Neonatal infection (early onset): antibiotics for prevention and treatment

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14 September 2018 to 12 October 2018

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Croydon University Hospital	General	General	In the South West London Neonatal Network we have observed a very significant increase in the number of babies receiving IV antibiotics from birth, apparently as a result of the current 'red flag' risk factor where parenteral antibiotic treatment is given to mothers for confirmed or suspected invasive bacterial infection. Recent changes in the Obstetric "Green Guide" means there is now a lower threshold (temperature ≥37.5° x2 or ≥38° x1) for starting IV antibiotics in labouring and postpartum women. These cases are labelled as 'maternal sepsis'. Our clinical observation suggested that many newborn babies are being treated with antibiotics where there is minimal evidence of invasive bacterial infection or sepsis in their mothers. We hypothesised that the use of a more rigorous objective assessment of maternal sepsis, such as the MEOWS (modified early obstetric warning scores) could reduce the number of asymptomatic babies unnecessarily treated with intravenous (IV) antibiotics at birth. A one month pilot study was conducted in May 2018, analysing the numbers of asymptomatic babies treated from birth in one of our network units. This gave rise to some very significant results. We demonstrated that 44 asymptomatic babies were treated at birth in this unit, and of those 68% (n=30) were for maternal sepsis. We applied the MEOWS to the observations of their mothers, and defined 'MEOWS Positive' as MEOWS of 5 across all parameters, or 3 in one parameter. This is the standard currently applied in some trusts already using MEOWS to help guide the use of antibiotics for the baby.	Thank you for your comment. The draft question "Which maternal and fetal risk factors for early-onset neonatal infection should be used to guide management?" will consider risk factors for intrapartum and neonatal antibiotic use. The update of the guideline will follow the processes and methods described in Developing NICE guidelines: the manual. Evidence reviews will be conducted for each of the review questions described in the scope which will include all published evidence which meet the review protocols developed for the guideline. The evidence that you refer to relates to clinical questions that are being updated in this guideline. If this evidence meets the review protocol, this will be considered by the guideline committee during the update. We have amended the scope to state that the guideline will cross refer to the NICE guideline on sepsis: recognition, diagnosis and early management (NG51).

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			We found that 63% of babies treated for maternal sepsis (n=19)(43% of all babies treated from birth) would not have met a MEOWS Positive threshold for treatment, and 64% (n=7) of babies in the MEOWS positive group, but only 16% (n=3) in the MEOWS negative group had a significant CRP rise. Given these results, we are now conducting a 6 month audit across 3 trusts in the network, looking to see if these results are reproducible, and what impact the use of MEOWS would have had. We would be happy to share our findings with the review, with a view to potentially incorporating an objective assessment tool (such as MEOWS) in order to reduce the number of babies treated where maternal parenteral antibiotics are currently mandating treatment; essentially by downgrading this to a standard risk factor where the MEOWS is not raised. If incorporated, it should probably be the case that maternal parenteral antibiotic use OR Pyrexia be treated as one single standard risk factor, (in the same way as pyrexia and chorioamnionitis currently are) unless MEOWS determines that it be treated as a red flag.	
Group B Strep Support	1	25-26	The evaluation of need for fungal prophylaxis and prophylaxis to reduce catheter-associated infection is timely and will hopefully be	Thank you for your comment. The draft questions "What is the clinical

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			conducted rigorously. There is significant variation in current practice which warrants this critical evaluation	and cost effectiveness of starting prophylactic antifungal treatment when starting antibiotic treatment for suspected late-onset neonatal infection?" and "What is the clinical and cost effectiveness of intravascular catheters impregnated with antibiotics in reducing the risk of the baby developing late-onset neonatal infection?" will consider fungal prophylaxis and prophylaxis for catheter-associated late-onset neonatal infection.
Group B Strep Support	1	7-8	We welcome the extension of this guideline to cover late-onset neonatal infection. The UK-neonIN database can be utilised to guide recommendations for antibiotic choices, which is timely considering the imperative global drive to implement sound antibiotic stewardship. Please consider the group of babies who are >37 weeks following gut surgery or other causes of intestinal failure, especially when they have IFALD (intestinal failure associated liver disease), carefully with experts in the field. There are limited published data in this group to	Thank you for your comment. No new evidence was identified in the surveillance review or scoping searches that would impact the current recommendations on antibiotic treatment for early-onset neonatal infection. Therefore this area will not be included in this update. The guideline focusses on infections acquired during late pregnancy, during intrapartum and

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			guide the NICE CGDG but these babies are extremely vulnerable to infection.	during the first 28 days old (using corrected age for preterm babies)after birth. The draft question "Which risk factors in the baby (including symptoms and signs) should raise suspicion of late-onset infection?" will consider risk factors for late-onset neonatal infection.
Group B Strep Support	11	16-21	Please expand this question to include not only the clinical/cost effectiveness question for women with known GBS carriage/history, but also testing women with prelabour preterm rupture of membranes for GBS carriage	Thank you for your comment. Screening is covered nationally by the National Screening Committee and is therefore out of remit for NICE to consider for its guidance.
Group B Strep Support	11	24-5	The question "4.1 Which maternal risk factors for late-onset neonatal infection/sepsis should be used to guide management?" is unclear – is this management of the pregnant mother, or of the baby once it is born, or both?	Thank you for your comment. The question will cover management of the pregnant mother and the neonate.
Group B Strep Support	11	8-9	The question "1.1 Which maternal and fetal risk factors for early-onset neonatal infection/sepsis should be used to guide management?" is unclear – is this management of the pregnant mother, or of the baby once it is born, or both? And will all of the existing RCOG risk factors and triggers for IAP plus any new risk factors be included?	Thank you for your comment. The question will cover management of the pregnant mother and the neonate, where appropriate, as it is in the current guideline. The update

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				of the guideline will follow the processes and methods described in Developing NICE guidelines: the manual. Evidence reviews will be conducted for each of the review questions described in the scope which will include all published evidence which meet the review protocols developed for the guideline. The evidence that you refer to relates to clinical questions that are being updated in this guideline. If this evidence meets the review protocol, this will be considered by the guideline committee during the update.
Group B Strep Support	2	15	Please amend the statement "but is even higher in premature babies" to "but is even higher in preterm babies".	Thank you for your comment. The scope has been amended accordingly.
Group B Strep Support	2	26	The current NICE guidelines recommend risk-based antibiotic prophylaxis in labour and neonatal antibiotic treatment to reduce all-cause neonatal sepsis, though this paragraph then goes on to talk about the EOGBS specific RCOG guideline. We think the distinction should be made clearer, so ask that you amend "To reduce mortality	Thank you for your comment. This section of the scope has been amended following stakeholder comments on the scope.

