National Institute for Health and Clinical Excellence

Feverish illness in children
Guideline Consultation Comments Table
23 November 2012 - 11 January 2013

Comment number	Stakeholder	Order No	Document	Page No	Line No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
1.	**Alder Hey Children's NHS Foundation Trust**	1	NICE	9	15	Add ***CSF analysis if focus for fever is unclear***	Thank you for your comment. There is a recommendation as to when CSF analysis should be performed in the main body of recommendations (1.5.2.3).
2.	**Alder Hey Children's NHS Foundation Trust**	2	NICE	9	26	Consider changing***/adding*** other agent if the child's distress is not alleviated	Thank you for your comment. After discussion the GDG believed that the suggested wording change would be inconsistent with the rest of the recommendation, and potentially confusing to readers. Therefore no change has been made.
3.	**Alder Hey Children's NHS Foundation Trust**	3	NICE	13	6	Add, ***reduced or poor respiratory effort***	Thank you for your comment. As much as possible, the recommendations directly refer to the terms used in the primary studies on which the reviews are based. As no evidence was found for the term "reduced or poor respiratory effort" it was not included and cannot be added now.
4.	**Alder Hey Children's NHS Foundation Trust**	4	NICE	21	12	Meningitis: neck stiffness ***(absence of neck stiffness does not exclude meningitis)***	Thank you for your comment. The GDG acknowledge that neck stiffness is often absent in young children. However, the traffic light table is not a tool for diagnosing meningitis. It is a tool for translating the risk of

							serious illness if a symptom or sign is present. As such, the present wording is correct. The presence of neck stiffness does confer a high risk of having a serious illness. In addition, a specific recommendation on this point “Healthcare professionals should be aware that classic signs of meningitis (neck stiffness, bulging fontanelle, high-pitched cry) are often absent in infants with bacterial meningitis. [2007]”
5.	**Alder Hey Children's NHS Foundation Trust**	5	NICE	13	1	To include ***parental concerns as a part of the assessment process.***	Thank you for your comment. All parents and carers must have sufficient concerns about the child’s health in order to seek help. Therefore, adding this to the traffic light table would not be appropriate as it is universal. However, the guideline does highlight that parental concerns are valid and must be taken seriously - “Reported parental perception of a fever should be considered valid and taken seriously by healthcare professionals. [2007]” and “ In addition to the child's clinical condition, healthcare professionals should consider the following factors when deciding whether to admit a child with fever to hospital …parental anxiety and instinct (based on their knowledge of their child)…”
6.	**Alder Hey Children's NHS Foundation Trust**	6	Full	18	33	Should highlight in the table that neck stiffness is not usually seen in young children	Thank you for your comment. The GDG acknowledge that neck stiffness is often absent in young children. However, the traffic light table is not a tool for diagnosing meningitis. It is a tool for translating the risk of serious illness if a symptom or sign is present. As such, the present wording is correct. The presence of neck stiffness does confer a high risk of having a serious illness.

							In addition, a specific recommendation on this point “Healthcare professionals should be aware that classic signs of meningitis (neck stiffness, bulging fontanelle, high-pitched cry) are often absent in infants with bacterial meningitis. [2007]”
7.	**Association of Anaesthetists of Great Britain and Ireland**					The AAGBI has no comment on this consultation.	Thank you for your response and taking the time to read the updated guideline.
8.	**British Association of Paediatric Nephrology**	1	Full	general		This is a comprehensive guideline but does not seem to address the case of children who are immunosuppressed. While the detailed management of these patients may not be appropriate for this document it would be appropriate to mention the need to be aware of the potential lack of associated symptoms and signs in the immunosuppressed patient and the need for a low threshold for treatment of pyrexia prior to investigation results being available.	Thank you for this comment. The GDG agree this should to be clearer. The scope for the guideline outlines groups not covered, including immunosuppressed. This list has been added to the main guideline document and the NICE version of the guideline.
9.	**British Association of Paediatric Nephrology**	2	Full	45	14	Delphi statement 7.4 seems to be interpreted incorrectly. The statement “Healthcare professionals should not routinely use electronic thermometers by the rectal route (back 15 passage) to measure body temperature in children aged 3 months to 2 years” is disagreed with-suggesting that the rectal route should be used-I don’t believe this is what was meant as the conclusion is that the rectal route shouldn’t be used (which is appropriate).	Thank you for your comment. Unfortunately use of thermometers was not selected to be included in the 2013 update of the feverish illness guideline. Therefore, we cannot take your comments forward or make any substantive changes to the existing topic in the final version of the Guideline. However, your comment will be kept on record for the next update of the guideline.
10.	**British Association of Paediatric Nephrology**	3	Full	124	18	Peritonitis is not included in the list of serious infections with specific signs and symptoms. Peritonitis is most likely due to appendicitis, nephrotic syndrome (and in children on peritoneal dialysis).	Thank you for your comment. Unfortunately the management of peritonitis was not raised by stakeholders during the scoping process and therefore was not included in the 2013 update of the feverish

							illness guideline. Therefore, we cannot take your comments forward or make any substantive changes the Guideline. However, your comment will be kept on record for the next update of the guideline.
11.	**British Infection Association**	1	Full	General		From the title the remit of this document sounds broad but this is misleading as it excludes many (most) common febrile illnesses. It probably should be titled: 'Feverish illness in children. Assessment and initial management to exclude serious illnesses that may have immediate consequences to the child's life expectancy or long-term quality of life'. In particular there is no mention of rash illnesses other than meningococcal disease and Kawasaki disease, yet there are clearly important illnesses other than these that I feel should be included at least for differential diagnosis. A section on rash and fever might be included, or at the least information on **measles** and **HHV6** infection in the specific infections section. HHV6 in particular is a common infection in this age group, with or without a rash, so should be considered in differential diagnosis of febrile illness in young children. In addition to febrile illnesses with potential for serious illness a section pointing out those needing early infection control and public health intervention eg measles, meningococcal infection, febrile illnesses acquired abroad (mentioned briefly on p134 section 5.6), respiratory infections such as influenza might be helpful.	Thank you for your comment. The Department of Health sets the remit for clinical guidelines and NICE agrees the short and long titles. The focus of the guideline is the initial identification of potentially serious illness. Initial advice is then provided on the most serious illnesses. The list of serious illnesses included in the guideline was agreed by consensus during the production of the original guideline (see section 1.2). Serious illnesses were agreed to be those "that could cause death or disability if there were a delay in diagnosis and treatment'. The GDG agree that measles and HHV6 are significant illnesses but they do not fit the GDG's precise definition of serious illness.

