Suspected Sepsis: recognition, diagnosis and early management (update)

Consultation on draft guideline - Stakeholder comments table
24/03/23 to 21/04/23

Comments forms with attachments such as research articles, letters or leaflets cannot be accepted.

Stakeholder	Document	Page No	Line No	Comments Please insert each new comment in a new row	Developer's response Please respond to each comment
Aneurin Bevan University Health Board	General	General	General	*Would it be challenging to implement of any of the draft recommendations? Please say why and for whom. Please include any suggestions that could help users overcome these challenges (for example, existing practical resources or national initiatives.* Given the flow of junior doctors and other medical staff on rotations within Wales we would be concerned that any implementation of these recommendations should be done across Wales simultaneously. Currently no acute sites in Wales use NEWS2 scoring system and the IT infrastructure does not yet support this, so for us this would be of concern, although we largely support the switch to NEWS 2 scoring system. We will need to carry out significant education and training to help roll out this change. Currently ABUHB respiratory team use CREWS scoring system and there may be some resistance to switching to NEWS2 scoring, due to the adjustment of target O2 level for those at risk of hypercapnic respiratory failure.	Thank you for your comment and for raising these implementation issues. Your comments will be considered by NICE where relevant support activity is being planned.
Aneurin Bevan University Health Board	General	General	General	*Would implementation of any of the draft recommendations have significant cost implications?* Unable to comment on this from the information I have available, sorry.	Thank you for your comment.
Aneurin Bevan University Health Board	Guideline	006	011	Rec 1.1.8 - Currently Wales and ABUHB do not utilise NEWS2 scoring system. There is support to switch over to NEWS 2 from several clinicians and groups in ABUHB, although not all. The IT	Thank you for your comment and for raising these implementation issues. Your comments will be considered by NICE

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				infrastructure does not yet support NEWS 2, which could be a challenge.	where relevant support activity is being planned.
Biocartis	Guideline	019	011	We suggest that NICE consider listing commercially available and clinically validated sepsis-specific biomarkers, (both protein biomarkers and gene expression signatures) along with the other blood tests, which could be used at the discretion of the attending physician. This is suggested for the following reasons: 1. To determine likelihood of poor outcomes in patients with sepsis first requires accurate identification of sepsis. 2. CRP is not a biomarker of sepsis. Rather, it is a biomarker of systemic inflammation in response to infectious and/or non-infectious stimuli (CRP is an acute phase protein). 3. Use of clinical parameters alone has not been demonstrated to accurately identify patients with sepsis (e.g. qSOFA, SOFA, MEWS). 4. Numerous references describe use of biomarkers for determining degree of systemic inflammation, likelihood of poor outcome and likelihood of sepsis, many of which are commercially available and clinically validated (see references below). One such product is SeptiCyte RAPID from Immunexpress which provides a likelihood of sepsis within a 1-hour turnaround. 5. NEWS2 does not differentiate sepsis from systemic inflammatory response syndrome in ICU patients. Our own clinical trials on acutely ill patients (n=419) in intensive care and suspected of sepsis have shown the following (www.SeptiCyte.com/references):	Thank you for your comment. Biomarker diagnostic tests were outside the scope of this guideline update. A further update of the guideline is planned and NICE are considering updating recommendations on rapid antigen tests for guiding treatment of suspected sepsis. Details can be found in the scope for this further update here: Project information | Suspected sepsis: recognition, diagnosis and early management – source control, rapid antigen tests, indicators of organ hypoperfusion, intravenous fluids, and vasopressors in the NEWS2 population | Guidance | NICE

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				• ~50% of patients initially suspected of sepsis were retrospectively determined not to have sepsis. • ICU patients on the day of ICU admission have a range of NEWS2 Scores from zero to greater than seven, with 30% having scores between zero and four. • NEWS2 scores greater than 5 clearly identified 74% of the patients diagnosed with sepsis as patients at risk. • NEWS2 scores of less than 5 were seen in 26% of patients retrospectively diagnosed with sepsis. • 26% of patients retrospectively diagnosed with sepsis did not have an elevated single component NEWS2 score of 3. • Therefore, patients suspected of sepsis, presenting with two or more SIRS criteria, and despite their NEWS2 scores, need to be evaluated for likelihood of sepsis. References: • Opal SM, Wittebole X. Biomarkers of Infection and Sepsis. *Crit Care Clin*. 2020;36(1):11-22. doi:10.1016/j.ccc.2019.08.002 • Pelaia TM, Shojaei M, McLean AS. The Role of Transcriptomics in Redefining Critical Illness. *Crit Care*. 2023;27(1):89. doi:10.1186/s13054-023-04364-2 • Singer M. Biomarkers for sepsis – past, present and future. Qatar Med J. 2019 Nov 7;2019(2):8. doi: 10.5339/qmj.2019.qccc.8. PMCID: PMC6851944. • Barichello T, Generoso JS, Singer M, Dal-Pizzol F. Biomarkers for sepsis: more than just fever and	

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				leukocytosis—a narrative review. *Crit Care*. 2022;26(1):14. doi:10.1186/s13054-021-03862-5 • Turgman O, Schinkel M, Wiersinga WJ. Host Response Biomarkers for Sepsis in the Emergency Room. *Crit Care*. 2023;27(1):97. doi:10.1186/s13054-023-04367-z • Miller III RRM, Lopansri BK, Burke JP, et al. Validation of a Host Response Assay, SeptiCyte LAB, for Discriminating Sepsis from Systemic Inflammatory Response Syndrome in the ICU. *Am J Resp Crit Care*. 2018;198(7):903-913. doi:10.1164/rccm.201712-2472oc	
British Paediatric Allergy Infection and Immunity Group	Guideline	General	General	The updated guideline applies to adults over 16 years and does not include children and young people under 16 years of age. The UK's National Early Warning Score (NEWS2) is widely accepted, but the National Paediatric Early Warning Score (PEWS) is currently being piloted. Paediatric Early Warning System (PEWSystem) - developing a standardised tool for England | RCPCH NEWS2 is well-validated and while PEWS is still undergoing piloting, both provide a suitable framework for a structured approach to the initial management of acutely ill patients with suspected sepsis.	Thank you for your comment. The risk assessment and treatment of children and young people with suspected sepsis (PEWS) is outside the scope of this guideline update. In the future, we plan to review the use of the paediatric early warning score (PEWS) and maternity early warning score (MEWS) tools, and consider making recommendations on them in the guideline.
British Paediatric Allergy Infection and Immunity Group	Guideline	General	General	A paediatric Sepsis Organ Failure Assessment (pSOFA) has been developed for sepsis but cannot be used in the first hour or so following presentation because of the inclusion of bilirubin and creatinine (1). A National Paediatric Early Warning Score (PEWS) has been developed (2), and evaluated in febrile children presenting to the Emergency Department (3, 4). PEWS, like NEWS, presents an	Thank you for your comment. The risk assessment and treatment of children and young people with suspected sepsis is outside the scope of this guideline update. In the future, we plan to review the use of the paediatric early warning score (PEWS),

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				opportunity to have a "common language" across pre-hospital, ED and critical care. PEWS could be a useful tool for identifying and tracking physiological changes, and the introduction of a standardised score would potentially allow improvement or deterioration to be tracked from ED to ward to critical care. In England, there has been no single, nationally validated system for recognising and responding to acutely unwell children, similar to the NEWS score used in patients over 16 years of age. There are versions of the Scottish and Irish PEWS in use (5-7), (8), but the National PEWs is not widely used in England. This significant patient safety risk has been addressed by the National PEWS Programme Board with representation from NHS England and NHS Improvement, the Royal College of Paediatrics and Child Health and the Royal College of Nursing (RCN). An English national PEWS called 'system-wide paediatric observations tracking' (SPOT) has been developed and is undergoing piloting to recognise deterioration across primary and community care, through ambulance services, EDs and into hospitals (9), (2). Using a common language could help to address the high false positive rate and consequent over-treatment of children associated with the use of the NICE Guidance 51 sepsis thresholds (10), (4), (11). Mortality as the primary outcome in paediatric ED settings has too low an event rate (<1%) for calibration. Critical care admission is a	and consider making recommendations on this in the guideline

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				more suitable outcome as this allows assessment of whether the score can identify those patients requiring additional support, regardless of survival. The use of the age-adjusted quick SOFA (qSOFA) for paediatric sepsis has demonstrated poor or insufficient sensitivity in predicting in-hospital mortality and PICU admission (12), (13). A recent retrospective analysis of over 11,000 febrile children attending a tertiary paediatric ED demonstrated excellent and relatively comparable performance across seven different PEWS scores currently used in the UK, including the proposed National PEWS, in predicting critical care admission and sepsis-related mortality (4). National PEWS in combination with the biomarkers procalcitonin and mid-regional pro-adrenomedullin (MR-proADM) was shown to improve risk stratification of febrile children presenting to the ED (14). These findings support the use of the National PEWS in the ED to improve standardisation and reduce variability in escalation of care for sepsis. This will need to be validated in prehospital and inpatient settings, and for non-sepsis presentations. We recommend this proposed update should be an opportunity to carefully consider the roll out of national PEWS (as well as consideration of applying updates to paediatrics for other guidance such as time to administration of first antibiotics) at the same time as updating the guidance on adult practice, rather than in a staggered	

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				fashion. This will ensure harmonisation of practice across all age ranges and patient groups, ensuring that the evidence considered in order to provide this consultation document is consistently reviewed and applied consistently across patient groups. Staggered implementation runs the risk of causing confusion in relation to important guidance such as time to administration of antibiotics if there is one document for adults and one for paediatrics. <u>References</u> 1. Matics TJ, Sanchez-Pinto LN: Adaptation and Validation of a Pediatric Sequential Organ Failure Assessment Score and Evaluation of the Sepsis-3 Definitions in Critically Ill Children. *JAMA Pediatr* 2017; 171(10):e172352 2. Roland D, Stilwell PA, Fortune PM, Alexander J, et al: Case for change: a standardised inpatient paediatric early warning system in England. *Arch Dis Child* 2021; 106(7):648-651 3. Romaine ST, Potter J, Khanijau A, McGalliard RJ, et al: Accuracy of a Modified qSOFA Score for Predicting Critical Care Admission in Febrile Children. *Pediatrics* 2020; 146(4) 4. Romaine ST, Sefton G, Lim E, Nijman RG, et al: Performance of seven different paediatric early warning scores to predict critical care admission in febrile children presenting to the emergency department: a retrospective cohort study. *BMJ Open* 2021; 11(5):e044091 5. Corfield AR, Booth KL, Clerihew L, Staines H, et al: Association of out of hospital paediatric early warning score with need for hospital admission in a Scottish emergency ambulance population. *Eur J Emerg Med* 2020; 27(6):454-460	

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				6. Corfield AR, Clerihew L, Stewart E, Staines H, et al: The discrimination of quick Paediatric Early Warning Scores in the pre-hospital setting. *Anaesthesia* 2020; 75(3):353-358 7. Corfield AR, Silcock D, Clerihew L, Kelly P, et al: Paediatric early warning scores are predictors of adverse outcome in the pre-hospital setting: A national cohort study. *Resuscitation* 2018; 133:153-159 8. Hannon C, Roland D, O'Sullivan R: Prediction of Pediatric Patient Admission/Discharge in the Emergency Department: Irish Pediatric Early Warning Score, Pediatric Observation Priority Score, and Irish Children's Triage System. *Pediatr Emerg Care* 2022; 38(6):e1320-e1326 9. RCPCH: Paediatric Early Warning System (PEWSystem) - developing a standardised tool for England. Available at: https://www.rcpch.ac.uk/resources/paediatric-early-warning-system-pewsystem-developing-standardised-tool-england. Accessed 10. Nijman RG, Jorgensen R, Levin M, Herberg J, et al: Management of Children With Fever at Risk for Pediatric Sepsis: A Prospective Study in Pediatric Emergency Care. *Front Pediatr* 2020; 8:548154 11. Gomes S, Wood D, Ayis S, Haliasos N, et al: Evaluation of a novel approach to recognising community-acquired paediatric sepsis at ED triage by combining an electronic screening algorithm with clinician assessment. *Emerg Med J* 2021; 38(2):132-138 12. Schlapbach LJ, Straney L, Bellomo R, MacLaren G, et al: Prognostic accuracy of age-adapted SOFA, SIRS, PELOD-2, and qSOFA for in-hospital mortality among children with suspected infection admitted to the intensive care unit. *Intensive Care Med* 2018; 44(2):179-188	

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				13. van Nassau SC, van Beek RH, Driessen GJ, Hazelzet JA, et al: Translating Sepsis-3 Criteria in Children: Prognostic Accuracy of Age-Adjusted Quick SOFA Score in Children Visiting the Emergency Department With Suspected Bacterial Infection. *Front Pediatr* 2018; 6:266 14. Lenihan RAF, Ang J, Pallmann P, Romaine ST, et al: Mid-Regional Pro-Adrenomedullin in Combination With Pediatric Early Warning Scores for Risk Stratification of Febrile Children Presenting to the Emergency Department: Secondary Analysis of a Nonprespecified United Kingdom Cohort Study. *Pediatr Crit Care Med* 2022	
British Society of Antimicrobial Chemotherapy	General	General	General	BSAC does not have any comment to submit currently.	Thank you for your comment.
DiaSorin UK Ltd	Evidence Review B	022	127	We agree with the committee's viewpoint that antibiotic delivery is most beneficial when treatment priorities are matched to severity of illness and that early administration of antibiotics in people in lower NEWS2 risk categories may lead to potential harms that could otherwise be avoided. We do however feel that there is a missed opportunity with respect to infection-specific diagnostic tests. It would be helpful to consider the benefits of biomarker analysis combining TRAIL, IP-10 and CRP, which is supported by evidence distinguishing between bacterial and viral infection (Oved et al, PLoS One, 10(3):e0120012. doi:10.1371/journal.pone.0120012; Ashkenazi-Hoffnung et al, Eur J Clin Microbiol Infect Dis, 37(7):1361-1371)	Thank you for your comment. Diagnostic tests were outside the scope of this guideline update. NICE is planning a further update to the guideline and will consider making recommendations on rapid antigen tests for diagnosing infection in people with suspected sepsis and guiding treatment. Details can be found in the scope for this further update here: Project information | Suspected sepsis: recognition, diagnosis and early management – source control, rapid