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			from early-onset neonatal sepsis" to "To reduce mortality from all-cause early-onset neonatal sepsis".	
Group B Strep Support	2	4-5	We are concerned at the definition of early-onset infection being within 72 hours of birth – this is out of step with early-onset group B Strep (GBS) infection, which is usually defined 0-6 days. Since group B Strep is the most common cause of severe infection in newborn babies, it would be helpful if these timeframes aligned. Similarly, late-onset GBS infection is usually defined as 7-90 days. We suggest that the timeframe for late-onset neonatal infection is defined.	Thank you for your comment. The definition of 72 hours after birth for early-onset neonatal infection was defined in the original guideline as there is no internationally agreed definition of early-onset neonatal infection. No new evidence was identified in the surveillance review or scoping searches that suggests this definition should be amended. Therefore this area will not be included in this update. The scope has been amended to include a definition of late-onset neonatal infection.
Group B Strep Support	2	9	Please amend the statement "82% occur in premature babies (born before 37 weeks) to "82% occur in preterm babies (born before 37 completed weeks of pregnancy)".	Thank you for your comment. The scope has been amended accordingly.

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Group B Strep Support	2/3	P2 28-9, p3 1	The statement that "guidance from the Royal College of Obstetricians and Gynaecologists recommends only giving antibiotics to women who are proven GBS carriers" is incorrect. RCOG recommends offering antibiotics in labour to women testing positive for GBS in the current pregnancy. However, they also recommend offering intrapartum antibiotics to women who are not known to carry GBS this pregnancy who have previously had a baby with GBS infection and to those who have intrapartum fever, and recommends intrapartum antibiotics for women in preterm labour. They also recommend that women who tested positive in a previous pregnancy where their baby was well should be offered the option of antibiotics in labour in a subsequent pregnancy or the option of GBS-specific testing with antibiotics offered in labour if the test is positive. Since it is helpful if national guidelines align, it would be helpful if the scope this review included consideration of each of the risk factors that RCOG highlights as increasing the risk of EOGBS infection (the above, plus prolonged rupture of membranes >18-24 hours in babies >37 weeks as well as <37 weeks) as well as all of those that should trigger the offer of or recommendation of intrapartum antimicrobial prophylaxis. https://obgyn.onlinelibrary.wiley.com/doi/full/10.1111/1471-0528.14821	Thank you for your comment. This section of the scope has been amended following stakeholder comments on the scope. The draft questions "Which maternal and fetal risk factors for early-onset neonatal infection should be used to guide management?" and "What risk factors in the baby (including symptoms and signs) should raise suspicion of infection within 72 hours of birth?" will consider risk factors for neonatal infection. The update of the guideline will follow the processes and methods described in Developing NICE guidelines: the manual. Evidence reviews will be conducted for each of the review questions described in the scope which will include all published evidence which meet the review protocols developed for the guideline. The evidence that you refer to relates to clinical questions

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				that are being updated in this guideline. If this evidence meets the review protocol, this will be considered by the guideline committee during the update.
Group B Strep Support	3	3-8	The impact of peripartum / neonatal antibiotic exposure extends well beyond the increased risk of antibiotic resistance. There is now a significant literature describing the dysregulating effects on immune and metabolic health, including the development of obesity in later life.	Thank you for your comment. Antibiotic administration for neonatal infection and its effects on the immune system and metabolic health is outside the remit of this guideline.
Group B Strep Support	4	13-15	We welcome the addition of babies with suspected or confirmed late-onset neonatal bacterial infection.	Thank you for your comment.
Group B Strep Support	4	13-15	Please would you add to the scope a new category for babies with an increased risk of late-onset neonatal bacterial infection, for example preterm babies are at raised risk of late onset GBS infection, as are those where the mother carries GBS and of young maternal age (2016 Pintye https://academic.oup.com/jpids/article/5/4/431/2631344). Additionally, babies who have recovered from GBS infection (early or late onset) are at increased risk of developing a subsequent late-onset GBS infection.	Thank you for your comment. The draft questions "Which risk factors in the baby (including symptoms and signs) should raise suspicion of late-onset infection?" and "Which maternal risk factors for late-onset neonatal infection should be used to guide management?" will consider risk factors for late-onset neonatal bacterial infection.

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Group B Strep Support	5	16-17	Please would you add to the scope consideration of both prophylaxis for women with preterm prelabour rupture of membranes, and of testing these women for GBS carriage using appropriate tests, to the topic of the timing of delivery. It is important to note that this is not a universal screening programme, rather it is testing individual women for GBS carriage because of one or more specific indications.	Thank you for your comment. The NICE guideline "preterm birth" NG25 covers antenatal prophylaxis for women with preterm prelabour rupture of membranes. The draft question "What is the clinical and cost effectiveness of immediate delivery versus expectant management in women between 34 and 37 weeks gestation with preterm prelabour prolonged rupture of membranes and vaginal or urine group B streptococcus colonisation?" will consider the management of preterm prelabour rupture of membranes. No new evidence was identified in the surveillance review or scoping searches that would impact the current recommendations on testing for GBS in preterm prelabour rupture of membranes. Therefore this area will not be included in this update.

