NICE National Institute for Health and Care Excellence

Appendix B: Stakeholder consultation comments table

2018 surveillance of Meningitis (bacterial) and meningococcal septicaemia in under 16s: recognition, diagnosis and management (2010)

Consultation dates: 27 July to 9 August 2018

Do you agree with the proposal to partially update the guideline?			
Stakeholder	**Overall response**	**Comments**	**NICE response**
Department of Health and Social Care	Not answered	The Department of Health and Social Care has no substantive comments to make, regarding this consultation.	Thank you.
Royal College of Nursing	Not answered	Nurses caring for people with Meningitis have reviewed the proposal and have no comments to submit at this stage.	Thank you.

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Imperial College Healthcare NHS Trust	Yes	No comment provided	Thank you.
UK Clinical Pharmacy Association (UKCPA)	Yes	No comment provided	Thank you.
Meningitis Now	Yes	1.5 Long term management – we agree with the Meningitis Research Foundations comment that a 6-week follow-up in babies recovering from GBS meningitis would fail to detect significant cognitive and neuromotor sequelae. We would support a review of this, once the results from the ongoing cohort study are known.	Thank you for your comment. No new evidence was identified in the current or previous surveillance review to impact on recommendation 1.5.5 for children and young people to be reviewed by a paediatrician with the results of their hearing test 4–6 weeks after discharge from hospital. Clinical feedback highlighted ongoing research that includes duration of follow up, which will be monitored for potential future impact. The need for longer term follow up of infants under 3 months who are diagnosed with meningitis may be explored as part of the scoping process.
Roche Diagnostics Ltd	Yes	We support the inclusion of Procalcitonin (PCT) in this guideline as it is shown to have value in diagnosis and prognosis of meningitis in under 16s. Please see the references below which provide evidence to support this. 1. Bell JM, Shields MD, Agus A, Dunlop K, Bourke T, Kee F, et al. Clinical and Cost-Effectiveness of Procalcitonin Test for Prodromal Meningococcal Disease–A Meta-Analysis. Plos One. 2015Aug;10(6). 2. Henry BM, Roy J, Ramakrishnan PK, Vikse J, Tomaszewski KA, Walocha JA. Procalcitonin as a Serum Biomarker for Differentiation of Bacterial	Thank you for your comment and supporting references. We will pass these references onto the developer for consideration during the update of the guideline.

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		Meningitis From Viral Meningitis in Children. Clinical Pediatrics. 2015;55(8):749–64. 3. Hu R, Gong Y, Wang Y. Relationship of Serum Procalcitonin Levels to Severity and Prognosis in Pediatric Bacterial Meningitis. Clinical Pediatrics. 2015Mar;54(12):1141–4. 4. Hubert-Dibon G, Danjou L, Feildel-Fournial C, Vrignaud B, Masson D, Launay E, et al. Procalcitonin and C-reactive protein may help to detect invasive bacterial infections in children who have fever without source. Acta Paediatrica. 2018;107(7):1262–9. 5. Li W, Sun X, Yuan F, Gao Q, Ma Y, Jiang Y, et al. Diagnostic Accuracy of Cerebrospinal Fluid Procalcitonin in Bacterial Meningitis Patients with Empiric Antibiotic Pretreatment. Journal of Clinical Microbiology. 2017Aug;55(4):1193–204. 6. Park BS, Kim SE, Park SH, Kim J, Shin KJ, Ha SY, et al. Procalcitonin as a potential predicting factor for prognosis in bacterial meningitis. Journal of Clinical Neuroscience. 2017;36:129–33. 7. Trippella G, Galli L, Martino MD, Lisi C, Chiappini E. Procalcitonin performance in detecting serious and invasive bacterial infections in children with fever without apparent source: a systematic review and meta-analysis. Expert Review of Anti-infective Therapy. 2017Feb;15(11):1041–57. 8. Umran RM, Radhi NH. Diagnostic value of serum procalcitonin level in differentiating bacterial from nonbacterial meningitis in children. Iranian journal of pediatrics. 2014 Dec;24(6):739-744.	