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					antigen tests, indicators of organ hypoperfusion, intravenous fluids, and vasopressors in the NEWS2 population | Guidance | NICE
DiaSorin UK Ltd	Guideline	015	004	Rec 1.5.3 – We agree with the addition of NEWS2 score introduced in section 1.5, but believe that 1.5.3 could go further, especially if there is cause for concern because of deterioration or lack of improvement. There is peer-reviewed UK evidence examining the combination of the NEWS score with the blood biomarker mid-regional proadrenomedullin (MR-proADM). This demonstrated that even in patients with a NEWS score < 4 points, when those patients had an MR-proADM score of ≥1.54 points, they had significantly higher mortality and ICU admission rate, significantly longer length of hospitalisation, and a significantly higher number of disease progression events versus patients in the same NEWS category but an MR-proADM score of <1.54 points (Saeed et al, Critical Care, 2019, 23:40). We therefore consider that there would be merit in including MR-proADM as a biomarker to assist in evaluating a patient's risk.	Thank you for your comment. Diagnostic tests were outside the scope of this guideline update. A further update of the guideline is planned and NICE are considering updating recommendations on rapid antigen tests for guiding treatment of suspected sepsis. Details can be found in the scope for this further update here: Project information | Suspected sepsis: recognition, diagnosis and early management – source control, rapid antigen tests, indicators of organ hypoperfusion, intravenous fluids, and vasopressors in the NEWS2 population | Guidance | NICE
DiaSorin UK Ltd	Guideline	018	004	Rec 1.9 – This recommendation risks being very top-line in describing the process of microbiological sampling, whereas it could be bolder. It is stated at the outset of the draft guideline that antimicrobial stewardship improvement is a priority (page 2). However, Rec 1.9 does not explicitly consider tools that may assist in this endeavour. For example, a biomarker assay combining TNF-related apoptosis-inducing ligand (TRAIL), Interferon gamma-induced protein 10 (IP-10) and C-reactive protein (CRP) host protein	Thank you for your comment. Diagnostic tests were outside the scope of this guideline update. A further update of the guideline is planned and NICE are considering updating recommendations on rapid antigen tests for guiding treatment of suspected sepsis. Details can be found in the scope

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				biomarkers in an applied machine learning algorithm has been shown to discriminate bacterial versus viral infections in sepsis patients (Stas et al, JAC Antimicrob Resist. 2022 Jun; 4(Suppl 2): dlac052.002). Inclusion of biomarkers and biomarker combinations such as this would be an important step to the goal of supporting antimicrobial stewardship.	for this further update here: Project information | Suspected sepsis: recognition, diagnosis and early management – source control, rapid antigen tests, indicators of organ hypoperfusion, intravenous fluids, and vasopressors in the NEWS2 population | Guidance | NICE
DiaSorin UK Ltd	Guideline	031	009	Rec 1.17 – This recommendation to find the source of infection in all people with suspected sepsis is unchanged from 2016. In some cases, this could benefit from being more specific. We feel that the evidence landscape has evolved sufficiently over the last 7 years to include a suggestion in 1.17.1 that assaying biomarker and/or biomarker combinations would be an appropriate approach. As an example, a biomarker assay combining TRAIL, IP-10 and CRP host protein biomarkers in an applied machine learning algorithm has been shown to discriminate bacterial versus viral infections in sepsis patients (Stas et al, JAC Antimicrob Resist. 2022 Jun; 4(Suppl 2): dlac052.002).	Thank you for your comment. Biomarker diagnostic tests were outside the scope of this guideline update. A further update of the guideline is planned and NICE are considering updating recommendations on rapid antigen tests for guiding treatment of suspected sepsis. Details can be found in the scope for this further update here: Project information | Suspected sepsis: recognition, diagnosis and early management – source control, rapid antigen tests, indicators of organ hypoperfusion, intravenous fluids, and vasopressors in the NEWS2 population | Guidance | NICE
Faculty of Intensive	Guideline	General	General	We welcome this new NICE Guideline that incorporates the use of NEWS2 and the work of Professor Bion and colleagues on producing	Thank you for your comment.

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Care Medicine				the 2022 Academy of Medical Royal Colleges, 'Statement on the initial antimicrobial treatment of sepsis'.	
Faculty of Intensive Care Medicine	Guideline	General	General	There was some concern expressed that the unintended consequence of incorporating NEWS 2 is that complexity is increased. There are multiple ways to reach the same point. The change in antimicrobial evidence, particularly the time frames for administration now stratified by NEWS 2 risk, only adds to the complexity. The Guideline is very confusing to read as text and keeping distinct the concepts of high risk, moderate to high risk, low to moderate risk, low risk; matched against different antibiotic timing. We found the table in the 2022 Academy of Medical Royal Colleges, 'Statement on the initial antimicrobial treatment of sepsis' very helpful in understanding the stratification and what actions were required by healthcare professionals. We would urge NICE to incorporate explanatory tables in the Guideline.	Thank you for your comment. The names of the risk levels have been revised to very low, low, moderate and high in line with stakeholder feedback. We are unable to incorporate explanatory tables into this guideline as these do not meet the NICE editorial accessibility standards. However, we have prepared algorithms to be published alongside the updated guideline to assist users. The algorithms can be viewed here: https://www.nice.org.uk/guidance/indevelopment/gid-ng10310/documents
Faculty of Intensive Care Medicine	Guideline	General	General	While this is not a NEWS2 guidance, we wondered if there is a place for highlighting more clearly how often the NEWS2 should be measured. More emphasis could be placed on emphasising the need for repeated observations. The trend is more important than a static number. Better for example is Page 16, Line 17 (1.6.3) which talks about 'consecutive NEWS2'. Given that all people who die from sepsis start with a NEWS2 of zero (were it measured early on in their sepsis), highlighting the need for consecutive testing could be made stronger. This is touched upon on Page 39 but would be better higher and more prominently.	Thank you for your comment. The committee considered this issue and have added a recommendation outlining the need to re-calculate a NEWS2 score and re-evaluate the risk of sepsis in line with the AoMRC report in this guidance.

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Faculty of Intensive Care Medicine	Guideline	General	General	It is a strong concern that the repeated sentence "The NEWS2 should not be used for women who are or have recently been pregnant" offers no alternative, or link to another guidance. We recognise this is acknowledged in the Guideline and that the 'care pathway described in this guideline is disjointed.' If no new guidance for this cohort is available, would it not be safer to suggest that an elevated NEWS2 score in this group, with suspected sepsis should trigger the same pathway as for other population groups?	Thank you for your comment. In the future, we plan to review the use of the maternity early warning score (MEWS) tools, and consider making recommendations on this in the guideline.
Faculty of Pharmaceutical Medicine	Guideline	000	000	Section 1.3 is entitled "Face to Face assessment" could it be changed to 'assessing diagnosis of suspected sepsis'? Whilst some of the symptoms and signs are common to both diagnosis and severity, the initial trigger for the guidelines is level of concern the patient has sepsis. Over 60% of cases of severe sepsis are community acquired and deciding whether to hospitalise or not is based on both diagnosis and severity, so diagnosis is particularly important in this patient group. Page DB, Donnelly JP, Wang HE. Community-, Healthcare-, and Hospital-Acquired Severe Sepsis Hospitalizations in the University Health System Consortium. Crit Care Med. 2015 Sep;43(9):1945-51. doi: 10.1097/CCM.0000000000001164. PMID: 26110490; PMCID: PMC4537676.	Thank you for your comment. The committee considered this issue but agreed to keep the current heading of face-to-face assessment as it is clearer.
Faculty of Pharmaceutical Medicine	Guideline	002	000	We agree with the change, and suggest that the reference is provided to the source ID 1.10 and also a reference for the risk factors mentioned in 1.2	Thank you for your comment. The committee considered this and agreed that further changes were not required. The NICE editorial style for guideline

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					recommendations does not include the use of references.
Faculty of Pharmaceutical Medicine	Guideline	003	000	We suggest that the reference should be provided to section 1.3 face to face assessment on people with suspected sepsis. Considering the introduction of NEWS2 in the hospital setting within this guidance in section 1.1.8, is there a risk of confusion between NEWS2 and section 1.1.7 regarding the guidance to "evaluating risk level in people with suspected sepsis" in the community, links to section 1.4 P.11? Should NEWS2 replace "evaluating risk level in people with suspected sepsis" in section 1.1.7?	Thank you for your comment. To create a joined up pathway, we have subsequently updated the recommendations that are not about antibiotics, but that relate to the initial management of suspected sepsis in an acute hospital setting. As NEWS2 has not been implemented in community settings, the recommendations covering these settings retain the criteria for stratification of risk of severe illness or death from sepsis if they are in the community or in a custodial setting.
Faculty of Pharmaceutical Medicine	Guideline	004	000	Whilst conventional chemotherapy has a nadir at 5-10 days with recovery by 30, some of the combination therapies potentially suppress for longer, this is what the CKS neutropenic sepsis guideline says that in CG151 is not that specific. There is a CKS on neutropenic sepsis, but the guideline is CG151 neutropenic sepsis in cancer, we wonder whether both be referenced?	Thank you for your comment. This issue is outside the scope of this guideline update and is covered by the NICE Neutropenic sepsis guideline (CG151). NICE guidelines do not reference Clinical Knowledge Summaries. We commission an external company to develop Clinical Knowledge Summaries (CKS) and publish them on our website. CKS contain summaries of published evidence and guidance on a wide range of topics. They are written for health professionals working in primary care and may include references to NICE guidance

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					(if there is any that is relevant) but they use lots of other sources too. The CKS do not contain new recommendations and are not subject to quality assurance. They do not constitute formal NICE guidance.
Faculty of Pharmaceutical Medicine	Guideline	006	000	Risk factors for sepsis: Should this section also specifically include people with other & localised infections, for example iGAS, viral/bacterial chest infections/pneumonia, chronic lung conditions e.g. cystic fibrosis, COPD/asthma, UTI, cellulitis/skin infections, meningitis etc.? iGAS attacks healthy young people, but can rapidly go into sepsis. Severe viral/bacteria pneumonia may also rapidly deteriorate into sepsis. GAS is only mentioned in the context of pregnancy and we would suggest broadening this. We would also suggest adding HIV/AIDS patients under people who have impaired immune function. We have noted that there is only a passing mention of diabetes in the guidance and interestingly, conversely, no mention of risk of sepsis in the NICE T1DM or T2DM guidances. According to the article below, those with T2 alone have 5-6 times risk of sepsis. We would suggest that diabetes should be both highlighted more prominently in this guidance AND consideration be given to cross referencing and including in the next update to the NICE T1DM or T2DM guidances. Costantini E, Carlin M, Porta M, Brizzi MF. Type 2 diabetes mellitus and sepsis: state of the art, certainties and missing evidence. Acta Diabetol. 2021 Sep;58(9):1139-1151. doi: 10.1007/s00592-021-01728-4. Epub 2021 May 10. PMID: 33973089; PMCID: PMC8316173.	Thank you for your comment. The issues raised are outside the scope of this guideline update. https://www.nice.org.uk/guidance/gid-ng10310/documents/final-scope

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				Again it is only mentioned for pregnant women	
Faculty of Pharmaceutical Medicine	Guideline	008	000	1.1.5 refers to this section 1.2 for this information.	Thank you.
Faculty of Pharmaceutical Medicine	Guideline	013	000	Making a definitive diagnosis of early sepsis in a hospital setting is difficult, in the community even more so – We suggest assigning a likelihood of diagnosis – i.e. unlikely / possible / probable / definite – and use the combined likelihood of diagnosis and NEWS2 score or equivalent together to guide hospitalisation. The statement on NEWS2 in the table on p13 in the report Statement on the Initial Antimicrobial Treatment of Sepsis recognised that people could have sepsis with a low NEWS2 score of 1-4. The international sepsis definition requires 2 or more of the following. Systolic BP≤100, RR ≥22 and some confusion, which could be a NEWS2 score of 3. Suspected sepsis could be even lower. However, in Table 1 of this guidance, while you only need one criterion, it would still allow some people with sepsis with a source of infection that is not skin or soft tissue to remain at home and have a higher potential to progress to moderate risk if they have a high likelihood of the diagnosis being correct compared to patients with low likelihood of sepsis and low risk. The first line of Table 1 seems very limited and may apply to likelihood of diagnosis as well as severity. Could it be clarified this is severity and risk of progression to or being in septic shock. Also, whilst history and physical examination are in Table 1, age is not, unless it is assumed age compromises immune function.	Thank you for your comment. The names of the risk levels have been revised to very low, low, moderate and high in line with stakeholder feedback. The committee considered this issue and have added a recommendation acknowledging the need to elevate the person's risk of sepsis in the context of certain clinical signs.

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				In 1.5.2 for hospital patients NEWS2 is still included – we wonder why, where possible, NEWS2 is not recommended to be used in the community. We would like to recommend other aspects of vulnerability be taken into account, such as recent viral infection or complicated urinary infection.	This issue is outside the scope of this guideline update as NEWS2 has not yet been validated, or endorsed by NHS England, for use in primary care. The committee discussed this issue and agreed this will be covered by considering the clinical history of the patient.
Faculty of Pharmaceutical Medicine	Guideline	016	000	Same comments as the rest of 1.4	Thank you.
Faculty of Pharmaceutical Medicine	Guideline	016	000	This section 1.6 "When to transfer immediately to an acute hospital setting" from the community/custodial setting is using the different guidance to NEWS2 for "stratification of risk from sepsis". However, in section 1.6.3 & 1.6.4. row 16 & beyond "Transfer by ambulance for people with a NEWS2 score of 5 or above", indicates that NEWS scoring had to be used in the community in order to determine the need for transferring to hospital. This is inconsistent guidance in the community, please see comments also made in section 1.1.7 & section 1.4.1.	Thank you for your comment. The recommendations in section 1.7 have been split by setting into a) primary care (GPs) and b) ambulance services to provide greater clarity. NEWS2 has been endorsed by NHS England for use in ambulance settings, but has been neither endorsed nor validated for use in community or custodial settings, and the recommendations reflect that. The revised recommendations outline that in remote and rural locations where transfer to emergency department and handover times to emergency department are greater than 1 hour, ensure ambulance services have mechanisms in place to give

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					antibiotics to people at high risk of severe illness or death from sepsis. We have asked a specific question regarding implementation of the recommendations flagged in the consultation for a further update of NG51. The consultation documents can be viewed here: Consultation | Suspected Sepsis: recognition, diagnosis and early management (update) | Guidance | NICE
Faculty of Pharmaceutical Medicine	Guideline	020	000	Scoring systems like CURB65 and PSI for pneumonia are often distorted by age and NEWS2 might be more accurate in younger people.	Thank you for your comment. The issue raised is outside the scope of this guideline update. https://www.nice.org.uk/guidance/gid-ng10310/documents/final-scope
Faculty of Pharmaceutical Medicine	Guideline	022	000	Comment as before re Table 1. We recommend to simply use a NEWS2 score + likelihood of sepsis as per the AoMRC guidance, which uses NEWS2 vs likelihood.	Thank you for your comment. The issue raised is outside the scope of this guideline update. https://www.nice.org.uk/guidance/gid-ng10310/documents/final-scope
Faculty of Pharmaceutical Medicine	Guideline	023	000	Making a definitive diagnosis of early sepsis in a hospital setting is difficult. In the community even more so. We would recommend assigning a likelihood – i.e. unlikely / possible / probable / definite – and use the NEWS2 score to guide hospitalisation. We would propose the inclusion of some guidance in here for primary care healthcare professionals, whose patients remain at home to	This issue is outside the scope of this guideline update as NEWS2 is not validated for use in primary care.