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Group B Strep Support	5	16-17	Please would you add to the scope consideration of prophylaxis for women with preterm prelabour rupture of membranes with known GBS colonisation, in addition to the topic of the timing of delivery.	Thank you for your comment. The NICE guideline "preterm birth" NG25 covers antenatal prophylaxis for women with preterm prelabour rupture of membranes. The draft question "What is the clinical and cost effectiveness of immediate delivery versus expectant management in women between 34 and 37 weeks gestation with preterm prelabour prolonged rupture of membranes and vaginal or urine group B streptococcus colonisation?" will consider prophylaxis for women with preterm prelabour rupture of membranes.

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Group B Strep Support	7		In information and support – can the guideline be updated to recognise and/or incorporate the new recommendation from RCOG 2017 GTG #36 that all pregnant women should be provided with an information leaflet about group B Strep? The leaflet that we have co-written with the RCOG lists the key signs of EOGBS infection https://gbss.org.uk/wp-content/uploads/2018/01/2017-Joint-RCOG-GBSS-PIL_final.pdf so may help new parents identify the key signs of EOGBS infection in their baby's first week of life	Thank you for your comment. The "information and support" section of the current guideline includes recommendation 1.1.1.8 that may help new parents identify the key signs of EOGBS infection in their baby. The guideline update will include a new area on Information and support for parents and carers of babies with late-onset neonatal infection. NICE is also developing a new guideline on Shared decision-making (GID-NG10120), expected to be published in 2021.
Group B Strep Support	8		In timing of delivery in women with preterm prelabour rupture of membranes, please also include prophylaxis and, in women not identified as carrying GBS this pregnancy, the issue of testing for GBS carriage using appropriate GBS-specific tests. It is important to note that this is not a universal screening programme, it is testing individual women for GBS carriage because of one or more specific indications.	Thank you for your comment. The NICE guideline on preterm birth (NG25) covers antenatal prophylaxis for women with preterm prelabour rupture of membranes. This is considered by the draft question "What is the clinical and cost effectiveness of immediate delivery versus expectant

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				management in women between 34 and 37 weeks gestation with preterm prelabour prolonged rupture of membranes and vaginal or urine group B streptococcus colonisation?". No new evidence was identified in the surveillance review or scoping searches that would impact the current recommendations on testing for GBS in preterm prelabour rupture of membranes. Therefore this area will not be included in this update.
Group B Strep Support	8	12-13	Important to highlight this relates to a universal screening programme, not testing individual women for GBS carriage because of specific indications.	Thank you for your comment. The scope recognises that the UK National Screening Committee covers screening of GBS.
Healthcare Improvement Scotland - Scottish Antimicrobial Prescribing Group	General	General	Our group welcomes the update of this guideline and agrees with the planned scope of the update	Thank you for your comment.

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Little Heartbeats	5	16	Re. timing of delivery in women with preterm prelabour prolonged rupture of the membranes. We would welcome a review of the evidence in this area in general, in addition to the specific case of group B strep colonisation, with particular attention to how management and delivery should take into account the gestation at which PPROM occurred and the latency period. The evidence in the recent Cochrane review as to when to deliver is heavily weighted towards cases of PPROM occurring at later gestations and specifically states in its text that further consideration needs to be given to the subgroups where expectant management is not suitable, but so far this point keeps being missed, in both clinical practice and in the development of new guidance products (including in the new draft RCOG PPROM guideline which has just come out for peer review, despite Little Heartbeats explicitly asking for it to be considered). We know full consideration of the various contraindications and risk factors will be beyond the scope of this guideline, but a careful review remaining within the limits of this scope would still be very much appreciated.	Thank you for your comment. The current recommendation 1.3.1.3 says "Consider intrapartum antibiotic prophylaxis using intravenous benzylpenicillin to prevent early-onset neonatal infection for women in preterm labour if there is prelabour rupture of membranes of any duration." The NICE guideline on preterm labour and birth (NG25) covers antenatal prophylaxis for women with preterm prelabour rupture of membranes and the NICE guideline on inducing labour (CG70) covers timing of delivery before 34 weeks in preterm prelabour rupture of membranes.
London Neonatal Operational Delivery Network		General	**Current advice has led to 10% of babies in post-natal wards being exposed to antibiotics**, https://www.nice.org.uk/guidance/cg149.chapter/guidance#risk-factors-for-infection-and-clinical-indicators-of-possible-infection-2 "parental antibiotic treatment given to the woman for confirmed or	Thank you for your comment.

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			suspected invasive bacterial infection (such as septicaemia) at any time during labour, or in the 24-hour periods before and after birth"	
London Neonatal Operational Delivery Network	2	25	https://www.nice.org.uk/guidance/GID-NG10111/documents/draft-scope **GBS screening.** Most developed countries offer this. In my view the national screening committee (NSC) is out of step here. When we offered screening locally (with only 70% uptake), GBS disappeared. Papers embedded here. **Give colostrum in first hour. This is not mentioned here. Use probiotics**. **These are not even mentioned**. (Cochrane review 2014 supports this and we have been doing this for years. "Enteral supplementation of probiotics prevents severe NEC and all cause mortality in preterm infants" 1.7.1.2 Consider performing a lumber puncture to obtain cerebrospinal fluid sample in a baby who did not have a lumber puncture at presentation who is receiving antibiotics, if it is thought safe to do so and if the baby: Has a C-reactive protein concentration of 10mg/litre or greater, or **There are many non-infective causes of a raised CRP (papers embedded). This should be acknowledged, There are too many limber punctures being done for moderately raised CRP, with little return.**	Thank you for your comment. Population screening is covered nationally by the National Screening Committee and is therefore not within the remit of NICE to consider for its guidance. The guideline considers antibiotic management of suspected or confirmed neonatal infection in this guideline. Care for babies in the first few weeks after birth is covered in the NICE guideline on Postnatal care up to 8 weeks after birth (CG37). No new evidence was identified in the surveillance review or scoping searches that would impact the current recommendations on CRP