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		9. Wei T-T, Hu Z-D, Qin B-D, Ma N, Tang Q-Q, Wang L-L, et al. Diagnostic Accuracy of Procalcitonin in Bacterial Meningitis Versus Nonbacterial Meningitis. Medicine. 2016;95(11).	
Public Health England (PHE)	Yes	**NICE Guideline Introduction** PHE comment: Paragraph 3 of the introduction in the NICE version of guideline CG102 should be amended to take account of the introduction of both the infant MenB vaccination programme and the MenACWY vaccination programme for teenagers, including routine vaccination at 13-15 years of age, into the schedule in 2015. The text should be amended accordingly taking into account the change in recent MenW epidemiology as noted later. **Table 1 Symptoms and signs of bacterial meningitis and meningococcal septicaemia** PHE agree that the way the table is constructed at present is confusing. Please note there is evidence that diarrhoea, abdominal pain can feature with meningococcal septicaemia (*http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=21422)*. **Immune testing** New intelligence indicates a potential impact on recommendations 1.5.8–1.5.10, to take account of the MenB vaccine that has been introduced since publication of NICE guideline CG102. The wording of these recommendations should be reviewed, so that any child	Thank you for your comments. **NICE Guideline Introduction** As part of the surveillance proposal, an amendment is proposed to the paragraph in question to take account of the introduction of both the infant MenB vaccination programme and the MenACWY vaccination for teenagers. **Table 1 Symptoms and signs of bacterial meningitis and meningococcal septicaemia** Thank you for your comment in support of the proposed restructuring of Table 1. The evidence submitted indicating that diarrhoea and abdominal pain can feature with meningococcal septicaemia was derived from a small case series of teenagers, aged 15-19 years. This study in isolation is unlikely to impact on the established signs and symptoms of the guideline until the findings are substantiated by further, larger studies. The proposed restructuring of Table 1 will be reviewed by the committee to include consideration of the column entries for meningococcal septicaemia. **Immune testing** Thank you for commenting that the MenB vaccine does not protect against all MenB disease. The highlighted evidence focused on the effectiveness of the vaccine, which is outside the remit of the guideline, and therefore was not included in the surveillance review.

		who has received meningococcal vaccination and subsequently develops meningococcal disease should be tested for complement deficiency. MenB vaccine does not protect against all MenB disease; the vaccine has been shown to protect against 73-88% of MenB strains (https://www.ncbi.nlm.nih.gov/pubmed/28100432). MenB disease in a fully MenB vaccinated child is therefore as likely to be due to a non-vaccine preventable strain. Any serogroup causing Invasive meningococcal disease in a child, other than MenB or MenC or currently MenW, would merit additional investigation unless recent travel history would help explain acquisition of a serogroup that is unusual in the United Kingdom (UK). MenW135 is now routinely referred to as MenW disease globally.	Nonetheless, this feedback will be passed on to the developer for consideration in the update process for this section of the guideline. Topic experts advised that the reason that MenB disease was excluded (recommendation 1.5.8 2nd bullet point) was that as there was no vaccine, cases could not reasonably be considered to represent unusual susceptibility. Now that there is a vaccine, it was suggested that the wording of these recommendations be reconsidered, so that any child who has received meningococcal vaccination and subsequently develops meningococcal disease should be tested for complement deficiency.
Alder Hey Children's NHS Foundation Trust	Yes	No comment provided	Thank you.
GlaxoSmithKline	Yes	NICE Guideline Introduction, Paragraph 3 Introduction of Meningococcal B vaccine on to the childhood immunisation schedule. We suggest adding in a link to the NHS schedule https://www.gov.uk/government/publications/the-complete-routine-immunisation-schedule	Thank you for your suggestion. An amendment is already included in the surveillance review proposal to update the paragraph in question. This will take account of the introduction of both the infant MenB vaccination programme and the MenACWY vaccination for teenagers.

Scottish Antimicrobial Prescribing Group	Yes	No comment provided	Thank you.
Meningitis Research Foundation	Yes	1. MRF would like to see stronger safety netting recommendations within CG102. Currently safety netting is only addressed in recommendation 1.3.5 of the CG102 guidance where it states – "*If the child or young person is assessed as being at low risk of meningococcal disease and is discharged after initial observation, advise parents or carers to return to hospital if the child or young person appears ill to them.*" However, there is much clearer guidance within the Quality Standard (QS51) which we would like to see reflected in the guidance itself. This is particularly relevant considering the recent recommendations from the Meningococcal working group report published in April 2018 and available from: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/721475/Meningococcal_Working_Group_Report.pdf which states: *Documentation (in addition to verbal instruction) should be given to any patient (particularly parents/carers of a child or teenager), who has been assessed because of concerns about infection and is being sent home. This information should:* • *set out what to look for in terms of deterioration or causes for concern for the child in question;* • *empower patients and carers with appropriate knowledge so they can seek further advice and assessment if concerned.* *It should be recorded in the patient's notes that this information has been provided and there should be mechanisms in place to monitor and audit that this is taking place so that, for example, the CQC could consider*	Thank you for your comments, which presumably refer to Quality Standard 19 on bacterial meningitis rather than Quality Standard 51 (Autism). **Safety netting guidance** The NICE pathway on Bacterial meningitis and meningococcal septicaemia in under 16s includes both NICE guideline CG102 and the Quality Standard QS19, and thereby incorporates the additional guidance on safety netting. In addition, the NICE version of CG102 contains a section on patient-centred care, which states that: 'Good communication between healthcare professionals and children and young people, and their parents and carers, is essential. It should be supported by evidence-based written information tailored to their specific needs. Treatment and care, and information given about it, should be culturally appropriate. Information should also be accessible to people with additional needs such as physical, sensory or learning disabilities, and to people who do not speak or read English.' No evidence was identified to impact on recommendation 1.3.5 and no impact on NICE guideline CG102 is anticipated in this area. This area is also covered in more detail in NICE's guideline on patient experience in adult NHS services **Symptoms information**