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				meet NEWS2 monitoring criteria they may be at risk of developing sepsis.	
Faculty of Pharmaceutical Medicine	Guideline	024	000	As an example, for a previously healthy man with a complicated urinary infection secondary to catheterisation following urinary retention and a systolic BP of 102, possible sepsis would potentially not receive formal treatment or observation. Perhaps there should be a recommendation for assessment of source identification in this section and frequency of monitoring. Simply leaving the patient to self-diagnose deterioration seems a potential risk.	Thank you for your comment. Assessment of source identification is covered in section 1.7 of the guideline. The committee considered the frequency of monitoring and have added a recommendation outlining the need to re-calculate a NEWS2 score and re-evaluate risk of sepsis periodically in line with the AoMRC report.
Faculty of Pharmaceutical Medicine	Guideline	025	000	In 1.6 there should perhaps be mention of source identification for suspected sepsis, even if source identification appears by cross referencing to 1.17. Patients not currently severely ill enough to be hospitalised may still need source identification but most of the text refers to tests that are done in hospital.	Thank you for your comment. Source identification for suspected sepsis is covered in section 1.17 of the guideline. The committee considered these tests should be conducted in secondary care.
Faculty of Pharmaceutical Medicine	Guideline	025	000	There should potentially be a mention of the microbiologist/ID expert as appropriate, as this could be ICU patients in a unit with MDR bugs. There is no mention of frequency of monitoring, it is important to provide this guidance.	Thank you for your comment. The committee considered this issue and agreed that this level of detail re: the need for a microbiologist/ ID expert was not needed. The committee also considered the frequency of monitoring and have added a recommendation outlining the need to re-calculate a NEWS2 score and re-evaluate risk of sepsis periodically in line with the AoMRC report.

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Faculty of Pharmaceutical Medicine	Guideline	027	000	These patients would be considered to be in septic shock - should this term be used in the next three sections?	Thank you for your comment. The management of septic shock is outside the scope of this current guideline update. https://www.nice.org.uk/guidance/gid-ng10310/documents/final-scope
Faculty of Pharmaceutical Medicine	Guideline	028	000	In NHSE this would follow NEWS2 frequency of monitoring. FPM recommends NEWS2 monitoring guidance is followed to simplify this.	Thank you for your comment. The committee considered this issue and have added a recommendation outlining the need to re-calculate a NEWS2 score and re-evaluate risk of sepsis periodically in line with the AoMRC report.
Faculty of Pharmaceutical Medicine	Guideline	029	000	This section implies antibiotics that should work within 1h, but this does not apply to all antibiotics. It is unclear what is the guidance /action for the consultant. Presumably it is to transfer to ICU, but we suggest further clarification.	Thank you for your comment. This issue is outside the scope of this guideline update. https://www.nice.org.uk/guidance/gid-ng10310/documents/final-scope
Faculty of Pharmaceutical Medicine	Guideline	035	000	Appropriate may include more than AKI and lactate... for discharge and whilst this does not say they should be discharged, failure to respond to antibiotics could be worrying and there might be an issue timing of recovery etc. Perhaps some further text would be helpful here regarding recovery length of treatment required for parenteral antibiotics (endocarditis for example needs 3 weeks parenteral antibiotics).	Thank you for your comment. The issue raised is outside the scope of this guideline update. https://www.nice.org.uk/guidance/gid-ng10310/documents/final-scope
Faculty of Pharmaceutical Medicine	Guideline	035	000	It depends on what the criterion that 'moderate' was based on was. In almost all cases of suspected sepsis (unless it was simply been immunosuppressed and no symptoms (line 1 of Table 1)) there may need to be source identification and other assessments. FPM recommends evaluating whether the AoMRC recommendations on timing of evaluation prescribing should be followed in this section.	Thank you for your comment. The issue raised is outside the scope of this guideline update. https://www.nice.org.uk/guidance/gid-ng10310/documents/final-scope

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Faculty of Pharmaceutical Medicine	Guideline	037	000	Can there be clarification of what "a definitive condition" is in this setting? FPM suggests a clarification.	Thank you for your comment. The issue raised is outside the scope of this guideline update. https://www.nice.org.uk/guidance/gid-ng10310/documents/final-scope
Faculty of Pharmaceutical Medicine	Guideline	045	000	This is possibly one of the most important aspects for patients in pre-septic shock. We recommend that it should be brought forward to be more prominent in the guidance. Furthermore, much of this aspect could not be managed in primary care, we would suggest updating this to reflect possible mention of this which may need specialist care – for example renal abscess.	Thank you for your comment. This issue is outside the scope of this guideline update. https://www.nice.org.uk/guidance/gid-ng10310/documents/final-scope
Faculty of Pharmaceutical Medicine	Guideline	050	000	We suggest that it could be useful to provide more information on what to monitor and whether there will be follow up and by whom?	Thank you for your comment. The committee considered this issue and have added a recommendation outlining the need to re-calculate a NEWS2 score and re-evaluate risk of sepsis periodically in line with the AoMRC report.
Faculty of Pharmaceutical Medicine	Guideline	051	000	For patients who have had sepsis and particularly septic shock there is an increased risk of mental health problems – Consideration should be given to mentioning this separately, particularly for the young – see below reference. Lund-Sørensen H, Benros ME, Madsen T, et al. A Nationwide Cohort Study of the Association Between Hospitalization With Infection and Risk of Death by Suicide. JAMA Psychiatry. 2016;73(9):912–919. doi:10.1001/jamapsychiatry.2016.1594	Thank you for your comment. This issue is outside the scope of this guideline update. https://www.nice.org.uk/guidance/gid-ng10310/documents/final-scope
Hywel Dda University Health Board	Guideline	006	011	In Wales we use NEWS2 in a Welsh context, scoring system is 3, 6 & 9, and we encourage staff to consider Sepsis at a NEWS of 3, which	Thank you for your comment and for raising these implementation issues. Your comments will be considered by NICE

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				in its self is more sensitive than what is advocated. The aim is about getting a clinician to the bedside to make a decision.	where relevant support activity is being planned.
Hywel Dda University Health Board	Guideline	014	008	From a GP perspective the assessment does not only take into consideration the NEWS score also considers the patients history and previous sepsis episodes.	Thank you for your comment. The committee considered this issue and agreed this would be covered in the clinical history of the patient.
Hywel Dda University Health Board	Guideline	016	017	Within rural localities within the HDUHB region transportation and transfers are relied heavily on Ambulance transport which regularly are over stretched having an impact on the golden hour. Has consideration been made in relation to rurality and the impact of this on assessment and treatment particularly within Primary Care/ Community setting	Thank you for your comment and for sharing your local practice. Recommendations 1.7.1 and 1.7.2 in the guideline update have made consideration for patient transfer in remote and rural locations We have asked a specific question regarding implementation of the recommendations flagged in the consultation for a further update of NG51. The consultation documents can be viewed here: Consultation | Suspected Sepsis: recognition, diagnosis and early management (update) | Guidance | NICE
Hywel Dda University Health Board	Guideline	017	001	Wording "ensure" should when available/ when possible be considered, the rurality of Wales and capacity of ambulance service can cause delays and GPs are not always available to support in the community, they will assist if able to but not always able.	Thank you for your comment and for sharing your local practice.
Hywel Dda University Health Board	Guideline	019	026	Welcome antibiotic choice in line with recommendations	Thank you for your comment.

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Institute of Biomedical Science	Guideline	General	General	Provide link to UKSMI *S12: Sepsis and systemic or disseminated infections* in the reviewed guidance where relevant. The document highlights the significant changes needed in both clinical and laboratory practice to improve the sensitivity and utility of blood cultures. This is critical in the endeavour to tackle the significant issue of antimicrobial resistance and inappropriate use of antimicrobials. Key points of *S12 – Sepsis and systemic or disseminated infections*: • Collecting adequate volume of blood for culture is critical. Every mL of blood increases the sensitivity of blood culture by 3%. • A minimum of 2 blood culture sets (2x2 bottles, 40mL) are recommended to detect bacteriaemia in adults. These can be collected in one draw. • Collecting a third set (total of 3x2 bottles, 60mL) is recommended if candidaemia is suspected. All three sets can be collected in one draw. • If endocarditis is suspected, 3 blood culture sets (3x2 bottles, 60mL) should be collected as separate draws over a 24h period. • Samples are ideally collected before starting antimicrobial therapy. However certain clinical conditions may dictate giving antimicrobials prior to blood culture collection e.g., unstable septic patients, patient with suspected meningococcal disease etc. Blood cultures should still be taken if clinical condition dictates in patients receiving ongoing antimicrobials.	Thank you for your comment. A link to the UK Health Security Agency guidance on UK Standards for Microbiology Investigations has been added to section 1.9.

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				• The blood culture bottles should be transported to the laboratory and loaded into a blood culture analyser without delay, ideally within 4 hours from collection, subject to local constraints and agreements. • List of auditable outcomes are provided. The document is endorsed by the 24 professional colleges and societies who are the partner organisations that develop UK SMIs including the Royal College of Pathologists (RCPath) and Institute of Biomedical Science (IBMS).	
Liverpool Heart and Chest Hospital NHS Foundation Trust	Guideline	General	General	As a trust we do not currently implement NEWS2 in any of our clinical areas due to the nature of our patient cohort. Therefore, this new guidance does not seem to apply to us, despite our patients being aged over 16 that are not or have not been recently pregnant. Therefore, we are not going to be able to implement this new guidance. I, as a sepsis practitioner, will not be able to use this guidance to update our local policy.	Thank you for your comment. The committee considered this issue and have added a recommendation outlining that NEWS2 can be less accurate in people with certain conditions and to interpret the NEWS2 scores within the context of the persons' underlying physiology and comorbidities.
Liverpool Heart and Chest Hospital NHS Foundation Trust	Guideline	General	General	There seems to be lots of bold statements stating that certain recommendations will be amended in a future update, does this mean that these statements are wrong? Or that there is new evidence for/against these statements? We are concerned that this update is not fully up to date with latest evidence.	Thank you for your comment. NICE has carried out a further update of the recommendations on the initial management of suspected sepsis in the NEWS2 population. These recommendations will soon be published.
MeMed Diagnostics Ltd	Guideline	General	General	Question 1: As diagnostic device manufacturer, we are unable to comment on this question.	Thank you for your comment.

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MeMed Diagnostics Ltd	Guideline	General	General	Question 2: As diagnostic device manufacturer, we are unable to comment on this question.	Thank you for your comment.
MeMed Diagnostics Ltd	Guideline	General	General	The driver for the NG51 guideline update centres around the incorporation of NEWS2 for risk stratification and to improve antimicrobial stewardship at the earliest opportunity without compromising patient safety. However, both improvements are linked to a different clinical question: (i) NEWS2 focuses on risk stratification and early identification of potential severe patient outcome (i.e., prognostic value), and (ii) antimicrobial stewardship focuses on understanding the underlying infection in terms of source identification and infection aetiology. Both improvements require a different approach to be optimally effective and the draft guideline recommendations provide a framework on how this could be achieved through NEWS2. However, there is a missed opportunity within the recommendations to align risk stratification and antimicrobial stewardship through the use of biomarker-guided decision making. Novel biomarkers and biomarker sets (both protein and mRNA-based) have come to market with the aim of complementing clinical assessment to improve antimicrobial stewardship and risk stratification. Consideration should be given to these novel biomarkers and biomarker sets to guide clinical assessment in suspected-sepsis patients.	Thank you for your comment. Biomarker diagnostic tests were outside the scope of this guideline update. NICE is planning a further update to the guideline and will consider making recommendations on rapid antigen tests for diagnosing infection in people with suspected sepsis and guiding treatment. Details can be found in the scope for this further update here: Project information | Suspected sepsis: recognition, diagnosis and early management – source control, rapid antigen tests, indicators of organ hypoperfusion, intravenous fluids, and vasopressors in the NEWS2 population | Guidance | NICE
MeMed Diagnostics Ltd	Guideline	018	004	The draft guidelines provides a general description on the collection of microbiological samples and blood cultures before antibiotics are given (not updated from NG51 guideline, 2016). However, as antimicrobial stewardship is one of the drivers for the guideline update, there is a missed opportunity to highlight novel microbiological approaches that are now available to aid with the	Thank you for your comment. The issue you've raised was outside the scope of this guideline update. A further update of the guideline is planned and NICE are considering updating recommendations on rapid antigen tests for guiding treatment of