12.	**British Infection Association**	2	Full	32	24	Streptococcus pneumoniae should be italicized	Thank you for your comment. This formatting error has been amended.
13.	**British Infection Association**	3	Full	11	49	Add: stool virus PCRs if diarrhoea present	Thank you for your comment. The GDG agree that stool virus PCR can be useful in the management of a child presenting with diarrhoea as the main complaint. However, the GDG are not aware of any evidence that stool virus PCR is immediately useful in the assessment and initial management of children with a feverish illness.
14.	**British Infection Association**	4	Full	179	16	**17** italicize bacterial names and add space between *Haemophilus*and *influenzae*(also line 23), also italics needed for names in Recommendations Box on same page	Thank you for your comment. This formatting error has been amended.
15.	**British Infection Association**	5	Full	237	8	**'…**higher overall cost **that** the highest..' should read 'than'	Thank you for your comment. This typographical error has been amended.
16.	**British Medical Association**	1	Full	General		We would like to highlight the importance of listening to the child's parents. The 24 hour knowledge of a child, and of a child's normal behaviour, is occasionally dismissed by health professionals. A parent's perception of their child's state of health is valid.	Thank you for your comment. The GDG agree with your comment and a specific recommendation has already been made to highlight this - "Reported parental perception of a fever should be considered valid and taken seriously by healthcare professionals. [2007]"
17.	**British Medical Association**	2	Full	224	30	Recommendation 80 ('Do not use antipyretic agents with the sole aim of reducing body temperature in children with fever.') needed to be explained a bit better – we are not sure what is meant by this statement.	Thank you for this comment. After discussion with the NICE editorial team, it has been concluded that this recommendation is clear. Therefore, no change will be made.
18.	**British Medical Association**	3	Full	224	30	Recommendation 81 ('When using paracetamol or ibuprofen in children with fever: continue only as long as the child appears distressed	Thank you for your comment. Justification for each recommendation is provided in the 'evidence to recommendation' section of each chapter. Throughout the

						• consider changing to the other agent if the child's distress is not alleviated • do not give both agents simultaneously • only consider alternating these agents if the distress persists or if it recurs before the next dose is due.') is thought to be confusing as it is unclear why the anti-pyretic should only be administered whilst the child is distressed. We also consider the wording of the final bullet point to be confusing and would benefit from 'it' being changed to 'the fever'.	guideline the GDG state that reduction in distress of a child is the primary aim of management. In addition, we have edited the recommendation, so it now reads. *When using paracetamol or ibuprofen in children with fever:* • *continue only as long as the child appears distressed* • *consider changing to the other agent if the child's distress is not alleviated* • *do not give both agents simultaneously* • only consider alternating these agents if the distress persists or recurs before the next dose is due. [new 2013]
19.	**British Society for Antimicrobial Chemotherapy**	1	NICE summary	24		Consider introducing a flow chart for management. See example attached (below)	Thank you for your comment. NICE have introduced 'NICE pathways' (http://pathways.nice.org.uk/) which replaces the static flows charts that were included in previous guidelines.
20.	**British Society for Antimicrobial Chemotherapy**	2	NICE summary	29		The BSAC suggests that ampicillin in children under 3 months should be used to cover for Group B Streptococci and Listeria. Late presentation of Group B Strep infection should be mentioned	Thank you for your comment. Unfortunately the management of specific conditions was not selected to be included in the 2013 update of the feverish illness guideline. Therefore, we cannot take your comments forward or make any substantive changes to the existing topic in the final version of the Guideline. The GDG would also highlight that bacterial meningitis and meningococcal septicaemia NICE clinical guideline 102 (2010) and antibiotics for early-onset neonatal infection NICE clinical guideline 149 (2012) address this

							issue in detail.
21.	**British Society for Antimicrobial Chemotherapy**	3	NICE summary	29		"an antibiotic active against listeria" is recommended for children younger than 3 months. However, the BSAC understand from the HPA that since the NICE guideline 47 was published in 2007 there have been no recorded cases of listeria infection in this country in children older than 4 weeks of age (there have been 41 cases in children =< 4weeks of age). The guideline development group may therefore wish to reconsider the cut-off age for listeria cover.	Thank you for your comment. Unfortunately the management of specific conditions was not selected to be included in the 2013 update of the feverish illness guideline. Therefore, we cannot take your comments forward or make any substantive changes to the existing topic in the final version of the Guideline. However, your comments will be taken forward for consideration at the next update. We wish to highlight that this recommendation was made to ensure the safest treatment possible. The GDG would also highlight that the NICE guidelines on bacterial meningitis and meningococcal septicaemia (CG102 [2010]) and antibiotics for early-onset neonatal infection (CG149 [2012]) address this issue in detail.
22.	**British Society for Antimicrobial Chemotherapy**	4	NICE summary	29		The BSAC is concerned that microbiology colleagues will object to the choice of third-generation cephalosporins as empirical therapy. We understand that cefotaxime has been used empirically for over 20 years in one SCBU with only rare instances of antibiotic resistance to date.	Thank you for your comment. Unfortunately the management of specific conditions was not selected to be included in the 2013 update of the feverish illness guideline. Therefore, we cannot take your comments forward or make any substantive changes to the existing topic in the final version of the Guideline. However, your comments will be taken forward for consideration at the next update Also, the scope of the guideline does not cover management of children cared for in SCBU settings. However, the recommendations are in line with