		this metric during inspections of acute trusts and primary care. Additionally, recently published research highlights the requirement for better safety netting information for parents especially in the context of meningitis in infancy. In a study of infants aged <90 days with bacterial meningitis diagnosed between July 2010 and July 2013, 70% of parents first sought help for their child by phoning the GP (n=21, 32%), calling the 24-hour NHS direct telephone service (n=15, 23%), or contacting the community midwife (n=10, 15%); of these, 13 (28%) were advised to stay at home. In total 30% of the infants were assessed to have received inappropriate pre-hospital management. Examples of inappropriate advice given to parents included being told that their child's fever was due to a change in milk formula, or to an umbilical hernia, or where prune juice was recommended for fever and irritability[1]. This highlights the need for clinicians to "think meningitis" and provide safety netting information to parents if this diagnosis cannot be ruled out particularly as symptoms of meningitis in young infants are typically non-specific. 2. A review of the symptoms information within CG102 would be useful to ensure that it remains up to date considering the recent rise in disease caused by a virulent strain of MenW which has a more unusual clinical presentation. We would also like symptoms information to be reviewed in alignment with recently published research on the clinical features of meningitis in infants under 90 days[1, 2] 3. MRF would like there to be a recommendation for longer term follow up of babies under 3 months who are diagnosed with meningitis. A recent study found that as many as 32% of infants surviving GBS meningitis were left with a neurodevelopmental	No evidence was identified in the surveillance review to impact on Section 1 Symptoms, signs and initial assessment. However, the section includes Table 1 covering symptoms and signs of bacterial meningitis and meningococcal septicaemia. The proposed restructuring of Table 1 will be reviewed by the committee to include consideration of the column entries for bacterial meningitis and meningococcal septicaemia. The scoping process will define the final parameters of the update, which may include the signs and symptoms section. **Follow up** No new evidence was identified to impact on the recommendation 1.5.5 for children and young people to be reviewed by a paediatrician with the results of their hearing test 4–6 weeks after discharge from hospital. Clinical feedback highlighted ongoing research that includes duration of follow-up, which will be monitored for potential future impact on the guideline. The cited study on neurodevelopmental impairment among infants surviving GBS meningitis will be passed on to the developer for consideration in the update. The need for longer term follow up of infants under 3 months who are diagnosed with meningitis may be explored as part of the scoping process. **Empirical antibiotics** Recommendations 1.4.2 and 1.4.15 state that children younger than 3 months with suspected bacterial meningitis should be treated without delay using intravenous cefotaxime plus either amoxicillin or ampicillin, for at least 14 days. If the clinical course is complicated,