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			Success rate for LP is around 80% Could NICE advise what to do when unable to obtain CSF (or blood culture gets lost) as these are real life considerations.	and lumbar punctures. Therefore this area will not be include in this update. Recommendations in this area will be reviewed and the presentation amended to add cross references to other recommendations within the guideline. This will be prioritised by NICE.
London Neonatal Operational Delivery Network	3	2	https://www.nice.org.uk/guidance/GID-NG10111/documents/draft-scope **GBS screening.** Most developed countries offer this. In my view the national screening committee (NSC) is out of step here. When we offered screening locally (with only 70% uptake), GBS disappeared. Papers embedded here. **Give colostrum in first hour. This is not mentioned here. Use probiotics**. **These are not even mentioned**. (Cochrane review 2014 supports this and we have been doing this for years. "Enteral supplementation of probiotics prevents severe NEC and all cause mortality in preterm infants" 1.7.1.2 Consider performing a lumber puncture to obtain cerebrospinal fluid sample in a baby who did not have a lumber puncture at presentation who is receiving antibiotics, if it is thought safe to do so and if the baby: Has a C-reactive protein concentration of 10mg/litre or greater, or	Thank you for your comment. Population screening is covered nationally by the National Screening Committee and is therefore out of remit for NICE to consider for its guidance. The guideline considers antibiotic management of suspected or confirmed neonatal infection in this guideline. Care for babies in the first few weeks of birth are given in the NICE guideline for Postnatal

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			There are many non-infective causes of a raised CRP (papers embedded). This should be acknowledged, There are too many limber punctures being done for moderately raised CRP, with little return. **Success rate for LP is around 80% Could NICE advise what to do when unable to obtain CSF (or blood culture gets lost) as these are real life considerations.**	care up to 8 weeks after birth (CG37). No new evidence was identified in the surveillance review or scoping searches that would impact the current recommendations on CRP and lumbar punctures. Therefore this area will not be include in this update. Recommendations in this area will be reviewed and the presentation amended to add cross references to other recommendations within the guideline. This will be prioritised by NICE.
London Neonatal Operational Delivery Network	5		The consultation should consider the evidence for screening swabs on neonatal units (admission and /or regular) that aim to find bacteria with antibiotic resistance in order to direct antibiotic therapy.	Thank you for your comment. No new evidence was identified in the surveillance review or scoping searches that would impact the current recommendations on investigations before starting antibiotics in the baby. Therefore

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				this area will not be included in this update.
London Neonatal Operational Delivery Network	5	12	The current guideline mandates that the baby gets treated for possible sepsis (ie a 'red flag' sign) when there is 'Parenteral antibiotic treatment given to the woman for confirmed or suspected invasive bacterial infection (such as septicaemia) at any time during labour, or in the 24-hour periods before and after the birth'. There is great variability in the thresholds for instituting maternal antibiotics across maternity units and great variability of the definition of 'high temperature' in women in labour, with some units having very low thresholds. This results in many babies getting antibiotics after birth when there is probably not chorioamnionitis. What is required is a suggested definition of chorioamnionitis, or more guidance for neonatal teams about when to treat maternal temperature as simply a 'risk factor' and when to treat it as a 'red flag'.	Thank you for your comment. The tables in current recommendation 1.2.1 list risk factors and clinical indicators to be used with current recommendation 1.2.3.2, which gives guidance on how to use those risk factors and clinical indicators when considering antibiotics for early-onset neonatal infection. Evidence in the area of red flags and risk factors will be reviewed as part of the update by draft questions "Which maternal and fetal risk factors for early-onset neonatal infection should be used to guide management?" and "What risk factors in the baby (including symptoms and signs) should raise suspicion of infection within 72 hours of birth?". Providing a definition for chorioamnionitis is not within the remit of this guideline.

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				The guideline will provide recommendations on which maternal and fetal risk factors for early-onset neonatal infection should be used to guide management,
London Neonatal Operational Delivery Network	5	General	There is very good evidence from the US that the use of computer algorithms (i.e. early onset sepsis calculator) for assessing risk in EOS are useful for deciding on management, which can reduce the use of antibiotics without increasing risk to the neonate. It is essential that the evidence around these tools is assessed in this review. Recommendations to use such tools are very likely to lead to significant cost savings and reduction in length of stay for babies on post-natal wards, neonatal units and transitional care units.	Thank you for your comment. The draft questions "Which risk factors in the baby (including symptoms and signs) should raise suspicion of late-onset infection?" and "Which maternal risk factors for late-onset neonatal infection should be used to guide management?" will consider risk factors for late-onset neonatal bacterial infection. The update of the guideline will follow the processes and methods described in Developing NICE guidelines: the manual. Evidence reviews will be conducted for each of the review questions described in the scope which will include all published evidence which meet the

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				review protocols developed for the guideline. The evidence that you refer to relates to clinical questions that are being updated in this guideline. If this evidence meets the review protocol, this will be considered by the guideline committee during the update.
London Neonatal Operational Delivery Network	7	General	There is very good evidence from the US that the use of computer algorithms (i.e. early onset sepsis calculator) for assessing risk in EOS are useful for deciding on management, which can reduce the use of antibiotics without increasing risk to the neonate. It is essential that the evidence around these tools is assessed in this review. Recommendations to use such tools are very likely to lead to significant cost savings and reduction in length of stay for babies on post-natal wards, neonatal units and transitional care units.	The draft question "Which risk factors in the baby (including symptoms and signs) should raise suspicion of late-onset infection?" and "Which maternal risk factors for late-onset neonatal infection should be used to guide management?" will consider risk factors for late-onset neonatal bacterial infection. The update of the guideline will follow the processes and methods described in Developing NICE guidelines: the manual. Evidence reviews will be conducted for each of the review questions described in the scope which will include all

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				published evidence which meet the review protocols developed for the guideline. The evidence that you refer to relates to clinical questions that are being updated in this guideline. If this evidence meets the review protocol, this will be considered by the guideline committee during the update.
London North West University Healthcare NHS Trust	5	12	The draft scope will not look at using antibiotics in babies. Yet across England many units do not use gentamicin because of local resistance. It would be good if the NICE guidance recognised this as prudent good management and it was in the guideline	Thank you for your comment. The issue of local resistance to gentamicin is addressed in current recommendation 1.6.1.1 **"**Use intravenous benzylpenicillin with gentamicin as the first-choice antibiotic regimen for empirical treatment of suspected infection unless microbiological surveillance data reveal local bacterial resistance patterns indicating a different antibiotic." Effective use of antimicrobials is covered in the NICE guideline on Antimicrobial stewardship (NG15).