							the NICE guidelines on bacterial meningitis and meningococcal septicaemia (CG102 [2010]) and antibiotics for early-onset neonatal infection (CG149 [2012]).
23.	**Commissioning**	1	Full	29		Are there any more recent figures for prevalence and incidence given that these figures were published prior to the publication of the previous guideline?	Thank you for your comment. We have provided more recent figures under the section “Need for 2013 update.”
24.	**Croydon Health Services NHS Trust**	1	Full	12	Section 9	“Learning difficulties” no longer the correct phrase. “Developmental delay” not ideal either, so preferable to use “learning disability” (or possibly “intellectual disability”)	Thank you for your comment. As suggested, we have changed the phrase "learning difficulties” to NICE's preferred terminology "learning disabilities ".
25.	**Croydon Health Services NHS Trust**	2	Full	51	31	As above	Thank you for your comment. As suggested, we have changed the phrase "learning difficulties” to NICE's preferred terminology " learning disabilities ".
26.	**Croydon Health Services NHS Trust**	3	Full	108	42	As above	Thank you for your comment. As suggested, we have changed the phrase "learning difficulties” to NICE's preferred terminology "learning disability".
27.	**Croydon Health Services NHS Trust**	4	Full	294	Section 9	As above	Thank you for your comment. As suggested, we have changed the phrase "learning difficulties' with the NICE's preferred terminology " learning disabilities ".
28.	**Croydon Health Services NHS Trust**	5	NICE	13	1.2.2.2	As above	Thank you for your comment. As suggested, we have changed the phrase "learning difficulties” to NICE's preferred terminology " learning disabilities ".
29.	**Croydon Health Services NHS Trust**	6	Full	122	11	Typing error: APSL (instead of APLS)	Thank you for your comment. This typographical error has been amended.
30.	**Croydon Health Services NHS Trust**	7	Full	125	Table	Change “cervical lymphadenopathy” in Kawasaki disease entry of table to “cervical lymphadenopathy $\geq$1.5cm diameter”	Thank you for your comment. The GDG agree that the diagnostic criteria of Kawasaki disease include “cervical lymphadenopathy $\geq$1.5cm diameter”. However, the GDG believe that the diagnosis should be considered if cervical

							lymphadenopathy of a lesser degree is present with other features of Kawasaki disease. Please note that the table is for features suggestive of a particular illness, not diagnostic of that illness.
31.	**Croydon Health Services NHS Trust**	8	NICE	21	Table	As above	Thank you for your comment. The GDG agree that the diagnostic criteria of Kawasaki disease include "cervical lymphadenopathy ≥1.5cm diameter". However the GDG believe that the diagnosis should be considered if cervical lymphadenopathy of a lesser degree is present with other features of Kawasaki disease. Please note that the table is for features suggestive of a particular illness, not diagnostic of that illness.
32.	**Department of Health**					Thank you for the opportunity to comment on the draft for the above clinical guideline. **I wish to confirm that the Department of Health has no substantive comments to make, regarding this consultation.**	Thank you for your response and taking time to read the updated guideline.
33.	**Expert adviser**		Full	6	35-36	The GDG decided that the entry point into the guideline would be a child presenting to health services with a measured or perceived fever. How was this subsequently operationalized in selecting the evidence? The selection criteria for the evidence only mention 'fever' and several studies were excluded because they did not select children based on fever.	Thank you for your comment. The GDG believed it was important to include a range of definitions of fever in the guideline to ensure all relevant studies were included. Therefore, studies were selected for detailed review if they stated that their inclusion criteria were: • children with a temperature above any cut off of 37^{o}C or higher • children with fever, • children with fever reported by their parents Similarly, if studies stated they reported on sub-groups of children with fever then they were assessed for inclusion.

34.	**Expert adviser**		Full	53	11-21	The YOS is considered diagnostically useful by the GDG. Our meta-analysis published in The Lancet suggests otherwise: sensitivity 32.5% (95% CI 21.7–45.5), specificity 78.9% (95% CI 73.9–83.1).	This is an important question. For the 2007 guideline, the GDG looked at the usefulness of the YOS and the Young Infant Observation Scale (YIOS). They concluded that whilst neither scale alone could reliably detect serious illness, the YOS did improve the detection of serious illness when combined with a physician-taken history and examination. As part of the 2013 update, the YOS was re-reviewed and the evidence was summarised as follows: *'The Yale Observation Scale was reported in twelve studies. The sensitivity, specificity, and predictive value ranged from high to low for detecting serious illness, bacteraemia, pneumonia, serious bacterial infection, bacterial disease, and/or urinary tract infection, but were not correlated with YOS score. The negative predictive value ranged from moderate to high and was also not correlated with YOS score. The positive and negative likelihood ratios ranged from not strong to convincing.' (see 'evidence statements' in section 5.4 of the full guideline)* The GDG stated in the evidence to recommendations section of the symptoms and signs chapter that *'The evidence suggests that the Yale Observation Score was good at identifying children who do not have a serious illness. However, it was less good at identifying children who do have a serious illness. This was in line with the evidence found for the 2007 review that the YOS alone was not a good detector of serious illness. As highlighted in the 2007 review, the GDG acknowledged that the usefulness of the YOS was increased*

							when it was used in combination with a physician-taken history and examination' (see 'evidence to recommendations' in section 5.4 of the full guideline). Based on the knowledge that the usefulness of the YOS was increased when it was used with a physician-taken history and examination, the GDG used the YOS as the starting point for the traffic light table. However, each symptom or sign in the YOS was then reviewed separately to determine whether it was useful as an indicator or predictor of serious illness. Other symptoms and signs that were not included in the YOS were also added to the traffic light table, based on reported evidence and GDG opinion. Whilst our review did identify the paper ('Diagnostic value of clinical features at presentation to identify serious infection in children in developed countries: a systematic review', 2010) we were unable to include it as the GDG needed more detail regarding the inclusion criteria of included studies. Therefore, a review of individual studies had to be undertaken. However, this paper was used to ensure we had identified all relevant papers. Reference: Van den Bruel A, Haj-Hassan T, Thompson M, Buntinx F, Mant D. Diagnostic value of clinical features at presentation to identify serious infection in children in developed countries: a systematic review. Lancet. 2010 Mar 6;375(9717):834-45
35.	**Expert adviser**		Full	99	26-36	It is stated that high specificity and negative predictive value mean that	Thank you for your comment.