		impairment (NDI) when followed up at least 18 months after illness[3] However detection of such effects is challenging particularly in infants and one follow up appointment four to six weeks after hospital discharge may not be sufficient to detect such effects. The same research found that the prevalence of moderate to severe NDI following GBS infection increased with follow-up to 18 months compared to 6 months (18% [95% CI, 13%–22%] vs 15% [95% CI, 11%–20%]) and the authors speculate that the upward trend suggests that longer follow-up is needed for accurate case ascertainment. We would like to see a review of the timeframes for follow up particularly for young infants recovering from meningitis to ensure that those with NDI following meningitis are not missed. 4. There may be a need to review empirical antibiotics for babies under 3 months of age after research has shown that meningitis caused by Listeria in babies over 1 month of age is very rare[4, 5]. Further research into this is ongoing (https://www.rcpch.ac.uk/bpsu-study-listeria-infection-infants). 5. NICE sepsis guideline (NG51) was published in 2016. This update is an opportunity to align CG102 with the NICE sepsis guidelines. For example the sepsis guidelines recommend the administration of antibiotics within 1 hour. Likewise the QS19 states that "*Children and young people with suspected bacterial meningitis or meningococcal septicaemia receive intravenous or intraosseous antibiotics within an hour of arrival at hospital.*" We would like to see the guidance amended to align with these other resources. 1. Okike, I.O., et al., Assessment of healthcare delivery in the early management of bacterial meningitis in UK young	consideration should be given to extending the duration of treatment and consulting an expert in paediatric infectious diseases. Clinical feedback highlighted some new evidence to suggest a shorter duration (30 days or less) of treatment for infants under 90 days of age. However, additional clinical feedback stated that existing evidence showed cases of listeria occurring up to 60 days and that the risk, although decreasing, could remain up to 90 days of age. The cited ongoing study Listeria infection in infants aims to establish the incidence of proven and possible listeria, age, geographical and ethnic distribution, management and outcome at diagnosis and at one year follow-up. This data is expected to provide stronger and more conclusive evidence to inform a potential future impact on NICE guideline CG102. The study has already been included in the surveillance evidence summary for monitoring. The other cited evidence will be passed on to the developer for consideration in the update and this area may be explored as part of the scoping process. **NICE sepsis guideline** The surveillance review proposal includes an amendment to the introductory text to the guideline to cross refer to the subsequently published NICE guideline on Sepsis. The proposed text will state: This guideline assumes that if a child presents with signs or symptoms that indicate possible infection, the child will be managed according to NICE's guideline on Sepsis: recognition, diagnosis and early management until bacterial meningitis or meningococcal septicaemia is suspected.

		infants: an observational study. BMJ Open, 2017. 7(8): p. e015700. 2. Okike. I., et al., Clinical characteristics and risk factors for poor outcome in infants less than 90 days of age with bacterial meningitis in the United Kingdom and Ireland (IN PRESS). PIDJ,. 3. Kohli-Lynch, M., et al., Neurodevelopmental Impairment in Children After Group B Streptococcal Disease Worldwide: Systematic Review and Meta-analyses. Clin Infect Dis, 2017. 65(suppl_2): p. S190-S199. 4. Okike, I.O., et al., Incidence, Aetiology and Outcome of Bacterial Meningitis in Infants Aged <90 days in the UK and Republic of Ireland: prospective, enhanced, national population-based surveillance. Clin Infect Dis, 2014. 5. Okike, I.O., et al., Empirical antibiotic cover for Listeria monocytogenes infection beyond the neonatal period: a time for change? Arch Dis Child, 2015. 100(5): p. 423-5.	This amendment will ensure alignment with NICE guideline NG51 for relevant sections of CG102. The NICE pathway on Bacterial meningitis and meningococcal septicaemia in under 16s includes both NICE guideline CG102 and the Quality Standard QS19, and thereby links to the related quality statements
Royal College of Paediatrics and Child Health	Yes	Happy with decision to update this guideline, Yes, it is interesting and very relevant	Thank you for your comment.
Royal College of Physicians	Not answered	Our experts believe that the proposal is uncontroversial apart from the part about procalcitonin. This is an expensive test and not routinely available in most NHS hospitals. There are relatively few cases of meningococcal	Thank you for your comment. The potential impact of PCT testing will be considered in the update process in the context of cost effectiveness and availability in NHS secondary care. A topic expert confirmed that PCT is being used more now than it was when the guideline was published and there have been a number of publications recently arguing for its wider

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		disease these days, so our experts believe that introducing this test does not seem sensible.	use. Evidence was identified in the surveillance review indicating that PCT, plus standard recommended tests, improved the discriminatory ability for fatal meningococcal disease and was more cost-effective than standard testing alone. It was considered important to review the evidence in the update process.
Biomerieux	Yes	No comment provided	Thank you.

Do you have any comments on areas excluded from the scope of the guideline?			
Stakeholder	**Overall response**	**Comments**	**NICE response**
Imperial College Healthcare NHS Trust	Yes	I want to ensure that the recent evidence regarding use of plasmalyte or other balanced crystalloid infusions is taken into account. Currently the recommendation is for Normal saline or albumin. There is a lot of evidence to support the use of balanced crystalloid solutions rather than N saline for resuscitation to avoid hyperchloremic acidosis. (Association between the choice of IV crystalloid and in-hospital mortality among critically ill adults with sepsis*. Raghunathan K, Shaw A, Nathanson B, Stürmer T, Brookhart A, Stefan MS, Setoguchi S, Beadles C, Lindenauer PK. Crit Care Med. 2014 Jul;42(7):1585-91), Crystalloid Fluid Choice and Clinical Outcomes in Pediatric Sepsis: A Matched Retrospective Cohort Study.	Thank you for your comment. The surveillance review did not identify any evidence to impact on recommendation 1.4.30 for intravenous (IV) fluid resuscitation in meningococcal septicaemia, which advises the use of IV or intraosseous sodium chloride 0.9% or human albumin 4.5% solution over 5–10 minutes. The submitted evidence either did not meet the surveillance study design eligibility criteria or was published prior to the surveillance period. However, this area may be explored as part of the scoping process for the update.