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				clinical decision to administer (or withhold) antibiotics in a safe way. In particular, a set of biomarkers (i.e., CRP+TRAIL+IP-10 measurements with an applied machine learning decision algorithm on automated platforms) demonstrated promise in better discriminating bacterial from viral infections in suspected-sepsis patients (O02 TRAIL, IP-10, CRP host-protein signature score distinguishes between viral and bacterial infection in sepsis patients | JAC-Antimicrobal Resistance | Oxford Academic (oup.com)). If used in conjunction with NEWS2, it may be feasible to further improve antimicrobial stewardship practice in suspected-sepsis patients (i.e., primarily in the stable 'low to moderate' & 'moderate to high risk' patient groups).	suspected sepsis. Details can be found in the scope for this further update here: Project information | Suspected sepsis: recognition, diagnosis and early management – source control, rapid antigen tests, indicators of organ hypoperfusion, intravenous fluids, and vasopressors in the NEWS2 population | Guidance | NICE A link to the UK Health Security Agency guidance on UK Standards for Microbiology Investigations has been added to section 1.9.
MeMed Diagnostics Ltd	Guideline	023	009	Within the draft guideline, the antimicrobial prescribing decision for the moderate to high risk of severe illness NEWS2 group is extended to 3 hours to gather more information for a more specific diagnosis. Within this patient subgroup, a set of biomarkers (i.e., CRP+TRAIL+IP-10 measurements with an applied machine learning decision algorithm on automated platforms) could improve antimicrobial stewardship decisions by providing insights on the underlying infectious aetiology. As standard venous blood sampling is recommended within this patient group, consideration could be given to use the biomarker-set as part of the clinical assessment to inform the diagnosis and antimicrobial prescribing decision.	Thank you for your comment. Biomarker diagnostic tests were outside the scope of this guideline update. A further update of the guideline is planned and NICE are considering updating recommendations on rapid antigen tests for guiding treatment of suspected sepsis. Details can be found in the scope for this further update here: Project information | Suspected sepsis: recognition, diagnosis and early management – source control, rapid antigen tests, indicators of organ hypoperfusion, intravenous fluids, and

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					vasopressors in the NEWS2 population | Guidance | NICE
MeMed Diagnostics Ltd	Guideline	025	018	Within the draft guideline, the antimicrobial prescribing decision for the low to moderate risk of severe illness NEWS2 group is extended for up to 6 hours to gather more information for a more specific diagnosis. Within this patient subgroup, a set of biomarkers (i.e., CRP+TRAIL+IP-10 measurements with an applied machine learning decision algorithm on automated platforms) could improve antimicrobial stewardship decisions by providing insights on the underlying infectious aetiology. Although standard venous blood sampling is not recommended (i.e., perform blood tests if indicated), the low to moderate risk of severe illness NEWS2 group likely represents the patient group where antimicrobial stewardship interventions will have the biggest impact. Consideration could be given to use the biomarker-set as part of the clinical assessment to inform the diagnosis and antimicrobial prescribing decision.	Thank you for your comment. Biomarker diagnostic tests were outside the scope of this guideline update. A further update of the guideline is planned and NICE are considering updating recommendations on rapid antigen tests for guiding treatment of suspected sepsis. Details can be found in the scope for this further update here: Project information | Suspected sepsis: recognition, diagnosis and early management – source control, rapid antigen tests, indicators of organ hypoperfusion, intravenous fluids, and vasopressors in the NEWS2 population | Guidance | NICE
MeMed Diagnostics Ltd	Guideline	036	014	Epidemiological studies on the presentation and management of sepsis in England are of tremendous value. On the other hand, the COVID-19 pandemic has clearly demonstrated that sepsis can be triggered by different infectious aetiologies and understanding this aetiology distribution in sepsis and suspected-sepsis patients would provide slightly different but valuable epidemiological insights. Through application of the currently available diagnostic tool that differentiates bacterial from viral infections (i.e., 'CRP+TRAIL+IP-10'	Thank you for your comment. Diagnostic tests were outside the scope of this guideline update. A further update of the guideline is planned and NICE are considering updating recommendations on rapid antigen tests for guiding treatment of suspected

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				biomarker signature score), the underlying infection aetiology distribution triggering sepsis can be studied to inform future clinical practice related to antimicrobial prescribing in suspected-sepsis patients.	sepsis. Details can be found in the scope for this further update here: Project information | Suspected sepsis: recognition, diagnosis and early management – source control, rapid antigen tests, indicators of organ hypoperfusion, intravenous fluids, and vasopressors in the NEWS2 population | Guidance | NICE
Meningitis Research Foundation	Guideline	039	013	The committee point out that acute illness is a dynamic state, and we agree. As such, we think it would be appropriate to include suggested monitoring frequencies especially for certain groups such as adolescents for whom the NEWS2 score may be unreliable.	Thank you for your comment. The committee considered this issue and have added a recommendation outlining the need to re-calculate a NEWS2 score and re-evaluate risk of sepsis periodically in line with the AoMRC report.
Meningitis Research Foundation	Guideline	005	017	Whilst we are aware that we can only comment on the yellow highlighted changes we believe that the new risk stratification which relies on NEWS2 score compared to the previous risk stratification based on meeting any high risk criteria in order to receive broad spectrum antibiotics within one hour of assessment risks delaying life-saving treatment with antibiotics in adolescents presenting with Invasive meningococcal disease (IMD). Adolescents with sepsis are a special case and should be specifically mentioned as such, with a warning in the guidance not to overly rely on NEWS for this age group because:	Thank you for your comment. The risk assessment and treatment of children and young people with suspected sepsis (PEWS) is outside the scope of this guideline update. In the future, we plan to review the use of the paediatric early warning score (PEWS), and consider making recommendations on this in the guideline The committee considered the issue of the move from PEWS to NEWS2 and agreed that clinical judgement should apply in this

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				• There is no evidence on what age, physiologically, one should move from using PEWS to NEWS2, so reliance on NEWS2 in adolescents is risky. • Adolescents can display low NEWS2 scores despite being very unwell. At MRF we often hear of deaths that occur in adolescents aged 16 and over in which cardiovascular parameters and blood pressure are well preserved by teenagers and by the time they decompensate with meningococcal or any other type of sepsis, it's too late for them due to cardiac compensation. We have real concerns that over reliance on a NEWS2 assessment in this age group could lead to delays in treatment with antibiotics and subsequently result in more preventable deaths. • Junior Ds are fallible in their clinical assessments. Research looking at the effect of suboptimal healthcare delivery on outcomes of patients with IMD[1] found that: o Optimal early management of IMD at the admitting hospital can improve outcomes o Children being looked after by doctors without paediatric training were at increased risk of dying. Often this was as a result of drs trained to recognise serious illness in adults failing to recognise compensated shock in children where hypotension can be a late sign due to the maintenance of blood pressure through vasoconstriction and tachycardia. Whilst the maximum age of children participating in this study we are in contact with families of fatal cases of young adults who presented similarly.	situation and remain a key component of risk assessment for sepsis. Clinical tools are not accurate enough to be used without clinical judgement but can help with decision making.

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				We would like to see adolescents and young adults be mentioned within those people who are most vulnerable to sepsis, particularly IMD. The reasons for this are as follows: • A recent multicentre study which took place across Europe concluded that despite accounting for a relatively small fraction of all ED visits, febrile adolescents have an increased risk of serious bacterial infections, including sepsis/meningitis, in comparison with younger children[2]. The authors state that more research is needed to be able to provide detailed guidelines for this age group. • Recent data from UKHSA has shown a rapid increase in IMD during epidemiological year 21/22 in the 15 to 24 year old age group particularly as a result of group B meningococcal disease with the incidence in this age group now higher than in children aged 1 to 4. During the same year there were an estimated 12 deaths in all ages with at least 3 of these within the 19-22 year old age group[3,4]. Levels of disease in this age group are now similar to the levels we saw pre-pandemic, but if they continue to increase at this rate they could soon exceed this. The recent elevated levels of GAS infections in this age group also highlight the need for this group to be considered at increased risk. • IMD is rapidly fatal, especially in adolescents. An analysis of 8 years worth of deaths from IMD in England between 2008 and 2015 showed that around 90% of all deaths as a result of confirmed IMD took place within the first 24 hours of diagnosis. In the 15 to 24 year old age group this was even higher at 96%[5].	

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				References 1) Ninis, Nelly, et al. "The role of healthcare delivery in the outcome of meningococcal disease in children: case-control study of fatal and non-fatal cases." Bmj 330.7506 (2005): 1475. 2) Borensztajn, Dorine, et al. "Characteristics and management of adolescents attending the ED with fever: a prospective multicentre study." BMJ open 12.1 (2022): e053451. 3) Invasive meningococcal disease in England: annual laboratory confirmed reports for epidemiological year 2021 to 2022. Available from Invasive meningococcal disease in England: annual laboratory confirmed reports for epidemiological year 2021 to 2022 - GOV.UK (www.gov.uk) 4) JCVI minutes - Extraordinary JCVI meeting to discuss polio and meningococcal B Minute of the meeting held on 25 July 2022. Available from Extraordinary JCVI polio and meningococcal B meeting draft minute July 2022.pdf | Powered by Box 5) Beebeejaun, Kazim, et al. "Invasive meningococcal disease: timing and cause of death in England, 2008–2015." Journal of Infection 80.3 (2020): 286-290	
Meningitis Research Foundation	Guideline	014	General	There is a lack of clarity within this guidance about how often the NEWS2 assessment should be repeated and results considered. The NEWS2 report[1] suggests that for those in the low-score group, the minimum frequency of monitoring should be 12 hourly, increasing to 4–6 hourly for an aggregate NEW score of 1–4. They also recommend that the frequency of monitoring should be increased to a	Thank you for your comment. The committee considered this issue and have added a recommendation outlining the need to re-calculate a NEWS2 score and re-evaluate risk of sepsis periodically in line with the AoMRC report.

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				minimum of every hour for those patients with an aggregate NEW score of 5–6, or a red score of 3 in a single parameter and while any patient can be considered for continuous monitoring, it is essential for patients with a score of 7 or more. References 1) NEWS2 Final Report. Available from https://www.rcplondon.ac.uk/projects/outputs/national-early-warning-score-news-2	
Meningitis Research Foundation	Guideline	014	General	In those aged 16 and over in acute hospital settings, acute mental health settings and ambulances, there is no longer any mention of the presence of a non-blanching rash of the skin, mottled or ashen appearance, cyanosis of the skin, lips or tongue being a trigger to: • arrange an immediate review with a senior clinical decision maker • administer broad spectrum antibiotics within an hour. Suspected sepsis with a non-blanching rash is indicative of Invasive Meningococcal disease (IMD) which needs urgent treatment with antibiotics. We are very concerned that this is no longer addressed in this setting and the defined population. We suggest that Rec 1.5.3 includes mention of the presence of non-blanching rash of the skin, mottled or ashen appearance, cyanosis of the skin, lips or tongue as a reason to consider someone at high risk of severe illness or death from sepsis.	Thank you for your comment. The committee considered this issue and have added a recommendation acknowledging the need to elevate the person's risk of sepsis in the context of certain clinical signs. The committee wanted to highlight that mottled or ashen appearance, non-blanching rash of skin or cyanosis of skin, lips or tongue are signs of meningococcal disease.

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Meningitis Research Foundation	Guideline	019	007	Rec 1.10.1 is now ambiguous. It is now unclear what is "1 or more high risk criteria" because risk is no longer stratified in this way for those aged over 16 in acute hospital settings. Presumably for over 16s in the acute hospital setting this should now be referred to using the same language as is used in line 11 of page 18 i.e amend line 7 to " For people aged 16 or over with suspected sepsis and at high risk of severe illness or death from sepsis:"	Thank you for your comment. To create a joined up pathway, we have subsequently updated the recommendations that are not about antibiotics, but that relate to the initial management of suspected sepsis in an acute hospital setting.
Meningitis Research Foundation	Guideline	020	006	Rec 1.10.3 is ambiguous. Page 18 Lines 12 to 14 and page 19, lines 1 to 6 defines what makes a patient at "high risk of severe illness or death from sepsis". Recommendation 1.10.2 outlines the antibiotics to be provided to those with high risk. Then recommendation 1.10.3 provides an alternative for those who have already been defined to be at high risk. This is unnecessarily confusing. We would suggest simplifying the language to make the distinction between the two different categories of high risk clearer to make this easier for busy clinicians to implement as intended.	Thank you for your comment. This recommendation and rationale has undergone further revision to improve its clarity.
Meningitis Research Foundation	Guideline	023	General	It would be helpful to include some recommendations about monitoring and when the NEWS2 assessment should be carried out again to check to deterioration.	Thank you for your comment. The committee considered this issue and have added a recommendation outlining the need to re-calculate a NEWS2 score and re-evaluate risk of sepsis periodically in line with the AoMRC report.
Meningitis Research Foundation	Guideline	035	General	It would be helpful to include some recommendations about monitoring and when the NEWS2 assessment should be carried out again to check to deterioration.	Thank you for your comment. The committee considered this issue and have added a recommendation outlining the need to re-calculate a NEWS2 score and re-evaluate risk of sepsis periodically in line with the AoMRC report.