						absence of a sign allows ruling out, and high sensitivity and positive predictive value allows ruling in. All other reasoning depends on this assumption - for example, you state that absence of focal seizures is indicative of no meningitis (p 105). Of course, high negative predictive value allows ruling out, but high specificity indicates ruling in. And high positive predictive value allows ruling in, but high sensitivity allows ruling out. Predictive values are likely to be high in this context, because most studies were done in low prevalence studies. In fact, most negative predictive values do not exceed the prevalence, indicating little diagnostic gain. We do not want clinicians to rule out meningitis because the child has no neck stiffness where in fact the probability of meningitis is basically unchanged. Signs with high specificity are red flags: their presence increases the probability of the condition. I would therefore like to advise you to carefully revise the guideline to make sure this potentially dangerous reasoning is corrected.	We recognise that it is misleading to infer that the absence of a symptom or sign on the basis of the predictive values gives strong reassurance of the absence of serious disease. We agree that many children with meningitis will not have neck stiffness or focal seizures. We agree that the previous wording was confusing as it was meant to provide a description of statistical findings rather than a clinically meaningful interpretation of them. We have removed statements of that effect from the guideline. We have also amended the relevant statements in the evidence to recommendation section. We would also like to explain the assessment of the evidence in the context of how the 2007 traffic light was created and how the 2013 up-date was undertaken. The 2007 traffic was based on three sources: the Yale Outcome Score, reviews of general symptoms and signs of serious bacterial illness, and reviews of symptoms and signs of specific conditions: namely bacterial meningitis, septicaemia, bacteraemia, pneumonia, urinary tract infection, encephalitis (herpes simplex), septic arthritis/osteomyelitis and Kawasaki disease. The actual location of individual items in the traffic light was determined by the strength of association between an item and serious illness and the GDG's clinical opinion. The 2013 update aimed to reassess the symptoms and signs contained in the 2007 traffic light table to ensure that the evidence supporting their inclusion was up to date and

							to explore whether there was new evidence to add any symptoms and signs that were not included in the 2007 traffic light table. The reviews focused on diagnostic usefulness of signs and symptoms. This differed from the 2007 approach that focused on associations between symptoms and serious illness. Any changes to the existing traffic light were based on both the diagnostic outcome measures (positive likelihood ratio, negative likelihood ratio, sensitivity, specificity, positive predictive value, and negative predictive value) and the GDG's expert opinion regarding the use of a symptom or sign in current clinical practice. Particular emphasis was given to likelihood ratios, with a positive likelihood ratio of 5 or higher used as a good indicator that a symptom or sign should be presented in the red column of the traffic light table. As a result of this process the following changes were made to the 2007 traffic light: • 'A new lump > 2cm' was removed from the table • 'Bile-stained vomiting' was removed from the table • 'Age 3–6 months, temperature ≥ 39°C' was moved from the red column to the amber column • 'Rigors' was added to the table, in the amber column • 'Tachycardia' was added to the table, in the amber column.
36.	**Expert adviser**			Gener al		Overall the review provides a further benchmark assessment of the evidence in this important area, and	Many thanks for your responses and taking the time to read the updated guideline.

						the GDG and technical team are to be commended on their excellent work. My comments below are intended to be constructive, to correct omissions that I have noted, and to further improve the guideline and maximise its impact on clinical care.	
37.	**Expert adviser**			General		The methods section specifies that systematic reviews are sought. However, on reviewing the evidence identified for the 2013 update, I note that at least 2 SR (funded by the HTA) which exactly address the clinical questions in the guideline - diagnostic value of clinical features for identifiying children with serious infection, and comparison of blood tests for identifying children with serious infection (Van den Bruel Lancet, Van den Bruel BMJ - references added to end of this document), appear to have been overlooked. This created a significant additional workload for the GDG and technical team, and excludes the already published highest quality evidence. My apologies if I am incorrect and these reviews were used, I did not see them cited in relevant chapters, nor in the reference sections. These reviews were funded and conducted in part in response to the previous version of this guideline.	Thank you for your comment. The systematic reviews you refer to were identified by the searches. The standard process would be to include high quality reviews such as these. However, there were several reasons why this could not be included: • The inclusion criteria for the reviews differed considerably from those used in the guideline (e.g. age range above 5 in some studies, no temperature reported as an inclusion criteria in some studies). • The GDG wanted to know the sensitivity, specificity, and predictive values of the symptoms and signs to make their recommendations, and unfortunately not all of these were not reported in the systematic reviews. • In addition, a number relevant studies published after these reviews were published were identified by our searches. Therefore, reviews of the individual primary studies had to be undertaken.

38.	**Expert adviser**			General		The search for prediction rules appeared to only identify and examine evidence for the Yale Score. Again, an HTA funded systematic review addressed this exact question, and there have been additional studies which have attempted to cross validate such prediction rules. These identify prediction rules which offer better performance than the YOS. THis SR evidence should be included in the guideline evidence. (References added to end of this document)	Thank you for your comment. The HTA report was not published when the main NCC-WCH search on prediction rules was undertaken. However, it was identified by the re-run searches undertaken at the end of the guideline. We checked the references identified by the HTA report to ensure we had captured all the relevant literature. Reference: Systematic review and validation of prediction rules for identifying children with serious infections in emergency departments and urgent-access primary care. Thompson M, Van den Bruel, Verbakel J et al. ***Health Technology Assessment*** 2012;16:1-100
39.	**Expert adviser**			General		I noted that the GDG included searching for and using evidence from middle and/or low income countries. This was not necessary and for most of the guideline, evidence from these settings is of much less relevance. Indeed, prevalence of the setting in which the studies were undertaken did not appear to be taken into account in the Grade tables and in some of the discussion, not just referring to high vs low income settings, but also high prevalence (eg hospitalised children) vs low prevalence (eg GP settings)	Thank you for your comment. The searches were not restricted by location. The GDG were aware of the location, setting and prevalence. This was acknowledged in the description of included studies: 'The settings of the studies varied, including GP's offices, emergency departments and paediatric wards of general hospitals, emergency departments of paediatric hospitals, tertiary care paediatric units, and tertiary care medical centres.' (see ' description of included studies' section 5.4 chapter 5 of the full guideline) In the evidence to recommendations section of the chapter, when discussing the quality of the evidence, we also state that: '…the included studies varied in their

							approach, including … the setting of the study (e.g. GP offices, hospital). These variations in the studies meant that data could not be pooled and made it difficult for the GDG to compare evidence from multiple studies for a symptom or sign.' (p108 of the full guideline) The GDGs interpretation of the evidence took into account the setting of the studies, each of which was highlighted in the full GRADE profiles in Appendix I. All settings (and therefore all studies, regardless of prevalence) were relevant to the review, as the aim of the guideline is to provide recommendations for any settings in which children with unexplained fever could present. The GDG therefore did not downgrade the evidence based on the setting or prevalence reported in each study.
40.	**Expert adviser**			Gener al		The use of the terms non-paediatric practitioner and paediatric specialist are unfortunate. I am not sure that these terms are used for other NICE guidelines that cross primary-secondary care. Children form a considerable component of the patient population consulting in primary care, and GPs who look after the majority of children with acute illness. It seems somewhat unfortunate to refer to such practitioners as not being specialists in child care. I acknowledge there are ongoing debates about who is the best type of doctor to look after children, how much training they should have, and what the training should comprise of etc, But for this guideline, It would have been preferable to use more acceptable and less vague terms,	The GDG agree that the terms referred to may not be perfect. However, they were agreed with NICE during the production of the first version of the guideline and they arose in large part from stakeholder comments on the draft for consultation of that guideline. The sections on management in various settings were not included in the scope for the update of the guideline, so the GDG have not looked at the terms used for healthcare workers in these settings