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		Weiss SL, Keele L, Balamuth F, Vendetti N, Ross R, Fitzgerald JC, Gerber JS. J Pediatr. 2017 Mar;182:304-310.e10.	
UK Clinical Pharmacy Association (UKCPA)	No	No comment provided	Thank you.
Meningitis Now	No	No comment provided	Thank you.
Roche Diagnostics Ltd	Yes	We would also recommend the inclusion of Interleukin-6 (IL-6), as a biomarker for the differential diagnosis of bacterial meningitis. There is evidence to support the diagnostic value of IL-6 below. 1. Dano ID, Sadou H, Issaka B. Measurement of Interleukin-6 in Cerebrospinal Fluid for the Diagnosis of Bacterial Meningitis. Pakistan Journal of Biological Sciences. 2016Jan;19(4):185–90. 2. Hamedi A, Ayatollahi H, Nakhaee AA. Evaluation of IL-6 and High Sensitive C Reactive Protein Value in CSF and Serum Children Suspected Meningitis Referred to Pediatric Emergency Room. Iranian Red Crescent Medical Journal. 2012;14(12):822–5. 3. Srinivasan L, Kilpatrick L, Shah SS, Abbasi S, Harris MC. Cerebrospinal fluid cytokines in the diagnosis of bacterial meningitis in infants. Pediatric Research. 2016;80(4):566–72. 4. Takahashi W, Nakada T-A, Abe R, Tanaka K, Matsumura Y, Oda S. Usefulness of interleukin 6 levels in the cerebrospinal fluid for the diagnosis of bacterial meningitis. Journal of Critical Care. 2014;29(4).	Thank you for your suggestion to include Interleukin-6. Evidence for CSF cytokines, including IL-6, was considered in the surveillance review. The new evidence showed potential diagnostic value, but no impact on the guideline is anticipated until the findings are substantiated by further prospective larger studies in UK settings. The cited studies were either included in the surveillance evidence summary (1, 3) or preceded the surveillance search period (2,4)

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Public Health England (PHE)	Yes	**Investigation and management in children and young people with suspected bacterial meningitis** PHE note that there is no mention of the role of throat swabs in surveillance. See section 6 Laboratory investigation of suspected cases in Guidance for the public health management of meningococcal disease in the UK available at: https://www.gov.uk/government/publications/meningococcal-disease-guidance-on-public-health-management	Thank you for your comment. Through current and previous surveillance reviews, there has been insufficient new evidence on the use of throat swabs to impact on recommendation 1.3.14. However, opposing recommendations between the NICE and Public Health England guidelines was recognised as a source of potential confusion. In February 2015, reference to throat swabs was removed from recommendation 1.3.14, to bring it in line with guidance for public health management of meningococcal disease in the UK. The recommendation had explicitly advised against taking throat swabs and topic experts agreed with the amendment to remove this.
Alder Hey Children's NHS Foundation Trust	Yes	1.4.2 Treat children younger than 3 months with suspected bacterial meningitis without delay using intravenous cefotaxime plus either amoxicillin or ampicillin. New UK data shows that empiric amoxicillin is only needed in neonates, not infants < 3 months. Okike IO, Awofisayo A, Adak B, Heath PT.Empirical antibiotic cover for Listeria monocytogenes infection beyond the neonatal period: a time for change? Arch Dis Child. 2015 May;100(5):423-5. Incidence, etiology, and outcome of bacterial meningitis in infants aged <90 days in the United kingdom and Republic of Ireland: prospective, enhanced, national population-based surveillance. Okike IO, Johnson AP, Henderson KL,	Thank you for your comment. Recommendations 1.4.2 and 1.4.15 state that children younger than 3 months with suspected bacterial meningitis should be treated without delay using intravenous cefotaxime plus either amoxicillin or ampicillin, for at least 14 days. If the clinical course is complicated, consideration should be given to extending the duration of treatment and consulting an expert in paediatric infectious diseases. Clinical feedback highlighted some new evidence to suggest a shorter duration (30 days or less) of treatment for infants under 90 days of age. However, additional clinical feedback stated that existing evidence showed cases of listeria occurring up to 60 days and that the risk, although decreasing, could remain up to 90 days of age. The ongoing study Listeria infection in infants aims to establish the incidence of proven and possible listeria, age, geographical and ethnic distribution, management and outcome at diagnosis and at