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London North West University Healthcare NHS Trust	general	general	The scope does not intend to look into recommendations for investigations carried out on neonates at risk of infection. We feel this should be addressed. There is lots of evidence to suggest: - CRP at zero hours has little clinical significance, would it be better to do first CRP at 24 hours and maybe a second later at 36/48 hours? - Current guidelines suggest doing an LP at initial screen if there is a 'strong clinical suspicion of infection'. We feel this should be looked into, should it worded as 'do an LP if clinical suspicion of meningitis' rather than infection.	Thank you for your comment. No new evidence was identified in the surveillance review or scoping searches that would impact the current recommendations on CRP and lumbar puncture. Therefore this area will not be included in this update. Recommendations in this area will be reviewed and the presentation amended to add cross references to other recommendations within the guideline. This will be prioritised by NICE.
London North West University Healthcare NHS Trust	general	general	Consideration of amending wording of guideline to 'consider' when discusses the need to do an LP, otherwise may be interpreted as 'do' an LP for high CRPs. Once again this is outside the remit of the current scope, but indications for when to do an LP vary widely between neonatal units and perhaps this should be reviewed as part of the guideline review.	Thank you for your comment. No new evidence was identified in the surveillance review or scoping searches that would impact the current recommendations on CRP and lumbar punctures. Therefore this area will not be include in this update. Recommendations in this area will be reviewed and the

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				presentation amended to add cross references to other recommendations within the guideline. This will be prioritised by NICE.
NHS England – Neonatal Critical Care Clinical Reference Group	3	4-5	We recommend consideration of the use of the Kaiser Permanante Sepsis Calculator to assess the risk of early onset neonatal infection. This has been widely established in the USA and has reduced the need for invasive investigations and use of IV antibiotics as well as shortening length of stay on postnatal wards. In these settings it has been assessed as safe. However, the evidence base for implementation of this in the UK does have some limitations, due to the different background population risk for GBS, E. coli and other organisms and lack of routine maternal screening for GBS olonisation in UK. It is disappointing that a proposed cluster RCT has not as yet been funded as this could provide a more robust evidence base relatively quickly. Current assessment of EONS risk using the existing NICE guidelines results in a significant number of newborn babies being screened by blood tests and other investigations as well as large numbers receiving IV antibiotics on the postnatal ward (up to 20%). Many neonatologists believe that this approach is too risk averse and local guidelines have often been adjusted and are therefore not consistent with the current NICE guideline.	Thank you for your comment. The draft questions "Which maternal and fetal risk factors for early-onset neonatal infection should be used to guide management?" and "What risk factors in the baby (including symptoms and signs) should raise suspicion of infection within 72 hours of birth?" will consider risk factors for early onset neonatal infection. The update of the guideline will follow the processes and methods described in Developing NICE guidelines: the manual. Evidence reviews will be conducted for each of the review questions described in the scope which will include all published evidence which meet the review

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				protocols developed for the guideline. The evidence that you refer to relates to clinical questions that are being updated in this guideline. If this evidence meets the review protocol, this will be considered by the guideline committee during the update.
NHS England – Neonatal Critical Care Clinical Reference Group	5	12-14	We recommend consideration of the use of the Kaiser Permanante Sepsis Calculator to assess the risk of early onset neonatal infection. This has been widely established in the USA and has reduced the need for invasive investigations and use of IV antibiotics as well as shortening length of stay on postnatal wards. In these settings it has been assessed as safe. However, the evidence base for implementation of this in the UK does have some limitations, due to the different background population risk for GBS, E. coli and other organisms and lack of routine maternal screening for GBS olonisation in UK. It is disappointing that a proposed cluster RCT has not as yet been funded as this could provide a more robust evidence base relatively quickly. Current assessment of EONS risk using the existing NICE guidelines results in a significant number of newborn babies being screened by blood tests and other investigations as well as large numbers receiving IV antibiotics on the postnatal ward (up to 20%). Many neonatologists	Thank you for your comment. The draft questions "Which risk factors in the baby (including symptoms and signs) should raise suspicion of late-onset infection?" and "Which maternal risk factors for late-onset neonatal infection should be used to guide management?" will consider risk factors for late-onset neonatal bacterial infection. The update of the guideline will follow the processes and methods described in Developing NICE guidelines: the manual. Evidence reviews will be conducted for each of the review questions described in

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			believe that this approach is too risk averse and local guidelines have often been adjusted and are therefore not consistent with the current NICE guideline.	the scope which will include all published evidence which meet the review protocols developed for the guideline. The evidence that you refer to relates to clinical questions that are being updated in this guideline. If this evidence meets the review protocol, this will be considered by the guideline committee during the update.
Royal College of General Practitioners	General	General	The RCGP welcomes the opportunity to comment on the draft scope 3 herpes viruses (cytomegalovirus, herpes simplex virus, and varicella zoster virus) have potentially serious effects from perinatal infection on obstetric outcomes, specifically maternal and neonatal morbidity. Will the guideline committee consider future directions of work in reducing the morbidities associated with these viral pathogens? https://www.sciencedirect.com/science/article/pii/S1473309917301433	Thank you for your comment. Viral infections are not within the remit of this guideline. The update will only consider bacterial infections in neonates.
Royal College of General Practitioners	General	General	Will hospital building and unit design be considered in order to can be used to aid infection prevention? https://www.tandfonline.com/doi/abs/10.1080/00140139.2017.1330967	Thank you for your comment. Hospital building and unit design are not within the remit of this guideline. The update will only