						although I recognise this is not an easy task	
41.	**Expert adviser**		Full	56	29	As noted above I was surprised that the search did not identify and then use the HTA funded systematic review of clinical predictors of serious infection in ambulatory settings.	Thank you for your comment. Unfortunately, the HTA report was not published when the main NCC-WCH review on prediction rules was undertaken. However, it was identified by the re-run searches undertaken at the end of the guideline. We checked the references identified by the HTA report to ensure we had captured all the relevant literature.
42.	**Expert adviser**			53	11	We have conducted and published systematic review of scoring systems/prediction rules for serious infection in children, funded by the HTA (as noted above). The decision to use and base this section on the YOS is not ideal, the YOS performs poorly in analyses (eg the above mentioned systematic review and subsequent external validation studies)	Thank you for your comment. The HTA was not published when the NCC-WCH review on prediction rules was undertaken. However, the GDG came to the same conclusion as the HTA report. As stated in the full guideline, in the 2007 guideline the GDG concluded that whilst neither the YOS or YIOS scale alone could reliably detect serious illness, the YOS did improve the detection of serious illness when combined with a physician-taken history and examination. The GDG acknowledged the weaknesses of the YOS, as stated in the evidence to recommendations section of the chapter: 'The evidence suggests that the Yale Observation Score was good at identifying children who do not have a serious illness. However, it was less good at identifying children who do have a serious illness. This was in line with the evidence found for the 2007 review that the YOS alone was not a good detector of serious illness. (p109 of the full guideline)' Based on the knowledge that the usefulness of

							the YOS was increased when it was used with a physician-taken history and examination, the GDG used the YOS as the starting point for the traffic light table. Each symptom or sign in the YOS was then reviewed separately to determine whether it was useful as an indicator or predictor of serious illness. Other symptoms and signs that were not included in the YOS were also added to the traffic light table, based on reported evidence and GDG opinion. Whilst the GDG agree with the conclusion of the HTA (that the YOS as it stands is not diagnostically useful), they believed that it provided a starting point for development of the traffic light table. The diagnostic usefulness of each symptom or sign in the YOS was reviewed individually so that the GDG could decide whether to include it in the traffic light table or not.
43.	**Expert adviser**			Gener al		Section 5- the GRADE tables and subsequent discussion about findings appear to ignore the type of setting - prevalence.	Thank you for your comment. See previous response - the settings of the studies are outlined in the footnotes of the full GRADE profiles which can be found in Appendix I, and this was discussed by the GDG. We no longer include footnotes on quality issues in the GRADE profiles presented in the main text of the full guideline, but full footnotes can be found in the appendix.
44.	**Expert adviser**			96	46	there is evidence of leg pain/limb pain for detection of meningococcal disease that appears to have been missed here.	Thank you for your comment. We agree this is an important specific sign of meningococcal disease and it is included in the bacterial meningitis and meningococcal septicaemia NICE clinical guideline 102 (2010) to which we cross refer. The reason it is not included in the 2013 update of the traffic light relates to the aims of the review, which were to

							- Identify any new evidence on signs and symptoms already included in the traffic light table. Leg pain/limb pain was assessed, but was not found to be a useful indicator for serious illness in general. - Identify any new signs and symptoms of undifferentiated serious illness; we did not update the reviews for signs and symptoms of specific conditions, such as meningococcal disease. - Following comments from yourself and others, we have cross referenced the bacterial meningitis and meningococcal septicaemia NICE clinical guideline 102 (2010) in the section on symptoms and signs meningitis and meningococcal septicaemia
45.	**Expert adviser**			99	5	cold hands and feet - same comment as 4. And further discussion of this on page 107 seems to ignore the potential role of this sign (in children with fever) for identifying those at risk of possible SBI, which should be the role of the current guideline, not solely the meningitis NICE guideline	Thank you for your comment. We agree this is an important specific sign of meningococcal disease and it is included in the bacterial meningitis and meningococcal septicaemia NICE clinical guideline 102 (2010) to which we cross refer. The reason it is not included in the 2013 update of the traffic light relates to the aims of the review, which were to - Identify any new evidence on signs and symptoms already included in the traffic light table. Cold hands and feet was assessed, but was not found to be a useful indicator. - Identify any new signs and symptoms of undifferentiated serious illness; we did not update the reviews for signs and symptoms of specific conditions, such as meningococcal disease. - Following comments from yourself and others, we have cross referenced the

							bacterial meningitis and meningococcal septicaemia NICE clinical guideline 102 (2010) in the section on symptoms and signs meningitis and meningococcal septicaemia
46.	**Expert adviser**			98	13	pallor or poor periph circulation - evidence has been missed for this section.	Thank you for your comment. This was assessed for inclusion in the traffic light table but no evidence was found for its inclusion as a general symptom of serious illness.
47.	**Expert adviser**			100	27	Gut feeling - there is evidence for this in GP settings, and by parents, so I strongly disagree with the statement that is shoudl be only used in those HCPs with paediatric training.	Thank you for your comment. We have changed the wording in the evidence to recommendations section to highlight that when we say '.. trained…' we include GPs and practice nurses in this. The issue of parent 'gut feeling' was discussed at length by the GDG. No evidence was found assessing the accuracy of parental 'gut feeling' for identifying serious illness. Furthermore in recommendations 6 (in the full guideline) – defining fever - and 70 – referral to hospital - it is stated that the parents' opinion on the severity of a condition is valid and should be taken in decision-making.
48.	**Expert adviser**			101	40	Oxygen saturations - there is evidence regarding the diagnostic value that appears to have been overlooked. Plus the selection of the cut of value chosen needs to be justified.	Thank you for your comment. No new evidence for oxygen saturation levels in febrile children was identified for this update.. We are aware of the papers examining oxygen saturation in children with infection, for example: Thompson,M., Coad,N., Harnden,A., Mayon-White,R., Perera,R., Mant,D. How well