		Blackburn RM, Muller-Pebody B, Ladhani SN, Anthony M, Ninis N, Heath PT; neoMen Study Group. Clin Infect Dis. 2014 Nov 15;59(10):e150-7.	one year follow-up. This data is expected to provide stronger and more conclusive evidence to inform a potential future impact on NICE guideline CG102. The evidence submitted (Okike et al. 2014, Okike et al. 2015) will be passed on to the developer for consideration in the update and this area may be explored as part of the scoping process. .
GlaxoSmithKline	Yes	Carriage of Meningococcal B. Suggest adding in to the introduction that there are ongoing studies in adolescents 16+ years of age to determine whether there is a reduction in carriage in vaccinated cohorts. (Australia and UK) https://www.ncbi.nlm.nih.gov/pubmed/29991629 https://www.ovg.ox.ac.uk/news/be-on-the-team-teenagers-against-meningitis The Meningococcal B vaccine is available privately for those age groups not included in the current National Immunisation Schedule. Research recommendations, No. 4. Update Outbreak recommendations Guidance 1.1.8/1.1.9 Update HPA title, now PHE.	Thank you for your comments. **Carriage of Meningococcal B.** The scope of the guideline covers children and young people from birth up to their 16th birthday who have or are suspected to have bacterial meningitis or meningococcal septicaemia. Adolescents over the age of 16 are not covered and ongoing studies relating to this group would not be directly relevant to the guideline. **Amendments to footnotes** Editorial corrections are already proposed to the footnote references to the Health Protection Agency in recommendations 1.1.8 and 1.1.9, to redirect to Public Health England. These corrections will be made as part of the update to the guideline.
Scottish Antimicrobial Prescribing Group	No	No comment provided	Thank you.

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Meningitis Research Foundation	Yes	1. There is considerable overlap between the NICE Sepsis guidelines (NG51), this guideline (CG102) and the feverish illness guideline (CG160). However the normal values of vital signs within these different guidelines are not in alignment. A recent report from the meningococcal working group https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/721475/Meningococcal_Working_Group_Report.pdf recognised the need for a tool such as a paediatric early warning score (PEWS) that would help hospital Drs and GPs rule out sepsis. We would like to see the CG102 GDG work alongside others in the development of such a score to ensure that cases of meningitis as well as sepsis are not missed. It will be important for CG102 to align with any PEWS score which is developed nationally. 2. The NICE Sepsis guideline encourages clinicians to think "Could this be sepsis?" when a person presents with signs of possible infection. It would be helpful if the sepsis guideline also encouraged clinicians to think "could this be meningitis?" in cases where the risk of sepsis is considered to be low and referred out to the CG102 guideline.	Thank you for your comments **Overlap with other guidelines** The surveillance review proposal includes an amendment to the introductory text to the guideline to cross refer to the subsequently published NICE guideline on Sepsis. The proposed text will state: > This guideline assumes that if a child presents with signs or symptoms that indicate possible infection, the child will be managed according to NICE's guideline on Sepsis: recognition, diagnosis and early management until bacterial meningitis or meningococcal septicaemia is suspected. This amendment will ensure alignment with NICE guideline NG51 for relevant sections of CG102. In the introductory text to the guidance section 1, the cross referral to Feverish illness in children (NICE clinical guideline 47) will be amended to cross refer to the NICE guideline on fever in under 5s: assessment and initial management. The accompanying text ensures alignment with this guideline: > This guideline assumes that fever in children younger than 5 years will be managed according to Feverish illness in children (NICE clinical guideline 47) until bacterial meningitis or meningococcal septicaemia is suspected. **Cross referral from NICE guideline NG51** NICE guideline NG51 already cross refers to NICE guideline CG102 for antibiotic treatment in people with suspected sepsis, finding the source of infection in people with suspected sepsis and information