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Meningitis Research Foundation	Guideline	039	001	We strongly agree that use of clinical judgement is of utmost importance when considering NEWS2 scores. But we know that clinical judgement is fallible[1]. We would recommend that adolescents be mentioned in this guidance as a special case due to the fact that there is no evidence on when, physiologically, one should move from using PEWS to NEWS2. Anecdotally at MRF we have heard many stories of young adults over the age of 16 who tragically died of invasive meningococcal disease but who had relatively low NEWS2 scores at the time they presented to hospital. References 1) Ninis, Nelly, et al. "The role of healthcare delivery in the outcome of meningococcal disease in children: case-control study of fatal and non-fatal cases." Bmj 330.7506 (2005): 1475.	Thank you for your comment. The risk assessment and treatment of children and young people with suspected sepsis (PEWS) is outside the scope of this guideline update. In the future, we plan to review the use of the paediatric early warning score (PEWS), and consider making recommendations on tis in the guideline
National Spinal Injuries Centre	Guideline	General	General	Patients with spinal cord injury often require alternative parameters for diagnosis and treatment of sepsis due to their altered baseline physiology (much like the obstetric and paediatric populations) and so it is strongly recommended that the guidance include a caveat regarding this.	Thank you for your comment. The committee considered this issue and have added a recommendation outlining that NEWS2 can be less accurate in people with certain conditions, such as people with spinal injury or heart or lung disease, because of their altered baseline physiology.
National Spinal Injuries Centre	Guideline	006	011	Rec 1.1.8 NEWS2 specificity can be as low as 35% (Ahmed et al 2018, PMID 31358907) in patients with spinal cord injury. Sensitivity of NEWS2 in the spinal injuries population is currently being investigated and so NEWS2 as a screening tool for sepsis must be used with caution.	Thank you for your comment. The committee considered this issue and have added a recommendation outlining that NEWS2 can be less accurate in people with certain conditions, such as people with

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					spinal injury or heart or lung disease, because of their altered baseline physiology.
National Spinal Injuries Centre	Guideline	007	005	Rec 1.2 Those with spinal cord injury are not necessarily more vulnerable to sepsis but this would be a logical section in which to include a caveat regarding altered presentation in the spinal injury population.	Thank you for your comment. The committee considered this issue and have added a recommendation outlining that NEWS2 can be less accurate in people with certain conditions, such as people with spinal injury or heart or lung disease, because of their altered baseline physiology.
National Spinal Injuries Centre	Guideline	010	005	Rec 1.3.8 We strongly recommend "people with a spinal cord injury" be added to this list.	Thank you for your comment. We have added people with a spinal cord injury to this recommendation.
National Spinal Injuries Centre	Guideline	010	025	Rec 1.3.11 In patients with a spinal cord injury the blood pressure will vary in the first months after injury and their long term pressure will relate to their grade and level of cord injury. Low blood pressure as defined by NEWS2 can be unreliable in this group. Acute presentations can result in raised blood pressure, possibly leading to the potentially fatal condition of autonomic dysreflexia with systolic pressure 20mmhg above baseline. This is frequently not detected by NEWS2 screening.	Thank you for your comment. The committee considered this issue and have added a recommendation outlining that NEWS2 can be less accurate in people with certain conditions, such as people with spinal injury or heart or lung disease, because of their altered baseline physiology.
National Spinal Injuries Centre	Guideline	014	004	Rec 1.5 NEWS2 should be used with caution in the spinal injuries population due to concerns over sensitivity and specificity.	Thank you for your comment. The committee considered this issue and have added a recommendation outlining that NEWS2 can be less accurate in people with certain conditions, such as people with spinal injury or heart or lung disease,

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					because of their altered baseline physiology.
National Spinal Injuries Centre	Guideline	018	002	NEWS2 should be used with caution in the spinal injuries population due to concerns over sensitivity and specificity.	Thank you for your comment. The committee considered this issue and have added a recommendation outlining that NEWS2 can be less accurate in people with certain conditions, such as people with spinal injury or heart or lung disease, because of their altered baseline physiology.
National Spinal Injuries Centre	Guideline	025	003	Rec 1.12 Due to concerns over sensitivity and specificity of NEWS2 scoring in the spinal injuries population, it is felt that a score of 1-4 CANNOT be equated to a low-moderate risk.	Thank you for your comment. The committee considered this issue and have added a recommendation outlining that NEWS2 can be less accurate in people with certain conditions, such as people with spinal injury or heart or lung disease, because of their altered baseline physiology.
National Spinal Injuries Centre	Guideline	027	002	Rec 1.13 Due to concerns over sensitivity and specificity of NEWS2 scoring in the spinal injuries population, it is felt that a score of 0 CANNOT be equated to a low risk.	Thank you for your comment. The committee considered this issue and have added a recommendation outlining that NEWS2 can be less accurate in people with certain conditions, such as people with spinal injury or heart or lung disease, because of their altered baseline physiology.

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NHS England	Guideline	General	General	We strongly suggest that where there is reference to information gathering throughout the guideline, this is expanded to include and consider the importance of communication. Staff should communicate with and try to understand the person they are caring for. Check with the person themselves, their family member or carer or their hospital or communication passport for the best way to achieve this and involve families and carers in conversations regarding their care, where requested or stated as a preference. Use simple, clear language, avoiding medical terms and 'jargon' wherever possible. Some people may be non-verbal and unable to tell you how they feel. Pictures may be a useful way of communicating with some people, but not all. There are risks of a Sepsis diagnosis being missed in people with a learning disability resulting from people being unable to communicate their needs and communication preferences not being followed by healthcare staff. We also strongly suggest the guideline referencing diagnostic overshadowing: This occurs when the symptoms of physical ill health are mistakenly either attributed to a mental health or behavioural problem or considered inherent to the person's learning disability or autism diagnosis. People with a learning disability or autism have the same illnesses as everyone else, but the way they respond to or communicate their symptoms may be different and not obvious. Their presentation with Sepsis may be different from that for people without a learning disability or autism. We strongly suggest adjusted assessment tools are utilised by clinical staff.	Thank you for your comment. The committee considered this issue and have addressed your concerns by the following: • In recommendation 1.3.14 learning disability was added as a factor that may cause a change in cognitive function. • In recommendation 1.18.1 the needs of people with additional needs has been added such as autism or learning disabilities when tailoring the timing, content and delivery of information. We are not aware of an adjusted assessment tool for NEWS2. At the beginning of the guideline there is a 'making decisions about your care' box which links to guidelines around shared decision making and patient experiences, which highlights the importance of communication.

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NHS England	Guideline	General	General	Given the evidence surrounding Sepsis being one of the main causes of deterioration (as referenced by the LeDeR report) in people with a learning disability, we strongly suggest staff learn from experiences for caring with people with a learning disability or autistic people. We strongly suggest there is reference to raising and listening to feedback and concerns from people and family members and the availability of Ask Listen Do resources.	Thank you for your comment. The committee considered this issue and have addressed your concerns by the following: • In recommendation 1.3.14 learning disability was added as a factor that may cause a change in cognitive function. • In recommendation 1.18.1 the needs of people with additional needs has been added such as autism or learning disabilities when tailoring the timing, content and delivery of information.
NHS England	Guideline	General	General	NEWS2 is not universally used in primary care and would encourage and support an increased awareness of this scoring system.	Thank you for your comment. This issue is outside the scope of this guideline update as NEWS2 has not yet been validated, or endorsed by NHS England, for use in primary care.
NHS England	Guideline	010	002	Where the guideline makes reference to 'Confusion, mental state and cognitive state in suspected sepsis', we strongly suggest making reference to diagnostic overshadowing. This occurs when the symptoms of physical ill health are mistakenly either attributed to a mental health or behavioural problem or considered inherent to the person's learning disability or autism diagnosis. People with a learning disability or autism have the same illnesses as everyone else, but the way they respond to or communicate their symptoms may be different and not obvious. Their presentation with Sepsis may be different from that for people without a learning disability or autism.	Thank you for your comment. The committee considered this issue and have addressed your concerns by the following: • In recommendation 1.3.14 learning disability was added as a factor that may cause a change in cognitive function. • In recommendation 1.18.1the needs of people with additional needs has been added such as autism or learning

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				It is critical ensure health professionals understand existing issues with mental capacity and 'cognitive state' arising from a learning disability and how this differs from confusion, mental state and cognitive state associated with a Sepsis infection.	disabilities when tailoring the timing, content and delivery of information.
NHS England	Guideline	014	12-21	This paragraph could be interpreted that high NEWS2 scores always relate to sepsis. Suggest amending the wording to reflect that not all patients with high NEWS2 scores have sepsis as in p18 L12-14	Thank you for your comment. The committee considered this issue and agreed that no further changes were needed because the recommendation already states that NEWS2 scores are being used here in people with suspected or confirmed infection.
NHS England	Guideline	014	04-05	Box in between lines 4 and 5 – amend 'The NEWS2 should not be used…' to 'The NEWS2 score should not be used…'	Thank you for your comment however this sentence is referring to the NEWS2 tool rather than the score.
NHS England	Guideline	014	006	Where the guideline references "history taking and physical examination results", we strongly suggest this is expanded to give reference to include and consider the importance of communication. Staff should communicate with and try to understand the person they are caring for. Check with the person themselves, their family member or carer or their hospital or communication passport for the best way to achieve this and involve families and carers in conversations regarding their care, where requested or stated as a preference. Use simple, clear language, avoiding medical terms and 'jargon' wherever possible. Some people may be non-verbal and unable to tell you how they feel. Pictures may be a useful way of communicating with some people, but not all.	Thank you for your comment. The committee considered this issue and have addressed your concerns by the following: • In recommendation 1.3.14 learning disability was added as a factor that may cause a change in cognitive function. • In recommendation 1.18.1 the needs of people with additional needs has been added such as autism or learning disabilities when tailoring the timing, content and delivery of information.

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				We strongly suggest the guideline references the possibility that when caring for a person with a learning disability and some autistic people, they may not be able to articulate their response to pain in the expected way: for example, they may say that they have a pain in their stomach when the pain is not there; may say the pain is less acute than you would anticipate; or not say they are in pain when they are. Some may feel pain in a different way or respond to it differently: for example, by displaying challenging behaviour; laughing or crying; trying to hurt themselves; or equally may become withdrawn or quiet. We strongly suggest reference to making reasonable adjustments: This is a legal requirement as stated in the Equality Act 2010 and is important to help you make the right diagnostic and treatment decisions for an individual. You can ask the person and their carer or family member what reasonable adjustments should be made. Adjustments aim to remove barriers, do things in a different way, or to provide something additional to enable a person to receive the assessment and treatment they need. Possible examples include allocating a clinician by gender, taking blood samples by thumb prick rather than needle, providing a quiet space to see the patient away from excess noise and activity.	At the beginning of the guideline there is a 'making decisions about your care' box which links to guidelines around shared decision making and patient experiences, which highlights the importance of communication. As reasonable adjustments are a legal requirement, we expect that these are being implemented and therefore didn't include them as part of the recommendations. The requirement for them to be made applies across all sections of the current guideline and to every NICE guideline.

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NHS England	Guideline	016	026	Where the guideline references advance care planning, we strongly suggest this makes reference to the existence of healthcare passports and their use. Some people with a learning disability and some autistic people may have a healthcare passport giving information about the person and their health needs, preferred method of communication and other preferences. Ask the person or their accompanying carer if they have one of these. We strongly suggest reasonable adjustments are in place during advance care planning: These are a legal requirement as stated in the Equality Act 2010 and is important to help you make the right diagnostic and treatment decisions for an individual. You can ask the person and their carer or family member what reasonable adjustments should be made. Adjustments aim to remove barriers, do things in a different way, or to provide something additional to enable a person to receive the assessment and treatment they need. Possible examples include allocating a clinician by gender, taking blood samples by thumb prick rather than needle, providing a quiet space to see the patient away from excess noise and activity. We strongly suggest this section is expanded to include consideration for existing multidisciplinary input into the care of the person. This may include but is not limited to epilepsy, cardiology, syndrome specific specialists. Consideration should also be given to the role of an organisation's learning disability team or liaison nurse on issues of communication, reasonable adjustments, pain assessment etc. Further resources to ensure appropriate care for people with a learning disability and autistic people are as follows:	Thank you for your comment. The committee considered this issue and have addressed your concerns by the following: • In recommendation 1.3.14 learning disability was added as a factor that may cause a change in cognitive function. • In recommendation 1.18.1 the needs of people with additional needs has been added such as autism or learning disabilities when tailoring the timing, content and delivery of information. As reasonable adjustments are a legal requirement, we expect that these are being implemented and therefore didn't include them as part of the recommendations. The requirement for them to be made applies across all sections of the current guideline and to every NICE guideline.

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				• https://www.england.nhs.uk/long-read/dnacpr-and-people-with-a-learning-disability-and-or-autism/ • https://www.local.gov.uk/our-support/partners-care-and-health/care-and-health-improvement/autistic-and-learning-disabilities/training • https://www.england.nhs.uk/learning-disabilities/improving-health/summary-care-records/ • https://digital.nhs.uk/services/reasonable-adjustment-flag	
NHS England	Guideline	016	029	There is a concern around the advocating of antibiotic administration in pre-hospital settings. While most people will live within an hour travel time of a hospital, delays in handovers may bring all areas into scope for this recommendation. This has the potential to greatly increase administration of broad spectrum antibiotics, and missing opportunities to fulfil the recommendations around diagnosis in 1.9 and 1.10. Choice of antibiotic is recommended to be determined locally but, as paramedics serve multiple hospitals, this may again lead to increase broad spectrum antibiotics. As the diagnostic process will not have been followed, the option to give source specific, narrower spectrum antibiotics will also be missed. Would suggest that if NICE is advocating pre-hospital antibiotics in these situations the guidelines must also advocate pre-hospital diagnostics. Cheng et al demonstrated that administering antibiotics before blood culture draw in patients with sepsis reduced the positivity rate for blood cultures from 31% to 19%, which would have a deleterious impact on the subsequent management of patients with sepsis (Cheng MP, Stenstrom R, Paquette K, Stabler SN, Akhter M, Davidson AC, Gavric M, Lawandi A, Jinah R, Saeed Z, Demir K, Huang K, Mahpour A, Shamatutu C, Caya C, Troquet JM, Clark G,	Thank you for your comment. The committee considered this issue but based on their clinical experience agreed that diagnostic processes outside of the hospital setting is problematic. These tests should be conducted in secondary care.

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				Yansouni CP, Sweet D; FABLED Investigators. Blood Culture Results Before and After Antimicrobial Administration in Patients With Severe Manifestations of Sepsis: A Diagnostic Study. Ann Intern Med. 2019 Oct 15;171(8):547-554. doi: 10.7326/M19-1696. Epub 2019 Sep 17. PMID: 31525774.)	
NHS England	Guideline	018	000	Strengthen wording on the time critical nature of blood cultures. The chance of obtaining a positive blood culture is closely related to the volume of blood sampled and their optimal (timely) processing. Aside from pre-test probability, the volume of blood cultured in adults is key to detecting bacteraemia, and the scientific evidence supporting this is extremely strong (Bouza 2012). Ideally, between 40 to 60 ML of blood should be cultured. For example, when blood cultures containing a standard vs low volume of blood were compared, the sensitivity of blood cultures for the diagnosis of blood stream infection was 92% vs 69%, respectively[1]. Multiple other studies have confirmed the effect of blood culture volume for optimising the diagnostic yield of these crucial clinical samples[2,3]. Notably, in particularly ill patients (with an APACHE II score of >18), the blood stream infection detection rate increased by 3% for each extra millilitre of blood cultured[4]. 1) Mermel L. A., Maki D. G. (1993). Detection of bacteremia in adults: consequences of culturing an inadequate volume of blood. *Ann. Intern. Med.* 119, 270–272.	Thank you for your comment. The issue you've raised is outside the scope of this guideline update. A link to the UK Health Security Agency guidance on UK Standards for Microbiology Investigations has been added to section 1.9.

