to diagnose infection but to stratify those thought to have sepsis, and available evidence is that temperature was not discriminating in this. The GDG were aware that people who are very unwell may not have a raised temperature and dependence on temperature is potentially misleading.
Integrated Care 24 Ltd	Short	3	Algorithms	(p3,6,8) Green boxes referencing HR in pregnancy. We believe it suggests that when assessing HR don't forget that HR is higher in pregnancy, however this is specified in the amber and red boxes so it is a little confusing, consider rewording, removing, or putting as a footnote?	Thank you for your comment. This has been removed from the algorithm as it was confusing.
Integrated Care 24 Ltd	Short	16	21	We read this paragraph to mean that patients identified with low risk criteria require review by a GP/Doctor? In clinical services where non medical practitioners (nurse, paramedic) routinely see patients	Thank you for your comment. These recommendations have been altered to specify appropriate safety netting.

				this would appear to duplicate effort, would not be possible in out of hours, nurse led services, WiCs and negate the clinical assessment of other healthcare professionals. This would be extremely difficult to manage.	
Integrated Care 24 Ltd	Short	30	16	There are concerns around the community administration of IV antibiotics from local acute hospital formularies as they may not always be suitable for community services in terms of complexity of administration and reconstititution. The acute sector can be poor at disseminating guideline updates. Services working across multiple acute trust footprints will struggle to get consensus over the recommended option and variable drugs in neighbouring localities could have safety implications for dosing and administration. It would be preferable if NICE (via HPA ?) could recommend ONE or TWO antibiotics suitable for generic administration for treating Sepsis if prompt transfer to secondary care is not possible.	Thank you for your comment. The recommendations have been clarified to indicate that antibiotics outside acute hospital settings should only be considered in those geographical locations where transfer time will routinely be more than one hour and the GDG were not aware that this is a common problem. The GDG do not consider it appropriate for them to make recommendations for antibiotic use in any more detail than they have done already. Patterns of infection can be different in different areas and patterns of anti-microbial resistance changes.
Integrated Care 24 Ltd	Short	30	22	The recommendation for Ceftriaxone referenced from CG102 is for treatment of patients diagnosed in hospital – it is not clear in this paragraph if it is secondary care based. Ceftriaxone (SmPC) recommends intravenous infusion in young children – this facility is not routinely available in out of hospital settings.	Thank you for your comment. The recommendations on ceftriaxone from the 'meningitis (bacterial) and meningococcal septicaemia in under 16s' NICE guideline are for management in secondary care. We have altered the recommendations to indicate that out of hospital use of antibiotics should only be considered in those geographical locations where transfer time will routinely be more than one hour and the GDG were not aware that this is a common problem.

Medicines and Prescribing Programme	Full	25	footnote	Use 'prescribing responsibilities' rather than 'prescribing rights'. This is the preferred term used in the single competency framework for prescribers	Thank you for your comment, this has now been amended.
Medicines and Prescribing Programme	Full	25-27	Whole section	Are recs 45,46,47 in addition to 44? The whole section is very complex and unclear. It Might be better if structured around what you do for everyone plus additional steps depending on criteria being present or not	Thank you for your comment. We have tried to improve signposting in the Full version with additional headings.
Medicines and Prescribing Programme	Full	33		P33 – consider adding reference to this rec around review of initial antibiotic from NG15 in this section. It might be that a shorter timeframe for review is required, but there doesn't seem to be any reference to this in the recs: 1.1.39 Consider reviewing intravenous antimicrobial prescriptions at 48–72 hours in all health and care settings (including community and outpatient services). Include response to treatment and microbiological results in any review, to determine if the antimicrobial needs to be continued and, if so, whether it can be switched to an oral antimicrobial.	Thank you. We had added reference to the guideline as a whole to cover this.
Medway NHS Foundation Trust	Short	Short	General	We accept that all information in the algorithms is important but it does make the algorithm difficult to follow and to read due to amount of information present	Thank you for your comment. We have worked to improve the layout and wording of the algorithms.
Medway NHS Foundation Trust	Short	Short	Gene	We accept that all information in the algorithms is important but it does make the	Thank you for your comment. We have worked to improve the layout and wording of the algorithms.

			ral	algorithm difficult to follow and to read due to amount of information present	
Medway NHS Foundation Trust	Short	General	General	It is a bit confusing that at time you are talking about …"adult and children and young people aged 12 and older…" and yet at others your are making clear distinctions about the ages e.g. under fluids section on Page 31 you talk about people aged over and under 16	Thank you for your comment. The recommendations on fluids come from the IV fluids in children guideline and this covers children to age 16 years.
Medway NHS Foundation Trust	Short	3	1.2.1 Line 19	For adults should you not be specially saying use the National Early Warning Score	'Consider' is used to indicate the lack of evidence for early warning scores. The GDG recognise that NEWS is commonly used but there was inadequate evidence to recommend this.
Medway NHS Foundation Trust	Short	3	1.2.1 Line 19	For adults should you not be specially saying use the National Early Warning Score	'Consider' is used to indicate the lack of evidence for early warning scores. The GDG recognise that NEWS is commonly used but there was inadequate evidence to recommend this.
Medway NHS Foundation Trust	Short	3	1.2.3	Assess temperature, heart rate etc…… in children **under 12 years** with suspected sepsis (this recommendation is adapted from NICE guideline on fever **in under 5's**)	This is correct. The original recommendation is taken from the Fever in Under 5s guideline and the GDG agreed that it was also relevant to the older group.
Medway NHS Foundation Trust	Short	31	1.7.1 & 1.7.2	Throughout the guideline we are talking about young people aged 12 years and older and then in these sections it talks about 16 years and over	Thank you for your comment. NICE guideline on use of intravenous fluids in children and young people covers young people under 16 years. These recommendations cross refer to that guideline.
Medway NHS Foundation Trust	Short	34	1.10	Should it not be made clearer that organisations should provide written	Thank you for your comment. The recommendations in this guideline should be used in conjunction with other NICE

			.4 Line26	information	guidance, for example the Patient Experience guideline, where communication is covered in more detail.
Medway NHS Foundation Trust	Short	35	1.10.7 Lines 13 to 15	This needs to be more explicit	Thank you for your comment. Following stakeholder comments the GDG reviewed the recommendation but considered they could not make it more explicit.
Medway NHS Foundation Trust	Short	36	General	(p36-37)It would be useful to define what "regular appropriate training is" – should this perhaps be annually	Thank you for your comment. The GDG agree that annual training appropriate to setting would be ideal. NICE guidelines do not have a remit to make recommendations for education authorities and/or competencies for professional groups.
Medway NHS Foundation Trust	Short	36	1.10.11 Lines 8 to 9	Organisations should provide written information	Thank you for your comment. The recommendations in this guideline should be used in conjunction with other NICE guidance, for example the Patient Experience guideline, where communication is covered in more detail.
Medway NHS Foundation Trust	Short	38	27	This UK sepsis registry should be mandatory	Thank you for your comment. The GDG felt that a UK-wide sepsis registry could be of great benefit for patients and potentially improve outcomes. Stating that such a registry should be mandatory would go beyond the remit of NICE guidance.
Meningitis Now	Short	34	Section	(p34-36) Is it possible for specific charities to be listed here, with contact details, so healthcare professionals can easily direct	Thank you for your comment. Recommendations do not usually contain this level of detail. The implementation team will consider your comment where relevant support activity is

			1.10	patients for additional information and support?	being planned.
Meningitis Now	Short	36	Section 1.11	We are pleased that there is a section on training, but how will this be implemented, monitored and evaluated. Can it be mandatory?	Thank you for your comment. The GDG agree that mandatory training appropriate to setting would be ideal. NICE guidelines do not have a remit to make recommendations for education authorities and/or competencies for professional groups.
Meningitis Now	Short	38	Context	You acknowledge an overlap between several different guidelines, and whilst we fully support the need for improved recognition, diagnosis and treatment of severe sepsis, is there a danger that this new guideline doesn't have the impact it should have because of this overlap. Health professionals need to be familiar with so many guidelines – is there a way to combine the relevant elements e.g. the algorithms for recognising severe illness, of these guidelines, to make it easier for those who use them?	Thank you for your comment and this suggestion which will be considered by the implementation team when support activity for the guideline is planned.
Meningitis Now	Short	38	Research	We feel that all these questions are important, but particularly No. 2. This links with our comments 2 & 3 above.	Thank you for your comment.
MRSA ACTION UK	Full	General		Which areas will have the biggest impact on practice and be challenging to implement? Please say for whom and why. MRSA Action UK supports this guideline review, but has reservations about the breadth and scope of research questions used in the review. Of particular concern is the significance (or lack of significance)	Thank you for your comment. The guideline remit included all people with sepsis in all settings and the GDG have attempted to emphasise issues for particular groups where relevant. This does include recommendations of the need for careful note of parental and carer concerns. The algorithms included in the guideline are not decision tools as may be required for services such as 111 and the

				given to 111 and 999 call handlers. The questions on training and education and how 'useful' this is do not place enough emphasis on the difficulties in diagnosing sepsis in the very young. The use of algorithms for 111 call handlers, who are not clinically trained, needs more attention. Training is not 'useful', it is absolutely essential. The use of information and education for the public should include campaigns to raise awareness, and if in any doubt seek immediate medical advice. If patients present at A&E or their GP surgeries and are concerned, particularly those with young children or babies, care should be taken to listen and take account of their concerns, as parents / carers are more likely to know when things are not right. The question of whether the 111 service is equipped to deal with calls relating to very young children and babies remains unclear. Sepsis should always be a consideration with a poorly child, algorithms need to be robust enough to keep this condition at the forefront of call-handlers' minds for <u>all</u> patients. Record keeping is particularly important to ensure anyone involved in assessing the patient is fully aware of the risks.	GDG recognise that services such as 111 will need to implement the recommendations in a way that is appropriate to the challenges of 111 triage. The GDG discussed your comment about record keeping and agree that record keeping is important but did not think there were issues about record keeping specific to sepsis. The GDG have altered the recommendations to highlight the need to consider sepsis when someone presents with possible infection.

				Any clinician assessing a patient with signs of infection should be asking the question "could this be sepsis?"	
MRSA ACTION UK	Full	General		What would help users overcome any challenges? (For example, existing practical resources or national initiatives, or examples of good practice.) The Sepsis Trust range of toolkits are a resource that can be tapped and used in the guideline development and should be signposted, both for clinicians and patients.	Thank you for your comment and this information. The GDG are aware of the resources available from the Sepsis Trust. These are not signposted in the guideline as they are implementation tools rather than recommendations and implementation tools were not included in guideline scope. The UK Sepsis Trust plan to update the Sepsis Trust algorithms to reflect the NICE guideline.
MSD	Full	General	General	MSD welcomes the focus on timely initiation with regard to antibiotic therapy, when sepsis is present or suspected. MSD suggests that local retrospective reviews of antibiotic use would be appropriate, both to understand the effectiveness of the antibiotics chosen, and to inform future practice and antibiotic protocols with regard to sepsis.	Thank you for your comment. Further detail on antimicrobial stewardship is outside the scope of the guideline. However, this guideline cross-refers to the antimicrobial stewardship guidance which provides more detail.
MSD	Full	33	13 - 17	MSD welcomes recommendation 95 and the alignment with NICE Guideline 15 (Antimicrobial Stewardship). MSD suggests that the recommendation's wording should be expanded to state that evidence summaries (where available) are a national reference point for evidence	Thank you for your comment. NICE recommendations do not usually contain reference to evidence summaries because these are not formal guidance.

				relating to the use of a new antibiotic.	
MSD	Full	37	31 - 34	MSD welcomes the inclusion of recommendations on training relating specifically to the use of antibiotics. MSD suggests that recommendation 130, line 34, be expanded to state that an up to date knowledge of local epidemiology and resistance patterns is an essential component of choosing an effective antibiotic.	Thank you for your comment. Choice of antimicrobials is dependent on local arrangements. The recommendation states that local protocols for antimicrobial treatment should be included in training schemes.
Newcastle-upon-Tyne Hospitals NHS Trust	General	General		Good to see that SIRS has been removed.	Thank you for your comment.
Newcastle-upon-Tyne Hospitals NHS Trust	General	General		There are concerns that the neutropaenic patient is under-triaged and comments have focused on clinical discomfort in withholding antibiotics from patients with febrile neutropenia.	Thank you for your comment. It was not the intention to hinder the care of people likely to have neutropenic sepsis. We have added additional recommendations and cross reference to make it clear that people with suspected neutropenic sepsis should be treated according to CG151.
Newcastle-upon-Tyne Hospitals NHS Trust	General	General		Source control is perhaps the one area (including antibiotics within one hour) which has been shown to improve outcome. Perhaps consideration of this should figure?	Thank you for your comment. The recommendations on finding the source of infection have been altered to provide more emphasis on source control.
Newcastle-upon-Tyne Hospitals NHS Trust	General	14	General	There has been concern amongst acute medical consultants that the moderate criteria will lead to unmanageable over-triage of the acute medical admission cohort. This has implications for service delivery.	Thank you for your comment. The wording of the recommendations has been changed to indicate that this population in the guideline are people with infection and a suspicion of sepsis. People in this group are at moderate to high risk of serious morbidity and mortality and the recommendations are planned to ensure they are assessed.

					The assessment can be done by a suitably qualified clinician and not a senior medical decision maker.
Newcastle-upon-Tyne Hospitals NHS Trust	General	14	General	Use of lactate >2mmol/l to place moderate risk straight to high risk without treatment or assessment of response to treatment will also result in over-triage and potentially inappropriate use of broad spectrum antibiotics.	Thank you for your comment. People in this category will already have been seen by a healthcare professional and alternative actions can be considered. The evidence suggests that if the person has 2 or more moderate to high risk criteria, infection and suspected sepsis, a raised lactate indicates an increased risk of mortality.
Newcastle-upon-Tyne Hospitals NHS Trust	General	14	General	Should the seniority of the reviewing doctor for high risk patients be *At least ST3 or ST3+*? Rather than simply ST3. This highlights the urgency of the patients in the high risk group.	Thank you for your comment. The wording has been altered and does say a doctor of grade CT3/ST3 or above or equivalent depending on local arrangements.
Newcastle-upon-Tyne Hospitals NHS Trust	General	14	General	Should other cultures as appropriate be included in the flow diagram? It would be easy to see how a false positive culture from blood could occur and a urine culture be missed.	Thank you for your comment. The algorithms are a balance between indicating main actions in a flow diagram and ensuring they are readable. For that reason only main actions such as taking blood cultures before giving broad spectrum antibiotics are listed.
Newcastle-upon-Tyne Hospitals NHS Trust	General	14	General	Consultant review is suggested after the second bolus of fluid or failure to improve after 30 minutes. This may have implications for service delivery. Which consultant do they mean? Base team? Critical care?	Thank you for your comment. The GDG discussed this recommendation at length and reviewed it following stakeholder comment. This group of patients are those who are not responding to initial resuscitation and therefore likely to have highest risk of mortality. The GDG intended that this could be a consultant covering patients who may be critically unwell. As such this could be a consultant from acute medicines, anaesthetics, or the emergency department. This has been clarified in a footnote.
Newcastle-upon-Tyne Hospitals NHS Trust	General	34	9	The rate of fluid administration of 500mls in 15 mins is 2000mls/hour which exceeds the maximum delivery speeds	Thank you for your comment. The IV fluids recommendations are from published NICE guidelines.

				of most pumps by a factor of two. Whilst this may encourage physician bolus which would improve monitoring, it may lead to the risk of over resuscitation if IV lines are just “opened up.”	
Newcastle-upon-Tyne Hospitals NHS Trust	Short	3	23	1.2.3 Suggest to add blood pressure also for under 12s why separate in 1.2.5.	Thank you for your comment. There is a paucity of evidence for blood pressure value in children and potential issues with measurement because of lack of correct cuff size. Blood pressure changes can be a late sign in children. For these reasons the GDG agreed to follow the Fever in Under 5s guideline and make different recommendations for blood pressure measurement in children.
Newcastle-upon-Tyne Hospitals NHS Trust	Short	17	8	1.5.1 To add glucose.	Thank you for your comment. This has been added to the recommendation.
Newcastle-upon-Tyne Hospitals NHS Trust	Short	19	7	1.5.8 To add glucose.	Thank you for your comment. This is already included in the recommendation for children under 11years and has now been added to recommendations for young people and adults over 12 years.
Newcastle-upon-Tyne Hospitals NHS Trust	Short	21	21	1.5.16 To add glucose.	Thank you for your comment. This is already included in the recommendation for children under 11years and has now been added to recommendations for young people and adults over 12 years.
Newcastle-upon-Tyne Hospitals NHS Trust	Short	30	22	1.6.7 Ceftriaxone dose as registered with European Medicines Agency(EMEA)is 100mg/kg with the same max of 4 g.	Thank you for this information. The dose as listed is that in BNF.
Newcastle-upon-Tyne Hospitals NHS Trust	Short	31	8	1.6.11 in neonates under one month of age (also those born at 40 weeks gestational age) cefotaxim rather than ceftriaxone are advised to avoid interaction with albumin particularly in neonates with jaundice.	Thank you for your comment. The GDG have reviewed the recommendations and the information in the BNF regarding ceftriaxone in neonates and have re-worded the recommendations for neonates.
Newcastle-upon-Tyne Hospitals NHS Trust	Short	33	1	1.9.3 Consider at least urine analysis in patients of ALL ages, x ray if clinically indicated.	Thank you for your comment. We have made this change as you suggest.
Newcastle-upon-Tyne	Sh	33	22	1.9.6 Sometimes a minimum platelet count	Thank you for your comment. This recommendation is

Hospitals NHS Trust	ort			of 50 is regarded sufficient for lumbar puncture.	adapted from the NICE meningococcal sepsis guideline. Coagulopathy in sepsis will accompany thrombocytopenia and while in non-septic conditions we accept that a platelet count of 50 may be acceptable for lumbar puncture, this may not be safe in sepsis. The recommendation has been clarified however to recognise that a decision can be made to do a lumbar puncture in early management of sepsis if this is a consultant decision.
Newcastle-upon-Tyne Hospitals NHS Trust	Short	40	General	I would not limit biomarker studies to PCT.	Thank you for your comment. The research recommendations listed are those prioritised by the GDG and are developed on the basis of the areas reviewed in the guideline or in other NICE guidance. The GDG recognise that there are other biomarkers that may be of interest and require to be researched.
NHS Choices	Full	General		Assessment for remote triage either over the telephone or digitally has been omitted. The guideline would benefit from this information	The GDG aimed to identify symptoms and signs that help in diagnosis of sepsis or are indicators of poor outcome. The risk criteria chosen are those for which there is most evidence. The GDG recognise the challenge of remote assessment and triage and considered that this problem is also relevant to general practitioners doing triage and general practice out-of-hours services. The GDG recognise that assessment for remote triage is difficult, however they did not think it appropriate to change the criteria listed. They do recognise that different services have to consider how they perform triage and that different services may implement triage in different ways. Following stakeholder comments, additional recommendation have been added which emphasise risk factors and disorders of behaviour, breathing and circulation as important factors to consider when deciding if someone needs a face to face assessment. The GDG considered they could not define these further.

NHS England	General	General	General	I was pleased to see this guidance and that it explicitly addresses people of different ages, although I recognise that this makes it quite a long and complex document. The algorithms at the front are useful. I note the research recommendation that there should be a sepsis registry and we will discuss what could be done about this. My question back to NICE is what impact do they think the new international definitions of sepsis (due out in a few weeks) will have on this guidance?	Thank you for your comment. We have included a section on the new sepsis definitions and clinical parameters in this guideline. This guideline does not aim to define sepsis but offer clinical trigger points that can help identify people at risk of developing sepsis and ensure that those people receive appropriate care. As a result, the new sepsis definitions do not contradict the recommendations in this guideline. Please note that the research recommendation has been changed to reflect the NICE process for research recommendations. The GDG agreed to change the wording and recommend that an epidemiological study on the presentation and management of sepsis in England be conducted.
NHS England	Short	General	General	Clear guidance for clinicians in primary care – easy to interpret using low, mod or high risk. Algorithms are easy to follow.	Thank you for your comment.
NHS England	Short	1	12	From page 16 – line 9 1.4.2 need to ensure that the recommendation of within 1 hour is translated into the algorithms	Thank you for your comment. This recommendation has been changed.
NHS England	Short	1	17	May need definition of 'very frail' or some frailty indicators would be helpful. No mention here of the impact of multi-morbidity.	Thank you for your comment. Following stakeholder consultation explicit mention of de-escalation of care has been added to the Full guideline when discussing actions of senior decision maker. The GDG were aware of research in the area of frailty but in this context did not consider further definitions were helpful. The recommendation is intended to alert healthcare professionals to situations when presentations may be atypical. Most indicators of frailty are performance based and not appropriate to be used when people are acutely unwell.