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				consider bacterial infections in neonates. NICE's guideline on Health-care associated infections: prevention and control (PH36) gives recommendations in this area.
Royal College of General Practitioners	General	General	There is some evidence that Infection prevention and control strategies in neonates should focus on prevention of bloodstream infections. Will the guidelines committee ensure due consideration for this important area? https://www.sciencedirect.com/science/article/pii/S1473309916305175	Thank you for your comment. The draft questions "Which risk factors in the baby (including symptoms and signs) should raise suspicion of late-onset infection?" and "What is the clinical and cost effectiveness of intravascular catheters impregnated with antibiotics in reducing the risk of the baby developing late-onset neonatal infection?" will consider the prevention of bloodstream infections in neonates.
Royal College of Midwives	General	General	The RCM welcomes the ambition to align NICE guidance and RCOG guidance on intrapartum prophylactic antibiotics based on current evidence.	Thank you for your comment.
Royal College of Nursing			This is just to inform you that the feedback I have received from nurses working in this area of health suggests that there are no comments to submit on behalf of the Royal College of Nursing to	Thank you for your comment.

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			inform on the consultation of the draft scope of neonatal infection (early onset): antibiotics for prevention and treatment. Thank you for the opportunity to participate. We look forward to participating at the next stage.	
Royal College of Obstetricians and Gynaecologists		12, 13, 14	Regarding antibiotics for preterm prelabour rupture membranes with RCOG green top guidelines, all centres provide intrapartum antibiotics	Thank you for your comment. The NICE guideline "preterm birth" NG25 covers antenatal prophylaxis for women with preterm prelabour rupture of membranes. The draft question "What is the clinical and cost effectiveness of immediate delivery versus expectant management in women between 34 and 37 weeks gestation with preterm prelabour prolonged rupture of membranes and vaginal or urine group B streptococcus colonisation?" will consider the management of preterm prelabour rupture of membranes.
Royal College of Obstetricians	1	22	Full details of why the update is needed are given in the 'surveillance review decision'. This linked document has sections on intrapartum antibiotics and a new area: maternal GBS status to guide the decision on timing of delivery in women with preterm prelabour rupture of the	Thank you for your comment. The surveillance report is made based on the evidence available at the time of publication. The draft

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and Gynaecologists			membranes (PPROM). The linked update page was last updated on 09 January 2017. Since then, the RCOG has published a revised Green-top guideline on the prevention of early-onset group B streptococcus (September 2017), which has updated the evidence on intrapartum antibiotics and includes a section on maternal GBS status to guide the decision on timing of delivery in women with PPROM. The surveillance review decision refers to, and includes quotations from, the 2nd edition of the RCOG GBS guideline that has now been archived. I would highly recommend that the surveillance review report is updated before work on this guideline continues.	question in the scope "What is the clinical and cost effectiveness of immediate delivery versus expectant management in women between 34 and 37 weeks gestation with preterm prelabour prolonged rupture of membranes and vaginal or urine group B streptococcus colonisation?" will consider prophylaxis for women with preterm prelabour rupture of membranes. The update of the guideline will follow the processes and methods described in Developing NICE guidelines: the manual. Evidence reviews will be conducted for each of the review questions described in the scope which will include all published evidence which meet the review protocols developed for the guideline.
Royal College of Obstetricians	1	7	Maternal obesity as a risk factor need evidence and will have huge impact on the management of mothers intrapartum	Thank you for your comment, the draft question "Which maternal and fetal risk factors for early-onset

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and Gynaecologists				neonatal infection should be used to guide management?" will consider risk factors for neonatal infection. The update of the guideline will follow the processes and methods described in Developing NICE guidelines: the manual. Evidence reviews will be conducted for each of the review questions described in the scope which will include all published evidence which meet the review protocols developed for the guideline.
Royal College of Obstetricians and Gynaecologists	2	25	The scope says that: 'guidance from the RCOG recommends only giving antibiotics to women who are proven GBS carriers'. This sentence is entirely inaccurate and this section of the draft scope needs to be revisited. Regarding the prevention of early-onset GBS disease, the RCOG (2017) recommends offering antibiotics (IAP) to: • Women with a previous baby with early- or late-onset GBS disease	Thank you for your comment. This section of the scope has been amended following stakeholder comments on the scope.

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			• Women who are found to have GBS bacteruria during the current pregnancy • Women who are found to be colonised with GBS • Women who are pyrexial in labour (a broad-spectrum antibiotic that also covers GBS) • Women with preterm rupture of membranes when they are in labour • Women in confirmed preterm labour • Women who were found to be colonised with GBS in a previous pregnancy (who may instead choose to be tested in the current pregnancy)	
Royal College of Obstetricians and Gynaecologists	General		Well written and detailed scope.	Thank you for your comment.
Royal College of Paediatrics			There is evidence from various neonatal units that the Kaiser Permanante App, which calculates risk along the current practice to	Thank you for your comment. The draft questions "Which maternal

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and Child Health			see what the discrepancy in risk scoring is, has reduced their use of antibiotics in new-borns.	and fetal risk factors for early-onset neonatal infection should be used to guide management?" and "What risk factors in the baby (including symptoms and signs) should raise suspicion of infection within 72 hours of birth?" will consider risk factors for intrapartum and neonatal antibiotic use. The update of the guideline will follow the processes and methods described in Developing NICE guidelines: the manual. Evidence reviews will be conducted for each of the review questions described in the scope which will include all published evidence which meet the review protocols developed for the guideline. The evidence that you refer to relates to clinical questions that are being updated in this guideline.. If this evidence meets the review protocol, this will be