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				2) Fabre V, Carroll KC, Cosgrove SE. Blood Culture Utilization in the Hospital Setting: a Call for Diagnostic Stewardship. J Clin Microbiol. 2022 Mar 16;60(3):e0100521. 3) Lamy B, Dargere S, Arendrup MC, Parienti JJ, Tattevin P. 2016. How to optimize the use of blood cultures for the diagnosis of bloodstream infections? A state-of-the art. Front Microbiol 7:697. 4) Bouza E, Sousa D, Rodríguez-Créixems M, Lechuz JG, Muñoz P. Is the volume of blood cultured still a significant factor in the diagnosis of bloodstream infections? J Clin Microbiol. 2007 Sep;45(9):2765-9.	
NHS England	Guideline	018	000	Strengthen wording on review of antimicrobial therapy in light of microbiological testing results. Refer to Start Smart- Then Focus programme.	Thank you for your comment. The committee considered this issue and have clarified in the recommendation the need to review the choice of antibiotic and change to a narrower spectrum antibiotic once the source of infection has been confirmed.
NHS England	Guideline	018	000	No reference to blood culture standards required for an accurate diagnosis of suspected sepsis. Even though diagnosis is part of the guidance and even though it states the requirement to make a definitive diagnosis of the condition, this is by Physical examination i.e., Blood Pressure, temperature, oxygen saturation, colour of skin etc. It at no point indicates the role of microbiological testing to diagnose or in appropriate modification (escalation/de-escalation) of antimicrobial treatments. Given this NICE guidance covers 'the recognition, diagnosis and early management of sepsis for all populations' and that one of the drivers behind the 2023 review of this guidance is to "improve	Thank you for your comment. The issue you've raised is outside the scope of this guideline update. A link to the UK Health Security Agency guidance on UK Standards for Microbiology Investigations has been added to section 1.9.

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				antimicrobial stewardship at the earliest opportunity", we feel that this section needs to be covered more fully. Propose expanding this section so it outlines the key requirements of using blood cultures to diagnose sepsis, also outlined in the *UK Standards for Microbiology Investigations - Sepsis and systemic or disseminated infections*: (a) 2 blood culture sets to be taken, (b) 8-10ml of blood per bottle, (c) time from collection to analyser to be no more than 4 hours In an optimised blood culture pathway, most blood cultures placed on the analysers within 4 hours will register positive within twelve hours of collection (most within 8 - 12 hours). The delay in time will have further negative impact on blood culture sensitivity as with each hour delay of placement on analyser there is a loss of organism viability. NHS England colleagues very happy to support in developing this section. Please contact england.cso@nhs.net if needed.	
NHS England	Guideline	018	000	Link to NICE's 2016 guideline on antimicrobial stewardship is not the most relevant reference in this instance. Suggest updating section 1.9 to include link to S12 guidance *UK SMI S 12: Sepsis and systemic or disseminated infections'* and NHS England's report into the appropriate use of blood cultures to diagnose sepsis. Suggest these links as they explicitly reference the standards required for blood culture collection, transportation and analysis	Thank you for your comment. The issue you've raised is outside the scope of this guideline update. A link to the UK Health Security Agency guidance on UK Standards for Microbiology Investigations has been added to section 1.9.

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				which is a vital diagnostic test for sepsis. This will make it easier for the reader to access the relevant information quickly.	
NHS England	Guideline	018	002	Box in between lines 2 and 3 – amend 'The NEWS2 should not be used…' to 'The NEWS2 score should not be used…'	Thank you for your comment however this sentence is referring to the NEWS2 tool rather than the score.
NHS England	Guideline	018	005	Consider rewording to increase the scope of advice around timing of cultures and antibiotics to encourage best practice in patients who are diagnosed out of hospital. Whilst it must be acknowledged that this is more challenging to do outside of hospital settings there are some instances where it may be prudent and possible to take some samples if giving antibiotics prior to admission.	Thank you for your comment. The committee considered this issue but based on their clinical experience agreed that diagnostic processes outside of the hospital setting is problematic. These tests should be conducted in secondary care.
NHS England	Guideline	019	028	Consider changing 'a broad-spectrum antibiotic' to 'a broad-spectrum antibiotic regimen'. This allows flexibility for providers to recommend appropriate combinations of narrower spectrum agents rather than a single broad-spectrum agent such as a carbapenem.	Thank you for your comment. The committee considered this issue and have amended the wording to broad spectrum antibiotic treatment.
NHS England	Guideline	019	030	The phrase "if it has not been given before" could be misconstrued as "if the chosen antibiotic has not been given before". Consider changing to "unless a broad-spectrum antibiotic regimen has already been administered".	Thank you for your comment. The committee considered this issue but felt that further amendments were not needed.
NHS England	Guideline	021	000	Consider adding "Review antimicrobial therapy in light of microbiological testing results". This is an opportunity to ensure the patient is given the most targeted treatment as soon as possible in line with the stated aims of this guidance review.	Thank you for your comment. The committee considered your feedback and agreed that the current wording is clear.

Suspected Sepsis: recognition, diagnosis and early management (update)

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24/03/23 to 21/04/23

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Stakeholder	Document	Page No	Line No	Comments Please insert each new comment in a new row	Developer's response Please respond to each comment
NHS England	Guideline	023	012	Consider rewording this bullet point, as the current use of term 'broad spectrum antibiotic' and expressed as a singular, implies that this should be monotherapy with a single agent such as pipercillin/tazobactam or a carbapenem. Such a broad spectrum choice may not be necessary, depending on the context and broad spectrum coverage (if required) can also be achieved with the administration of a number of narrower spectrum agents which provide a combined broad spectrum of cover. Recommendation 1.11.3 talks about antibiotics in the plural, and reinforces the point above about the implications of the wording around a broad-spectrum antibiotic in recommendation 1.11.2 Suggest change wording to '…deferring administration of antibiotic treatment for up to 3 hours…'	Thank you for your comment. The committee considered this issue and have amended the wording to broad spectrum antibiotic treatment.
NHS England	Guideline	023	015	In addition to using the available time to gather information for a more specific diagnosis, it would also be helpful to recommend using the time to review previous microbiology culture & susceptibility results if available and check for evidence of past colonisation or infection with multi-resistant organisms, which may require alteration of empiric antibiotic choice.	Thank you for your comment. The issue raised is outside the scope of this guideline update. https://www.nice.org.uk/guidance/gid-ng10310/documents/final-scope A further update of the guideline is planned and NICE are considering updating recommendations on rapid antigen tests for guiding treatment of suspected sepsis. Details can be found in the scope for this further update here: Project information | Suspected sepsis: recognition, diagnosis and early management – source control, rapid antigen tests, indicators of organ

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					hypoperfusion, intravenous fluids, and vasopressors in the NEWS2 population | Guidance | NICE
NHS England	Guideline	025	018	Similar to comment number 4 above, use of the term 'broad-spectrum antibiotic' in the singular implies that a monotherapy with a single agent is required for patients with a low to moderate risk of severe illness or death from sepsis and may drive inappropriately broad-spectrum antibiotic use which is associated with longer term harmful consequences for patients, given that these are low risk patients. Consider rewording to '…deferring administration of antibiotic treatment for up to 6 hours…'	Thank you for your comment. The committee considered this issue and have amended the wording to broad spectrum antibiotic treatment.
NHS England	Guideline	025	021	Similar to comment 5 above; there should be sufficient time to review previous microbiology culture & susceptibility results to ensure that antibiotic choice is appropriate based on past history.	Thank you for your comment. The issue you've raised is outside the scope of this guideline update. https://www.nice.org.uk/guidance/gid-ng10310/documents/final-scope
NHS England	Guideline	028	015	Note switch to the term 'antimicrobials' here when the guideline has referred to antibiotics throughout prior to this. Unusual choice of terminology to class antimicrobials as 'source-specific', they tend to be more pathogen specific as multiple different sources of infection could be treated with one antibiotic. Additionally, it will be important to tailor antibiotic treatment to the available relevant culture & susceptibility results. Consider rewording this statement to 'Tailor the choice of antibiotic (or antimicrobials if this is the preferred term here) to the anticipated pathogens once the source of infection is confirmed and/or microbiology culture & susceptibility results are available, in line with Start Smart then Focus recommendations'. Compliance with this recommendation is likely to be improved by providing a rationale	Thank you for your comment. The committee considered this issue and have clarified in the recommendation the need to review the choice of antibiotic and change to a narrower spectrum antibiotic once the source of infection has been confirmed.

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				that targeted antimicrobial therapy is preferred to limit collateral damage to host microbiota and the associated risk of opportunistic infection (for example with Candida spp. or *C. difficile*) and to preserve the effectiveness of broad-spectrum antimicrobials.	
Nottingham University Hospitals NHS Trust	General	General	General	Unsure whether the process of dissemination is robust enough to ensure a thorough approach to consultation as draft for revision not received via normal communication routes – this has been found based on interest only periodic checking of the NICE guidelines website.	Thank you for your comment. As a registered stakeholder you should have received the draft guideline for stakeholder comment.
Nottingham University Hospitals NHS Trust	Guideline	General	General	Overall this is an unexpected altogether disappointing revision of what has been a very thorough and technically well evidenced and fundamental guideline in the management of patients with sepsis over the last 7 years. It was expected that this revision would provide some degree of sensible harmonisation between the current 2016 NICE Sepsis guidelines and the recently published Academy of Medical Royal Colleges (AoMRC) Statement on the initial antimicrobial treatment of sepsis, trying to solve the clinical disparity between the urgent treatment for those whom are critically unwell with sepsis versus a more measured response in those not as unwell and simplifying the differences in opinion between conflicting academic interests. Instead this revision has focussed almost exclusively on NEWS2 in the NICE guideline for sepsis. With significant emphasis on its now mandated use since it was shoehorned into the compliance criteria during the last quarter of the sepsis CQUIN 2017-2019. It is unclear why there is such emphasis on NEWS2 scores, an arbitrary	Thank you for your comment. The drivers for this update were the endorsement by NHS England of NEWS2 for risk stratification in people aged 16 or over who are not and have not recently been pregnant in acute mental health, hospital and ambulance settings, and new evidence about the timing of administration of antibiotics for people with suspected sepsis. To improve antimicrobial stewardship at the earliest opportunity, we updated these areas of the guideline as a priority and as such, these are the only areas within scope of this update. To create a joined up pathway, we have subsequently updated the recommendations that are not about antibiotics, but that relate to the initial

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				aggregate general physiology scoring system for which there is little available evidence in general or specific to sepsis. What has resulted is a very disjointed and somewhat confusing document with heavy reliance of the NEWS2 score, but then also *"to consider higher risk of severe illness or death than the NEWS2 score suggests if there is cause for concern"*. This is not only difficult to read and digest, and follow at individual clinician level, but also difficult to operationalise at organisational level and to defend medicolegally should the need arise. This partial revision is unworkable without revision of the full guideline.	management of suspected sepsis in an acute hospital setting. A further update of the guideline is planned and NICE are also considering updating recommendations on source control, rapid antigen tests, indicators of organ hypoperfusion, intravenous fluids, and vasopressors. Details can be found in the scope for this further update here: Project information | Suspected sepsis: recognition, diagnosis and early management – source control, rapid antigen tests, indicators of organ hypoperfusion, intravenous fluids, and vasopressors in the NEWS2 population | Guidance | NICE Recommendation 1.5.4 outlines the need to consider elevating the person's risk of severe illness or death from sepsis as being higher than suggested by their NEWS2 score alone if there is cause for concern because of deterioration or lack of improvement. The committee agreed that clinical judgement should apply in this situation and remains a key component of risk assessment for sepsis. Clinical tools are not accurate enough to be used without

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					clinical judgement but can help with decision making.
Nottingham University Hospitals NHS Trust	Guideline	General	General	The instruction that the new revision is only for use adults who are not and have not recently been pregnant is an immediate red flag for complexity, with partial inexplicit qualification of the statement of recent pregnancy some 7 pages after its first mention. Data from UK Obstetric Surveillance Study (UKOSS) suggests that two thirds of maternal sepsis with high risk of morbidity and mortality occurs post partum. Of all occurrences, close to 80% have organ failure and require critical care. It is therefore surprising for this guideline to specifically exclude patients whom are or recently have been pregnant. Especially the latter statement as postpartum patients may be more vulnerable to sepsis as stated in section 1.2 but are now subject to different guidance. Again it is anticipated that this will be difficult to follow at individual clinician level and to operationalise as a standard of care, would those excluded be those who are obviously pregnant from examination or history or should the clinician specifically seek to exclude pregnancy in any patient with the capacity for pregnancy. For example at what point should the pregnancy status be determined during the presentation of acute deterioration which may or may not be sepsis, should one withhold application of interventions in a guideline that specifically excludes those who are pregnant until enough urine can be produced and obtained for a bedside dipstick (difficult if sepsis and acute kidney injury) or wait for laboratory blood	Thank you for your comment. In the future, we plan to review the use of the maternity early warning score (MEWS), and consider making recommendations on this in the guideline

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				analysis, prior to using NEWS2 to direct urgency of care for a time critical condition.	
Nottingham University Hospitals NHS Trust	Guideline	General	General	The phrase "recently pregnant" needs to be replaced throughout with a defined period of time –women who have been pregnant within the previous 6 weeks with specific reference to medical or surgical management of miscarriage or instrumentation of the genital tract and to also cover for termination of pregnancy.	Thank you for your comment. A definition of 'recently pregnant' has now been added to the guideline to provide further clarification.
Nottingham University Hospitals NHS Trust	Guideline	General	General	It is noted that there are several sections suffixed in bold font that "the recommendation will be amended in a future update". In particular this seems to occur for the management of the patient in the acute hospital setting. Here the guidelines begin to revert back to the original NICE sepsis 2016 criteria for physiological observations, despite much of the initial document focussing on NEWS2 scores. Publication at this stage with these comments removes what little confidence there was from the guidelines. By writing they are for review, but not changing them it a) leaves the reader to speculate whether they will change and to what, and b) it leaves the clinician to speculate whether they are incorrect or inadequate or even unsafe, as if they were correct or adequate then they would not need such as disclaimer. It makes it seem like this revision work is unfinished and published anyway, which makes it seem like it has been rushed through, and with the dominant focus on incorporation of NEWS2 does make the experienced clinician further question the utility and credibility of this document and the NICE guideline process as a whole.	Thank you for your comment. To create a joined up pathway, we have subsequently updated the recommendations that are not about antibiotics, but that relate to the initial management of suspected sepsis in an acute hospital setting.