NHS England	Short	3	19	Should this section recommend potentially using an early warning score in the community as well?	Thank you for your comment. We have included a research recommendation for early warning scores in the community as the evidence available did not support a recommendation.
NHS England	Short	8	3	Column 3 line 2- “not behaving normally or wanting to play” it may be clearer to say “not behaving normally or **not** wanting to play”	Thank you for your comment. This has been amended.
NHS England	Short	16	all	The guidelines on this page are excellent and easier to remember than the	Thank you for your comment.
NHS England	Short	16	21	Is a timescale appropriate for this?	Thank you for your comment. This recommendation has been changed following stakeholder comment to specify safety netting rather than assessment by a GP.
NHS England	Short	36	19	Could have specific mention of staff in care homes – huge need for training and education in this area.	Thank you for your comment. We have changed the recommendation following stakeholder comment to make the need to include care home staff explicit.
NHS England	Short	36	20	Suggest this sentence includes regular appropriate training in both hospital community and primary care setting.	Thank you for your comment. We have changed the wording of the recommendation in line with your suggestion.
NHS England	Short	37	9	Should this section be at the start of the guideline – excellent context and explains the seriousness of sepsis in terms of mortality and the need for awareness for all clinicians.	Thank you for your comment. This is the standard format for short guidelines.
Northumbria Healthcare NHS Foundation Trust	Short	17	16	There needs to be an expansion of what “maximum recommended dose” means e.g. for Meropenem is that 1g or 2g? For some antibiotics it may be more straightforward e.g. Piperacillin-Tazobactam but for the majority the maximum dose depends upon the source of the sepsis. For most patients using Meropenem as an example 2g would	Thank you for your comment. The GDG reviewed the recommendation following your comment. They were concerned about use of sub-optimal doses of antibiotic in patients who are critically ill. They recognise that maximum dose may differ according to clinical scenario but that the detail has to be left to local and regional experts. It is beyond the scope of this guidance to provide detailed guidance on this.

				not be necessary unless there are concerns regarding the possibility of meningitis. Careful thought is required into the rewording of this sentence otherwise we will require organisations to prescribe Meropenem 2g initially for all their septic patients to comply with NICE guidance. I can understand what the authors are trying to say e.g. give the maximum **systemic** dose of an antibiotic but they are not necessarily the maximum dose available for other conditions. It is also not clear for many antibiotics what he maximum dose is to be effective e.g. clindamycin and there are huge region variations in maximum doses recommended by "experts" in the fluid. Gentamicin is another drug where review of the BNF lists the dose as 5-7mg/kg – so should we give 7mg/kg to everyone? I feel the current wording is not helpful to facilitate the intention of the authors.	
Northumbria Healthcare NHS Foundation Trust	Short	30	22	I am concerned this would result in a more appropriate antibiotic than ceftriaxone not being administered. If for example a person under 17 years of age presented "septic" with a painful ankle – IV Flucloxacillin and Clindamycin (for toxin) control would be far more appropriate than ceftriaxone. Could we change the wording to use ceftriaxone only when a clear source for the infection is unknown (as you have for adults)? Would this not potentially improve outcomes rather than a blanket	Thank you for your comment. Following stakeholder consultation we have added a recommendation for all people where the source of infection is clear that existing local antimicrobial guidance should be used (recommendation 1.7.6).

				treat every infection with Ceftriaxone even when the source is obvious and there are more effective antibiotics for that source available?	
Nottingham University Hospitals NHS Trust	General	General		Whilst we welcome this review and guidance, the algorithms look too complicated and will be difficult for clinical staff to follow	Thank you for your comment. We have worked with the NICE editors to improve the algorithms.
Nottingham University Hospitals NHS Trust	General	short version guideline algorithms page 4—6, table page 8-9 table 3 page		• The high risk criteria of no urine output in 18 hours is too long to wait for children	Thank you for your comment. This recommendation has been changed and this criterion has been removed.

		10-12, full guideline			
Nottingham University Hospitals NHS Trust	General	short version guideline algorithms page 4—6, table page 8-9 table 3 page 10-12, full		The comment in the algorithm adult low risk box in full and short version guidance ‘ Baseline heart rate is 10-15 beats/minute more in pregnancy ‘ needs extra text to clarify or be removed as different heart rate in pregnancy referred to in high to moderate risk box anyway	Thank you. This had been removed.

		guideline			
Nottingham University Hospitals NHS Trust	General	short version guideline algorithms page 1 , table 1 page 4—6, table page 8-9 table 3 page 10-		The titles of criteria boxes in the algorithms and tables should be labelled as high, moderate or *no* risk, i.e. not use the moderate to high risk title - short version guideline algorithms page 1 , table 1 page 4—6, table page 8-9 table 3 page 10-12, full guideline	Thank you for your comment. The GDG discussed altering the labelling of risk categories but agreed to leave them as low, moderate to high, and high risk. The GDG wished to emphasise that some people in the moderate to high risk group have a significant risk of mortality and careful assessment is required.

		12, full guideline			
Nottingham University Hospitals NHS Trust	General	short version guideline algorithms page 1, table 1 page 4—6, table page 8-9 table 3 pag		Concerned with the difficulty to identify/ assess if existing or new confusion in the elderly patient , which will mean that the default will be to treat as new and managed as high risk. As there is no route back into moderate or no risk criteria even if no other markers of high or moderate risk after further investigation, resulting in overuse of antibiotics and missed alternative diagnoses	Thank you for your comment. Following stakeholder comments the recommendations have been altered to increase emphasis on clinical judgement for alternative diagnosis and management decisions. Altered mental status was noted in the evidence review for the guideline and is also included in literature on new definitions as one of the indicators of increased mortality.

		e 10-12, full guideline			
Nottingham University Hospitals NHS Trust	General	Full page 21 Short Table 1 page 5 Pg 6	Line 2 Line 7	Concerned that the threshold in the 12 and above guidance of oxygen saturation of less than 92% is too low for young adults	Thank you for your comment. The GDG, which includes four paediatricians, reviewed the recommendations following stakeholder comment and considered the recommendation appropriate.
Oxford University Hospitals NHS Foundation Trust	Full	General	General	Main issue is when to use this guideline- Flow chart starts with a person who has "an infection/fever/unwell". What does unwell mean- for example asthmatics are unwell but there would be no indication to use this guideline. Seems overinclusive – Those of us who work regularly in ED would find a good number of URTI/OM/Bronchiolitics who would fit in the moderate risk groups. What is the definition of infection- does this guideline cover all likely viral as well as bacterial infection	Thank you for your comment. The wording of recommendations has been changed and additional recommendations have been added to clarify that the intention is to consider if someone might have sepsis and to include appropriate emphasis on clinical judgement to ensure people are not treated as suspected sepsis inappropriately. The recommendation in the under 5 years group uses bronchiolitis as a specific example of an alternative diagnosis. The emphasis in the guideline is on early assessment and at that stage it may be not be possible to know whether infection is bacterial or viral so no distinction is made in the guideline.

Oxford University Hospitals NHS Foundation Trust	General	General	General	It also isn't clear who the hospital part of the guideline is aimed for- are these guidelines for adult physicians seeing children or paediatricians and if for both who is 'a senior decision maker?'	Thank you for your comment. The guideline covers all groups and senior decision maker is described in the guideline both for adults and for children and young people.
Oxford University Hospitals NHS Foundation Trust	General	General	General	No definition of what is sepsis- although the definition may change in the near future surely this is fundamental to this guideline. This would help decide which patients this guideline should be used for. Most of the points in this document are sensible for patients who are truly "septic". However, certainly in paediatrics, many patients who will be assessed with this document will have minor febrile illnesses with a clear focus but will end up following the high risk criteria pathway requiring blood tests, IV fluid and IV antibiotics and therefore hospital admission and invasive investigation often unnecessarily. This will have cost implications as well as patient flow implications for most Trusts who potentially won't have the capacity for resultant increases in admission numbers	Thank you for your comment. We have included a section on the new sepsis definitions. It is not the aim of this guideline to define sepsis but to help identify people who have suspected sepsis and are at risk of severe illness or dying from sepsis and to ensure they have early and appropriate treatment. The recommendations have been changed following stakeholder consultation to increase the emphasis on clinical judgement and to consider alternative diagnoses.
Oxford University Hospitals NHS Foundation Trust	General	General	General	There is an assessment for predicted risk factors for sepsis (e.g. immunodeficiency) but these are then ignored when moving to next steps of the flow charts (although there is some mention in the document- although not entirely clear)	Thank you for your comment. The risk factors should be part of the decision-making of the person doing the assessment. We have worked with the NICE editors to improve the algorithms and clarify the intended pathway.
Oxford University Hospitals NHS	Gener	Gener	Gene	It is mentioned in the text that BP should be measured in children <5 years if abnormal	Thank you for your comment. We have worked with the NIE editors to improve the algorithms and make steps clear. We

Foundation Trust	al	al	ral	HR/CRT but this is not mentioned in the flow chart (in the middle of the night SpRs/SHOs are only going to look at the flow chart)	are also aware that the Sepsis Trust plan to update their pathways in line with the NICE recommendations.
Oxford University Hospitals NHS Foundation Trust	General	General	General	Very heavy reliance on lactate testing- the evidence from the full guideline seems fairly thin especially for children (only 1 study only in children which was deemed "very seriously biased"). To use lactate > 4 as sole arbiter of when to call PITU seems worrying, and to use lactate levels as main criterion for giving fluid, ditto. Surely more reliance should be placed on CRT, HR, general clinical assessment and whether the child is clinically deteriorating. Lactate should be used in conjunction with these- rather than being used as a single indicator. It may be more useful to say – 'lactate that remains high despite adequate antipyretics/ fluid resuscitation' as we often see highish capillary lactates in children with poor peripheral perfusion who respond to adequate antipyretics/ fluid etc and which then subsequently drops as part of management .	Thank you for your comment The recommendations do not use lactate alone to decide on treatment. All those with high risk criteria have clinical assessment with a senior clinical decision maker, antibiotics and discussion with consultant. Lactate is used when considering fluids and critical care referral.
Oxford University Hospitals NHS Foundation Trust	General	General	General	Once on the pathway and another diagnosis is made (other than sepsis- which is often going to be the case) it is difficult/impossible to get off the pathway of giving fluid and antibiotics. This has been a major concern voiced by most members of the team and will lead to over investigation , once the guideline is in place	Thank you for your comment. The recommendations have been amended following stakeholder consultation to increase the emphasis on clinical assessment and consideration of other diagnoses.

Oxford University Hospitals NHS Foundation Trust	General	General	General	No clear mention of measuring blood glucose , even on 'severe' pathway	Thank you for your comment. This has been added.
Oxford University Hospitals NHS Foundation Trust	General	General	General	No clear mention of examining for a source, rash etc	Thank you for your comment. This guideline includes recommendations for source identification. The GDG agreed that a thorough clinical examination should be carried out to look for sources of infection tailored to a person's clinical history and findings on examination.
Oxford University Hospitals NHS Foundation Trust	General	General	1.5.8-	Suggests review with blood results within 1 hour of meeting the mod-high risk criteria (at triage for many patients)- most hospitals will struggle to get all the blood results back within 1 hour from them being sent, let alone including the time to assess the patient & take the blood esp in children.	Thank you for your comment. The recommendation has been amended to have consideration of lactate only at this stage as the other results are not required for early management.
Oxford University Hospitals NHS Foundation Trust	General	General	1.9.4/ 1.9.5	Gives advice of considering abdominal imaging/surgical assessment to find a source if none identified. Why just this rather than seeking other sources (cardiac, CSF esp small children, etc which should probably be mentioned and if child too unwell for LP that meningitis doses of antibiotics should be considered).	Thank you for your comment. The recommendations suggest use of clinical judgement when deciding on appropriate tests. The recent ombudsman's report highlighted the need to consider sources of infection that may need, for example, surgical drainage, and the recommendation was included to remind healthcare professionals of this possibility.
Oxford University Hospitals NHS Foundation Trust	General	General	General	How would one would know that urine output is > 0.5 ml/kg/hour in a child outside hospital ?	Thank you for your comment. The pathways have now been adapted. The cut-off of 1 ml/kg/hour is only intended for catheterised children.
Oxford University Hospitals NHS Foundation Trust	General	General	1.10.12	Do parents (carers) of children have a right to a carer's assessment of their needs? This probably won't be relevant to many children and is ambiguous	Thank you for your comment. Parents of children with disability are entitled to support and we have therefore not changed the recommendation.
Oxford University Hospitals NHS Foundation Trust	General	General	1.4.1	<17years AND immunocompromised AND mod-high risk criteria needs hospital referral. Adults with suspected sepsis with	Thank you for your comment. The GDG discussed this at length. We have added cross referral to the NICE Neutropenic Sepsis guideline and agreed that referral was

				immunocompromise AND mod-high risk criteria don't need hospital review? Seems unlikely in most circumstances	appropriate for children where this is an uncommon occurrence. The GDG considered that there are many adults who are on low dose steroids or disease modifying drugs for example who do require assessment but that recommending hospital review for all would be inappropriate.
Oxford University Hospitals NHS Foundation Trust	General	General	1.10.5	Advises giving written advice about sepsis to people assessed for sepsis but not diagnosed with sepsis. Surely every patient we see and review in ED is "assessed" for sepsis- will everyone need a leaflet?	Thank you for your comment. The GDG reviewed the recommendations following stakeholder comment and have distinguished the population with suspected sepsis from all people with infection. The GDG acknowledge that some judgement is required in the type of information supplied to patients but that providing a safety net of information is useful in all cases.
Oxford University Hospitals NHS Foundation Trust	General	General	1.5.15	patients >12 years old with "suspected sepsis" and no mod-high risk factors can be managed according to clinical judgement- the definition of sepsis is also needed here. Why "sepsis" is suspected if there are not even moderate risk factors?	Thank you for your comment. The stratification of risk uses criteria of physiological abnormalities. It may be appropriate to suspect sepsis on the basis of factors such as reduced immunity and a person feeling unwell even if there are no abnormal findings on examination.
Oxford University Hospitals NHS Foundation Trust	General	General	1.5.16	Give antibiotics within 1 hour of high risk criteria- often these criteria will be met at triage. Will every febrile child with a raised HR & RR need antibiotics within 1 hour of triage? Feasible? Desirable?	Thank you for your comment. The recommendations have been altered to increase emphasis on clinical assessment and consideration of other diagnoses.
Oxford University Hospitals NHS Foundation Trust	General	General	1.5.22	Consultant to attend in person if child fails to respond within 1 hour of fluid/antibiotics- the criteria for failure to respond seem overly conservative.	Thank you for your comment. The GDG aimed to strike a balance between appropriate input and resource impact.
Oxford University Hospitals NHS Foundation Trust	General	General	1.5.31	Doesn't suggest max dose of antibiotic for <5 year olds but does for >5 year old groups? Correct?	Thank you. This was an error and has been corrected.

Oxford University Hospitals NHS Foundation Trust	General	General	1.7.2	The advice for fluid resuscitation for patients <16 years is from the NICE guideline for OVER16s- surely is should be from the guideline for children (newly published).	Thank you for your comment. We have proofread the document and corrected typos and spelling errors.
Oxford University Hospitals NHS Foundation Trust	General	General	1.5.5	Suggests using a physiological track & trigger system for adults. Surely children too?	Thank you for your comment. This recommendation is from an adult guideline. The GDG considered that using track and trigger systems in children had less evidence and could not suggest their use in all settings.
Oxford University Hospitals NHS Foundation Trust	General	General	1.10.9	Ensure GP discharge letter includes diagnosis of sepsis. If they have a UTI causing a fever does sepsis count as a separate diagnosis?. Again unclear as no definition of what constitutes sepsis	Thank you for your comment. Detail of recent new definitions has been added to the guideline. The GDG considered that clinically it is possible to differentiate a person with a UTI from a person who has sepsis.
Oxford University Hospitals NHS Foundation Trust	General	General	1.3.9	Sats≤95% in air is mod-high risk in children <5years- most paediatricians this think is overly conservative, and unclear where evidence for this is from. Again depends partly on who the guideline is used for.	Thank you for your comment. This has been altered following stakeholder comment and detail added to the Full guideline. It is informed by the recent study by Cunningham et al (2015) and the reference has been added.
Oxford University Hospitals NHS Foundation Trust	General	General	1.9.3	Consider urinalysis/CXR if >5 years. Surely < 5 year olds (probably more relevantly) too?	Thank you. We have altered this recommendation.
Oxford University Hospitals NHS Foundation Trust	General	General	1.7.7	Suggests considering 4.5% albumin for sepsis with shock. If there is sepsis without shock (no definition given) why are boluses of fluid being given?	Thank you for your comment. We acknowledge that the terminology is confusing. This recommendation is from IV Fluids guideline. The new definition of shock applies when people have not responded to fluid resuscitation and require inotropes so is a definition that is not appropriate outside critical care settings.

					This guideline has therefore avoided the use of the term sepsis in new recommendations.
Paediatric Intensive Care Society	Full	38	General	Research recommendations: NIHR HTA is currently funding a combined feasibility and external pilot study of different size fluid bolus therapy - (10 vs 20 ml/kg) in paediatric sepsis beyond the first 20 ml/kg fluids. The study is called “Fluids in Shock”, FiSh (13/04/105, http://www.nets.nihr.ac.uk/projects/hta/1304105). It does not appear that the NICE guideline will impact significantly on FiSh as the NICE guidance is primarily concerned with recognition and very early management and FiSh is concerned with management beyond the first 20 ml/kg fluid bolus. However, FiSh will target therapy beyond the first 20 ml/kg fluid bolus to SBP and capillary refill time (not HR or lactate), as SBP and CRT were determined to be the most helpful clinical parameters to target by our clinical steering group. It would be useful, therefore, for NICE to recognise as a Research Recommendation a well organised UK clinical trial comparing recommended fluid bolus resuscitation (20 ml/kg) to a more restrictive strategy (10 ml/kg), to determine which strategy is associated with improved outcomes for children presenting to UK EDs with presumed septic shock. We would be happy to share our trial protocol if that would be helpful.	Thank you for this information. We will alert the NICE surveillance team so that they can be aware of this study when considering updates of the IV fluids in children guideline and this guideline.
RCGP	Full	Ge	Ge	RCGP generally support this document,	Thank you for your comment.

		neral	neral	however it is important to see if empirically this works in a lower risk primary care setting. In a low prevalence setting this "test of sepsis" may generate large numbers of false positives for instance patients that are rated as possible sepsis and 999 ambulances are called who are not that ill. Is any modelling available? As I suspect our practice would be sending at least 1 patient per day by 999 on the basis of this guidance. (MJ)	The population the guideline is trying to capture is people with infection plus a suspicion of sepsis. The guideline aims to empower healthcare staff to make a diagnosis based on assessment and clinical judgement but also to lead to a cultural change where people think about sepsis. The wording of recommendations has been changed and additional recommendations have been added to clarify that the intention is to consider if someone might have sepsis and to include appropriate emphasis on clinical judgement to ensure people are not treated as suspected sepsis inappropriately. Unfortunately modelling was not feasible on this guideline because of the large number of unknowns around the epidemiology of sepsis. However, the criteria in the guideline are consistent with those included in new Sepsis-3 criteria for people at elevated risk of morbidity and mortality which are based on large cohorts of patients.
RCGP	Full	General	General	The overall premise of this document is to start from knowledge about the presentation of sepsis patients by looking back at how patients with sepsis presented. Unfortunately, this does not necessarily produce a coherent strategy for the management of infection which is the predominating presentation and from which sepsis is a remarkably small subset. Indeed, the recommendations made here would potentially exacerbate the challenges faced by the out of hospital clinician by	Thank you for your comment. In order to identify evidence for the diagnosis and management of people with sepsis, we identified studies in people with suspected sepsis or confirmed sepsis to inform the recommendations. We recognise that much of the evidence was retrospective and the findings of the studies have been evaluated accordingly. When formulating the recommendations the GDG had to strike a balance of how wide the net should be with regards to wanting to be inclusive enough to not miss people, but also not too wide to overburden the NHS, and also taking the

				increasing the number of people presenting to GPs with infection to have sepsis ruled out if this is indeed possible. (SS)	evidence identified into account. Sepsis is currently missed because clinicians do not consider it. The GDG discussed the stakeholder concern about over triggering and the resulting impact on services and have made a number of changes to the recommendations and summary algorithms to clarify their intentions. These include making it clear that the population are people with suspected infection and increasing the emphasis on the importance of the clinical judgement in assessment of people with infection.
RCGP	Full	General	General	The minimum output of the algorithm is assessment by a GP or other healthcare professional for all people with infection, fever or “feeling unwell”, there is no pathway for infection or symptoms being managed without access to healthcare. If applied by 111 all patients would come to GPs etc who would only have a limited capacity to rule out sepsis at that point, and potentially could refer to hospital who would face the same challenge. The risk of over diagnosis and treatment is significant as is the burden it would place on health services. The safe management of people with infection at home without involvement of health services doesn’t seem to be considered, and given that this is what most people do and are encouraged to do, seems odd. (SS)	Thank you for your comment. Following stakeholder comments the wording of recommendations has been altered and recommendations have been added to clarify that not all people with infection have to be seen by a GP or other healthcare professional and that if people do contact health services about infection safety-netting is appropriate. The wording has been changed to clarify that the emphasis is on considering sepsis and ensuring appropriate assessment of people who might have sepsis. The GDG considered that sepsis is missed because health care professionals do not think of the possibility of sepsis.
RCGP	Full	Gener	Gene	The symptoms and signs for moderate to high risk are curious, particularly the	Thank you for your comment. The first step in the pathway is that sepsis is considered and the presence of certain

		al	ral	selection of pulse rate and temperature. These represent my concerns about the retrospective rather than prospective nature of the evidence used derived to achieve these guidelines and I suspect will run counter to the evidence provided to support the new definitions of sepsis due for publication in February. Particularly, they fall within the normal ranges for adult pulse and temperature (60-100bpm, and low normal temp of 35.5 female 36.7 male) which means that people with these normal ranges and an infection fall into a high to moderate risk of sepsis. This in itself a problem as it makes normal values high risk in the presence of infection. It is particularly the case for the elderly where the range of resting heart rates is greater. The placing of inflamed or discharging wounds in this group isn't clear when it is then tied to a one-hour response from GPs where this is found in primary care. I suspect the evidence for this being linked to sepsis is hospital derived and the response is potentially disproportionate with the knowledge regarding sepsis risk. (SS)	underlying problems or treatments particularly requires careful consideration. The evidence for the new sepsis definitions was not available when the guideline went for consultation. These have been reviewed following their publication and are discussed in the Full guideline chapter 6. Of note is that there is significant overlap between the criteria included in the guideline and those developed by the specialist societies as Sepsis- 3 as being associated with increased risk of mortality. The recommendations include the need to consider factors that may alter usual physiological responses. The GDG acknowledge that clinical judgement must also be used in patient assessment. The one hour response review by a GP has been removed from the recommendations.
RCGP	Full	General	General	The speed of response required in the presence of septic shock is widely understood with timely fluids oxygen, antibiotics and fluids but I am unaware of evidence for the timeliness of response in the presence of sepsis without circulatory collapse. It is assumed that a timely	Thank you for your comment. The recommendations have been altered and the need for GPs to respond within an hour to moderate to high risk criteria has been removed.