							do vital signs identify children with serious infections in paediatric emergency care? 2009. This paper was included in height of fever because it compared serious illness based on temperature. It was also included in heart rate, as that review was not restricted to febrile illness. However, it could not be included for oxygen saturation as the groups would include non-febrile children. Also, Oostenbrink R, Thompson M, Lakhanpaul M, Steyerberg E, Coad N Children with fever and cough at the emergency care: diagnostic accuracy of a clinical model to identify children at low risk of pneumonia.. European J Emerg Med 2012. Again, this paper was not included as it examined a specific illness. The inclusion of oxygen saturation in the 2007 guideline was based on one study (Mahabee-Gittens EM, Grupp-Phelan J, Brody AS, *et al.* Identifying children with pneumonia in the emergency department. *Clinical Pediatrics* 2005;44(5):427–35) and the clinical opinion of the GDG.
49.	**Expert adviser**			107	48	Limiting the search and evidence revivew to the YOS alone was not acceptable, as our HTA funded systematic review and subsequent publications indicate there are other clinical prediction rules that perform better than the YOS, though most with caveats in terms of performance related to age group, setting, state of validation etc. THis includes one clinical prediction rule conducted in primary care (van den Bruel & Buntinx, BJGP)	Thank you for your comment. As stated previously, one of the aims of the 2013 review was to update the reviews undertaken in 2007 to create the traffic light table, and YOS was the only scoring system included in the 2007 review.

50.	**Expert adviser**			115		states only one study has looked at effect of HR on SBI (Brent), however others have now examiend this (references added to end of this document).	Thank you for your comment and providing the additional references. The review of heart rate includes three studies and recommendations were based on these: References: Brent,A.J., Lakhanpaul,M., Ninis,N., Levin,M., MacFaul,R., Thompson,M., Evaluation of temperature-pulse centile charts in identifying serious bacterial illness: observational cohort study, Archives of Disease in Childhood, 96, 368-373, 2011 Craig,J.C., Williams,G.J., Jones,M., Codarini,M., Macaskill,P., Hayen,A., Irwig,L., Fitzgerald,D.A., Isaacs,D., McCaskill,M., The accuracy of clinical symptoms and signs for the diagnosis of serious bacterial infection in young febrile children: prospective cohort study of 15 781 febrile illnesses, BMJ, 340, c1594-, 2010 Thompson,M., Harnden,A., Perera,R., Mayon-White,R., Smith,L., McLeod,D., Mant,D., Deriving temperature and age appropriate heart rate centiles for children with acute infections, Archives of Disease in Childhood, 94, 361-365, 2008
51.	**Expert adviser**			111	15-18	The use of GRADE to examine the quality of these studies - unclear why the specific study designs here are rated as very low, perhaps I have biases being the author of one of these, but given the research question for these, I disagree that superior design to the cross sectional study would have been preferable or higher	Thank you for your comment. Studies are often downgraded when using the GRADE system not because they were poorly conducted but because they do not directly match the review question being asked or the findings were inconclusive. Appendix I contains the full GRADE profiles

						quality. Is grade too crude of a tool here?	with footnotes highlighting any quality issues with the studies. The methodology section chapter 3 section 3.1 of the full guideline explains the GRADE approach used in the Feverish illness in children guideline: ‘‘In the GRADE approach, the quality of the evidence identified for each outcome listed in the review protocol is assessed according to the factors listed below, and an overall quality rating (high, moderate, low, or very low) is assigned by combining the ratings for the individual factors. • Study design (as an indicator of intrinsic bias; this determines the initial quality rating). • Limitations in the design or execution of the study (including concealment of allocation, blinding, loss to follow up; these can reduce the quality rating). • Inconsistency of effects across studies (this can reduce the quality rating). • Indirectness (the extent to which the available evidence fails to address the specific review question; this can reduce the quality rating). • Imprecision (reflects the confidence in the estimate of effect and this can reduce the quality rating). • Other considerations (including large magnitude of effect, evidence of a dose-response relationship, or confounding variables likely to have reduced the magnitude of an effect; these can increase the quality rating in observational studies, provided no downgrading for other features has occurred). The type of review question determines the

							highest level of evidence. … For questions on prognosis, the highest possible level of evidence is a controlled observational study (a cohort study or case–control study), and a body of evidence based on such studies would have an initial quality rating of high, which might be downgraded to moderate, low, or very low, depending on the factors listed above. For diagnostic tests, studies examining the performance of the test were used if information on accuracy was required, but where an evaluation of the effectiveness of the test in the clinical management of the condition was required, evidence from RCTs or cohort studies was considered optimal. For studies evaluating the accuracy of a diagnostic test summary statistics - sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and likelihood ratios for positive and negative test results (LR+ and LR–, respectively) - were calculated or quoted where possible. The GRADE system described above covers studies of treatment effectiveness. However, it is less well established for studies reporting accuracy of diagnostic tests or prognostic factors. For such studies, NICE recommends using the Quality Assessment of Studies of Diagnostic Accuracy (QUADAS) methodology checklist or the NICE prognostic study checklist, respectively, to assess study quality (see the NICE guidelines manual). These were then mapped onto the GRADE system.”
52.	**Expert adviser**			122		I agree overall with the inclusion of HR in the traffic light table. I noted that the review group identified our SR	Thank you for this comment. There were a number of reasons for using the