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Nottingham University Hospitals NHS Trust	Guideline	General	General	Reasonable suggestion to delay the publication of this guideline revision until a more thorough review of the whole guideline and research needs section to be explored in enough detail to form part of the guidance which in itself should be more harmonious, easy to read and straightforward to implement, adhere to and audit against. Interim position can NICE release a statement advising Trusts whether they should independently decide to continue to follow NICE 2016 or AoRMC 2022 treatment guides or wait for the latest NICE sepsis revision?	Thank you for your comment. To create a joined up pathway, we have subsequently updated the recommendations that are not about antibiotics, but that relate to the initial management of suspected sepsis in an acute hospital setting.
Nottingham University Hospitals NHS Trust	Guideline	009	006	Initial assessment would be better structured and described as an A-E assessment. This would maintain the familiarity of this structured prompt for examination of the acutely unwell patient based on a hierarchy of need and importance (eg airway and breathing before blood pressure and temperature) which is used in many well known and publicised multi-professional and multi-disciplinary patient assessment systems such as basic, intermediate, paediatric and advanced life support (BLS, ILS, PLS, ALS), advanced trauma life support (ATLS), care of the critically ill surgical patient (CCrISP) and of course the NEWS2 score, described and recorded with headings A through to E.	Thank you for your comment. The issue raised is outside the scope of this guideline update. https://www.nice.org.uk/guidance/gid-ng10310/documents/final-scope
Nottingham University Hospitals NHS Trust	Guideline	014	004	Where the guideline states NEWS2 should not be used for women who are or recently have been pregnant, it should clearly signpost them back to original NICE sepsis criteria, otherwise clinicians are left not knowing how pregnant women should be assessed, risk stratified or managed.	Thank you for your comment. NICE will split the guideline into separate populations (children, adults and pregnant women and people) and publish each as a separate guideline. In the future, we plan to review the use of the maternity early warning score (MEWS),

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					and consider making recommendations on this in the guideline
Nottingham University Hospitals NHS Trust	Guideline	014	014	There is concern that the recommendations which incorporate an objective measure of NEWS2 to guide timeliness of antibiotics, then confuse this guidance with addition of subjective phrases such as "use clinical judgement". This leaves individual clinicians very open to criticism and at best defensive practice will be to give antibiotics whatever occurs, at worst poor and untimely care could be defended with the same judgement terminology. Guidance needs to be clear, and objective and this can be followed rigidly or deviated from with reasons given, rather than guidance written to be deliberately vague which is then difficult to interpret to follow or deviate from.	Thank you for your comment. The committee considered this issue and agreed that clinical judgement should remain a key component of risk assessment for sepsis. Clinical tools are not accurate enough to be used without clinical judgement but can help with decision making.
Nottingham University Hospitals NHS Trust	Guideline	015	001	For hospital adult patients using the objective NEWS2 scores to stratify risk, the presence of organ dysfunction by laboratory testing such as raised lactate or new acute kidney injury needs to be incorporated into the risk stratification for patients who by NEWS2 score alone do not meet criteria for high risk of severe illness or death. Having reassuring NEWS2 score and high lactate is not an unusual presentation of sepsis that does indeed lead to morbidity and mortality in young and generally fit patients. This has been seen locally several times in recent living memory.	Thank you for your comment. A further update of the guideline is planned and NICE are considering updating recommendations on indicators of organ hypoperfusion (including lactate).
Nottingham University	Guideline	019	026	The true time zero of the pathophysiological disease process of sepsis has usually begun long before the calculation of a NEWS2	Thank you for your comment. The recommendations in section 1.7 have been

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Hospitals NHS Trust				score. Time critical antibiotics should be given as soon as possible and ideally within an hour if the patient is unwell and in situations where the patient is meeting criteria *prior* to the set of observations and calculation of the NEWS2 score, the time should not really based on the first *calculated* NEWS2 score on admission to a certain geographical area. For example if there is physiological derangement at arrival to the emergency department the patient meets criteria then, therefore antibiotics should be given as soon as possible, ideally within 1hour of arrival to hospital, not by the time they are triaged and eventually have basic nursing observations taken and NEWS2 calculated. ie there is a need to accept that sepsis starts prior to NEWS2 score, and that late assessment and late NEWS2 scoring and prompt antibiotics is not necessarily a good treatment position.	split by setting into a) primary care (GPs) and b) ambulance services to provide greater clarity. In remote and rural locations where transfer to emergency department and handover times to emergency department are greater than 1 hour, ensure ambulance services have mechanisms in place to give antibiotics to people at high risk of severe illness or death from sepsis. This acknowledges the need to give antibiotics to people at high risk of severe illness or death from as soon as possible in pre-hospital settings. We have asked a specific question regarding implementation of the recommendations flagged in the consultation for a further update of NG51. The consultation documents can be viewed here: Consultation | Suspected Sepsis: recognition, diagnosis and early management (update) | Guidance | NICE
Royal College of Emergency Medicine	Guideline	006	011	Lack of specific times around defining recent pregnancy eg. 42 days for post-partum, 28 early pregnancy loss	Thank you for your comment. A definition of 'recently pregnant' has now been added to the guideline to provide further clarification.

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Royal College of Emergency Medicine	Guideline	014	004	If NEWS2 is not to be used, it would be useful to suggest what should be used instead e.g. MEWS	Thank you for your comment. NICE will split the guideline into separate populations (children, adults and pregnant women and people) and publish each as a separate guideline. In the future, we plan to review the use of the maternity early warning score (MEWS), and consider making recommendations on this in the guideline
Royal College of Emergency Medicine	Guideline	016	026	The caveats around considering individual patient circumstances and not just their NEWS2 score is welcome, and I wonder whether this patient centric approach should have more prominence throughout the whole document rather than merely relying on a NEWS2 score	Thank you for your comment. The committee considered this issue and have added a recommendation acknowledging the need to elevate the person's risk of sepsis in the context of certain clinical signs. The committee wanted to highlight that mottled or ashen appearance, non-blanching rash of skin or cyanosis of skin, lips or tongue are signs of meningococcal disease.
Royal College of Emergency Medicine	Guideline	016	029	Patients attend emergency departments (not admitted) and get admitted to wards. An emergency department attendance is not the same as a hospital admission. This also applies to the rest of the document e.g., 1.10.2 page 19 line 30	Thank you for your comment. The committee considered this issue and have removed 'time before admission to the emergency department' from this recommendation.
Royal College of General Practitioners	Guideline	General	General	The RCGP supports most of the recommendations within the updated guidance and in particular the criteria to assess patients in general practice and the community documenting vital signs, without the mandate to use NEWS2. This aligns with our position statement.	Thank you for your comment.

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Royal College of General Practitioners	Guideline	General	General	The RCGP would like to highlight the increasing evidence on the reliability of pulse oximetry in pigmented skin which is important to understand when assessing pulse oximetry.	Thank you for your comment. The issue has been addressed by a text box below recommendation 1.3.16 which outlines this issue.
Royal College of General Practitioners	Guideline	General	General	It would be useful to reiterate within the guidance that at the current time, the evidence base for use of NEWS within primary care has not reached the threshold required to recommend it's use within primary care as would align with the AoMRC report from 2022 and the RCGP position statement to ensure primary care colleagues understand why it is not currently being recommended.	Thank you for your comment. This issue is outside the scope of this guideline update as NEWS2 has not yet been validated, or endorsed by NHS England, for use in primary care.
Royal College of General Practitioners	Guideline	016	029	In the current NHS climate, it is much less likely that ambulances will arrive in primary care and reach A&E to be handed over within 60 minutes. This recommendation appears to put the onus onto general practice when there is a delay, rather than focussing on improving the transfer time to A&E. In addition, GP surgeries are not routinely set up to give IV antibiotics and only commonly stock one antibiotic for emergencies, IM benzylpenicillin, for those with suspected meningococcal septicaemia. To make a recommendation to "ensure" that all GP surgeries should have the facility to "give antibiotics" with transfer times greater than 1 hour in the current NHS climate will potentially add a huge burden to primary care and mean that every single GP surgery will have to stock a range of antibiotics which will be impractical. In addition, there is the risk that antibiotics will potentially be wasted, as the likelihood of seeing severe sepsis in primary care is low, therefore GP stocks, once out of date, will have to be disposed of. By using the word	Thank you for your comment. The committee considered this issue and the recommendations in section 1.7 have been split by setting into a) primary care (GPs) and b) ambulance services to provide greater clarity. They have also used your suggested recommendation wording. We have asked a specific question regarding implementation of the recommendations flagged in the consultation for a further update of NG51. The consultation documents can be viewed here: Consultation | Suspected Sepsis: recognition, diagnosis and early management (update) | Guidance | NICE

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				"ensure" means this recommendation may become 'mandated' for all GP practices, whereas on reading the evidence, the rationale states this is more likely to be aimed at rural and remote general practice rather than those in urban areas. Could NICE therefore consider amending this statement and separate it into 2 parts? This will then clarify that not all GP practices need to invest in further antibiotics. For example: In remote and rural locations where transfer times to A&E are routinely over 1 hour, ensure GP surgeries and paramedics have the facilities to give antibiotics. In areas where transfer to A&E *and* handover times to A&E teams are greater than 1 hour, ensure paramedics have the facilities to give antibiotics.	
Royal College of Nursing	Guideline	General	General	In light of viral infections such as COVID, should there also be recommendation on when antimicrobials should be administered?	Thank you for your comment. The issue raised is outside the scope of this guideline update. https://www.nice.org.uk/guidance/gid-ng10310/documents/final-scope
Royal College of Nursing	Guideline	002	000	We welcome this new and updated recommendations considering new evidence on the timing of administration of IV antibiotics for patients with sepsis and also to improve antimicrobial stewardship.	Thank you for your comment.
Royal College of Nursing	Guideline	002	000	We agree that further guidance that are not about antibiotics would be helpful.	Thank you for your comment. To create a joined up pathway, we have subsequently updated the recommendations that are not about antibiotics, but that relate to the initial

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					management of suspected sepsis in an acute hospital setting. A further update of the guideline is planned and NICE are also considering updating recommendations on source control, rapid antigen tests, indicators of organ hypoperfusion, intravenous fluids, and vasopressors. Details can be found in the scope for this further update here: Project information | Suspected sepsis: recognition, diagnosis and early management – source control, rapid antigen tests, indicators of organ hypoperfusion, intravenous fluids, and vasopressors in the NEWS2 population | Guidance | NICE
Royal College of Nursing	Guideline	006	011	We fully agree and support the use of NEWS2 to assess people with suspected sepsis.	Thank you for your comment.
Royal College of Nursing	Guideline	014	012	Agree with the emphasis on clinical judgment to interpret NEWS2 score.	Thank you for your comment.
Royal College of Nursing	Guideline	014	017	It would be good to understand the rational for using the terms 'moderate to high' and 'low to moderate'. For simplicity and clarity, can we suggest high, moderate, low, very low risk?	Thank you for your comment. The names of the risk levels have been revised to very low, low, moderate and high in line with stakeholder feedback.

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Royal College of Nursing	Guideline	015	001	AOMRC version 2 recommends that abnormal single parameter should be used to alert clinician but not as mandates for specific treatment.	Thank you for your comment. The committee considered this but agreed that an abnormal single parameter may require managing at a higher risk level than suggested by their NEWS2 score alone.
Royal College of Nursing	Guideline	015	004	Agree with the statement.	Thank you for your comment.
Royal College of Nursing	Guideline	020	006	Agree with the emphasis on clinical judgement to determine IV antibiotics within 1 hr or 3hrs. Suggest bringing forward the explanation on 1.11.2 here.	Thank you for your comment. This recommendation and rationale has undergone further revision to improve its clarity.
Royal College of Nursing	Guideline	028	015	Good to see the recommendation on using source specific antimicrobials.	Thank you for your comment.
Royal College of Pathologists	General	General	General	We welcome this stratification of risk using the NEWS2 score while stressing the importance of considering deterioration in clinical condition and/or a single parameter with a score of 3 or more as a reason to consider when to prescribe antimicrobial treatment 9wihtin 3 vs 6 hours). This very much puts the onus of clinical diagnosis and risk assessment back into the hands of the clinician but with appropriate safety netting. We believe this will help reduce the number of inappropriate antimicrobial prescriptions for non-infective conditions that may also be associated with high NEWS2 scores. We also welcome the inclusion of using source specific antimicrobials rather than a specific broad spectrum for all cases of sepsis, which again promotes good antimicrobial stewardship.	Late Comment – No formal response required

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				This updated guidance should help focus the need for prompt treatment on the patients at high risk of sepsis, allowing more time to confirm a diagnosis in those with a lesser risk of sepsis before prescribing antimicrobials. This should reduce unnecessary antimicrobial consumption and help to prevent the advent of antimicrobial resistance.	
Royal College of Physicians	General	General	General	The RCP is grateful for the opportunity to respond to the above consultation. We have liaised with our Patient Safety Committee and the NEWS2 Improvement Advisory Group and would like to comment as follows. Overall, there was broad support for the recommendation of using NEWS2 and we fully support the consensus position regarding the statement on the initial antimicrobial treatment of sepsis published by the Academy of Medical Royal Colleges (October 2022). There was concern about the lack of conciseness and potential challenge of implementing the guidance but acknowledgment that this will be addressed subsequently. Specific comments that we have received have been provided in the table below and may reflect similar feedback from other stakeholders such as the Royal College of General Practitioners.	Late Comment – No formal response required
Royal College of Physicians	Draft Guideline NEWS2 Update	9	19	Our experts question whether this would this include haematuria or dysuria as well as frequency.	Late Comment – No formal response required