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				considered by the guideline committee during the update.
Royal College of Paediatrics and Child Health			The guidance describes prelabour rupture of the membranes as a risk factor for EOI, as opposed to the more usually considered "prolonged rupture of the membranes". (The guidance does not define a criterion for considering when the condition of prelabour rupture of the membranes is satisfied – this is a significant operational problem). Clinical staff often assume that these two distinct, but sometimes coexistent risk factors are the same. The danger is that still more babies than would otherwise have received antibiotics do so as a result of this understanding of exactly what NICE mean by prelabour rupture of the membranes. That prolonged rupture of the membranes is described in other (obstetric) NICE guidance as NOT a reason to start babies on antibiotics is only confusing to NHS staff.	Thank you for your comment. The current recommendation 1.2.2.2 considers prelabour rupture of membranes and it currently refers to the Intrapartum care guideline (CG55). The updated guideline will cross refer to the NICE guideline on Intrapartum care for healthy women and babies (CG190), which replaced CG55.
Royal College of Paediatrics and Child Health			The risk to babies' developing microbiotia from administration of early onset antibiotics should be acknowledged as a disadvantage of the widespread administration of antibiotics to asymptomatic patients, where the actual benefit may be very low.	Thank you for your comment. No new evidence was identified in the surveillance review or scoping searches that would impact the current recommendations on antibiotic treatment for early-onset neonatal infection. Therefore this area will not be included in this update.

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Royal College of Paediatrics and Child Health			The suggestion that where EOI is strongly suspected, a course of antibiotics of 7 days should be administered, in place of the commonly used 5 days needs to be better evidenced, or the uncertainty acknowledged. To the reviewers knowledge, there is no evidence that 7 day courses are "better" than 5 day courses – and as all too often the only pathology being treated is a transient rise in CRP, it remains problematic to use longer courses.	Thank you for your comment. No new evidence was identified in the surveillance review or scoping searches that would impact the current recommendations on CRP and duration of antibiotic treatment. Therefore this area will not be included in this update.
Royal College of Paediatrics and Child Health			The guidance should be made clearer.	Thank you for your comment. Without further information, NICE cannot amend the scope based on this comment.
Royal College of Paediatrics and Child Health	1	25	Prophylactic use of antifungals; is this only to be included in babies who will be on prolonged antibiotics or all babies?	Thank you for your comment. Committee members noted that antibiotic use increases the risk of fungal infection in neonates. The guideline will consider the effectiveness of starting antifungal treatment for babies receiving antibiotic treatment for suspected late-onset neonatal infection in the draft review question "What is the clinical and cost effectiveness of starting prophylactic antifungal

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				treatment when starting antibiotic treatment for suspected late-onset neonatal infection?".
Royal College of Paediatrics and Child Health	11	Point 3.5	The threshold is currently low to investigate and treat babies according to current guidelines and perhaps a significant number do not need intervention, a review is most welcomed. Furthermore, streamlining/optimising maternal management will help with neonatal management.	Thank you for your comment.
Royal College of Paediatrics and Child Health	5		The consultation should consider the evidence for screening swabs on neonatal units (admission and/or regular) that aim to find bacteria with antibiotic resistance in order to direct antibiotic therapy.	Thank you for your comment. No new evidence was identified in the surveillance review or scoping searches that would impact the current recommendations on investigations before starting antibiotics in the baby. Therefore this area will not be included in this update.
Royal College of Paediatrics and Child Health	5	12	For truly patient centred care, some information is required of the absolute risks of neonatal sepsis with the different risk factors, and common combinations of risk factors. Currently, parents who are reluctant for their baby to have antibiotics have very little information on how to weigh up the true risks.	Thank you for your comment. The draft questions "Which risk factors in the baby (including symptoms and signs) should raise suspicion of early-onset infection within 72 hours of birth?" and "Which maternal risk

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				factors for late-onset neonatal infection should be used to guide management?" will consider risk factors for neonatal bacterial infection. The evidence review will present all the reviewed evidence in the area.
Royal College of Paediatrics and Child Health	5	12	It is very important that the guidance includes a consideration of when intrapartum antibiotic prophylaxis HAS been given. Do such babies need any observation? If a baby has two risk factors/one red flag but has received IAP, does this change the decision to perform partial septic screen?	Thank you for your comment. No new evidence was identified in the surveillance review or scoping searches that would impact the current guideline on management following antibiotic administration for early-onset neonatal infection. Therefore this area will not be included in this update.
Royal College of Paediatrics and Child Health	5 and 7		There is very good evidence from the US that the use of computer algorithms (i.e. early onset sepsis calculator) for assessing risk in EOS are useful for deciding on management, which can reduce the use of antibiotics without increasing risk to the neonate. It is essential that the evidence around these tools is assessed in this review. Recommendations to use such tools are very likely to lead to significant cost savings and reduction of length of stay for babies on postnatal wards, neonatal units and transitional care units.	The draft question "Which risk factors in the baby (including symptoms and signs) should raise suspicion of late-onset infection?" and "Which maternal risk factors for late-onset neonatal infection should be used to guide management?" will consider risk factors for late-

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				onset neonatal bacterial infection. The update of the guideline will follow the processes and methods described in Developing NICE guidelines: the manual. Evidence reviews will be conducted for each of the review questions described in the scope which will include all published evidence which meet the review protocols developed for the guideline. The evidence that you refer to relates to clinical questions that are being updated in this guideline. If this evidence meets the review protocol, this will be considered by the guideline committee during the update.
Royal College of Paediatrics and Child Health	7	3	'Maternal obesity as a risk factor for sepsis' - this is interesting and not widely known	Thank you for your comment.
Royal College of Paediatrics	7	Point 1.5 to 1.7	The draft scope proposes not to update these points; however, it is thought that if NICE guidelines are followed then too many LPs are done and the yield for these is low.	Thank you for your comment. No new evidence was identified in the surveillance review or scoping