				response is required for the latter to prevent the former but the relationship isn't proven. The leap then to require GPs to respond within an hour to moderate to high risk criteria where sepsis isn't even a given would potentially lead to a huge amount of work without any strong evidence of a positive impact upon the care of sepsis. There is also a question that if the volume and stress of work thus created produced a low yield that clinicians would disengage from the assessment to the detriment of the patient with sepsis. To make the stipulation that assessment is made within an hour without an impact assessment and no proven evidence of benefit is difficult to accept. (SS)	
RCGP	Full	General	General	In conclusion we have guidance derived largely from the retrospective study of sepsis passing judgement on the prospective management of infection. It seems to include values normally considered to be well within the normal range as abnormal when they appear in the presence of infection without clear reasoning. It uses these to define people at moderate to high risk of sepsis and expects a GP to be able to assess these patients within an hour. It also says that all people with infection should be assessed by a GP or healthcare professional which would be disproportionately burdensome and potentially counter-productive. (SS)	Thank you for this summary of your comments. We have responded to each of these points in responses above.
RCGP	Full	Ge	Ge	There seems to be little in the content to	Thank you for your comment. We have details about

		neral	neral	argue with; as sometimes happens it does gather together what most of us would regard as standard good medical care. What I have not be able to find in this document is an agreed definition of sepsis. It looks like the term has emerged in the last few years as a distinct entity, but I haven't come across any definition and it is unclear it can be found here. If that is correct, then the risk is that the necessarily vague criteria could be used after the event and in the light of subsequent developments to criticise doctors (especially GPs) for what they should have done. One later consequence is that the guidelines could lead to further overtreatment. I would personally feel much happier if it were acknowledged somewhere that the term is imprecise; and that the distinction between milder and more severe bacterial infection is likely to be uncertain. (DJ)	definitions of sepsis and how this guideline relates to them in Full guideline chapter 6.

RCGP	Full	13	General	There does not seem to be a pathway by which a patient with an infection is not assessed by a GP or other medical qualified professional. Is it the attention that all people who have an infection are assessed or just those who present to the health service for assessment? I am worried that we are going to become a sepsis rule out service and that telephone advice for infection will become ever more difficult when the requirement for physiological assessment is made so clearly. I fear that the NICE Guidance will be built into public advice and we will lose control of infection management. The impact on service delivery is a concern and unquantified (SS)	Thank you for your comment. Following stakeholder comment the wording of the recommendation has been changed to clarify that people need to be seen when there is suspicion of sepsis. The need to see a GP and perform a physical examination within a specified time period has been removed with more of an emphasis on clinical judgement. The guideline aims to empower healthcare staff to make a diagnosis based on assessment and clinical judgement but also to lead to a cultural change where people think about sepsis. The risk factors highlighted in the guideline, and recommended approach following identification of those, is not intended to be a management pathway that replaces clinical judgement, but a tool to encourage clinicians to be able to place patients on a pathway should they have concerns that a patient might have sepsis because of an infection and a definitive diagnosis cannot be made outside of hospital.
RCGP	Full	15	General	See previous. (SS)	
RCGP	Full	20	8	This requires that the assessment is done face to face with a medical professional, and precludes telephone consultations and advice where appropriate. It is unclear that this has been impact assessed when applied to out of hospital care. (SS)	Thank you for your comment. Following stakeholder comment the recommendations have been changed to indicate that remote assessment is possible and to indicate where the GDG thought assessment should be done face to face.
RCGP	Full	20	12	See previous	

			,13		
RCGP	Full	20	34	Not sure these comments correlate with the algorithm which suggests that these signs and symptoms in the presence of suspected infection raise the possibility of sepsis but on their own they don't necessarily suggest sepsis. (SS)	Thank you for your comment. The recommendations do refer to people who have infection and whom there is concern that they have sepsis. The recommendation needs to be understood in the context of the pathway.
RCGP	Full	21	1	The new international definitions suggest a rate of 22 breaths per minutes. (SS)	Thank you for your comment. The new definitions suggest a respiratory rate of 22 breaths per minute or more as an indicator that a person is likely to have a higher hospital mortality. The GDG wished to develop a pathway where those at highest risk have more immediate treatment but those at lower, but still significant risk are also seen as soon as possible. The evidence identified for this guideline showed that outcomes were consistently poor at rates above 24 breaths per minute in adults. Our pathways suggest a respiratory rate of 21-24 breaths per minute for people at moderate to high risk and 25 breaths per minute and more for people at high risk of severe illness or dying from sepsis. These cut-offs were used in the pathways as the GDG wished to

					balance antimicrobial stewardship and clinical judgement with physiological assessments.
RCGP	Full	21	11	See comment 5. (SS)	
RCGP	Full	21	21	A pulse rate of up to 100 is quoted as within normal range by numerous sources, including NHS Choices and texts on cardiology, suddenly in the context of infection a normal value is considered abnormal, and potentially needing urgent action / assessment. Not sure the retrospective use of pulse in septic patients informs the prospective management of infection. (SS)	Thank you for your comment. Following stakeholder comment the wording of recommendations have been altered to clarify the importance of clinical judgement. An isolated raised heart rate of 100 with no other criteria in a person with infection requires assessment for cause and treatment or safety netting only.
RCGP	Full	21	25	A temperature of less than 36.0 includes the normal adult range which is from 35.5 in women and 36,7 in men. Suddenly in the context of infection a normal value is considered abnormal, and potentially needing urgent action / assessment. (SS)	Thank you for your comment. Following stakeholder comment the wording of recommendations have been altered to clarify the importance of clinical judgement. An isolated temperature of less than 36 degrees with no other criteria in a person with infection requires assessment for cause and treatment or safety netting only.
RCGP	Full	21	31	See Comment 11. (SS)	
RCGP	Full	22	8	See comment 11. (SS)	
RCGP	Full	22	23	See comment 11. (SS)	
RCGP	Full	22	25	See comment 11. (SS)	
RCGP	Full	23	8	See comment 15. (SS)	
RCGP	Full	24	1	Neither fever or hypothermia are defined. (SS)	Thank you for your comment. The GDG reviewed these recommendations and agreed that further definition in the recommendation is unlikely to be helpful.
RCGP	Full	25	16	The use of language here might be	Thank you for your comment. These recommendations have

			-18	misunderstood; the non-medical practitioner does this mean anyone who isn't a doctor? Does it include parent, carer, midwife, nurse, paramedic or 111 operators. If so anyone with infection, unwell or feverish ultimately is needing to be seen by a GP or doctor because they are low risk and are sepsis suspects. The timing for this assessment isn't stated but the requirement previously made for physiological assessment almost completely precludes anything other than a face to face examination. GPs and Out of hours' services are not geared up to deliver assessment on this scale. You have written out any carer or parent's own judgement for the assessment of severity of infection GPs would see everybody with an infection potentially if this guidance was adopted. (SS)	altered following stakeholder consultation and this recommendation has been removed. The recommendations have also been altered to indicate appropriate remote assessment.
RCGP	Full	25	4	The use of the word ALL is unfortunate, suggest that an asthmatic or a patient with COPD or any other chronic condition will fall foul of meeting a high risk category by respiratory rate alone, you have made no allowance for a judgement to be made by the clinician. Every exacerbation of a respiratory illness gets an ambulance ride is that your intention? (SS)	Thank you for your comment. People with suspected sepsis outside acute hospital settings, who meet any of the high risk criteria, should be referred to emergency care services by the most appropriate means of transport. Risk stratification is intended for people who are thought to have an infection or fever and are suspected to have sepsis. The pathway offers exit points if a definite diagnosis other than sepsis is made.
RCGP	Full	25	7	The impact and reason for stating 1 hour is unclear and not supported by evidence as these people do not have septic shock. (SS)	Thank you for your comment. This recommendation has been removed.
RCGP	Full	25	7	Why just GPs and other doctors, Nurse	Thank you for your comment. Following stakeholder

				practitioners and Paramedics are excluded from assessing patients with these symptoms without evidence? (SS)	comments the need for assessment to be by a GP has been removed.
RCGP	Full	25	10	See comments 18. (SS)	
RCGP	Full	25	14	Why specify the emergency department and not include medical assessment unit or other appropriate hospital facility? (SS)	Thank you for your comment. The most appropriate place for a patient from either the high risk or moderate to high risk group could be the emergency department, or an acute admissions unit (such as a paediatric assessment unit) therefore the wording has been changed to reflect this. The best location for an emergency may vary locally and should be somewhere with resuscitation facilities.
RCGP	Full	33	11	This might be justified where septic shock is present but not all red categories indicate the presence of shock. It is not clear where the evidence for this derives in the pre-hospital arena. (SS)	Thank you for your comment. The GDG agreed that the priority should be to ensure rapid transport to hospital with the emergency department alerted to the patient's arrival. The GDG acknowledged that the majority of people in England are within an hour of a hospital. However in more remote areas where there is delay in getting to emergency departments it may be appropriate for local services to plan interventions by paramedics. Most of the evidence was derived from intensive, hospital or ED settings. The GDG however extrapolated the evidence and used their clinical experience to word recommendations.
RCGP	Full	38	10	It should first be considered and assessed if a sepsis register can collect appropriate clinical and epidemiological database given that much of the key information particularly out of hospital will need to be collated from lots of different sources. This is new and untested and would require significant GP and OOH commitment. Scope and assess first rather than just state we need a	Thank you for your comment. We agree that feasibility and piloting would be appropriate before a larger registry is rolled out.

				register without knowing if it might work, other registries have started small first. (SS)	
RCGP	Full	44	23	The second question ***In people with suspected sepsis how accurate are physiological signs and symptoms to identify whether sepsis is present?*** Is this actually the wrong question for the out of hospital arena, it is of necessarily retrospective in its analysis as it starts from the patients who are likely to be a different cohort of the patients with infection either in the community or GPs waiting rooms and determines which of their symptoms were indicative? Unfortunately, in the out of hospital arena that isn't the question we are faced with, it is prospective information we need to say what features of a septic patient make them stand out from the patients with infection or other medical condition such as asthma or COPD. This is why you have determined that normal physiological signs are abnormal in the presence of infection or feeling unwell. Is it possible that by asking the wrong question you have come up with the wrong answer? (SS)	Thank you for your comment. The guideline aims to effect cultural change, so presents a risk assessment to aid identification of the sickest patients. It does not try to provide management pathways for all patients with infection, but does aim for all clinicians to consider sepsis as a possible diagnosis in all cases of infection. The mentioned review aims to answer the question about which people with suspected infection are at risk of having sepsis and are therefore at risk of dying from sepsis. The identified evidence suggested that all signs and symptoms are indicators for sepsis. The low quality of the evidence meant that the GDG could not rely on the evidence alone but had to use their clinical experience to formulate recommendations in and out-of hospital settings. If a person is suspected of having an infection and presents with clinical signs and symptoms which could be an indication for sepsis, then that person should receive appropriate care as soon as possible. This approach is irrespective of the chronology of symptom presentation. Sometimes people with suspected infection will develop symptoms after having been seen by a clinician, sometimes a person will have developed those symptoms before having been assessed by a clinician. The evidence review looked for an association between signs and symptoms and the presence of sepsis in a defined population. The cause and effect relationship requires that signs and symptoms are present in order to then diagnose or assist in the diagnosis of sepsis. This clinical approach can

					however not be transposed onto study designs, which have to allow for a population (in this case people with sepsis) to be defined and identified first. This approach and the resulting findings are irrespective of whether the included studies are of a retrospective or prospective design.
RCGP	Full	67	37	Not clear how this was applied to GPs capacity to assess patients when non-medical feel that they have a low risk of sepsis? (SS)	Thank you for your comment. This recommendation has been removed.
RCGP	Full	68	15	Everyone with a possible infection is a huge group of the UK population at anyone time to suspect sepsis in particularly if they ALL have to be assessed by a GP or doctor. 111 for instance if they followed your guidance could not send anyone to a chemist for paracetamol or manage a single patient with flu. The impact of this is not considered in the economic considerations. (SS)	Thank you for your comment. Following stakeholder comments the recommendations have been altered and assessment by a GP has now been removed.
RCGP	Full	75	16 - 17	REMS uses mean arterial blood pressure which isn't readily available in primary care. (SS)	Thank you.
RCGP	Full	128	14	This recommendation removes the possibility of telephone assessment for people with infections so that makes 111s life easy and the GPs impossible. (SS)	Thank you for your comment. The recommendations have been changed following stakeholder comment.
RCGP	Full	133	6	If no evidence for hypothermia as a sign of sepsis yet it appears in your moderate to high risk groups, It is not understandable. (SS)	Thank you for your comment. The reference is unclear. Studies are included that looked at hypothermia and fever.
RCGP	Full	133	6	Ditto reduced urine output	Thank you for your comment. Reduced urine output is potentially a sign of acute kidney injury. This has been

					removed from high risk criteria following stakeholder comment.
RCGP	Full	134	28	Difficult to judge these as it is likely that the populations are wildly different and few if any are out of hospital presentations. Many are retrospective. (SS)	Thank you for your comment. All studies that fit the inclusion criteria as specified in the review protocol are included in this review. The quality of the evidence is assessed using validated tools and checklists. A retrospective study design does not automatically reflect poor quality of data. Furthermore, those studies retrospectively analyse variables that were prospectively collected and registered in medical records of patients.
RCGP	Full	175	30	See previous comments. (SS)	
RCGP	Full	192	General	Trade off between clinical benefits and harm, Sepsis with organ dysfunction (Organ dysfunction has to be present for there to be sepsis, new definitions). Will need to consider rephrasing in the light of the new Sepsis definitions. (SS)	Thank you for your comment. This sentence was misleading and has been removed.
RCGP	Full	192	General	No account is taken of burdensome interventions for those nearing the end of life. Not all sepsis or septic shock needs admission. Eventually in extremely sick or frail patients the aggressive treatment of infection becomes ultimately futile and burdensome for the individual, sepsis is an inevitable consequence and should be managed in line with the patient's wishes and or best interests. Ignoring this issue and option for managing both infection and sepsis is a weakness and a significant potential harm to a vulnerable group. (SS)	Thank you for your comment. The recommendations have been altered following stakeholder comment and include increased emphasis on clinical judgement. In acute hospital settings consideration of other diagnoses have been added to role of senior clinical decision maker. The GDG consider that appropriateness of care for each individual should also be considered and this has been added to the narrative.
RCGP	Full	192	General	Economic considerations are ducked here they have set the net so broad it is inevitable that there will be an economic	Thank you for your comment. Following stakeholder comment the recommendations have been changed to include recommendations about remote triage and to

				impact as everyone will be referred to a GP even those with low risk symptoms. You have also removed the possibility of telephone advice or support all now need physiological assessment. In deciding not to decide where the line should be drawn have thereby you have not guided GPs. (SS)	remove the need for GPs to see people as was present in the draft version.
RCGP	Full	192	General	There is no review of evidence as there is no evidence to review for these suggestions. (SS)	Thank you for your comment. It is highlighted that no specific evidence review was carried out. Recommendations presented here are developed using evidence from reviews on signs and symptoms and on interventions.
RCOG	Full	General	General	This is a very thorough and well-written guideline and was well received by the members of the RCOG Guidelines Committee. We note and welcome that you refer to our guidance on sepsis in pregnancy and sepsis in the puerperium.	Thank you for your comment.
RCOG	Full	General	General	It is difficult to read the algorithms and flowcharts in their current format and size is not great. These flowcharts are usually used as quick reference guides in practice. Sometimes posted as they are on walls in clinical areas.	Thank you for your comment. The algorithms are not intended to be decision tools to be used in practice but summarise the guidance.
RCOG	Full	General	General	We identified a few typos/spelling errors – we suspect this will be identified and corrected in later drafts:	Thank you for your comment. We have proofread the document and corrected typos and spelling errors.
RCOG	Full	Figures 1-6	13-18	Colour cannot be pale. it is the skin that can be pale. Hence for consistency suggest using 'colour of skin, lips or tongue - ashen, blue or mottled.'	Thank you for your comment. This has now been amended.
RCOG	Full	Figure	13	Presumably patients with a temperature ≥38 are high risk – wonder if we need to	Thank you for your comment. The evidence available on temperature as a predictor of poor outcomes was of very low

		1		state this?	quality and was not consistent with high temperature being a good predictor of high risk. In addition, the GDG were concerned that people with severe infection are not diagnosed because of the expectation that they will have a high temperature and the GDG therefore agreed not to include high temperature and to emphasise that people may not have a raised temperature.
RCOG	Full	Figure 1	13	Have a high index of suspicion - would anaemia also come under this category as the UKOSS (an Obstetric Surveillance System) have identified this in their sepsis study.	Thank you for your comment. Following your comment we have reviewed the UKOSS studies to check if they added anything to the information already included in the guideline. The evidence did not suggest that anaemia specifically was an additional risk factor but that presence of co-morbidities was relevant. On review the GDG considered that the recommendations had not adequately emphasised that woman who were pregnant or recently pregnant were at risk because of non-pregnancy related factors as listed in other recommendations and the recommendations were therefore changed to ensure this was clear.
RCOG	Full	Figure 1	13	Typo in caption of 'young' Typo in 'contact' not 'contract' wIth Gp A infection.	Thank you for your comment. We have proofread the document and corrected typos and spelling errors.
RCOG	Full	Figure 2	19	Outcome for low risk group – noun verb dysjunction. Either ‘clinically assess and manage' or 'clinical assessment and management'	Thank you for your comment. We have proofread the document and corrected typos and spelling errors.
RCOG	Full	19	30	**(also page 71)**The risk of sepsis also extends to women who have had ventouse (vacuum) delivery, hence the term 'operative delivery' which includes CS, forceps and ventouse would be more apt. We tend to use the term ‘pregnancy remains’ rather than 'products of	Thank you for your comment. This list contains examples only and is not intended to be comprehensive. The GDG reviewed the suggested wording and agreed that ‘products of conception’ was more widely understood than ‘pregnancy remains’.

				conception'	
RCOG	Full	19	30	**(also page 71)**Chorionic villous sampling and amniocentesis should be in example list of invasive procedures.	Thank you for your comment. This list contains examples only and is not intended to be comprehensive.
RCOG	Full	19	33	**(also page 71)**I think an example of Group A infection such as sore throat should be mentioned here	Thank you- we have added an example.
RCOG	Full	20	1	**(also page 71)**Prelabour ROM. There is no mention of time from ROM. I do think this is important as there is so much variability about the use of antibiotic prophylaxis in term prelabour ROM. Could say 'prolonged, prelabour rupture of the membranes'	Thank you for your comment. The guideline does not intend to define pre-mature rupture of membranes and recommend antibiotic prophylaxis, but rather to highlight that this is a risk factor for mother and baby.
RCOG	Full	20	12	Would be safer to simply state ' blood pressure' as specifically mentioning 'systolic', conveys the message that 'diastolic' is unnecessary.	Thank you. We have made this change.
RCOG	Full	30	34	Typo in 'parenteral'	Thank you for your comment. We have amended this.
RCOG	Full	70	14	Consensus and ...	Thank you for your comment. We have proofread the document and corrected typos and spelling errors.
Royal College of Anaesthetists	General	General		Good to see that SIRS has been removed but the moderate risk criteria look a lot like SIRS criteria.	Thank you for your comment. This guideline does not intend to define sepsis but offer clinical parameters that can help identify people at risk of severe illness or dying from sepsis. Some of the clinical parameters used in the pathways will inevitably look similar to clinical parameters suggested in the past.
Royal College of Anaesthetists	General	General		There are concerns that the neutropaenic patient is under-triaged and comments have focussed on clinical discomfort in withholding antibiotics from patients with febrile neutropaenia.	Thank you for your comment. This was not our intention and we have added additional reference to the NICE Neutropenic sepsis guideline.
Royal College of Anaesthetists	General	General		Source control is perhaps the one area (including antibiotics within one hour) which has been shown to improve outcome.	Thank you for your comment. The recommendations on finding the source of infection have been altered to provide more emphasis on source control.