						examining all available data on normal HR and RR in well chidlren. It is therefore inconsistent to then select the APLS reference ranges simply because they are well known in the UK. The new centile charts provide the GDG with exactly what is needed- new evidence based cut offs for all age groups, including the under 5s. These have been adopted by clinical groups and hospitals worldwide. They are right to point out that exactly which centile to select as the higher (and lower) cut off is still being investigated, and no doubt will trade sens/spec with higher or lower cutoffs. However, I urge the GDG to use current SR evidence for cut offs, rather than relying on non-evidence based APLS cut offs. This could be added to the 'research needed' section of course.	APLS cut-offs. • The Craig study from Australia provided much of the evidence for the inclusion of tachycardia in the traffic lights table. This study used cut offs for tachycardia that were almost identical to APLS • The recommendation to use the APLS was also based on other evidence showing that using specified heart rate cut-offs was a useful diagnostic tool. • The use of centile charts was examined, however without evidence on which centiles to use or the diagnostic value of these they could not be included. • Furthermore, for the children aged under 5, the APLS and the centile are reasonable well matched. For these reason the APLS reference ranges are used.
53.	**Expert adviser**			122	18-19	If the GDG chooses to use HR not corrected for temperature (and there seems v good agreement of the rise of 10bpm per 1 degree celsius), then there will be a considerable proportion of children who are febrile who will have HR above the cut offs selected. THis risks HR vvalues interpreted without concern to the whole child (including presence of fever) driving referral decisions and parent/practitioner anxiety.	Thank you for your comment. The recommendation was based on evidence showing that heart rate alone, based on specified cut-offs, was a useful diagnostic variable. Furthermore, evidence showed that the diagnostic usefulness of heart rate and temperature combined was worse than heart rate alone. However, the GDG agrees that the whole child needs to be taken into account, hence heart rate being in the amber (intermediate risk) rather than the red (immediate action) column.
54.	**Expert adviser**			123		The use of blood pressure in children is complicated and teh GDG have somewhat overlooked and	Thank you for your comment. The GDG did not find any evidence to change

						oversimplified this question, citing only that BP is a predictor of poor outcome in meningococcal disease, but not finding evidence for its diagnostic value in other diseases or settings. Thus including this as a diagnostic test to be used, appears to be unjustified. The same major research gaps exist with BP as exist with HR. As part of a review to be published in Pediatrics in March this year, we identified only 2 studies that have examined the diagnostic value of BP for detecting children with HTN (much more common than SBI of course), both showing limited sens/spec. There are issues with reference range for BP in children, different ways of measuring. The implications of this would be the need for infant and child BP cuffs,disseminating reference ranges, etc, and all to unclear additional diagnostic value. I would urge to clarify the lines page 123 lines 20-21 (and subsequent places eg Page 130) to highlight this and clarify when this should be used. IF as it currently reads, BP should be measured in children with HR above the APLS thresholds, this would lead to a lot of BPs being measured. I also suggest the GDG to add this to the 'research needed' section.	the recommendations made on blood pressure in the original version of the guideline. The rationale for the inclusion of blood pressure in the original guideline is explained in the “GDG translation” in the section to which you refer. The GDG are not aware of any published evidence that would lead them to alter the existing interpretation.
55.	**Expert adviser**			125/126	19	Again, perhaps as I am the author of these studies, I am concerned that the GDG has overlooked the evidence for possible early clinical features of meningo. The Lancet paper, and subsequent case-control study reported in BJGP (Haj-Hassan et al) provide data to indicate the diagnostic	Thank you for your comment. Unfortunately the management of specific conditions was not selected to be included in the 2013 update of the feverish illness guideline. However, cold hands/feet and leg pain were

						value of these features. The biases that the GDG identify, ie recall bias and retrospective analyses are well acknowledged (at least for the orginal study, less so for the subsequent publication) - yet as the GDG knows well, this is the only data that is ever likely to be generated in high income countries due to the decline in meningo cases. Even the type of prospective study suggested by the GDG in the evidence needed section will not be able to provide evidence for meningo or other invasive bacterial infections. In additon, the same evidence I noted above i believe was included in the NICE meningitis guideline. Thus, ignoring 'best available' evidence as it is not of the optimal study design is not appropriate. It is the interpretation of the evidence base in level and study design biases which is the key. CLinical users of the guideline are left with the classic meningitic features, all of which are late and when the disease is more likely to be clinically obvious.	assessed for inclusion in the traffic light table as general symptoms and signs of serious illness, but were not found to be useful indicators. In addition, in the relevant recommendations we do cross refer to the bacterial meningitis and meningococcal septicaemia NICE clinical guideline 102 (2010) which, as you say, includes a comprehensive list of symptoms and signs.
56.	**Expert adviser**			125/6		again, the justification for the O2 sats cut off needs to be justified.	Thank you for your comment. No new evidence for oxygen saturation levels in febrile children was identified for this update. We are aware of the papers examining oxygen saturation in children with infection, for example: Thompson,M., Coad,N., Harnden,A., Mayon-White,R., Perera,R., Mant,D. How well do vital signs identify children with serious infections in paediatric emergency care? 2009. This paper was included in height of fever because it compared serious illness based on temperature. It was also included in heart rate,

							as that review was not restricted to febrile illness. However, it could not be included for oxygen saturation as the groups would include non-febrile children. Also, Oostenbrink R, Thompson M, Lakhanpaul M, Steyerberg E, Coad N Children with fever and cough at the emergency care: diagnostic accuracy of a clinical model to identify children at low risk of pneumonia.. European J Emerg Med 2012. Again, this paper was not included as it examined a specific illness. The inclusion of oxygen saturation in the 2007 guideline was based on one study (Mahabee-Gittens EM, Grupp-Phelan J, Brody AS, *et al.* Identifying children with pneumonia in the emergency department. *Clinical Pediatrics* 2005;44(5):427–35) and the expert opinion of the GDG.
57.	**Expert adviser**			127	16	Not all relevant studies of clinical features associated with pneumonia have been identified here. The use of studies from low/middle income countries is not justified. The lack of evidence cited does not in its present form justify the cut offs selected for O2 sats and RR. There is more data on these than what the GDG identified, this needs to be included in the guideline.	Thank you for your comment. Unfortunately the section of the guideline regarding symptoms and signs of specific serious illnesses was not selected to be included in the 2013 update of the feverish illness guideline. Therefore, we cannot take your comments forward or make any substantive changes to the existing topic in the final version of the Guideline. However, your comment will be kept on recorded for the next update of the guideline.
58.	**Expert adviser**			139	35	reference cited for safety netting is not correct. Either cite the original Neighbour book, or a more recent paper of consensus of paediatricians and GPs' assessment of the core	Thank you for your comment. Unfortunately the section of the guideline regarding the management by the non-paediatric practitioner was not selected to be