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and Child Health				searches that would impact the current recommendations on CRP and lumbar punctures. Therefore this area will not be included in this update. Recommendations in this area will be reviewed and the presentation amended to add cross references to other recommendations within the guideline. This will be prioritised by NICE.
Royal College of Paediatrics and Child Health	8	5	Should the evidence for preventing LOS be reviewed? E.g. infection control, care bundles, Abx-impregnated longlines, hand hygiene, probiotics, feeding practices, VAP prevention, etc.	Thank you for your comment. Infection control is covered in the NICE guideline Healthcare-associated infections: prevention and control in primary and community care (CG139).
Royal College of Paediatrics and Child Health	9	3	Draft scope not to include early onset infections known/thought to be associate with maternal STI - is there an antimicrobial guideline to direct on this or will it be down to local micro advice?	Thank you for your comment. Early onset infections due to STIs are out of remit for this guideline.
Royal College of Paediatrics	General		There is a discernible difference between neonates who have been discharged and those who have not.	Thank you for your comment. Neonates who have been readmitted from home are listed

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and Child Health				under "specific considerations" in the "groups that will be covered" section in the scope.
Royal College of Paediatrics and Child Health	General		In babies who have been discharged home and then re-attend with a fever and signs of evolving sepsis, they seem to have enterovirus meningitis. Should babies with viral meningitis have their antibiotics stopped and when?	Thank you for your comment. Viral infections are out of remit for this guideline. The update will only consider bacterial infections in neonates.
Royal College of Paediatrics and Child Health	General	General	This guideline is necessary, the scope is agreed with.	Thank you for your comment.
Royal College of Paediatrics and Child Health	general	general	Current guidance does not define PROM in term babies. This leads to variation in interpretation and practice nationally. NICE guidance CG190 specifies that babies with ROM of more than 24 hours to onset of established labour should have observations, perhaps this could be specified in the current guidance too.	Thank you for your comment. The updated guideline will cross refer to the NICE guideline on Intrapartum care for healthy women and babies (CG190).
Royal College of Paediatrics and Child Health	general	general	The 2017 surveillance decision states that there is no new evidence relating to investigations. However, there is enormous controversy around how the existing guidance interprets the evidence relating to lumbar puncture and CRP values. No neonatal units in the reviewer's regional network have retained the guidance to consider LP at CRP of 10 as this led to an enormous increase in number of LPs performed,	Thank you for your comment. No new evidence was identified in the surveillance review or scoping searches that would impact the current recommendations on CRP and lumbar punctures. Therefore

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			with no increase in significant organisms identified, and substantial harm to babies who had unsuccessful or bloody taps with resultant long courses of antibiotics. Some units are also changing guidance on length of antibiotics based on new viral PCR testing of CSF that is coming into practice.	this area will not be include in this update. Recommendations in this area will be reviewed and the presentation amended to add cross references to other recommendations within the guideline. This will be prioritised by NICE.
Royal College of Paediatrics and Child Health	general	general	The revisions will be extremely helpful and necessary. They relate to areas that often cause confusion (different guidance on antepartum antibiotics) and the observation is that the use of antibiotics has increased since the guidance was implemented.	Thank you for your comment.
Royal College of Paediatrics and Child Health	General	General	When considering late onset sepsis, fungal infections (and viral infections) as a differential diagnosis should be considered including the necessary treatment options, not just antifungal prophylaxis.	Thank you for your comment. Diagnosis of fungal and viral infections is outside the remit for this guideline update. The guideline will consider the effectiveness of starting antifungal treatment for babies receiving antibiotic treatment for suspected late-onset neonatal infection in the draft review question "What is the clinical and cost effectiveness of starting prophylactic antifungal treatment

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				when starting antibiotic treatment for suspected late-onset neonatal infection?".
Royal College of Paediatrics and Child Health	General	General	There should be cross-referencing to EOS and LOS meningitis to ensure that it is in keeping with other NICE guidance on meningitis as there is overlap in the management.	Thank you for your comment. The current recommendation 1.2.3.5 refers to the NICE guideline on Bacterial meningitis and meningococcal septicaemia (CG102) for management of these conditions. In addition the updated guideline will also cross refer to the NICE guideline on Bacterial meningitis and meningococcal septicaemia (CG102) in section 1.5 of the current guideline
Royal College of Paediatrics and Child Health	General	General	Otherwise happy with document.	Thank you for your comment.
UK Clinical Pharmacy Association	11	3.5 Key Issues Q6	At Guy's & St Thomas Foundation Trust (GSTFT) we use IV flucloxacillin & gentamicin as our first line antibiotic regimen for the treatment of late onset neonatal infection on the Neonatal Unit with consideration to change flucloxacillin to vancomycin if failure to respond & central lines in place or if blood cultures grow CoNS. Local	Thank you for your comment. The draft question "What is the optimal antibiotic treatment regimen for suspected late-onset neonatal infection?" will consider antibiotics

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			preference is to use narrow spectrum agents to reduce risk of antimicrobial resistance. At GSTFT we start prophylactic antifungal treatment for babies that meet the following criteria: <26 weeks gestation <800g birth weight Therapy is continued for 6 weeks until unless ETT & all invasive plastic removed. Prophylactic antifungal treatment is not routinely started when antibiotics are started for empiric treatment of late onset neonatal infection however fungal sepsis is consisted in culture negative sepsis.	regimen for treating late-onset neonatal infection. The update of the guideline will follow the processes and methods described in Developing NICE guidelines: the manual. Evidence reviews will be conducted for each of the review questions described in the scope which will include all published evidence which meet the review protocols developed for the guideline.
UK Clinical Pharmacy Association	Comments Form	Q1	The current guidance recommends performing a lumbar puncture if CRP > 10. Locally our clinicians have chosen to use a CRP value of 20 rather than 10 since a positive CSF is so rare. Review of this recommendation could reduce the number of lumbar punctures performed.	Thank you for your comment. No new evidence was identified in the surveillance review or scoping searches that would impact the current recommendations on CRP and lumbar punctures. Therefore this area will not be include in this update. Recommendations in this area will be reviewed and the presentation amended to add cross references to other

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				recommendations within the guideline. This will be prioritised by NICE.