				Perhaps consideration of this should figure?	
Royal College of Anaesthetists	General	General		In light of the new international definitions, we would suggest the terminology be reviewed;Sepsis now clearly mandates the presence of organ dysfunction and his needs to be made clear. It would be preferable to launch after the new definitions had been released.	Thank you for your comment. We have included a chapter on the new sepsis definitions and clinical parameters in this guideline. This guideline does not aim to define sepsis but offer clinical trigger points that can help identify people at risk of developing sepsis and ensure that those people receive appropriate care. Organ dysfunction is represented by clinical parameters included in the pathways. Therefore, the new definitions do not contradict our recommendations.
Royal College of Anaesthetists	General	General		We would advise that the algorithms are reviewed and made more concise.	Thank you for your comment. We have worked with the NICE editors to improve the algorithms.
Royal College of Anaesthetists	General	General		Give fluids as soon as possible – but the algorithm says to wait until the lactate test comes back – contradictory.	Thank you for your comment. The GDG considered that lactate is a venous lactate which should be available quickly and would not significantly delay fluid delivery.
Royal College of Anaesthetists	General	General		Why not use a trigger point from a validated score such as NEWS score or the new qSOFA criteria to better quantify which patients with infection have, or at high risk, of having sepsis?	Thank you for your comment. The guideline did not find evidence of validation of NEWS and qSOFA has not been validated in UK settings. The GDG has however recommended that further research on whether early warning scores can improve the detection of sepsis in pre-hospital settings and the ED be conducted.
Royal College of Anaesthetists	General	Rec 18-19		Recommendations 18-19 – 'high risk or moderate-to-high-risk-of dying'. It would be useful to see how risk is quantified. The new qSOFA criteria show that having one of altered mentation OR Systolic BP ≤100 OR RR ≥22 gave a mortality risk of approximately 2-3%.	Thank you for your comment. The evidence used to inform the guideline was of low quality and expertise of the GDG group and knowledge of normal parameters influenced the criteria. The criteria chosen in moderate to high risk are slightly broader than those in qSOFA but as qSOFA does not predict 20% of people at high risk of mortality the GDG considered this acceptable. As qSOFA has not been validated in UK populations the GDG felt it was not appropriate to recommend qSOFA itself but to define criteria based on the evidence and expertise mentioned above.
Royal College of Anaesthetists	Gener	Rec 1		Recommendation 1 "suspect sepsis if a person presents with signs and symptoms	Thank you for your comment. The recommendations have been amended to clarify the importance of clinical judgement

	al			that indicate possible infection, even if they do not have a high temperature' This advice is rather non-specific and may not be useful in a clinical setting. . Infection can be posited for virtually any condition where a patient is unwell so this means blood gases, cultures etc. have to be done on every patient seen by a doctor?	in assessment. The wording hopes to ensure people think about the possibility of sepsis but does not suggest all people with infection need investigation.
Royal College of Anaesthetists	General	Rec 9		Recommendation 9 comprises 6 of the 7 criteria used for the NEWS score – why not use the NEWS scoring cut-offs (or the qSOFA criteria) for escalating care/assessment?	Thank you for your comment. The GDG did not consider there was adequate evidence to recommend NEWS or qSOFA. NEWS has not been validated in primary care or emergency departments and qSOFA has not been validated in UK populations. The GDG felt it was more appropriate to define criteria based on the evidence identified through this guideline and clinical expertise.
Royal College of Anaesthetists	General	13		(p13,14,25) Outside hospital settings - GPs see, on average, 1 septic patient every 1-2 years. The algorithms will completely swamp the GP service and the 999 service. For any patient with infection/fever/feeling unwell assessment by a GP is mandated e.g. for any patient on oral steroids (regardless of dose!); for any surgery (non-defined) in the last 6 weeks; for tachycardia 91-130 or for resp rate 21-24? How many patients normally have a HR of 91? How many have a HR of 91 or a respiratory rate of 21 with a cold (and a temperature)? Anxiety or pain may also cause these physiological changes. A GP has to see the patient within 1 hour if they fulfil any moderate-to-high risk criteria (page 25) – is this feasible in today's NHS?	Thank you for your response. Following stakeholder comment the recommendations have been altered to clarify the population included, to increase the emphasis on clinical judgement and the need to be seen by a GP within a time period has been removed.
Royal College of	Ge	14	Ge	There has been concern amongst acute	Thank you for your comment. The wording of the

Anaesthetists	neral		neral	medical consultants that the moderate criteria will lead to unmanageable over-triage of the acute medical admission cohort. This has implications for service delivery.	recommendations has been changed to indicate that this population in the guideline are people with infection and a suspicion of sepsis. People in this group are at moderate to high risk of serious morbidity and mortality and the recommendations are planned to ensure they are assessed. The assessment can be done by a suitably qualified clinician and not a senior medical decision maker.
Royal College of Anaesthetists	General	14	General	Use of lactate >2mmol/l to place moderate risk straight to high risk without treatment or assessment of response to treatment will also result in over-triage and potentially lead to inappropriate use of broad spectrum antibiotics.	Thank you for your comment. People in this category will already have been seen by a healthcare professional and alternative actions can be considered. The evidence suggests that if the person has 2 or more moderate to high risk criteria, infection and suspected sepsis, a raised lactate indicates an increased risk of mortality.
Royal College of Anaesthetists	General	14	General	Should the seniority of the reviewing doctor for high risk patients be At least ST3 or ST3+ rather than simply ST3? This is a level not usually associated with the description 'senior decision maker'. This highlights the urgency of the patients in the high risk group.	Thank you for your comment. The wording has been altered and does say a doctor of grade CT3/ST3 or above or equivalent depending on local arrangements.
Royal College of Anaesthetists	General	14	General	Should other cultures, as appropriate, be included in the flow diagram? It would be easy to see how a false positive culture from blood could occur and a urine culture be missed.	Thank you for your comment. The algorithms are a balance between indicating main actions in a flow diagram and ensuring they are readable. For that reason only main actions such as taking blood cultures before giving broad spectrum antibiotics are listed.
Royal College of Anaesthetists	General	14	General	Consultant review is suggested after the second bolus of fluid or failure to improve after 30 minutes. This may have implications for service delivery dependent upon which consultant they mean; i.e base team or critical care.	Thank you for your comment. The GDG discussed this recommendation at length and reviewed it following stakeholder comment. This group of patients are those who are not responding to initial resuscitation and therefore likely to have highest risk of mortality. The GDG intended that this could be a consultant covering patients who may be critically unwell and this could be a consultant from acute medicines, anaesthetics, or the emergency department. This has been clarified in a footnote.

Royal College of Anaesthetists	General	Rec 14		Recommendation 14 'Only measure oxygen saturation if equipment is available'. This recommendation seems a little obvious as oxygenation saturation cannot be measured if the equipment is not available. Perhaps this needs to be reworded?	Thank you for your comment. The wording of the recommendation has been altered slightly to clarify meaning.
Royal College of Anaesthetists	General	34	9	The rate of fluid administration of 500mls in 15 mins is 2000mls/hour which exceeds the maximum delivery speeds of most pumps by a factor of two. Whilst this may encourage physician bolus which would improve monitoring, it may lead to the risk of over resuscitation if IV lines are just "opened up."	Thank you for your comment. The IV fluids recommendations are from published NICE guidelines.
Royal College of Anaesthetists	General	38		NEWS has already been shown to work for detecting sepsis. Also see qSOFA criteria paper.	Thank you for your comment. The review for the guideline did not find evidence for early warning scores in all settings, specifically in primary care or emergency settings. The guideline already includes recommendations to consider use of early warning scores in hospital settings. Detail about qSOFA has been added to the Full guideline chapter 6. However, qSOFA has not been validated in UK settings.
Royal College of Anaesthetists	General	39		Sepsis is caused by the body's immune and coagulation systems being switched on by an infection". Please see new Sepsis definition – its organ dysfunction consequent to a dysregulated host response to infection that encompasses multiple pathways (including immune and coagulation). There is also a new definition for septic shock that includes hypotension and hyperlactatemia.	Thank you for your comment. Information about the new definitions has been added to chapter 6.
Royal College of	Ge	Re		Recommendation 44 – "give a broad	Thank you for your comment. The evidence in adults

Anaesthetists	neral	c 44		spectrum antimicrobial at the maximum recommended dose as soon as possible (within 1 hour of identifying any high risk criteria). What is the strength of the evidence base that antibiotics within one hour are beneficial? Sterling et al (Crit Care Med 2015; 43:1907-15) recently published a meta-analysis showing "no significant mortality benefit of administering antibiotics within 3 hours of emergency department triage or within 1 hour of shock recognition in severe sepsis and septic shock". Fitzpatrick et al (Clin Microbiol Infect. 2015 Nov 11. pii: S1198-743X(15)00974-X. doi: 10.1016/j.cmi.2015.10.034) looked prospectively at 679 adults with Gram negative bacteraemia in ten English hospitals and found inappropriate empiric antibiotic therapy was not associated with mortality. Many other studies not cited in the review show the same. In a prospective before-after study, Hranjec (Lancet Infect Dis 2012;12:774–80) showed major outcome improvement with a delay in initiating antibiotics, even in patients who were shocked. The guidelines rightly conclude (page 402 and 405) that "Comparison of the evidence for benefit for reduction in mortality for antibiotics within 1 hour versus 3 hours was inconclusive because of differences in populations and settings". Yet despite this statement, p405 states "The clinical evidence showed that	showed a reduction in all-cause mortality when antibiotics were administered within up to 3 hours. The GDG considered that recommending antibiotics within 1 hour for people in the high risk group would ensure a better benefit. The GDG also agreed that it was appropriate to recommend a 3 hour window for people at moderate to high risk without organ dysfunction. This is because the evidence suggested that there was only a minor additional benefit of early therapy when comparing the evidence for mortality reduction for antibiotics within 1 hour versus 3 hours. Evidence examining antibiotic delay in people with suspected sepsis is observational, and as such inherently open to bias not usually found in randomised studies. The Sterling systematic review conducted meta-analyses of observational data and the findings need to be interpreted with the strength of evidence in mind. The guideline clinical evidence report on antibiotic delay acknowledges the very low quality of the studies. None of the mentioned studies were included in the guideline for the following reasons. The Fitzpatrick 2016 study was published after the date cut-off for this guideline. The Sterling 2015 study was excluded due to an unclear methodology; the studies included in its meta-analysis were however assessed and, if appropriate, included in the analysis for this guideline. The other mentioned studies did not fulfil the criteria of the review protocol. The statement on page 405 was an error and has been corrected to reflect the uncertainty of the effect. No evidence on delay in antibiotic therapy was identified of sufficient quality to make a recommendation with confidence that antibiotics could wait until after a given time.

				for adults, administering antibiotics in less than one hour had a clear clinical benefit in terms of reduction in mortality" Isn't this directly contradictory? Where is the evidence for the recommendation that the highest risk patients would benefit if treatment is given within 1 hour? The duration of sepsis prior to presentation is not known. There is a distinct risk of unnecessary overuse of antibiotics. It is worth noting that the American College of Emergency Medicine have abandoned time to first dose of antibiotic as a quality metric because of a lack of evidence and antibiotic abuse. (e.g. Pines JM, Isserman JA, Hinfey PB. THE MEASUREMENT OF TIME TO FIRST ANTIBIOTIC DOSE FOR PNEUMONIA IN THE EMERGENCY DEPARTMENT: A WHITE PAPER AND POSITION STATEMENT PREPARED FOR THE AMERICAN ACADEMY OF EMERGENCY MEDICINE. J Emerg Med; 2009;37:335–40. and Sucov A, J Emerg Med 2013;45(1):1–7.	
Royal College of Anaesthetists	General	Rec 48		Recommendation 48 – Suggest using physiological track and trigger systems to monitor patients at a minimum of every 30 minutes. How feasible is 30 mins on a general ward? If the recommendation is 'such a system' it could be advisable to use NEWS from the outset.	Thank you for your comment. The patients specified in these recommendations are people with a high risk of severe illness or death from sepsis and the GDG considered that they are the group who require most intense monitoring. An earlier recommendation (recommendation 8 in the draft version of the guideline) does suggest use of EWS in hospital settings should be considered.
Royal College of	Ge	Re		Recommendation 50 'A consultant has to	Thank you for your comment. The GDG discussed this

Anaesthetists	neral	c 50		be notified to attend in person if the lactate doesn't fall by more than 20% within 1 hour'. Alternatively, consultant has to be notified if high risk patient fails to respond within 1 hour of initial antibiotic and/or iv fluid. This recommendation may be impractical, particularly during the early hours of the morning.	recommendation at length and reviewed it following stakeholder comment. This group of patients are those who are not responding to initial resuscitation and therefore likely to have highest risk of mortality. The GDG intended that this could be a consultant covering patients who may be critically unwell and this could be a consultant from acute medicines, anaesthetics, or the emergency department. This has been clarified in a footnote.
Royal College of Anaesthetists	General	Rec 115		Recommendation 115 - where is the evidence that an LP is contraindicated if coagulation results fall outside the normal range or platelets are below 100. Or for shock? This is poor advice as the LP result may be vitally important, especially in an immunosuppressed patient e.g. for fungus. Doing an LP is a judgment call based on individual benefitrisk assessment – a CT scan may be useful prior.	Thank you for your comment. The recommendation is adapted from the NICE guideline CG102 Bacterial meningitis and meningococcal septicaemia in children and young people. We have added the involvement of a consultant in making the decision to do an LP to the recommendations.
Royal College of Anaesthetists	General	352	and general	What evidence is there that lactate is so useful for all these conditions? Table 87 and Tables 108-112 on the lactate evidence shows the quality of evidence is very low. The paragraph on page 352 is equally damning. So why is the effort and cost to measure lactate being mandated? Lactate adds little to predictive validity over the new qSOFA criteria.	Thank you for your comment. The GDG acknowledged that the evidence was not strong enough to justify determining a particular lactate threshold on a rule in or rule out basis. The GDG considered that the context in which lactate would be used was important. The evidence suggested that specificity was higher at higher lactate levels indicating that those patients with higher lactate levels were more likely to have poor prognosis. Lactic acid is an indication of poor perfusion and higher levels of lactate are consistent with a more compromised circulatory system. The GDG considered that as a group mortality is higher in the group of patients who have higher lactate level. The GDG therefore agreed to make a recommendation informed by the evidence and their experience. Studies on the new sepsis criteria came to similar

					conclusions. The new qSOFA criteria are meant to function as an early warning trigger and lead to further investigation. They are not meant to function as a definite diagnosis for sepsis. While there was a statistical benefit of adding lactate to the qSOFA criteria, there was no meaningful improvement in predictive validity. The study authors concluded that lactate could potentially help in identifying people with intermediate risk of developing sepsis.
Royal College of Emergency Medicine	Full	General		There are several references to patients under the age of 18 needing senior review – ST4 or above. The evidence for this appears to be one study of patients managed during 1997-1999. The numbers in this case controlled study of meningococcal disease are small and circa 60% of cases were children under 5. NICE recognise that this study is of low quality. Question 1 – Has the GDG considered the degree to which medical training has changed for Emergency Medicine and Intensive Care medicine trainees in the last 16 years in making this recommendation?	Thank you for your comment. Following stakeholder consultation the definition of senior decision maker has been amended to recognise that doctors trained in emergency medicines will have the necessary skills as also may other health care professionals. The wording is therefore changed to specify people with paediatric or emergency care training or equivalent experience.
Royal College of Emergency Medicine	Full	General		**Paediatric ST4 or above** Question 2 – Has the GDG considered the barriers to achieving this if the only recommended route to hospital is 999 ambulance to the Emergency Department? (Not necessarily a Paediatric ED. Paediatric Assessment Units may be preferable)	Thank you for your comment. Following stakeholder comments this has been amended to clarify that the emphasis was on the ability to provide appropriate emergency care and this was not intended to specify emergency department only.

Royal College of Emergency Medicine	Full	General		Question 3 – If time zero is to be the time at which any high risk factor is identified, has the GDG considered the resource implications for Emergency Departments if they are to deliver antibiotics within an hour (when the clock started pre-hospital)?	Thank you for your comment. We have clarified this to indicate that this is within one hour of when criteria are assessed in a hospital setting, which may be on arrival in emergency department or when measured on the ward.
Royal College of Emergency Medicine	Full	General		The only advocated route to hospital for patients with moderate to high risk criteria assessed by GPs in the community is 999 ambulance to the Emergency Department. Question 4 – Has the GDG considered that paediatric assessment units or adult medical assessment units may be appropriate for patients assessed in the community with moderate to high risk criteria assessed by GPs?	Thank you for your comment. The recommendation says they should be sent urgently to emergency care. We have clarified this in the algorithm. Following stakeholder comments we have clarified the wording to emphasise that assessment units and other such settings may be appropriate depending on facilities available.
Royal College of Emergency Medicine	Full	General		The only advocated route to hospital for patients with moderate to high risk criteria assessed by GPs in the community is 999 ambulance to the Emergency Department. Question 5 – Has the GDG group considered the implications for increased attendances at EDs? Question 6 – Has the GDG considered that in some local health setups, children may be better served by being transferred direct to Paediatric Assessment Units (where “Paediatric ST4 and above” doctors are based)?	Thank you for your comment. The most appropriate place for a patient from either the high risk or moderate to high risk group could be the emergency department, or an acute admissions unit (such as a paediatric assessment unit), therefore the wording has been changed to reflect this. The best location for an emergency may vary locally and should be somewhere with resuscitation facilities. The population the guideline is trying to capture is people with infection plus a suspicion of sepsis. The guideline aims to empower healthcare staff to make a diagnosis based on assessment and clinical judgement but also to lead to a cultural change where people think about sepsis. The risk factors highlighted in the guideline, and recommended approach following identification of those, is not intended to

					be a management pathway that replaces clinical judgement, but a tool to encourage clinicians to be able to place patients on a pathway should they have concerns that a patient might have sepsis because of an infection and a definitive diagnosis cannot be made outside of hospital. It was a difficult balance and the GDG had to make a judgement about where they wanted to draw the line, as criteria too narrow would miss some people, and too wide would trigger many false positives. The GDG considered that although the recommendations may have some impact on hospital attendances, this would be in patients that would benefit from treatment, some of which would have been missed with sepsis. The GDG felt this was an appropriate balance and following stakeholder consultation altered the criteria that would trigger hospital admission even further. The guideline is not attempting to identify everyone with an infection and treat those, only to treat those who could have sepsis because clinical concern is raised following a thorough assessment and history taking. The population presenting to primary care are likely to be individuals who would have presented anyway, however if a clinician in the community is concerned about a patient based on their symptoms and assessment and a definitive diagnosis cannot be made and treated out of hospital, then the GDG considered it is warranted that those patients should be seen in hospital because they may have sepsis or be in septic shock. If that does not turn out to be the case, it is likely they may still have benefitted from treatment because, based on a clinician's judgement and assessment, they were deemed to be unwell. Following stakeholder comments we have clarified the wording to emphasise that assessment units and other such

					settings may be appropriate.
Royal College of Emergency Medicine	Full	General	General	The format of the guideline needs to be more workable, with a quick reference pathway for each age group. The content makes sense and doesn't suggest anything we don't really already know. Clinicians would just have to check their scoring observation charts for adults and children to see if they are scoring to recognize sepsis. They quote specific heart rates and resp rates for sepsis in children in age groups and we would need to ensure that paeds charts correspond. Most Emergency Departments (ED) may not have this on their observation charts.	Thank you for your comment. The algorithms now include separate algorithms for children under 5, 5-11 year olds, 11-17 year olds and those over 18 years.
Royal College of Emergency Medicine	Full	13		Fig 1 ...spelling / typo in title; reads youg rather than Young.	Thank you for your comment. We have proofread the document and corrected typos and spelling errors.
Royal College of Emergency Medicine	Full	13		Suggests that all moderate to high risk should be sent to the ED via 999 ambulance. This would be better “send to secondary care” as many children’s assessment units can manage these cases rather than overload the ED.	Thank you for your comment. The recommendation stated that the patients should be sent urgently to emergency care and does not specify 999 ambulance or that they are sent to the emergency department. We recognise that there may be different settings where appropriate care can be provided. The wording in the algorithm has been changed.
Royal College of Emergency Medicine	Full	14	General	(p14-16) Over reliance on the lactate to guide unspecified fluid challenges. If a patient triggers based on clinical findings having a normal lactate we would suggest amending to “give fluids” rather than “consider fluids”.	Thank you for your comment. We have changed the formatting to ensure emphasis is on the initial risk assessment. The lactate is used to direct the immediacy of fluid administration and senior support. The GDG were concerned with the possibility of fluid overload if fluids are not required. Of note these values are pre fluid resuscitation and so are