			at discharge for people who have had sepsis. An additional general cross reference is made to NICE guideline CG102 for follow up of people who have had meningococcal septicaemia. Further cross references were not considered necessary during the guideline development or subsequent surveillance reviews.
Royal College of Paediatrics and Child Health	No	The changes seem appropriate	Thank you for your comment.
Biomerieux	Yes	1.3.12 - Submit CSF to the laboratory to hold for PCR testing for N meningitidis and S pneumoniae, but only perform the PCR testing if the CSF culture is negative. We would suggest that PCR is done on receipt of CSF if there is a high suspicion of bacterial meningitis based on clinical presentation and the gram stain is negative. Pre-treatment may influence the detection by culture and gram stain. PCR could also include other bacterial causes of meningitis e.g. Escherichia coli K1, Haemophilus influenzae, Listeria monocytogenes, Streptococcus agalactiae. Please see the publications below not included in those referenced as evidence for the 2018 surveillance of this guideline; Arora HS1, Asmar BI, Salimnia H, Agarwal P, Chawla S, Abdel-Haq N . Enhanced Identification of Group B Streptococcus and Escherichia Coli in Young Infants with Meningitis Using the Biofire Filmarray Meningitis/Encephalitis Panel. Pediatr Infect Dis J. 2017 Jul;36(7):685-687. doi: 10.1097/INF.0000000000001551.	Thank you for your comment relating to recommendation 1.3.12. The surveillance review did not identify any evidence to warrant a change in this recommendation. The evidence submitted was excluded from the review due to either inadequate reporting of data in the abstract, ineligible study designs, low relevance to review questions or lack of directness to the UK NHS population. Further evidence in this area may be explored as part of the scoping process for the update.

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		Dien Bard J, Naccache SN, Bender JM. Use of a Molecular Panel To Aid in Diagnosis of Culture-Negative Meningitis. J Clin Microbiol. 2016 Dec;54(12):3069-3070. Liesman RM, Strasburg AP, Heitman AK, Theel ES, Patel R, Binnicker MJ. Evaluation of a Commercial Multiplex Molecular Panel for Diagnosis of Infectious Meningitis and Encephalitis. J Clin Microbiol. 2018 Mar 26;56(4). pii: e01927-17. doi: 10.1128/JCM.01927-17. Duff S, Hasbun R, Ginocchio CC, Balada-Llasat JM, Zimmer L, Bozzette S A. Economic analysis of rapid multiplex polymerase chain reaction testing for meningitis/encephalitis in pediatric patients Future Microbiol. 2018 May;13:617-629. doi: 10.2217/fmb-2017-0238. Messacar K, Breazeale G, Robinson CC, Dominguez SR. Potential clinical impact of the film array meningitis encephalitis panel in children with suspected central nervous system infections. Diagn Microbiol Infect Dis. 2016 Sep;86(1):118-20. doi: 10.1016/j.diagmicrobio.2016.05.020. Blaschke AJ, Holmberg KM, Daly JA, Leber AL, Dien Bard J, Korgenski EK, Bourzac KM, Kanack KJ. Retrospective Evaluation of Infants Aged 1 to 60 Days with Residual Cerebrospinal Fluid (CSF) Tested Using the FilmArray Meningitis/Encephalitis (ME) Panel. J Clin Microbiol. 2018 Jun 25;56(7). pii: e00277-18. doi: 10.1128/JCM.00277-18. Wootton SH, Aguilera E, Salazar L, Hemmert AC, Hasbun R. Enhancing pathogen identification in patients with meningitis and a negative Gram stain using the BioFire FilmArray(®) Meningitis/Encephalitis panel. Ann Clin Microbiol Antimicrob. 2016 Apr 21;15:26. doi: 10.1186/s12941-016-0137-1. Graf EH, Farquharson MV, Cárdenas AM. Comparative evaluation of the FilmArray meningitis/encephalitis molecular panel in a pediatric population. Diagn Microbiol	