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Royal College of Physicians		11	15	Our experts question whether there is a standard reason/cause for this alert being in turquoise.	Late Comment – No formal response required
Royal College of Physicians		13	Table	Our experts question whether this would include haematuria or dysuria as well as frequency/volume.	Late Comment – No formal response required
Royal College of Physicians		15	8/9	Our experts question what the time frames are between any previous NEWS2 score was calculated/any interventions have taken place.	Late Comment – No formal response required
Royal College of Physicians		33	16 to 20	Our experts question whether this could include seeking any further investigations required to establish if there is any underlying cause for the infection.	Late Comment – No formal response required
Royal College of Physicians		36	18	Our experts suggest that in any future research on incidence and outcomes of sepsis, the 'justification required' would benefit from broader research investigating initial causes.	Late Comment – No formal response required
Royal Wolverhampton NHS Trust	Guideline	General	General	Has the guideline been researched on the Oncology/Haematology cohort of patients and if so, can this be shared with us	Thank you for your comment. The patient groups raised are covered by the NICE Neutropenic sepsis guideline (CG151).
Royal Wolverhampton NHS Trust	Guideline	General	General	Would this document override both NG51 and Neutropenic Sepsis guideline CG151? If not, there will be a conflict of guidance	Thank you for your comment. The NICE Neutropenic sepsis guideline (CG151) will remain separate from the update of the NICE Sepsis guideline (NG51). Both cover distinct patient population groups.
Royal Wolverhampt	Guideline	General	General	We accept the significant concerns around the need for engaging with the antibiotic stewardship programme, however the need for rapid delivery of antibiotics in the Oncology/Haematology group of	Thank you for your comment. This issue is outside the scope of this guideline update

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on NHS Trust				patient has been clearly proven to be necessary. A multivariate analysis by Lin, et al., found that mortality was higher in patients with an absolute neutrophil count (ANC) of <0.1 x 10°L when time to antibiotic therapy was >24 hours in a non-ICU setting.	and is covered by the NICE Neutropenic sepsis guideline (CG151).
Royal Wolverhampton NHS Trust	Guideline	012	000	Document clearly states that Oncology/Haematology patients are vulnerable and in a higher risk category of developing sepsis but attempt to stratify risk in accordance with clinical parameters. The systemic inflammatory response to infection in this cohort of patients is attenuated therefore the diagnostic criteria for sepsis might not be fulfilled and a clear focus of infection might not be found. Stratifying risk cannot be reliant upon someone's vital signs meeting this criteria and there must remain a high index of suspicion for infection and proactive response in all patients undergoing immunosuppressive treatments.	Thank you for your comment. This issue is outside the scope of this guideline update and is covered by the NICE Neutropenic sepsis guideline (CG151).
Sheffield Teaching Hospitals NHS Trust	Guideline	037	General	There may be confusion arising from the assessment of mild to moderate high risk criterion. Concern that some people with sepsis will experience a relevant delay in receiving antibiotics. Operationalising the subtleties of assessing mild-moderate-severe risk will be difficult.	Thank you for your comment. The names of the risk levels have been revised to very low, low, moderate and high in line with stakeholder feedback.
Society For Acute Medicine	Guideline	General	General	that throughout the document it talks about people aged 16 and over however in section 1.14.5 They say for people up to age 17 and then in section 1.14.7 they talk about aged 18 and over. This causes confusion and needs to be more clear.	Thank you for your comment. The different ages used in the guideline are caused when we cross refer to other NICE guidelines that cover different age groups. The NICE meningitis guideline (CG102) covers children and young people up to their 16th birthday. The NG51 suspected sepsis guideline committee was happy to adapt this CG102 recommendation up to

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					young people's 18th birthday, but no further.
Society For Acute Medicine	Guideline	General	General	Too long and wordy. Will not be read by lots of people who are commonly dealing with this and then remembered. Would suggest authors consider an info graphic to accompany it to aid better use. We have also not been able to refrain from commenting on the section in grey. If you're going to update the paper then you need to update the paper and look at it in its entirety. It seems nonsensical to have parts of the paper that are "not to be reviewed".	Thank you for your comment. We have prepared algorithms to be published alongside the updated guideline to assist users. The algorithms can be viewed here: https://www.nice.org.uk/guidance/indevelopment/gid-ng10310/documents Sections in grey will also be addressed in future updates of this guideline.
Society For Acute Medicine	Guideline	019	000	Why would you liaise with a consultant in anaesthetics for your poorly sepsis patient?!	Thank you for your comment. The committee considered this issue and agreed to amend the recommendation.
Society For Acute Medicine	Guideline	020	000	Not keen on referring all patients with high lactate / low BP to Critical Care (especially if that is in fact just an Outreach nurse). Refer for senior input, sure, but mandating a Critical Care review does not seem sensible (I would expect an AIM trainee / Consultant to be able to deal with this)	Thank you for your comment. The committee considered this and amended the recommendation to refer or discuss with a critical care team.
Society For Acute medicine	Guideline	022	000	Suggest the bloods requested for the moderate-high risk patient should be the same as for the high risk patient (ie add a clotting). Unnecessarily complicates things to have two different panel of bloods for the unwell sepsis patient.	Thank you for your comment. Clotting screen has been added to the list of bloods requested for the moderate risk patient.
Society For Acute medicine	Guideline	031	000	Not comfortable with recommending urine analysis in elderly patients (would want that changed to under 65s)	Thank you for your comment. This issue is outside the scope of this guideline update. https://www.nice.org.uk/guidance/gid-ng10310/documents/final-scope

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Thermo Fisher Scientific	Guideline	036	General	As an addition to the current recommendation, it's important to highlight the NIHR Health Technology Assessment funded PRONTO study (PROcalcitonin and NEWS2 evaluation for Timely identification of sepsis and Optimal use of antibiotics in the Emergency **Department**) - Chief Investigator - Prof. Neil French. Sponsor - University of Liverpool. This study aligns with the research recommendation from NICE Diagnostic Guidance 18 (NICE DG18- "Procalcitonin testing for diagnosing and monitoring sepsis", 2015) related to the use of Procalcitonin testing in EDs for guiding antibiotic use in people with suspected sepsis. The study specifically assesses implementing the biomarker alongside the NEWS2 algorithm to demonstrate that addition of PCT measurement to NEWS2 scoring can lead to a reduction in intravenous antibiotic initiation in ED patients managed as suspected sepsis, with at least no increase in 28-day mortality compared to NEWS2 scoring alone. 20 NHS England Emergency Departments are enrolled in this evaluation with an expected recruitment of 7676 adult patients. As of April 2023, more than 6000 patients have been recruited, with target close date in the next 12 months. We are strongly convinced that B·R·A·H·M·S PCT (Procalcitonin) will demonstrate a clinically and economically relevant additional value, when combined with NEWS2, to safely improve early identification of systemic bacterial infection, initiation and timing of antibiotic therapy and aid to reduce unnecessary antibiotic use in the UK.	Thank you for your comment. Biomarker diagnostic tests were outside the scope of this guideline update. A further update of the guideline is planned and NICE are considering updating recommendations on rapid antigen tests for guiding treatment of suspected sepsis. Details can be found in the scope for this further update here: Project information | Suspected sepsis: recognition, diagnosis and early management – source control, rapid antigen tests, indicators of organ hypoperfusion, intravenous fluids, and vasopressors in the NEWS2 population | Guidance | NICE Procalcitonin (PCT) testing was also indicated by the guideline committee as a possible area for update. However, PCT testing is covered by the NICE diagnostics guidance on procalcitonin testing for diagnosing and monitoring sepsis. The ongoing PRONTO trial is comparing PCT-supported assessment with standard care for suspected sepsis in adults at emergency departments, to measure whether this approach reduces antibiotic prescriptions without increasing mortality.

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				We request that the guideline committee will consider the results of this study for extended guidance as soon as they are available.	We will decide whether to update our recommendations on PCT testing once this trial completes. .
UK Health Security Agency	EIA	001	3.2	Regarding the other potential equality issues, we disagree that no other consideration, such as those of ethical and equality nature should be anticipated. Our unpublished data above suggests there are other considerations which align with the Core20PLUS approach which should be considered. Whilst the risk stratification using the NEWS2 tool is based on the measurement of physiological parameters of people with suspected sepsis, the outcomes for patients and incidence of sepsis are not similar. This was clear from COVID-19 and has also been highlighted in our recent studies. It is important that the guideline acknowledges the considerations needed for the impact of factors commonly known to be associated with health inequalities and the additional factors we have highlighted as well as highlight the considerations to healthcare professionals.	Thank you for your comment. The EIA has been revised to acknowledge the need to consider factors commonly associated with health inequalities including those who are more deprived. We are aware of recent data published by the UKHSA and University of Manchester which reports on risk factors for sepsis that are not covered by NEWS2. NICE is planning a further update to the guideline and will consider revising the current recommendation on people who are most vulnerable to sepsis.
UK Health Security Agency	Guideline	029	006	We would list 'ceftriaxone 50 mg/kg unless there is a suspicion of meningitis, in which case 80 mg/kg would be the appropriate dose.'	Thank you for your comment. This issue is outside the scope of this guideline update. https://www.nice.org.uk/guidance/gid-ng10310/documents/final-scope
UK Sepsis Practitioner Forum	Guideline	General	General	We are concerned that the guidance is open to risk to follow in this format re safety, human factors.	Thank you for your comment. To create a joined up pathway, we have subsequently updated the recommendations that are not about antibiotics, but that relate to the initial management of suspected sepsis in an acute hospital setting.

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UK Sepsis Practitioner Forum	Guideline	General	General	We would like NICE to consider including a split guideline; 1) In-hospital trust using NEWS2, 2) pregnant/recently pregnant, 3) Children, 4) In-hospital trust not using NEWS2	Thank you for your comment. We will split the guideline into separate populations (children, adults and pregnant women and people) and publish each as a separate guideline.
UK Sepsis Practitioner Forum	Guideline	006	000	We would like to highlight that some NHS Trusts are not using NEWS2 e.g., Liverpool Heart and chest.	Thank you for your comment. The committee considered this issue and have added a recommendation outlining that NEWS2 can be less accurate in people with certain conditions, such as people with spinal injury or heart or lung disease, because of their altered baseline physiology. As a result, some NHS trusts are not using NEWS2. Your comments will be considered by NICE where relevant support activity is being planned.
UK Sepsis Practitioner Forum	Guideline	014	000	The guideline will be difficult to implement in practice with many trusts using electronic systems to ensure compliance e.g. Nervecentre– informed that will only make amends to AMRoC IF NICE adhere/align to AMRoC. Some trusts' medical staff very much welcome the AMRoC, Royal Cornwall hospital have already changed to AMRoC in ED.	Thank you for your comment and for raising these implementation issues. Your comments will be considered by NICE where relevant support activity is being planned.
UK Sepsis Practitioner Forum	Guideline	019	000	Amended to me made to ensure clear guidance for sepsis. Sepsis is challenging when ensuring screening, recognition and management are timely, creating disjointed guidance that differs per different specialties makes it even harder to operationalise.	Thank you for your comment. To create a joined up pathway, we have subsequently updated the recommendations that are not about antibiotics, but that relate to the initial management of suspected sepsis in an

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					acute hospital setting. Additionally, NICE will split the guideline into separate populations (children, adults and pregnant women and people) and publish each as a separate guideline.
University Hospitals Birmingham	Guideline	014	012	These categorisations are confusing and difficult to implement. Our nurse and junior doctor colleagues may conclude that a NEWS2 score that was 7 and on repeat an hour later declined to 5 would mean improvement of patient's conditions and further delay sepsis intervention? Another way of causing confusion is that when clinically a patient has severe sepsis and yet their NEWS2 is less than 7? The term 'moderate' would not help in management of those patients?	Thank you for your comment and for raising these implementation issues. The committee considered this issue and agreed that clinical judgement should remain a key component of risk assessment for sepsis. Clinical tools are not accurate enough to be used without clinical judgement but can help with decision making. Your comments will be considered by NICE where relevant support activity is being planned.
University Hospitals Birmingham	Guideline	016	016	This instruction is not in line with the instructions on the severity of sepsis? Are we saying that ambulance crew do not need to follow the moderate/ severe categories and should therefore administer antibiotics within an hour irrespective of the category of sepsis?	Thank you for your comment. The recommendations in section 1.7 have been split by setting into a) primary care (GPs) and b) ambulance services to provide greater clarity. In remote and rural locations where transfer to emergency department and handover times to emergency department are greater than 1 hour, ensure ambulance services have

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					mechanisms in place to give antibiotics to people at high risk of severe illness or death from sepsis We have asked a specific question regarding implementation of the recommendations flagged in the consultation for a further update of NG51. The consultation documents can be viewed here: Consultation | Suspected Sepsis: recognition, diagnosis and early management (update) | Guidance | NICE
University Hospitals Birmingham	Guideline	019	019	These categorisations and instructions may not be read as intended in the AoMRC statement. The AoMRC document mentions that the time frames are not intended to permit delay in treatment but to offer a chance to clinicians to make a safe decision. The evidence provided in AoMRC document is on choosing the correct antibiotic instead of aiming to give a broad spectrum antibiotic empirically within an hour of sepsis diagnosis and without obtaining a blood culture. The most helpful evidence for antimicrobial stewardship is having culture results (blood, urine, sputum, etc) available (normally within 48 hours). With those results, one can follow the SMART principles of antimicrobial stewardship. I therefore think the message should be that we should aim to administer antibiotics promptly and after obtaining blood culture.	Thank you for your comment. The committee agrees with the points you've raised. In recommendation 1.9.1 it states - For patients in hospital who have suspected infections, take microbiological samples before prescribing an antimicrobial and review the prescription when the results are available. For people with suspected sepsis, take blood cultures before antibiotics are given. See the UK standards for microbiology investigations.
University Hospitals Birmingham	Guideline	023	009	This intended aim of delay in administration of antibiotics is near impossible to achieve in practice. How do we expect a doctor working in busy acute settings who has assessed the patient and has	Thank you for your comment and for raising these implementation issues. Your comments will be considered by NICE

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				diagnosed sepsis, to then stop prescribing antibiotics pending the results of the investigations? In those settings, doctors would make their diagnosis, set up the management plan and move on to the next patient they have to see. Also, suppose because of long waits, by the time patient had their imaging, the three hour interval may elapse. Would that not cause more issues? Can I suggest that we should instead spell out obtain blood, urine, or CSF (where indicated) samples for m+c before administering antibiotic instead.	where relevant support activity is being planned. Sections 1.10, 1.11, 1.12 and 1.13 of the guideline outlines the management plan based on the risk of severe illness and death from sepsis. The committee highlighted that: • the purpose of deferring antibiotic delivery is not to delay treatment, but to have extra time to gather information for a more specific diagnosis, allowing for more targeted treatment. • the 1-, 3- and 6-hour time limits are a maximum (rather than an aim) for each risk level. • clinical judgement is key when considering someone's specific care needs.