				Quantify fluid bolus (e.g. up to 30ml/kg)	different from the current use in critical care guidelines or the Sepsis- 3 “new definitions” where criteria for septic shock are following fluid resuscitation. The GDG have therefore not changed this recommendation. Detail of fluid bolus is included in the recommendations.
Royal College of Emergency Medicine	Full	14	Lactate boxes	(p14-16) We recommend formatting boxes so mmol/L is on one line and remove spaces from mmol / L	Thank you for this suggestion. We have worked with the NICE editor to improve layout of the algorithms.
Royal College of Emergency Medicine	Full	14	Fig 2	Very prescriptive stating that all children with lactate >2 or high risk criteria need immediate review by ST4 paeds for children >12 – 17. This could be difficult to achieve for many units...better to state senior decision maker	Thank you for your comment. Following stakeholder consultation the wording has been altered to indicate that this may be paediatric or emergency care ST4 or equivalent.
Royal College of Emergency Medicine	Full	15	Fig 3	The document suggests all patients go to an ED via 999 ...for moderate to high our recommendation is to refer all to secondary care / hospital, as many children’s assessment units would manage these cases.	Thank you for your comment. We have clarified what is meant by emergency care in the recommendations and altered the wording in the algorithm.
Royal College of Emergency Medicine	Full	17	Fig 5	The document again suggests all patients go to an ED via 999 ...for moderate to high our recommendation is to refer all to secondary care / hospital, as many children’s assessment units would manage these cases.	Thank you for your comment. The most appropriate place for a patient from either the high risk or moderate to high risk group could be the emergency department, or an acute admissions unit (such as a paediatric assessment unit) therefore the wording has been changed to reflect this. The best location for an emergency may vary locally and should be somewhere with resuscitation facilities.
Royal College of	Full	20	10	“Consider using an early warning score in	Thank you for your comment. The GDG did not consider that

Emergency Medicine				hospital settings” Question 6 – Could the GDG consider just “Consider using an early warning score” There is discussion in the guideline that early warning scores may not be validated in primary care, but they can be useful in the pre-alert process to hospital.	the evidence supported use of an early warning score in this setting but recognised the need for further research in this area by developing a research recommendation.
Royal College of Emergency Medicine	Full	25	32	Investigations to include BM too? Or mention as part of blood gas to include lactate and Blood sugar	Thank you for your comment. The recommendations have now been changed and both glucose and lactate have been added.
Royal College of Emergency Medicine	Full	31	4	If followed this would vastly increase the number of PICU referrals	Thank you for your comment. Referral to critical care in this context meant having a discussion with a critical care consultant to seek their advice on escalation of care and make them aware that the patient may need critical care. It does not mean that all the high risk patients with a lactate level of 4 or above should be in critical care. The critical care consultant may feel that the patient is being adequately treated on the ward. The meaning of the term referral has been clarified further in the LETR.
Royal College of Emergency Medicine	Full	34	4	(p34 and 408, lines 4 and 6, and 100) Consider changing “postmenstrual age” to “corrected age” as per later in the document	Thank you for your comment. This has now been amended to ‘corrected gestational age’.
Royal College of Emergency Medicine	Full	466	and general	High flow oxygen is an element of many current sepsis bundles regardless of pulse oximetry saturation level. I have read the discussions presented in the guideline in detail.	Thank you for your comment. The guideline is making recommendations on the evidence available. Given the paucity of evidence it was not appropriate to make a ‘do not’ recommendation. The GDG felt that the lack of evidence for oxygen therapy could not lead to an explicit description of which patients do not need oxygen.

				Question 7 – In light of the current practice of some centres to administer high flow oxygen to **all** septic patients (evidence based or not) does the guideline need to be more explicit in describing which patients do not need oxygen?	
Royal College of Nursing	Full	General	General	Due to compensation in children, recommend continuous monitoring or observations every 15 minutes if high degree of suspicion/risk for sepsis. Reference local escalation policies for the deteriorating child	Thank you for your comment. The recommendation is for a minimum of monitoring every 30 minutes which the GDG considered appropriate if continuous monitoring is not available. In such circumstances the GDG considered that staff would also be completing other duties such as reviewing fluids and performing blood tests. The recommendation does not preclude more frequent monitoring if clinically appropriate.
Royal College of Nursing	Full	General		Document very lengthy in descriptions, greater impact on "Sepsis Six "sooner in the text recommended. Algorithm flow charts are very congested and difficult to follow, concern this may cause more time reading documentation and guidelines than treating the patient.	Thank you for your comment. The Full guideline provides the detail of the evidence reviews and GDG discussions. The NICE version contains the recommendations only. The algorithms present an overview of the guideline and will be available to download separately from the recommendations from the NICE website.
Royal College of Nursing	Full	General		'Patients' and 'people' used interchangeably. Suggest utilising one and maintaining it throughout document for consistency	Thank you for your comment. In the recommendations we have used 'people with suspected sepsis' or similar in line with the NICE convention. We appreciate that it would be good to be consistent throughout the documents, however using 'people with suspected sepsis' does not work well in some instances. We also refer to children and young people and so in some instances, patient is a less cumbersome term to use.
Royal College of Nursing	Full	General		The full guidance has useful information and guidelines, however it tends to be repetitive and disjointed. Information required on how to treat sepsis within a	Thank you for your comment. The Full guideline includes the evidence and discussion of the evidence for each recommendation. Some recommendations were informed by multiple evidence reviews and there are separate

				hospital environment occasionally jumps to community settings and back which disrupts flow of the document as a whole.	recommendations for different age groups so some repetition is inevitable. Following consultation we have re-ordered the recommendations to improve flow in the short version of the guideline.
Royal College of Nursing	Full	19	General	(p19-23) Consider subheadings such as 'Children 5-11yrs' 'Children under 5yrs' to guide the reader through the document easily and identify a specific section if needed	Thank you for your comment. We have added headings as you suggest.
Royal College of Nursing	Full	19	3	*(p19 onwards)* *'Identifying sepsis and people with increased risk of sepsis'* This new definition of sepsis seems complex and has too many variables. It would be helpful to have a simple and clear definition, which takes into consideration management of low risk and high risk patients. There is currently no guideline on how to monitor "low risk patients" with infection in order to prevent it getting worse and developing into sepsis. It simply says use clinical judgement. This advice has proven problematic and contributes to the current inconsistency and variation in practice. The proposed guidelines do not seem to include pyrexia in the definition. This is mentioned later in the guideline, in 1.3.11 where the advice is not to use temperature as the sole predictor of sepsis. This advice can however also be said for all the other	Thank you for your comment. We have clarified the wording following consultation. The guideline is not specifying a definition of sepsis rather aiming to use criteria to indicate those with suspected sepsis with potentially worst outcomes and ensure they receive appropriate assessment and treatment. The majority of people with infection will have low risk of sepsis so monitoring is not necessarily appropriate. NICE guideline CG50 already makes recommendations for use of track and trigger systems for unwell adults in hospital settings. The evidence available on temperature as a predictor of poor outcomes was of very low quality and was not consistent with high temperature being a good predictor of high risk. In addition the GDG were concerned that people with severe infection are not diagnosed because of the expectation that they will have a high temperature and the GDG therefore agreed not to include high temperature and to emphasise that people may not have a raised temperature. The GDG recognised that there is a small difference

				parameters described in the definition i.e. heart rate, respiratory rate, blood pressure, altered mental state and lactate. Also page 145 6.2.3.2.1 Table 47 states that there is very low quality of evidence with regards to pyrexia but low quality evidence is also applicable to other variables – heart rate and blood pressure. The symptoms or signs for high risk compared to moderate to high risk are not significantly different. From theoretical and academic points of view one can understand why this is separated, but from practical bedside point of view, this makes things complex. For example, a patient could present with the following: - heart rate is 131 (high risk) or 120 (moderate to high risk) - systolic blood pressure is 85 (high risk) or 93 (moderate to high risk) - not passed urine for 18 hrs (high risk) or 12 hours (moderate to high risk). Should this parameter not be in line with NICE Acute Kidney Injury guidelines for simplicity which states AKI is present if urine output is <0.5mL/kg/hr for more than 6 hours It is not clear why '*tympanic'* temperature is specified (page 21 - line 25)	between the high risk and moderate to high risk criteria. The GDG considered that a balance needed to be made between ensuring those at most risk are assessed quickly, and not overwhelming resources or leading to inappropriate antibiotic use. Parameters have been chosen to ensure those at highest risk have most urgent treatment but with a recognition that people with moderate to high risk criteria are also at risk. Clinical judgement is also always required. The recommendation about urine output in high risk criteria has been removed. Tympanic temperature is specified as the guideline aimed to be consistent with other related NICE guidance. The Fever in under 5s guideline made specific recommendations about use of tympanic temperature.
Royal College of	Full	20	11	Suggest using word "'recommend' using an	Thank you for your comment. The wording of

Nursing				Early Warning Score (EWS) in hospital settings" rather than 'consider'	recommendations reflects the strength of the evidence. It is NICE policy to use the word 'consider' for recommendations for which the evidence of benefit is less certain.
Royal College of Nursing	Full	21	General	Clear guidelines, but repeating previous pages. Symptoms documented haphazardly, would be easier to read if these were grouped in an order (for example: join lines 17&25,7&24,19&26,4&21,5&23)	Thank you for your comment. The recommendations are presented in a way that reflects the algorithms; they are based on age, setting and risk stratification.
Royal College of Nursing	Full	21	35-42; 1-2	(p21-22) Good information, could be highlighted to draw attention to parameters	Thank you for your comment.
Royal College of Nursing	Full	25	19	*'Managing and treating sepsis in hospital'* Should consideration for oxygen therapy be part of this section?	Thank you for your comment. As you suggest the recommendations for oxygen could be in this section. Oxygen therapy was however not included in this section because the GDG wanted to give prominence to aspects such as fluids, antibiotics and expert input. The lack of evidence for oxygen therapy and the cross-reference to other guidance for specific clinical scenarios contributed to the GDG's decision.
Royal College of Nursing	Full	25	32	*'Blood gas to include lactate measurement'* - Caution with venous lactate needs to be addressed. Particularly in the how and from where it is obtained process. Ideally it should be arterial lactate.	Thank you for your comment. The GDG recognised that arterial blood gases can be difficult to take and did not want to delay assessment and treatment by stipulating that arterial blood gas should be taken.
Royal College of Nursing	Full	26	1; 11; 15	These should read: 'give IV fluids' instead of "*give fluids"*	Thank you for your comment. We have added 'intravenous' when recommending fluids.
Royal College of Nursing	Full	35	1	*'Finding the source of infection'* There is no mention of the viral swabs.	Thank you for your comment. The GDG agreed that a thorough clinical examination should be carried out to look

					for sources of infection tailored to a person's clinical history and findings on examination. No evidence review was carried out because it was agreed that investigations should be specific to the clinical presentation of the patient with suspected sepsis. The recommendations are not intended to cover all possible scenarios but to make healthcare staff aware of sepsis and tailor their diagnostic and management approach accordingly.
Royal College of Nursing	Full	36	1	*Information and support for people with sepsis and their families and carers'* This section is welcomed. Consider additional recommendation for attendance at follow-up clinic for patients admitted to ICU with sepsis	Thank you for your comment. Follow up is included in CG82 Rehabilitation after critical illness in adults to which we cross refer.
Royal College of Nursing	Full	37	20	*'Training and education'* How is 'regular training' defined/interpreted - annually? Some trusts do this as part of an annual patient safety training but not all Consider recommendations for higher education authorities? Consider competency-based assessment, e.g. Critical care nurse training courses include sepsis as part of the syllabus and competency based assessment is also included in the course.	Thank you for your comment. The GDG agree that annual training appropriate to setting would be ideal. NICE guidelines do not have a remit to make recommendations for education authorities and/or competencies for professional groups.
Royal College of Nursing	Full	38	10	*Recommendations for research* We support the proposal to establish a UK Sepsis Registry. Utilization of electronic clinical early warning software and its impact could also be audited	Thank you for your comment. The research recommendation has been changed to reflect the NICE process for research recommendations. The GDG agreed to recommend that an epidemiological study on the presentation and management of sepsis in England be conducted.
Royal College of Nursing	Full	76	Scoring	Clearly set out and easy to read, this section could be inserted nearer the beginning of the document. An example of	Thank you for your comment. The guideline document was prepared following NICE templates.

			systems section	one of the flowcharts from Manchester Triage System (MTS) (table 18) would be useful to a reader unfamiliar with MTS	
Royal College of Nursing	Full	361	11	'Clinical evidence summary table: Initial Lactate: If quality of evidence has been found to be very low, why is lactate considered a major investigation for diagnosis and management of sepsis?	Thank you for your comment. The GDG agreed that lactate is a marker for illness severity but that the evidence did not warrant its use in initial risk stratification. Initial risk stratification for immediate antibiotics and for senior decision maker review does not use lactate but lactate level is used to guide fluid therapy and potential critical care involvement within the high risk group which the GDG considered was consistent with the quality of evidence.
Royal College of Nursing	Full	403	Recommendation 44	"arrange for immediate review" – what is the definition of immediate? Provision of a timeframe would be more realistic. "discuss with consultant" – is this any consultant or a specific consultant i.e. microbiology consultant? Or both?	Thank you for your comment. The GDG agreed that patients with high risk criteria should be seen immediately and did not want to define this further as this risked allowing delay before people are seen. A footnote has been added to the recommendation to indicate that the consultant who should attend can be the admitting consultant or a designated acute care consultant.
Royal College of Nursing	Full	425	105	Wording unclear around using/not using a pump	Thank you for your comment. The wording has now been changed.
Royal College of Nursing	Full	439	3	With regards to a sepsis registry establishment, whose responsibility will it be to enter data into the registry and what are the criteria for entry to ensure effective use of clinician time vs data input?	Thank you for your comment. The research recommendation has been changed to reflect the NICE process for research recommendations. The GDG agreed to recommend that an epidemiological study on the presentation and management of sepsis in England be conducted.
Royal College of	Ge	Ge	Ge	The Royal College of Nursing (RCN)	Thank you for your comment.

Nursing	neral	neral	neral	welcomes proposals to develop this guideline. The RCN invited members to review and comment on the draft guideline. The comments below also include the views of our members.	
Royal College of Nursing	Short	General		Due to compensation in children, recommend continuous monitoring or observations every 15 minutes if high degree of suspicion/risk for sepsis. Reference local escalation policies for the deteriorating child	Thank you for your comment. The recommendation is for a minimum of monitoring every 30 minutes which the GDG considered appropriate if continuous monitoring is not available. In such circumstances the GDG considered that staff would also be completing other duties such as reviewing fluids and performing blood tests. The recommendation does not preclude more frequent monitoring if clinically appropriate or escalation according to local policies.
Royal College of Nursing	Short	General		The shorter version of the guidelines is concise, with good short informative sentence construction.	Thank you for your comment.
Royal College of Nursing	Short	17	15	'*Blood gas to include lactate measurement'* - caution with venous lactate needs to be addressed, particularly in the how and from where it is obtained process. Ideally it should be arterial lactate.	Thank you for your comment. The GDG recognised that arterial blood gases can be difficult to take and did not want to delay assessment and treatment by stipulating that arterial blood gas should be taken. The GDG considered that a venous sample is usually adequate and that the relative ease of collection outweighed concerns about accuracy.
Royal College of Nursing	Short	17	24; 7; 13	(p17; 18) These should read: 'give IV fluids' instead of "give fluids"	Thank you for your comment. We have added 'intravenous' when recommending fluids.
Royal College of Nursing	Short	34	10	*Information and support for people with sepsis and their families and carers'* This section is welcomed. Consider additional recommendation for attendance at follow-up clinic for patients admitted to ICU with sepsis	Thank you for your comment. Recommendations about follow up following ICU admission are included in NICE guideline CG83 Rehabilitation after critical care.
Royal College of	Sh	36	19	*'Training and education'*	Thank you for your comment. The GDG agree that annual

Nursing	ort			How is 'regular training' defined/interpreted - annually? Some trusts do this as part of an annual patient safety training but not all Consider recommendations for higher education authorities? Consider competency-based assessment, e.g. Critical care nurse training courses include sepsis as part of the syllabus and competency based assessment is also included in the course.	and mandatory training appropriate to setting would be ideal. NICE guidelines do not have a remit to make recommendations for education authorities and/or competencies for professional groups.
Royal College of Nursing	Sh ort	38	26	*'Recommendations for research'* We support the proposal to establish a UK Sepsis registry. Utilization of electronic clinical early warning software and its impact could also be audited	Thank you for your comment and this suggestion. A study of the utilisation of early warning software and its impact is likely to require a different study design. Please note that the research recommendation has been changed to reflect the NICE process for research recommendations. The GDG agreed to change the wording and recommend that an epidemiological study on the presentation and management of sepsis in England be conducted.
Royal College of Paediatrics and Child Health	Full	18	Ge ne ral	As presented the algorithm is even less discerning than that published by UK Sepsis Trust and will result in an unacceptably large number of children being investigated for sepsis and treated with intravenous antibiotics. This has implications for patient safety and patient experience and so risks compromising quality of care. There are also issues around antimicrobial stewardship. The physiological parameters as defined will place a large number of children with essentially self-limiting viral illnesses in the "high-risk of sepsis" stratification group. The cut-offs are appropriate but there is no	Thank you for your comment. Following stakeholder comment the recommendations have been altered to clarify the importance of clinical judgement and the need to consider other diagnoses to ensure people are not treated inappropriately. Bronchiolitis is specifically included as an example of an alternate diagnosis in the under 5 age group. The Sepsis Six algorithms are developed by the Sepsis Trust which has agreed to work with NICE in implementing these guidelines as part of the NHSE Sepsis action plan. The UK Sepsis Trust plan to update the Sepsis Trust algorithms to reflect the NICE guideline.

				explicit scope for the application of clinical judgement in their interpretation. Importantly identification of only one high risk criterion is required in the context of suspected infection to force an aggressive response to sepsis. In fact any child with bronchiolitis is also likely to trigger the algorithm on the basis of two or more moderate criteria. The proposed clinical response for all these children is then senior medical review (fine) but with an imperative to cannulate, bleed and start antibiotics. I believe this is unnecessary. In contrast the new Sepsis 6 algorithm differentiates red flag sepsis criteria on which such a response would be based and still leaves room for the exercise of clinical discretion and regular, periodic review of patients in whom there is remaining doubt. This would appear to be a good operational solution to an old problem. A recent audit in our DGH suggests that 5-8% of children presenting for acute paediatric assessment satisfy SIRs criteria based on the presence of fever and tachycardia (APLS limits). Of these 2/3 end up with a diagnosis of viral illness and half of the rest with a focal infection which might be successfully treated with oral antibiotics. We estimated that application of the first Sepsis 6 algorithm (which was still more	

				stringent than that proposed by NICE) would have tripled the number of children we treat with intravenous antibiotics on our unit.	
Royal College of Paediatrics and Child Health	General	General	General	This guideline on sepsis management for children and adults is is very relevant and comprehensive and includes useful algorithms	Thank you for your comment.
Royal College of Paediatrics and Child Health	General	Definition of senior clinical decision maker for children.	Paediatric ST4 or above to review all children with high risk criteri	Unfortunately, many hospitals would not be able to meet this requirement, because ST3 doctors and speciality doctors often work as middle grades and there may not be a resident ST4 or consultant. Perhaps say “discussion with on call consultant recommended?”	Thank you for your comment. The GDG have now clarified that this is ‘paediatric or ED ST4 or above or equivalent’ in recognition of the fact that the original wording was unhelpful. Local arrangement may include an ST3 who is acting up for example.