		Infect Dis. 2017 Jan;87(1):92-94. doi: 10.1016/j.diagmicrobio.2016.09.022. Sheila F Lumley , Dave Pritchard , Atanu Dutta , Philippa C Matthews ,Kathy Cann , Multiplex PCR reveals high prevalence of Enterovirus and HHV6 in acellular paediatric cerebrospinal fluid samples, Journal of Infection (2018), doi: 10.1016/j.jinf.2018.05.008 Leber AL, Everhart K, Balada-Llasat JM, Cullison J, Daly J, Holt S, et al. Multicentre Evaluation of the BioFire FilmArray Meningitis Encephalitis Panel for the Detection of Bacteria, Viruses and Yeast in Cerebrospinal Fluid Specimens J Clin Microbiol 2016;54(9):2251–61. Duff S, Hasbun R, Ginocchio CC, Balada-Llasat JM, Zimmer L, Bozzette S A. Economic analysis of rapid multiplex polymerase chain reaction testing for meningitis/encephalitis in pediatric patients Future Microbiol. 2018 May;13:617-629. doi: 10.2217/fmb-2017-0238. Dien Bard J, Alby K. Point-Counterpoint: Meningitis/Encephalitis Syndromic Testing in the Clinical Laboratory. J Clin Microbiol. 2018 Mar 26;56(4). pii: e00018-18. doi: 10.1128/JCM.00018-18. Print 2018 Apr. Rhein J, Bahr NC, Hemmert AC, Cloud JL, Bellamkonda S, Oswald C, Lo E, Nabeta H, Kiggundu R, Akampurira A, Musubire A, Williams DA, Meya DB, Boulware DR; ASTRO-CM Team. Diagnostic performance of a multiplex PCR assay for meningitis in an HIV-infected population in Uganda. Diagn Microbiol Infect Dis. 2016 Mar;84(3):268-73. doi: 10.1016/j.diagmicrobio.2015.11.017. Balada-Llasat JM, Rosenthal N, Hasbun R, Zimmer L, Ginocchio CC, Duff S, Allison J, Bozzette S. Cost of managing meningitis and encephalitis among adult patients in the United States of America. Int J Infect Dis. 2018 Jun;71:117-121. doi: 10.1016/j.ijid.2018.04.799. Chang D, Okulicz JF, Nielsen LE, White BK A Tertiary Care Center's Experience with Novel Molecular	

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		Meningitis/Encephalitis Diagnostics and Implementation with Antimicrobial Stewardship. Mil Med. 2018 Jan 1;183(1-2):e24-e27. doi: 10.1093/milmed/usx025. Soucek DK, Dumkow LE, VanLangen KM, Jameson AP. Cost Justification of the BioFire FilmArray Meningitis/Encephalitis Panel Versus Standard of Care for Diagnosing Meningitis in a Community Hospital. J Pharm Pract. 2017 Jan 1:897190017737697. doi: 10.1177/0897190017737697. Llano López LH, Reischl AT, Gröndahl B, Kidszun A, Kowalzik F, Oetzmann von Sochaczewski C, Gehring S. The BioFireFilmArray enables point of care diagnostic in neonatal parechovirus meningitis. Infect Dis (Lond). 2017 Sep;49(9):705-707. doi: 10.1080/23744235.2017.1311417. Hanson KE. The First Fully Automated Molecular Diagnostic Panel for Meningitis and Encephalitis: How Well Does It Perform, and When Should It Be Used? J Clin Microbiol. 2016 Sep;54(9):2222-4. doi: 10.1128/JCM.01255-16. Launes C, Casas-Alba D, Fortuny C, Valero-Rello A, Cabrerizo M, Muñoz-Almagro C. Utility of FilmArray Meningitis/Encephalitis Panel during Outbreak of Brainstem Encephalitis Caused by Enterovirus in Catalonia in 2016. J Clin Microbiol. 2016 Dec 28;55(1):336-338. doi: 10.1128/JCM.01931-16. We are very surprised that the literature search to identify relevant new evidence for diagnosis of meningitis did not bring to light any of the publications we have included in the comments form. The last two or three years has seen the adoption of novel rapid molecular diagnostic assays launched with CE marking and in some cases FDA approval. These assays have broad panels that can test for a number of pathogens causing meningitis and encephalitis and aid in	

		rapid differential diagnosis especially where gram films are negative.	
Do you have any comments on equalities issues?			
Stakeholder	**Overall response**	**Comments**	**NICE response**
Imperial College Healthcare NHS Trust	-	No comment provided	Thank you.
UK Clinical Pharmacy Association (UKCPA)	No	Do all secondary care providers have access to in house PCT testing?	Thank you for your question. The potential impact of PCT testing will be considered in the update process in the context of access and availability in NHS secondary care. The Chair of the guideline committee confirmed that PCT is being used more now than it was when the guideline was published and there have been a number of publications recently arguing for its wider use. It was considered important to review the evidence in the update process.
Meningitis Now	No	No comment provided	Thank you.
Roche Diagnostics Ltd	No	None	Thank you.
Public Health England (PHE)	No	No comment provided	Thank you.
Alder Hey Children's NHS Foundation Trust	No	No comment provided	Thank you.

GlaxoSmithKline	No	No comment provided	Thank you.
Scottish Antimicrobial Prescribing Group	No	No comment provided	Thank you.
Meningitis Research Foundation	No	No comment provided	Thank you.
Royal College of Paediatrics and Child Health	No	No comment provided	Thank you.
Biomerieux	No	No comment provided	Thank you.