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Royal College of Paediatrics and Child Health	General	Managing children under 5 with suspected sepsis in acute hospital setting	Respiratory rate> 60 in children under 1 yr	Unfortunately, using this criteria on its own would lead to many children with viral bronchiolitis being given antibiotics and having unnecessary blood tests and X rays. The BTS/SIGN guidelines for bronchiolitis would suggest that antibiotics should not be given routinely. 80% of LRTIs in young children are viral.	Thank you for your comment. Following stakeholder comment the role of the senior clinical decision maker in considering alternative diagnoses and management has been emphasised to prevent over treatment. The consideration of bronchiolitis as an alternative diagnosis is included as an example in the under 5 group.
Royal College of Paediatrics and Child Health	General	Managing children under 5 with	Pulse rate >160 /min in chi	Unfortunately, using this criteria on its own would lead to many children under I yr with viral infections or acute wheeze being given antibiotics unnecessarily and having blood tests. A degree of judgement needs to be used by an experienced doctor, if other high risk symptoms and signs are NOT present. Tachycardia which does not improve after control of fever would be of greater concern.	Thank you for your comment. Following stakeholder comment the role of the senior clinical decision maker in considering alternative diagnoses and management has been emphasised to prevent over treatment.

		suspected sepsis in acute hospital setting	ldren under 1 yr		
Royal College of Paediatrics and Child Health	General	13		Need to include children with cancer and other immunodeficiencies or co-morbidities in statement about higher index of suspicion	Thank you for your comment. Impaired immunity associated with drugs or illness is included in the risk factor list.
Royal College of Paediatrics and Child Health	General	18		Children over 1 month but under 5 years? Separate algorithm for neonates needed?	Thank you for your comment. The GDG recognise that the current age groups could be sub-divided further and while this may be appropriate for different settings in implementing the guideline it risked making the guideline too unwieldy.
Royal College of Paediatrics and Child Health	General	31		Give parenteral antibiotics to all neonates who appear unwell even without fever?	Thank you for your comment. The wording in the recommendations has been changed to highlight that the population are people with suspected sepsis.
Royal College of Paediatrics and Child Health	Short	1		1.1 While it is important we recognise sepsis should there be at some point in this document a clear balance in some cases between sepsis recognition and treatment and antimicrobial stewardship, overtreatment and mis-diagnosis. Especially in children there is a real risk that services will become overloaded and increase patient harm if SEPSIS protocols	Thank you for your comment. The GDG considered the balance between sepsis recognition and treatment and antimicrobial stewardship throughout guideline development. Antibiotics within one hour are only recommended in those at highest risk because of this concern. Following stakeholder comment the recommendations have been changed to increase emphasis on clinical assessment and consideration of other diagnoses.

				are adequately utilised.	
Royal College of Paediatrics and Child Health	Short	1		Even in the short guidance I think that definitions need to be present. There is still confusion over sepsis, septicaemia, SIRS, red flag sepsis for both the public and health care professionals. *I note this has been included at the end but this should be brought to the beginning*	Thank you for your comment. We have added information to the short guideline and the Full guideline about definitions of sepsis. The 'context' section following the recommendations is standard NICE format.
Royal College of Paediatrics and Child Health	Short	1		The diagrams contain far too much text and detail to be useful. While I understand they are probably illustrative the amount of information contained is likely to get lost.	Thank you for your comment. We have worked to improve the layout and wording of the algorithms.
Royal College of Paediatrics and Child Health	Short	3	17	"*Consider using an early warning score in hospital settings*" would probably be more correct has consider using a 'scoring system or bespoke proforma". There is no evidence early warning scores are effective outside of ward environments.	Thank you for your comment. 'Consider' is used to indicate the lack of evidence for early warning scores and the recommendation is to use a structured assessment.
Royal College of Paediatrics and Child Health	Short	4	17	*Ask the person, parent or carer about frequency of urination in the past 18 hours* - what is the rational for 18 hours. This will be a difficult question to ask parents. Why not 24 hours which the parents/carers are likely to have a better understanding of. 1.2.9 – assessment of feeding should be added	Thank you for your comment. This recommendation has been amended following stakeholder comment.
Royal College of Paediatrics and Child Health	Short	4	24	Should be High, Moderate and Low – high to moderate is confusing	Thank you for your comment. The GDG preferred the term moderate to high to emphasise that some people within this group are at risk of significant morbidity or death.

Royal College of Paediatrics and Child Health	Short	7	5	1.3.3 – and burns (risk of TSS)	Thank you for your comment. Breeches of skin are included in risk factors and the GDG considered that this covered burns.
Royal College of Paediatrics and Child Health	Short	8	3	While I feel the term " *not responding to social cue*s" wasn't brilliant it seems odd to have different wording on the sepsis chart compared to the feverish illness one.	Thank you for your comment. In the case of children under 5 where we have adapted the risk stratification tool from the Fever in under 5s guideline (NICE guideline CG160) we do use the term 'not responding to social cues'. The GDG did not consider this wording was appropriate for older children and adults.
Royal College of Paediatrics and Child Health	Short	8	3	Practically this is not a useful way of highlighting risk of RR. While I understand the CDG must follow evidence at the same time the NHS is not paper lite, in fact in many places it is still completely paper based. The values for the HR and RR while be very difficult to enforce without e-systems. This will lead to poor implementation. I do think the GDG need to consider the implications of this.	Thank you for your comment. The GDG considered this at length but were also concerned about having ranges that were inappropriate and risked over treatment. Following stakeholder comment the ranges have been simplified and presentation improved.
Royal College of Paediatrics and Child Health	Short	11		Flushed – is there really evidence flushed is an independent predictor of sepsis? I am not sure that 'flushed' made it to the NICE fever guideline so not sure how it could be different for sepsis?	Thank you for your comment. This was an error and has been removed from the recommendations.
Royal College of Paediatrics and Child Health	Short	12	16	1.3.8 – assessment of feeding should be added	Thank you for your comment. The GDG reviewed this and agreed not to include feeding. Feeding difficulties has also been removed from the risk stratification criteria. The GDG agreed that feeding difficulties can be common in children who are unwell but were not a specific indication of children who might have sepsis. The inclusion of feeding difficulties in the draft guideline increased the risk of children being included in a sepsis pathway unnecessarily.
Royal College of	Sh	13	26	1.3.9 – assessment of feeding should be	Thank you for your comment. The GDG reviewed this and

Paediatrics and Child Health	ort			added	agreed not to include feeding. Feeding difficulties has also been removed from the risk stratification criteria. The GDG agreed that feeding difficulties can be common in children who are unwell but were not a specific indication of children who might have sepsis. The inclusion of feeding difficulties in the draft guideline increased the risk of children being included in a sepsis pathway unnecessarily.
Royal College of Paediatrics and Child Health	Sh ort	14	16	1.3.14 – children with diagnoses other than cancer and on immunosuppressive drugs/systemic steroids should also be in this risk group	Thank you for your comment. The list is not meant to be exhaustive and cannot include all possible examples.
Royal College of Paediatrics and Child Health	Sh ort	15	8	1.3.17 – recognise that if BP starts rising in unwell children, that this can be a sign of shock	Thank you for your comment. The GDG reviewed this recommendation following your comment. They considered that it was difficult to make more detailed recommendations about BP in children because of the paucity of data and preferred to emphasise that BP may appear normal in children with shock as this may be more useful information in early stages.
Royal College of Paediatrics and Child Health	Sh ort	23	15	1.5.23 – many children in this age group with a fever with focus - tonsillitis, otitis media, UTIs etc - will easily score 2 or more in the moderate risk group, necessitating blood tests. This will increase workload and impact on patient flow in the ED. Will the Guideline take this into account? I note that the GDG itself states: "The GDG considered that the evidence indicated that blood tests had poor performance overall for diagnosis or prognosis." (page 352 of Full Guidleline). While WBC and CRP are useful in decision making, there are many children with a focus for their fever who do not need these tests – simply a period of observation.	Thank you for your comment. The wording of recommendations has been changed to include appropriate emphasis on clinical judgement to ensure people are not treated as suspected sepsis inappropriately.

Royal College of Paediatrics and Child Health	Short	23	25	Is there really the evidence to justify a defining treatment decision on a lactate alone, particularly given the low quality evidence and the statement on p.370 that it has a poor sensitivity and serious consequences could arise if used to decide if a patient should be treated? I think much greater consideration should be given to the clinical picture in terms of treatment and fluids. Using lactate alone seems to take clinical decision making out of the equation.	Thank you for your comment. The recommendations do not use lactate alone to decide on treatment. All those with high risk criteria have clinical assessment with a senior clinical decision maker, antibiotics and discussion with consultant. Lactate is used when considering fluids and critical care referral. For people with 2 or more moderate to high risk criteria a raised lactate suggests that they should be treated as high risk.
Royal College of Paediatrics and Child Health	Short	27	8	1.5.38 – many infants 2-3 months presenting with bronchiolitis have a mild fever (<38.5°C) and we do not start antibiotics, or even perform blood tests	Thank you for your comment. The wording of recommendations has been changed and additional recommendations have been added to clarify that the intention is to consider if someone might have sepsis and to include appropriate emphasis on clinical judgement to ensure people are not treated as suspected sepsis inappropriately. The recommendation in the under 5 years group uses bronchiolitis as a specific example of an alternative diagnosis.
Royal College of Paediatrics and Child Health	Short	27	18	1.5.39 - many children in this age group with a fever with focus - tonsillitis, otitis media, UTIs etc - will easily score 2 or more in the moderate risk group, necessitating blood tests. This will increase workload and impact on patient flow in the ED. Will the Guideline take this into account? I note that the GDG itself states: “The GDG considered that the evidence indicated that blood tests had poor performance overall for diagnosis or prognosis.” (page 352 of Full Guideline). While WBC and CRP are useful in decision making, there are many children with a	Thank you for your comment. The wording of recommendations has been changed to consider if someone might have sepsis and to include appropriate emphasis on clinical judgement to ensure people are not treated as suspected sepsis inappropriately.

				focus for their fever who do not need these tests – simply a period of observation.	
Royal College of Paediatrics and Child Health	Short	34	16	1.10 – worth drafting short patient info leaflet explaining sepsis to go with published guideline	Thank you for your comment. NICE produce a document called Information for Patients which will accompany the guideline.
Royal College of Pathologists	Full	General	P 83 P 204 P 302 P 308 P 352 [*summary of wbc usage*]	[WBCS- band/absolute nos]…No mention of Panton Valentine leucocidin producing *S. aureus* contact/history in patient or contacts and effect on peripheral WBC [may be falsely low]	Thank you for your comment. Cytotoxins and cell physiology are beyond the scope of this guideline. The pathways use clinical parameters to identify people at risk of dying from sepsis and help ensure those people receive appropriate care. The use of specific serological and microbiological tests is determined by protocols at each trust and laboratory.
Royal College of Pathologists	Full	Ch 14		Of the team of 32 drawing up the GL none appear to be microbiologists, which is a shame given the expertise clinical microbiologists have in ensuring correct	Thank you for your comment. The GDG consists of 13 healthcare professionals and lay members. The emphasis in the guideline is on early recognition and early management of people at high risk of morbidity and mortality from sepsis

				tests are performed and empirical antimicrobials chosen.. The importance of a goo dhistory is mentioned but could be more emphasised since microbiologists often diagnosis the organism merely from pertinent questions, then thorough examination adds weight to the diagnosis.	and the GDG were primarily people involved in those early phases of the guideline when a microbiologist may not be involved. The GDG was aided by a co-opted microbiologist who provided expert advice.
Royal College of Pathologists	Full	14	Figure 2	This algorithm and indeed all the algorithms in the document are overly complicated and not suitable for use in routine clinical practice. The algorithm has been reviewed with acute medicine colleagues. The algorithm in the UK Sepsis Trust guidance is simpler and easier to use.	Thank you for your comment. We have worked with the NICE editor to improve the layout of the algorthims. The UK Sepsis Trust plan to update the Sepsis Trust algorithms to reflect the NICE guideline.
Royal College of Pathologists	Full	407		(p407, 510) No evidence for the choice of empirical antimicrobial agents given . Narrow/ broad spectrum agents- recommended- but often the underlying agent – Gram positive or negative may be more obvious…and can avoid unnecessarily broad spectrum antimicrobials. Ceftriaxone is a broad spectrum agent with no anti-pseudomonal cover or intrinsic anti-exotoxin activity, may be less effective in eg GAS sepsis. Cephalosporins are associated with C difficile, and narrower spectrum Gram positive spectrum agents such as flucloxacillin / daptomycin , [or broader spectrum such as gentamicin or pip-tazo]- are less likely to provoke *C difficile*. .	Thank you for your comment. No evidence review was carried out for choice of antimicrobial agents. This would not have informed national recommendations as choice of antimicrobial is influenced by local resistance patterns and requires local guidelines in many cases.
Royal College of	Ge	Ge		A workable definition of sepsis is needed-	Thank you for your comment. A section on the new

Pathologists	neral	neral		new sepsis definitions are due to be releas ed shortly by the Society of Critical Care Medicine (S CCM) and the European Society of Intensiv e Care Medicine (ESICM). The new definiti ons should address some of the already hig hlighted problems of lack of sensitivity and specificity of the current definition based on SIRS criteria.	definitions and clinical trigger points has been added to the guideline. This guideline does not aim to define sepsis but offer clinical trigger points that can help identify people at risk of developing severe illness or death from sepsis and ensure that those people receive appropriate care.
Royal College of Pathologists	General	Section 1.2		No mention of the effect on temperature of concomitant paracetamol or NSAIDS usage – the latter common in severe GAS SSTI presentation, causing late presentation and masking symptoms..	Thank you for your comment. The GDG considered that it was not possible to include all issues affecting presentation such as use of paracetamol or NSAIDS. The recommendations emphasise that temperature is not necessary to consider the possibility of sepsis.
Royal College of Pathologists	General	Section 1.2		'*In contact with Gp A Streptococcal infection'*- should also apply to general population and child sepsis not just pregnancy, and to raise the suspicion of the protean manifestations of exotoxin driven Gram positive sepsis [gastroenteritis/myalgia /rashes of some STSS] No mention of history of recurrent SSTi as clue to cause of sepsis – e.g. necrotizing pneumonia	Thank you for your comment. The GDG considered that group A streptococcal infection is generally common but of particular concern in this group.
Scottish Antimicrobial Prescribing Group	Full	14		(page 14-19) In any potentially septic patient it is important to know the formal lab glucose level (as opposed to a fingerprick test), both to help stratify how unwell the patient might be and to ensure that the important differential diagnosis of diabetic ketoacidosis does not go unrecognised. The management algorithms contain no mention of	Thank you for your comment. We have added glucose to the recommendations for adults following stakeholder comment.

				checking this for any group. While this should be self-evident to acute physicians, it should probably be stated explicitly that this is part of the assessment process, for non-expert users.	
Scottish Antimicrobial Prescribing Group	Full	14		(pages 14, 16, 18) The algorithms for community assessment state that the presence of any high risk criteria should place the patient in the high risk category. This is not stated for the inpatient algorithms. It would help those working in an emergency to include on the pathway a similar comment.	Thank you for your comment. We have amended the algorithms.
Scottish Antimicrobial Prescribing Group	Short	30	1	The recommendation for GPs and ambulance staff to give antibiotics if transfer time is likely to be more than 1 hour. There are 2 issues here – logistics for availability of stock of antibiotics in all locations where likely to be needed and more importantly training of ambulance staff to recognise sepsis accurately and give the correct choice and dose of antibiotic, acknowledging the issue of potential allergy.	Thank you for your comment. The recommendation has been re-worded to clarify that this should be considered in geographical locations where transfer time is routinely likely to be more than one hour. The GDG considered that transferring the patient to acute care is most important and agree that training of ambulance staff to recognise sepsis accurately, to take blood cultures and to give the correct choice and dose of antibiotic would not be appropriate.
Somerset Partnership	Full	General	General	clarify 'fluids' – as 'intravenous fluids', so this is not misinterpreted	Thank you for your comment. We have added 'intravenous' when recommending fluids.
Somerset Partnership	Full	General	General	Clarify 'hospital as 'acute hospital' as our Trust has community hospitals that don't offer acute services.	Thank you for your comment. We have made the change as you suggested.
Somerset Partnership	Full	180	30	Add patients who are anorexic	Thank you for your comment. The conditions included in this recommendation are examples. The GDG reviewed the

					recommendation following stakeholder comments and agreed that the conditions listed are the most common and that adding more examples would give the mistaken impression that the list was comprehensive.
Somerset Partnership	Full	Section 7	40, 43	Our Trust has emergency nurse practitioners who run the MIUs. They have advanced assessment and diagnostic skills – they would call an ambulance without referring to a GP or doctor. So the list of who should assess the patient needs to include practitioners with these skills, not just doctors or those 'medically trained'	Thank you for your comment. This recommendation has now been changed and could include nurse practitioners.
Somerset Partnership	Full	Section 7	40 - 41	This will be a challenge for our organisation as our community hospitals rely on an 'out of hours' medical service. This means that a DP or doctor assessing an unwell patient within an hour is often not practicable. In practice the ward nurses assess the patient, using the NEWs scoring system and the sepsis proforma, and if the doctor cannot attend quickly, they will call an ambulance if the patient is high risk. This is the same for our district nurses – if they found a patient at home who is unwell and triggering the high risk sepsis criteria, they would not call a doctor first, but would call an ambulance instead.	Thank you for your comment and this information. Following stakeholder comment the recommendations have been altered and the need for a GP to see a patient within one hour has been removed.
Somerset Partnership	Short	19	16	There are many advanced practice nursing and AHP roles where the practitioner has advanced assessment and diagnostic skills, as well as prescribing skills. Some may be in roles where it would be appropriate for them to be included in the list of practitioners.	Thank you for your comment. We are unsure which recommendation your comment refers to. Following stakeholder comment we have altered the description of clinicians to include people with equivalent skills to medical personnel previously listed.

Somerset Partnership	Short	36	2	In our organisation, patients are admitted with a range of Central venous access devices (CVADs), of which a PICC line is just one type. Please could this we broadened to reflect this.	Thank you for your comment. PICC lines are included here only as an example.
Somerset Partnership	Short	36	25	Add assistant Practitioners to the list – we have these roles throughout our organisation	Thank you for your comment. We have altered the recommendation following stakeholder comment and removed descriptions of types of practitioners to ensure no relevant personnel were excluded.
Somerset Partnership	Short	37	7	This would not be relevant to our staff as we do not provide acute care or critical care – our escalation is to call for a doctor or an ambulance. The escalation needs to be relevant to the practice area of the staff.	Thank you for your comment. We have altered the recommendation in response to your comment to ensure it is relevant to a wide group of healthcare professionals.
South Tees Hospitals	Short	3		(p3-9) Paediatric Algorithms: It's useful that they've stratified physiological criteria by age band but I think it's unnecessarily complicated, especially within the algorithms. As an example, 'respiratory rate in a child age 6-7 years, 24-26 breaths per minute'. Why not just say 26 breaths per minute? By the time they done this for every parameter in every age child it looks very complicated.	Thank you for your comment. The GDG considered this at length but were also concerned about having ranges that were inappropriate and risked over-treatment. Following stakeholder comment the ranges have been simplified and presentation improved.
South Tees Hospitals	Short	3		(p3-9) Paediatric Algorithms: It's interesting that they're putting so much reliance on lactate in determining treatment in the high risk group, particularly in younger children. I'm not sure where they've got this evidence from (I think it's probably extrapolated from adult data). Of course lactate is a useful measure but this should be in addition to other parameters, particularly in younger children who present	Thank you for your comment. The recommendations do not use lactate alone to decide on treatment. All those with high risk criteria have clinical assessment with a senior clinical decision maker, antibiotics and discussion with a consultant. Lactate is used when considering fluids and critical care referral. For people with 2 or more moderate to high risk criteria a raised lactate suggests that they should be treated as high risk. Studies with children are included in the evidence review.

				in cold shock much more readily than older patients. It seems to imply that lactate is the only thing that should be used to determine treatment.	The layout of the algorithms has been altered to make the place of lactate clear.
South Tees Hospitals	Short	3		(p3-9) Paediatric Algorithms: would like to see inotropes given greater prominence, even if given peripherally. As far as I understand, the reason children die of sepsis is because of a failure to restore cardiovascular normality. Fluids are of course important but I would like to see a statement along the lines of 'once 40ml/kg of fluid resuscitation has been given, consider starting inotropic support' or something along those lines. The reason I say this is partly due to the way paediatric critical care is organised. If an adult presents to a DGH with septic shock, it's likely that an intensivist will meet the patient relatively early as there will be an ICU on site. If a child presents to a DGH, the PICU will be some distance away and therefore we should try to encourage inotropes to be started early. This is reasonably anecdotal but I've had babies transferred to PICU with sepsis who have had 80ml/kg of fluid who are not on inotropes.	Thank you for your comment. The GDG recognise your concern and for this reason the recommendation is for early discussion with a relevant paediatric intensive care service to discuss and agree this approach.
South Tees Hospitals	Short	3		(p3-9) Algorithms: Low Risk category – *Baseline Heart rate is 10-15 beats/min	Thank you for your comment. This has been removed.

				more in pregnancy) ---we know what it means but this line there does not read right	
South Tees Hospitals	Short	3		(p3-9) Algorithms: new definition is being released same day of closing date for comments. How will this be reflected on the criteria, especially when new definition criteria is based on best available evidence and data	Thank you for your comment. Information about the new definitions has been added to the Full guideline in chapter 6. The GDG reviewed the recommendations in light of the new definitions and have not changed the criteria.
St George's University Hospitals NHS Foundation Trust	Full	General	General	**The population that should be managed as per these guidelines**- The 'High Risk' and 'Moderate to High Risk' populations. Whilst we understand the need to spread the net wide to include patients who fall outside the traditional presence of two or more SIRS criteria, the 'Action / Management' should be the same. In other words, the patient should have a minimum one 'High Risk' criteria or a minimum two 'moderate to high risk criteria'. Once a patient satisfies either (or both) they then should receive the same investigations and treatment.	Thank you for your comment. The GDG were concerned that the approach you describe was not in keeping with antimicrobial stewardship and would risk inappropriate use of broad spectrum antibiotics and may overwhelm resources. Following stakeholder comments they have reviewed this decision and did not think it should be changed.
St George's University Hospitals NHS Foundation Trust	Full	General	General	**Investigations** – All the recommended investigations are appropriate but we would include liver function tests as these are vital in sepsis, if not anything else as a baseline.	Thank you for your comment. Liver function tests were included in the evidence review and no evidence found. The tests specified are those the GDG considered most important for immediate assessment. The GDG recognised that other tests may be appropriate according to clinical presentation and judgement of senior clinicians but did not consider it appropriate to add it as a test at initial assessment. The review protocol to look for blood tests helpful in diagnosis of sepsis did include liver function tests but no evidence was found.

St George's University Hospitals NHS Foundation Trust	Full	General	General	**Little guidance on management** -The guideline seems to focus on identifying the 'high risk' population but gives very little guidance on how to manage this population. The triad of studies (Process, Arise and Promise) all compared EGDT with 'usual care'. But it must be recognised that 'usual care' included inserting a central line and commencing vasopressors early for refractory hypotension. The reduction in use of central lines in the 'usual care' group was due the lack of use in the purely hyperlactaemic shock group. All of the above studies treated early and aggressively in the 'usual care' group. These draft guidelines do not advise early and aggressive management of refractory hypotension. Similarly, there is no advice on titrating to lactate clearance in hyperlactaemic shock. The guidelines should also include resuscitation targets.	Thank you for your comment. The guideline has concentrated on early recognition and early management of people at high risk of morbidity and mortality from sepsis and ensuring that people who are at highest risk are directed towards healthcare professionals who can provide early and aggressive management as you describe. When the guideline was scoped it was recognised that excellent critical care guidelines already exist and that attention to earlier parts of the patient pathway were what was required. The title of the guideline has been changed to clarify that the guideline covers recognition, assessment and early management.
St George's University Hospitals NHS Foundation Trust	Full	General	General	**The guidelines stop at 'refer to critical care'**. The guidelines should concentrate on the treatment the patient should receive rather than limiting treatment to artificial boundaries. Each hospital should/ could decide where the treatment should be delivered. For instance the guidelines state that all patients with a systolic <90 mmHg or a lactate >4 should be referred to critical care. We do not think this is appropriate. Some departments will give a patient IV fluids and if the systolic is <90 mmHg or the	Thank you for your comment. The wording has been changed to clarify that people at highest risk should be discussed with critical care staff. The reference to admission to critical care has been removed.

				MAP is <65 mmHg after a 30ml/kg fluid bolus, they will either insert a central line and commence vasopressors and then refer the patient to critical care. If however if the blood pressure improves and the lactate is clearing, the patient may be admitted to or remain on the ward.	
St George's University Hospitals NHS Foundation Trust	Full	General	General	**The identification of the high risk population is complex and lends itself to errors in management**. If the guidelines are followed strictly, a patient who has not passed urine for 18 hours may not receive intravenous fluids if the lactate is <2.	Thank you for your comment. The criteria have been altered and some criteria removed following stakeholder comments and 'not passed urine for 18 hours' is no longer included for people under 12 years as the GDG considered it was too unreliable to be included as a high risk factor in children. It has been retained for young people and adults where the GDG considered it was more reliable and may be only evidence of AKI. People with high risk criteria should be assessed by a senior clinical decision-maker and condition discussed with a consultant. The GDG considered that the potential risk of fluid overload is such that a 'consider' recommendation remains appropriate when lactate is less than 2mmol/litre.
St George's University Hospitals NHS Foundation Trust	Full	General	General	**Acute Kidney Injury** – the presence of AKI is taken in to account only in the 'Moderate to High risk' flow chart but not under the 'High Risk' flow chart. Is this an error?	Thank you for your comment. This is not an error. People who are already in High risk category will be in receipt of treatment and the finding of AKI on a blood test may influence decision-making for further treatment but will not change their categorisation. The inclusion of AKI in people at moderate to high risk would indicate that they are at higher risk than other criteria suggest.
St George's University Hospitals NHS Foundation Trust	Full	General	General	**Lactate to risk stratify treatment**- Although lactate may risk stratify outcome, the way it is used in the flow chart to risk stratify treatment (IV fluids), seems risky. A lactate of >4 should mandate not just IV	Thank you for your comment. The guideline uses lactate to stratify primarily for discussion with or referral to critical care. All people who fulfil high risk criteria and have been assessed by a senior decision-maker do require re-assessment and this is included in the recommendations.

				fluids but repeated measures to ensure a minimum clearance of 10% every two hours. Patients with a lactate of 2-3.9 should also have their lactate re-measured to ensure clearance. All patients with 'High Risk criteria' should receive IV fluids until there is evidence against it.	The GDG reviewed the recommendations on fluids for people at high risk and agreed that 'consider' was appropriate for people with lactate less than 2. The GDG were concerned not to cause fluid overload as this is a recognised concern in the care of critically ill people.
St George's University Hospitals NHS Foundation Trust	Full	General	General	**Source control** - There is no guidance on source control and how soon it should be done. If there is no evidence to include it in the guideline, then it should be a research priority?	Thank you for your comment. The recommendations on finding the source of infection have been altered to provide more emphasis on source control.
St George's University Hospitals NHS Foundation Trust	Full	General	General	**Organ dysfunction** – The guidelines do not refer to or define organ dysfunction. Patients with increasing number of dysfunctional organs are at increased risk of mortality. There has to be some recognition of this.	Thank you for your comment. This guideline does not aim to define sepsis or organ dysfunction. Instead, it provides clinical parameters that function as trigger points for the management of people who are at risk of severe morbidity or mortality from sepsis. This is in keeping with the latest 'definition' of sepsis and is discussed in chapter 6.
St George's University Hospitals NHS Foundation Trust	Full	General	General	**De-escalation**- Whilst escalation of treatment is important, there must be recognition that it may not be in the patient's interest to escalate treatment. This must be acknowledged.	Thank you for your comment. Additional emphasis has been added to the role of clinicians in considering other diagnoses and appropriate management.
The British Society for Antimicrobial chemotherapy (BSAC)	General	general		The algorithms are too complicated and will be difficult for clinical staff to follow	Thank you for your comment. We have worked with the NICE editors to improve the algorithms.
The British Society for Antimicrobial chemotherapy (BSAC)	General	short ver		The titles of criteria boxes in the algorithms and tables should be labelled as high, moderate or *no* risk,	Thank you for your comment. The GDG discussed altering the labelling of risk categories but agreed to leave them as low, moderate to high, and high risk. The GDG wished to

		sion guideline algorithms page 1 , table 1 page 4-6, table page 8-9 table 3 page 10-12, full guideline		i.e. not use the moderate to high risk title - short version guideline algorithms page 1 , table 1 page 4—6, table page 8-9 table 3 page 10-12, full guideline	emphasise that some people in the moderate to high risk group have a significant risk of mortality and careful assessment is required.
The British Society for Antimicrobial	Gener	short		• The high risk criteria of no urine output in 18 hours is too long to	Thank you for your comment. This recommendation has been changed.

chemotherapy (BSAC)	al	version guideline algorithms page 4—6, table page 8-9 table 3 page 10-12, full guideline		wait for children	
The British Society for Antimicrobial chemotherapy (BSAC)	General	short version		The comment in the algorithm adult low risk box in full and short version guidance ‘Baseline heart rate is 10-15 beats/minute more in pregnancy‘ needs extra text to clarify or be removed as	Thank you. This had been removed.

		guideline algorithms page 4—6, table page 8-9 table 3 page 10-12, full guideline		different heart rate in pregnancy referred to in high to moderate risk box anyway	
The British Society for Antimicrobial chemotherapy (BSAC)	General	short version guideline		Concerned with the difficulty to identify/ assess if existing or new confusion in the elderly patient, which will mean that the default will be to treat as new and managed as high risk and no there is no route back into moderate or no risk criteria if no other markers of high risk on further after investigation, resulting	Thank you for your comment. Following stakeholder comments the recommendations have been altered to increase emphasis on clinical judgement for alternative diagnosis and management decisions. Altered mental status was noted in the evidence review for the guideline and is also included in literature on new definitions as one of the indicators of increased mortality.

		algorithms page 1, table 1 page 4—6, table page 8-9 table 3 page 10-12, full guideline		in overuse of antibiotics and missed alternative diagnoses	
The British Society for Antimicrobial chemotherapy (BSAC)	General	Full page 21 Short	Line 2	Concerned that the threshold in the 12 and above guidance of oxygen saturation of less than 92% is too low for young adults	Thank you for your comment. In the absence of other evidence the GDG agreed to use the NICE accredited British Thoracic Society guidelines (BTS) to inform their recommendations on oxygen level. The GDG, which includes four paediatricians, reviewed the recommendations following stakeholder comment and considered the

		Table 1 page 5 Pg 6	Line 7		recommendation appropriate.
The Intensive Care Society	Appendix L	139		In Appendix L p139, the 20% albumin trial of Caironi 2014 has been excluded due the “incorrect interventions”. However the trial of 20% albumin and 6% HES by Dolech 2009 has been included. Again trial inclusion consistency is required.	Thank you for pointing out this error. This study has now been included in the analysis. The inclusion of this study has not changed the overall results and thus the conclusions of the evidence review remain.
The Intensive Care Society	Full	General	General	We welcome the NICE sepsis guidance in particular that they acknowledge different levels of risk and different treatment strategies based on this risk stratification (summarised in Fig 2). However, we are aware that the new international sepsis definitions are due to be published this month and include risk stratification too. They have taken a different strategy to develop these risk levels but have identified similar clinical parameters (namely respiratory rate, hypotension, raised lactate levels and decreased level of consciousness). In order not to confuse clinicians it will be vital to ensure that the various trigger thresholds align so that uniform guidelines can be implemented in all hospitals.	Thank you for your comment. The GDG have reviewed the new definitions and the recommendations in light of these. This has not resulted in change to management algorithms. We have added information on how the guideline fits with new international definitions in chapter 6.
The Intensive Care Society	Full	Gener	Gene	The early & increased involvement of consultants and critical care in the high-risk	Thank you for your comment and support. The GDG considered it was important that consultants are

		al	ral	sepsis cases is to be welcomed (recommendations 45 and 50). However, this is likely to have significant staffing implications in some hospitals and this is acknowledged in the economic evaluation. It will be important for managers and funders to make appropriate changes before these guidelines can be implemented. Also it should be recognised that parameters that might trigger a consultant review on a general ward for failure to improve (eg systolic blood pressure <90 mmHg after 1 hour of fluid resuscitation) may not require the same consultant review whilst in the intensive care unit.	involved early on and at key stages of decision making for the high risk group. This is initially recommended as a discussion which could be over the phone. The GDG considered that this group of patients are potentially very unwell and that it would be expected that the consultant would be aware that they are being treated under his/her care. The recommendation to attend is only if a patient with a high risk of mortality is not responding to treatment. Following stakeholder comments we have now excluded people already in intensive care from the guideline.
The Intensive Care Society	Full	424	13 - 14	On p424 L13-14 it states “A multivariable analysis in one study indicated that patients receiving albumin had a higher chance of death at 28 days compared to those receiving saline.” Is this the SAFE study? As page 425 states “A follow-up paper (SAFE 2011) presented more detailed data on the severe sepsis subgroup. A multivariate analysis showed that albumin was independently associated with a decreased 28-day mortality.” Has p424 been written incorrectly?	Thank you for your comment. The multivariable analysis comparing albumin with saline is taken from the SAFE study. The study showed that people with severe sepsis receiving albumin had a lower chance of 28-day mortality compared to those receiving saline. This sentence has now been corrected in the evidence statement.
The Intensive Care Society	Full	428	Paragrap	On page 428 paragraph 2, the GDG excluded the 6S trial (Perner 2012) on the grounds that the EMA have stated that HES is contraindicated in sepsis. However,	Thank you for your comment. The 6S trial was excluded because the intervention had not started within 6 hours of diagnosis. This has now been made clearer in the relevant section.

			h 2	the GDG have included the CHEST trial (Myburgh 2012) that used a similar HES that is also contraindicated in sepsis after the EMA ruling. Surely the inclusion/exclusion of trials should be consistent. As HES is potentially still available for other (non-sepsis) indications it would be appropriate for the GDG to recommend that HES not be used for sepsis.	The GDG decided to use the recommendations in the IV fluid therapy in adults guideline (NICE guideline CG174) and recommended that HES should not be used for IV fluid resuscitation in people with sepsis.
The Intensive Care Society	Full	493	8	We are disappointed to see that the GDG does not offer any recommendation about early goal directed therapy (page 493 line 8) despite this being the one area with the most highest quality, direct evidence available. We understand the GDG concerns that any recommendation might be misunderstood but not to make a recommendation despite good evidence will not help everyday clinicians to improve their management of septic patients. Furthermore the PROMISE trial was conducted in 56 acute hospitals in the UK and to not use this high-quality evidence for directly relevant guidelines will be demoralising for clinicians and patients. Why conduct a trial or volunteer to be a trial patient if the evidence generated is not going to improve patient care? Possible recommendations could have been, "Protocolised early goal directed therapy does not need to be instituted for all sepsis patients but for high risk patients individual	Thank you for your comment. The guideline deals with recognition, assessment and early management of people with suspected sepsis and this is now clarified in the title. A review of EGDT was included to assess what could be learned about early management. The studies of EGDT deal with first six hours and recruitment criteria for the trials were of people who had already received antibiotics and fluids. The priority in this guideline has been to ensure that people who need early antibiotics and fluids get them and are referred to those with critical care expertise who can provide the treatment described in the EGDT trials. The GDG did not consider it appropriate to make a recommendation on EGDT. The available evidence indicated no difference between EGDT and routine care which would potentially lead to a recommendation not to do EGDT. The GDG considered that the standard of routine care in the trials was very high and they were concerned that a recommendation saying not to carry out EGDT would be misinterpreted.

				patient goals should be set by experienced clinical teams".	
The Royal College of Midwives	Full	19		(and pages 20, 71) There is some confusion here about the definition of prolonged rupture of membranes - it would be clearer if it described it as longer than 18 hours in all contexts	Thank you for your comment. The recommendations are not intending to define prolonged rupture of membranes but rather to draw attention to prolonged rupture of membranes as a potential risk factor separately in mothers and in neonates.
The Royal College of Midwives	Full	27		The guideline should address the issue of the potential for dangerous overuse of antibiotics - and the absolute need to be clear about duration and spectrum of their use.	Thank you for your comment. The GDG were aware of the importance of antimicrobial stewardship which is why different risk levels have been identified and only those at high risk are given immediate antibiotics. Cross reference to the NICE guideline on Anti-microbial stewardship has been added to the Short guideline.
The Royal College of Midwives	Full	36		It would be helpful to name some of the appropriate charities and support groups that are referred to here. *'Give people with sepsis and their families and carers information about national charities and support groups that provide information about sepsis and the causes of sepsis'.*	Thank you for your comment. Recommendations do not usually contain this level of detail. However, this information will be included in the information for the public that is published alongside the guideline.
The Royal College of Midwives	Full	38		We agree with all the research recommendations here and think that this one needs urgent attention *'Can early warning scores, for example NEWS (national early warning scores for adults) and PEWS (paediatric early warning score), be used to improve the detection of sepsis and facilitate 3 prompt and appropriate clinical response in pre-*	Thank you for your comment.

				hospital settings and in emergency departments'	
The Royal College of Midwives	Full	39		Reference to the number of children that die of sepsis should appear in the introduction to prevent the guideline becoming adult focused.	Thank you for this suggestion. We were unable to find reliable statistics for this so have not added this.
The Royal College of Midwives	Full	73		This sentence is not clear - there is a missing word *'A pregnant woman's reduced immunity mea close contacts such as family members hav streptococcal infections.'*	Thank you for your comment. We have proofread the document and corrected typos and spelling errors.
The Royal College of Midwives	General	General		The RCM welcomes the development of this important guideline.	Thank you for your comment.
The Royal College of Midwives	General	General		It would be clearer to recognise neonates as a separate subgroup - as management differs in this wide age spectrum.	Thank you for your comment. The GDG recognise that the current age groups could be sub-divided further and while this may be appropriate for different settings in implementing the guideline it risked making the guideline too unwieldy.
The Royal College of Midwives	General	General		We look forward to the early development of a quality standard from this guideline to move practice forward. We presume that useful implementation tools will be identified within that.	Thank you for your comment. Sepsis has been referred by the Department of Health for development of a Quality Standard and we would expect usual tools to support a quality standard to be developed.
The Royal College of Midwives	Short	36		*'Ensure all healthcare staff and professionals are given skills training appropriate to their role in sepsis recognition'* Options for the models for this training should be offered here eg as part of skills and drills training	Thank you for your comment. The GDG agree that this could be part of skills and drills training in some settings
The Royal College of Midwives	Short	36		It would be helpful if the guidance could make clear recommendations that could be used in education eg in the school curriculum that could raise awareness	Thank you for your comment. NICE clinical guideline recommendations are directed to health professionals and NHS settings and not educational settings.

				amongst young parents of the importance of recognising serious illness	
The Society for Acute Medicine	Full	General	Multiple references	We recommend that where taking a blood sample for urea and electrolyte is advised it should also specify a serum bicarbonate. The reason is that increasingly this is being withdrawn from biochemistry analysis unless specified and metabolic acidosis associated with elevated lactate or other causes will not be recognised.	Thank you for your comment. The tests specified are those the GDG considered most important for immediate assessment. The GDG recognised that other tests may be appropriate according to clinical presentation and judgement of senior clinicians but did not consider it appropriate to add it as a test at initial assessment. The review protocol to look for blood tests helpful in diagnosis of sepsis did include bicarbonate but no evidence was found.
The Society for Acute Medicine	Full	26	50	We are concerned that the recommendation for a Consultant to attend in person is not warranted. There is a lack of evidence for this recommendation. In most hospitals receiving Acute medical emergencies there will not be 24/7 Consultant presence and the financial and workforce implications of mandating such are prohibitive at present. We recommend this is changed to discussed with Consultant. Discussion with Consultant, track and trigger observations and use of a sepsis bundle provides effective patient care.	Thank you for your comment. The GDG discussed this recommendation at length and reviewed it following stakeholder comment. This group of patients are those who are not responding to initial resuscitation and therefore likely to have highest risk of mortality. The GDG agreed that such a scenario warrants a consultant to attend in person because of the high mortality risk. The GDG intended that this could be a consultant covering patients who may be critically unwell, and therefore a consultant from acute medicines, anaesthetics, or the emergency department. This has been clarified in a footnote.
UK Sepsis Trust	Full	General	General	The Clinical Advisory Group of the UK Sepsis Trust, comprising expert clinicians across all clinical environments and including specialist boards of Paediatricians, Obstetric Anaesthestists and Obstetricians, has reviewed the NICE sepsis draft guideline. The Group has been at the fore of delivering operational interpretations of international clinical	Thank you for your comment.

				guidelines for sepsis since 2004, these interpretations entering the NHS as a common language and having been widely adopted. The Clinical Advisory Group of the UK Sepsis Trust welcomes this draft document in its effort to produce a pragmatic, deliverable set of guidelines with operational interpretation for diverse clinical environments for patients across the range of ages.	
UK Sepsis Trust	Full	General	General	We are delighted to have been granted the opportunity to working in collaboration with NICE to produce a series of clinical tools and decision aids to support the Guideline's launch and commit to doing so.	Thank you for your comment.
UK Sepsis Trust	Full	General	General	We concur wholeheartedly with the Guideline Development Group's view that the qSOFA tool proposed by the international definitions task force as an optional bedside recognition aid is not useful operationally as bedside test in the NHS, due to our reliance on existing track-and-trigger scoring systems within hospitals, and the clear difficulties in operationalising care delivery governed by two separate aggregate scoring systems.	Thank you for your comment. The qSOFA tool was not published when the guideline was being developed and was therefore not evaluated for inclusion in the guideline. We have added further detail about how the guideline fits with the new sepsis definitions in chapter 6.
UK Sepsis Trust	Full	General	General	To facilitate acceptance and implementation of this Guideline, we suggest that the use of language already embedded in NHS practice be useful. The	Thank you for your comment. The GDG acknowledges the importance of the work of the UK Sepsis Trust. The recommended interventions in the guideline were agreed by the GDG following a review of the evidence and differ slightly

				traffic light system proposed by the GDG incorporates red 'high risk' criteria, 5 of which (Altered mental state, RR>25, HR>130, Systolic blood pressure <90, non-blanching rash) are very similar or identical in parameters and thresholds to the 'Red Flag Sepsis' recognition strategy promoted by the UK Sepsis Trust (including its multiple Clinical Toolkits) in collaboration with 6 of the Royal Colleges and NHS England since September 2014. The therapeutic strategies recommended by the GDG in essence describe the Sepsis Trust's 'Sepsis Six' treatment pathway, which following publication of the NCEPOD report in October 2015 we know to be used in 94% of hospitals (NHS and private) in the British Isles. We submit that supportive narrative reference to these terms would broaden appeal of the Guideline and help to ensure acceptance and uptake. It would be naïve to assume that language will change following publication of the Guideline, and it would be naïve to assume that these aspects of the recommendations won't be seen for what they are.	from the current Sepsis Six. The GDG preferred not to use a term already in use but to outline the criteria individually.
UK Sepsis Trust	Full	General	General	Whilst we agree with the utility of the traffic light system, and welcome the added margin of safety presented by the escalation recommendations following identification of one or more 'moderate to high risk criteria', we contest that from an algorithmic perspective within acute settings the 'low risk criteria' (for adults and	Thank you for your comment. The aim of the GDG was to use consistent criteria in all settings. The GDG recognise that different aspects of the guidance will be more relevant in some settings than others and that how the guidance is displayed and implemented is likely to also differ in different settings.

				for children) are almost entirely an exclusion of moderate/ high risk criteria and from a decision making perspective therefore add little value. Low risk is implied by an absence of moderate risk.	
UK Sepsis Trust	Full	General	General	In adults, lactate is frequently measured in the hospital environment when patients are suspected as being critically ill using point of care or near-patient testing, and many Emergency Departments routinely measure lactate in non-trauma patients triaged to majors: the patient is typically reviewed with the lactate result within minutes of first assessment. The presence of lactate in Red Flag Sepsis criteria has further embedded this practice. It is operationally illogical, therefore, to include the prompt to measure lactate within the battery of important blood tests sent to the laboratory. Further, as identified repeatedly within the literature (and acknowledged within the new definitions) high lactate not only defines shock but is also one of the most important predictors of mortality. To recommend lactate's inclusion in the immediate algorithm is welcome, but we suggest that to place it in the algorithm for a clinician review with results at 1 hour may delay identification of cryptic shock with potentially adverse consequence-outcomes for patients with cryptic shock are similar to those for overt shock.	Thank you for your comment. The recommendations do not include lactate as a test to be sent to the laboratory.
UK Sepsis Trust	Full	Gener	Gene	We believe that there is a significant gap in the need to consider the importance of fetal	Thank you for your comment. Recommendations on CTG monitoring from CG 190 are being updated and the GDG

		al	ral (maternal) and figure 2, p13	tachycardia (and the need for fetal monitoring to detect it). We propose that, in the pregnant population, this be both a trigger factor for initiating screening and a High Risk ('Red Flag' using UK Sepsis Trust language) criterion. We propose that, as per the NICE Guideline for Intrapartum Care (CG190) recommendations for cardiotocogram (CTG) monitoring, the 'non-reassuring' threshold of ≥161 BPM be used as a moderate risk criterion in this population, and the 'abnormal' threshold of >180 be used as a High Risk ('Red Flag') criterion.	therefore preferred not to add detail to the guideline. We have added reference to that guideline in development in the related guidance section.
UK Sepsis Trust	Full	General	General (maternal) and figure 2, p13	We submit that, in 'moderate to high risk criteria' in the pregnant population, distinguishing between spontaneous and artificial rupture of membranes is unnecessary and indeed potentially harmful. Women who have had labour induced frequently experience gaps of many hours between artificial rupture of membranes and delivery, and are at increased risk of infection.	Thank you for this comment. We have removed 'spontaneous' from the recommendation.
UK Sepsis Trust	Full	General	General (P	Sepsis is not always a binary diagnosis in children. While the algorithmic approach presented is generally clear it may be beneficial to include a clearer "stop and	Thank you for your comment. Following stakeholder comments the recommendations have been altered to ensure adequate prominence is given to the importance of clinical judgement and consideration of alternative

			ae dia tric)	think" section whereby individual clinical judgement (especially at a senior level) can be used to arbitrate or record when decisions that go against guidance (either give or withhold antibiotics). Such 'holding' steps are included in the UK Sepsis Trust's Paediatric Sepsis Six tools and are welcomed by users.	diagnoses.
UK Sepsis Trust	Full	13	(G P)	(p13, 15) There does not seem to be a pathway by which a patient with an infection is not assessed by a GP or other medical qualified professional. Is it the intention that all people who have an infection are assessed by Primary Care or just those who present to the health service for assessment? What role exists for services including Paramedics, 111, Walk-in and Urgent Care, Midwives, Health Visitors, etc; and (within hospitals) Medical Assessment Units or other appropriate facility? The impact on service delivery is a concern and unquantified: the cohort of patients with potential infection in the countries at any one time is vast and would immediately overwhelm services.	Thank you for your comment. The guideline is organised by setting with recommendations for outside an acute hospital setting and in an acute hospital setting. People presenting outside an acute hospital setting may present to a variety of services and personnel. Following stakeholder comment the wording of the recommendation has been changed so that the need to see a GP and/or have a physical examination within a specified time period has been removed with more of an emphasis on clinical judgement. The guideline aims to empower healthcare staff to make a diagnosis based on assessment and clinical judgement but also to lead to a cultural change where people think about sepsis. The risk factors highlighted in the guideline, and recommended approach following identification of those, is not intended to be a management pathway that replaces clinical judgement, but a tool to encourage clinicians outside an acute hospital setting to be able to place patients on a pathway should they have concerns that a patient might have sepsis because of an infection and a definitive diagnosis cannot be made outside of hospital.

UK Sepsis Trust	Full	14	Figure 2	In adults, we do not see added value in the hospital setting for adults of having a discriminator between 1 and 2 moderate risk criteria. It is straightforward and operationally deliverable to recommend the sampling of bloods and competent decision-maker review within one hour in the presence of any single moderate to high risk criterion. The key 'ask' is clinical review and evaluation for the presence of acute kidney injury- this can and should be achieved within one hour.	Thank you for your comment. The GDG did not want to overload services and considered that people with one moderate to high risk criterion were likely to be at lower risk and take a longer time to review and consideration of blood tests was likely to be appropriate.
UK Sepsis Trust	Full	14	Figure 2	We are concerned that a high risk patient who is hypotensive but without hyperlactataemia (for example, a blood pressure of 75/35 but with a lactate of 1.9 mmol/l) will not be considered as in urgent need of fluid resuscitation under this algorithm. We submit that the need of the hypotensive patient for IV fluid is as urgent as the need of the patient with high lactate.	Thank you for your comment. The algorithm and recommendations indicate that fluids should be given to people with systolic blood pressure of less than 90 mmHg.
UK Sepsis Trust	Full	16	Figures 4 and 6	(and p18) Whilst we recognise a need for consistency between children and adults, the lactate thresholds, especially the 2-4 range in children will appear (to paediatricians) a little arbitary. There are likely to be differences between the values obtained by venous, capillary and arterial samples- the sampling method should be stated. We are concerned that a high risk child who is hypotensive but has a relatively normal lactate (for example, a 65kg 11 year-old with a blood pressure of	Thank you for your comment. Following stakeholder comments the recommendations have been adjusted to ensure senior review and support. The GDG reviewed the recommendations in light of your comment and do not agree that all children with a lactate under 2 with one high risk criteria should necessarily receive an immediate fluid bolus. There is concern about the potential of fluid overload and bolus fluids in this scenario need to be at the direction of the experienced paediatric clinician present.

				75/35 but with a lactate of 1.9 mmol/l) will not be considered as in urgent need of fluid resuscitation under this algorithm. We submit that the need of the hypotensive child for consideration for IV fluid is as urgent as the need of the child with high lactate.	
UK Sepsis Trust	Full	25	4 (GP)	Whilst we understand the didactic nature of algorithms, the use of the word 'ANY' is unfortunate in the narrative, in that it is entirely possible that an asthmatic or a patient with COPD or many other chronic conditions will fall foul of meeting a high risk category by respiratory rate alone, with no allowance for a judgement to be made by the clinician. A caveat would be helpful.	Thank you for your comment. People with suspected sepsis outside acute hospital settings, who meet any of the high risk criteria, should be referred to emergency care services by the most appropriate means of transport. Risk stratification is intended for people who are thought to have an infection or fever and are suspected to have sepsis. The pathway offers exit points if a definite diagnosis other than sepsis is made.
UK Sepsis Trust	Full	25	32	Is a blood gas absolutely necessary outside an acute care environment? Would measurement of a serum lactate in isolation using point of care testing add similar value and be more readily deliverable?	Thank you for your comment. Lactate is only recommended in an acute hospital setting.
UK Sepsis Trust	Full	26	12	Review of elevated lactate important to monitor response to therapy. We suggest add EITHER 'repeat lactate within 1 hour' OR repeat lactate after each 10ml/kg of intravenous fluid resuscitation administered	Thank you for your comment. The guideline does not specify how to monitor, rather the need to act if lactate has not responded following resuscitation.
UK Sepsis Trust	Full	26	29	We suggest that having two discreet thresholds for respiratory rate might be potentially confusing, should the recommendation for the identification of non-response be 25 as it is in the high risk criteria?	Thank you. We have altered this to 25 as you suggest.
UK Sepsis Trust	Full	28	24 (R	We are concerned that the statement "refer to critical care for review of central access	Thank you for your comment. The wording has been changed to clarify that people with apparent septic shock

			ecommendation 60)	and initiation of inotropes or vasopressors and admission to critical care" may lead to units particularly in District General Hospitals not commencing inotropes/vasopressors in a timely manner. Personnel with specific paediatric critical care skills are unlikely to be immediately available, and recommendations from ACCM-PALS suggest vasoactive agents be administered peripherally during resuscitation pending definitive central access.	should be discussed with critical care staff. The reference to admission to critical care has been removed.
UK Sepsis Trust	Full	34	19 (maternal)	We note the existing reference to the importance of continued bleeding or offensive vaginal discharge as needing particular attention. We suggest the feature of pelvic pain/tenderness be added to this statement. This would then make this statement more consistent with the widely used criteria for features that may indicate a pelvic infection (NICE accredited "UK national guideline for the management of pelvic inflammatory disease 2011. London (UK): British Association for Sexual Health and HIV.")	Thank you for your comment. The criteria used were discussed with a co-opted expert. Following stakeholder comment the GDG considered additions but felt that pelvic pain is likely to be a common complaint and would risk over inclusion.
UK Sepsis Trust	Full	75	22 Table 17	(and p79) We respectfully feel that the UK Sepsis Trust Clinical Toolkits, developed in collaboration with relevant Royal Colleges and supported by NHS England in a Level 2 Patient Safety Alert in 2014, are misrepresented: • We submit that these should be described broadly as a group, and referenced appropriately to the UK	Thank you for your comment. The GDG recognise the work of the Sepsis Trust. The aim of this review was to identify scores and their usefulness in diagnosing sepsis or predicting outcomes. The UK Sepsis Trust information was included for completeness. We have amended the name and added some explanatory information to the start of this section.

				Sepsis Trust website. • In section 6.1.1, the toolkits are inappropriately referred to in the singular and cited as 'Sepsis trust UK toolkit' as an example of an Emergency Department screening tool only. Toolkits exist for Primary Care, Prehospital Services, Emergency Departments, Acute Medical Units and the 'general ward' with an additional Paediatric Toolkit, each endorsed by the relevant College/ Royal College/ Society. The correct name for the organization is the UK Sepsis Trust. Table 17 presents a hybridization and misinterpretation of the recognition strategies within the UK Sepsis Trust toolkits. It is an amalgam of a two stage process: the Systemic Inflammatory Response Syndrome criteria, published jointly by the Society for Critical Care Medicine and American College of Chest Physicians in 2001 which are currently used as an 'opt in' tool to initiate screening in the presence of suspected infection, and the Red Flag Sepsis criteria proposed by the UK Sepsis Trust as a set of bedside criteria identifying high risk patients in whom intervention should immediately be initiated in 2014. Could this be rectified please?	
UK Sepsis Trust	Full	192	(GP)	No account is taken of burdensome interventions for those nearing the end of life. Not all sepsis or septic shock needs	Thank you for your comment. The recommendations have been altered following stakeholder comment and include increased emphasis on clinical judgement. In acute hospital

				admission. Eventually in extremely sick or frail patients the aggressive treatment of infection becomes ultimately futile and burdensome for the individual, sepsis is an inevitable consequence and should be managed in line with the patient's wishes and or best interests. Ignoring this issue and option for managing both infection and sepsis is a weakness and a significant potential harm to a vulnerable group.	settings consideration of other diagnoses have been added to role of senior clinical decision maker. The GDG consider that appropriateness of care for each individual should also be considered and this has been added to the narrative.
UK Sepsis Trust	Full	406	3	The Health and Social Care Information Centre has recently released data on coded episodes of sepsis (primary and secondary diagnostic codes) in England for 2013/14. Incidence has risen over the last 3 available years by 5-8% per annum. Nearly 123,000 cases were identified in England. Extrapolating this across the UK, and taking into account that mortality in England is 30%, Wales 24% and Scotland 20% gives our revised incidence and mortality figures as 150,000 cases with 44,000 deaths annually in the UK.	Thank you for this information.
University Hospitals Southampton NHS Foundation Trust	Full	General		We are concerned that not enough emphasis is placed on the need for referral to secondary/tertiary care if a patient is receiving chemotherapy. If they fell into the moderate to high risk criteria box which includes the "impaired immunity" criteria then by following the algorithm they could be treated outside the hospital presumably with oral antibiotics which would be insufficient as these patients can rapidly	Thank you for your comment. It was not the intention to hinder the care of people likely to have neutropenic sepsis. We have altered the recommendations and made additional cross reference to make it clear that people with suspected neutropenic sepsis should be treated according to CG151.

				deteriorate.	
University Hospitals Southampton NHS Foundation Trust	Full	General		WE are concerned that the draft algorithms for management of acute inpatient sepsis do not address either identification of the source of sepsis or source control of sepsis. The algorithm that is given is really just the initial assessment and treatment and I think prompts should be included to ensure senior review with targeted investigations and identification of treatable/drainable sources of infection.	Thank you for your comment. The importance of source control is recognised in the recommendations. The algorithms are not intended to include all aspects of care but to highlight early immediate steps. On review the GDG agreed that adding source control to the algorithm made it less easy to read.
University Hospitals Southampton NHS Foundation Trust	Full	General		<u>NICE Stakeholder Feedback, UHS Paediatric data</u> We looked at 227 sets of paediatric notes retrospectively over a period of one week in January 2016. All patients had presented as an acute admission either via the Paediatric Emergency Department or the Paediatric Assessment Unit as acutely unwell and required screening for consideration of sepsis. We compared the available NICE sepsis guidance with our locally developed Wessex PCCN Paediatric Sepsis Screening Tool which has been developed regionally across 5 centres and refined over 10 PDSA cycles. The feedback that we have is listed in the points below : - The NICE guidance classifies all children >12yrs using a single set of data ranges. We feel that this requires further	Thank you for your comment and information. The GDG reviewed the findings of your submission. Following your submission and those of other stakeholders we have reviewed the risk criteria for children and the actions subsequent to those assessments. The review of criteria resulted in removal of criteria of not passed urine in last 18 hours in children under 11 years and also removal of skin turgor as high risk criteria in under 5s. The wording has also been changed to clarify that the population are people with possible infection. This should reduce the possibility of over-triggering. The GDG reviewed the categorisation by age and did not agree that further age ranges were either possible (because of lack of evidence) or helpful. The algorithms are not intended to be decision tools and the GDG recognise that different formats may be required As noted in the Full guideline people with sepsis may not

				assessment by age. - The tool in it's current format is not very concise and user friendly and unless accompanied by a computer programme where simple numbers (HR, RR etc) can be input to lead progression through the tool, then utilisation at the 'front line' is unlikely to happen. - Looking at our data, detailed below, the trigger to follow the 'red' pathway was too broad in our opinion, and we suggest that combining trigger criteria would result in many patients being more appropriately directed down the 'amber' pathway. - We felt that the start of the pathway at the point of entry was confusing and too broad and using the question 'infection / fever / unwell' was too vague. - One of the 'red' criteria for patients aged <5years was noted as 'skin turgor'. We did not feel that this was a useful criterion for sepsis. - As users, we found it confusing that although an entry criterion for the pathway was 'fever' in only one age group (patients <3 months old) was a documented fever used in assessment in the pathway. In all other age groups, the pathway reads '<36C' rather than a figure representing fever.	have a temperature which is why raised temperature is not included as a specific criteria. A person with suspected sepsis and hypothermia however is likely to be at raised risk of poor outcome. Some changes have been made to the algorithm to improve understanding. Thank you for these results. The changes made to the recommendations; in particular the clarification that clinical decision maker should consider alternative diagnoses, and the need for anti-microbial treatments.

				- As users, we felt that specifying source of blood for recording the lactate value (eg as arterial or venous rather than capillary) within the red lactate boxes would be helpful, rather than inside the text box where it is somewhat lost in the text. - Of the 228 sets of patient notes reviewed, **41 patients (18% of total) triggered activation of the NICE red pathway**. Of these : - ***4 patients were aged 0-1yrs***, and of these : 3 triggered on Heart Rate (min 165, max 186, IQR 174+/-10.5) 1 triggered on temperature (35.6C) - ***13 patients were aged 1-2 yrs***, and of these : 10 triggered on Heart Rate (min 150, max 180, IQR 159.5+/-8.25) 1 triggered on Temperature (35.8C) 2 triggered on Heart Rate	

				and Respiratory rate (HR min 160, max 178. RR min 52, max 60) - ***8 patients were aged 3-4 yrs***, and of these : 5 triggered on Heart Rate (min 147, max 164, IQR 154+/-7) 1 triggered on Respiratory Rate (56) 2 triggered on Heart Rate and Respiratory Rate (HR min 150, max 158) - ***3 patients were aged 5 yrs***, and of these : 1 triggered on HR (HR 145) 2 triggered on RR (RR min 32, max 37) - ***4 patients were aged 6-7 yrs***, and of these : 1 triggered on Heart Rate (HR 128) 2 triggered on Respiratory Rate (RR min 28, max 30) 1 triggered on Heart Rate and Respiratory Rate (HR 122, RR 32) - ***9 patients were aged 8-11yrs***,	

				and of these : 6 triggered on Heart Rate (min 122, max 140, IQR 135+/-5.25) 1 triggered on RR (28) 1 triggered on Temperature (35.7C) 1 triggered on Heart Rate and Respiratory Rate (HR 128, RR 36) - Of the 41 patients who triggered activation of the red NICE pathway, **10 patients also triggered the Wessex PCCN Paediatric Sepsis Screening Tool (4.4% of total cohort of 227).** Of the 10 patients who triggered both pathways, all required a prompt review by a senior clinician. **3 of these patients were treated with broad spectrum intravenous antibiotics** and had a discharge diagnosis consistent with a significant bacterial infection although none had positive cultures. The other 7 were appropriately not treated with iv antibiotics and were given alternative diagnoses. All had good outcomes. - **9 patients were tracked along the NICE amber pathway,** and only one of these	

				triggered the Wessex Paediatric Sepsis Screeing Tool. None of these had a discharge diagnosis of a significant bacterial infection and the single patient in this group that triggered the Wessex tool was given a diagnosis of viral URTI and not treated with antibiotics with a good outcome. All of the patients tracked along the NICE amber pathway triggered on the criteria of both HR and RR. - **Of the 227 set of notes studied, a total of 13 patients triggered the Wessex PCCN Paediatric Sepsis Screening Tool (5.7% of total cohort)**. 10 of these also followed the NICE red pathway, 1 followed the amber pathway, 2 would not have entered the NICE pathway at all. Of these patients : - 1 patient was aged 0-1 yrs and triggered the Wessex tool on the following criteria (Temp 38.9C, altered mental state, prolonged capillary refill time and clinical concern regarding sepsis. HR was 174 (borderline for triggering) and RR was 36) - 9 patients were aged 1-5 yrs, and of those : 2 triggered the Wessex tool on temperature (38.5, 38.7) and HR (154, 147) plus altered mental state.	

				1 triggered on temperature (39.8), HR (158) and RR (52) plus altered mental state and clinical concern regarding sepsis. 5 triggered on HR (min 142, max 192) and RR (min 41, max 65) plus altered mental state / clinical concern regarding sepsis. 1 triggered on HR (154) plus altered mental state, prolonged capillary refill and concern regarding sepsis. RR was 38, also borderline for triggering. - 3 patients were aged 6-11 years, and of those : 1 triggered on temperature (39.8), HR (122) and RR (32) and clinical concern 1 triggered on temperature (39.8C), RR (28) and altered mental state and clinical concern regarding sepsis. 1 triggered on temp (35.5C), HR (135) and altered mental state and prolonged capillary refill time.	

				We are continuing to audit patients screened using the Wessex Tool across the region and may refine the tool further based on our data analyses and user feedback. We are particularly interested in examining the fever criterion and age based range values for HR and RR (which were set using APLS guidelines) and continue to examine data collected regionally to do this.	
University Hospitals Southampton NHS Foundation Trust	General	4		My concern is how we would develop a sepsis screening tool based on these NICE criteria. Once a patient triggers High, Moderate or Low I think the pathway is fine. To have the initial box with 'feeling unwell' will in practice mean we have to screen all admissions and virtually every patient whose condition changes on the ward which I am not sure is required and runs the risk of reducing the impact when there is someone who will really benefit from the pathway. I would recommend that the first box on the adult pathway is removed	Thank you for your comment. This wording has been changed to indicate that the population are people with possible infection.