						features of safety netting (Almond S et al, BJGP).	included in the 2013 update of the feverish illness guideline. Therefore, we cannot take your comments forward or make any substantive changes to the existing topic in the final version of the Guideline. However, your comment will be kept on recorded for the next update of the guideline
59.	**Expert adviser**			150 and this chapter		Was the SR and meta analysis of lab tests for identification of SBI in children used in this section? This SR exactly addressed the questions concernign WBC, CRP, PCT and their comparisons.	Thank you for your comment. The review you reference was identified. However, the inclusion criteria for the review differed from those of our review. Therefore, we had to assess the individual primary studies to ensure they met our inclusion criteria. In addition, a number of studies have been published since the review was undertaken. Reference: Diagnostic value of laboratory tests in identifying serious infections in febrile children: a systematic review. Van den Bruel A, Thompson MJ, Haj-Hassan T et al. ***BMJ*** 2011;342:d3082
60.	**Expert adviser**					Given that CRP is now available as a rapid and cheap point of care test, which is used in many other countries in mostly adults, I would add the setting of primary care or out of hours care to the types of setting where evidence on the use of these tests is needed.	Thank you for your comment. This issue was discussed by the GDG, but it was concluded that point of care CRP testing is not readily available in primary healthcare and community settings in the UK. Furthermore, it was the view of the GDG if a child was ill enough to require a CRP test then they would have been referred to specialist care. Therefore, this recommendation was not included in the non-paediatric specialist section.

61.	**Expert adviser**					The recommendations not to use ibuprofen and paracetmol together does not appear to be based on the evidence which seemed to show a small benefit. The theoretical risks of overdosing needs to be balanced with similar risks of underdosing. I am not sure that the recommendation is justified	Thank you for comment. We have reworded this section to improve clarity. Recommendations are based on the GDG's interpretation of the evidence on benefit and harm. In the case of the antipyretics recommendations, the GDG concluded that potential problems of recommending an alternating strategy – incorrect administration, over-dosing – outweighed the small benefit found.
62.	**Expert adviser**					1. How well do clinical prediction rules perform in identifying serious infections in acutely ill chidlren across and international network of ambulatory care datasets? Verbakel J, Buntinx F, Thompson M et al. ***BMC Medicine*** - *published January 2013* 2. Children with fever and cough at the emergency care: diagnostic accuracy of a clinical model to identify children at low risk of pneumonia. Oostenbrink R, Thompson M, Lakhanpaul M, Steyerberg E, Coad N. ***European J Emerg Med*** 2012	Thank you for providing these references. All those published during the development period of the guideline were identified and assessed for inclusion. • Derivation and validation of age and temperature specific reference values and centile charts to predict lower respiratory tract infection in children with fever: prospective observational study. Nijman R, Thompson M, van Veem M et al. ***BMJ*** 2012:344;e4224 • Systematic review and validation of prediction rules for identifying children with serious infections in emergency departments and urgent-access primary care. Thompson M, Van den Bruel, Verbakel J et al. ***Health Technology Assessment*** 2012;16:1-100 • Diagnostic value of laboratory tests in identifying serious infections in febrile children: a systematic review. Van den Bruel A, Thompson MJ, Haj-Hassan T

						3. Clinicians' gut-feeling about serious infection in children: observational study. Van den Bruel A, Thompson M, Buntinx F, Mant D. ***BMJ*** 2012;345:e6144 4. Derivation and validation of age and temperature specific reference values and centile charts to predict lower respiratory tract infection in children with fever: prospective observational study. Nijman R, Thompson M, van Veem M et al. ***BMJ*** 2012:344;e4224 5. Systematic review and validation of prediction rules for identifying children with serious infections in emergency departments and urgent-access primary care. Thompson M, Van den Bruel, Verbakel J et al. ***Health Technology Assessment*** 2012;16:1-100 6. Diagnostic value of laboratory tests in identifying serious infections in febrile children: a systematic review. Van den	et al. ***BMJ*** 2011;342:d3082 • Which symptoms and clinical features correctly identify serious respiratory infection in children attending a paediatric assessment unit? Blacklock C, Mayon-White R, Coad N, Thompson M. ***Arch Dis Child*** 2011;96:708-14 • Which early "red flag" symptoms identify children with meningococcal disease in primary care? Haj-Hassan T, Thompson M, Mayon-White R, et al. ***Br J Gen Pract*** 2011;61:97-104 • Diagnostic value of clinical features at presentation to identify serious infection in children in developed countries: a systematic review. Van den Bruel A, Haj-Hassan T, Thompson M. et al. ***The Lancet*** 2010;375:834-45

						Bruel A, Thompson MJ, Haj-Hassan T et al. ***BMJ*** 2011;342:d3082 7. Which symptoms and clinical features correctly identify serious respiratory infection in children attending a paediatric assessment unit? Blacklock C, Mayon-White R, Coad N, Thompson M. ***Arch Dis Chil****d* 2011;96:708-14 8. Which early "red flag" symptoms identify children with meningococcal disease in primary care? Haj-Hassan T, Thompson M, Mayon-White R, et al. ***Br J Gen Pract*** 2011;61:97-104 9. Diagnostic value of clinical features at presentation to identify serious infection in children in developed countries: a systematic review. Van den Bruel A, Haj-Hassan T, Thompson M. et al. ***The Lancet*** 2010;375:834-45 10. Diagnostic safety netting. Almond S, Mant D, Thompson M. ***Br J Gen Pract***	

						2009;59:872-4	
63.	**Healthcare Infection Society**	1	Full	186	30	Use of anti-pyretics may increase the likelihood of serious infections (including meningococcal septicaemia) progressing more rapidly. Evidence may need to look at specific infections and laboratory studies. See for example how, speed of growth of N. meningitidis is reduced by a raised temperature -- see See Dixon et al BMJ 2010;340:c450	Thank you for your comment and providing a reference. This is an interesting issue. However, NICE guidelines do not routinely include laboratory studies. Therefore, we cannot take this forward or make changes to the guideline.
64.	**Herpes Viruses Association**	1	Full	General: both full and NICE version		The word 'meningitis' can apply to viral meningitis which is usually not a serious condition and bacterial meningitis which needs swift treatment. Does the guideline refer equally to both when the word is used? If not, the phrase 'bacterial meningitis' needs to be used every time. For instance, on page 3 of the NICE version, 'bacterial meningitis' is specified, but further down the document the word 'meningitis is used alone'.	Thank you for this comment. The term meningitis is used to describe bacterial meningitis. This term has been amended, as appropriate, throughout the guideline to ensure accuracy.
65.	**Johnson & Johnson Consumer**	1	Full	11	81	The fourth bullet point describes the potential for alternate dosing of paracetamol and ibuprofen if distress persists; but no posology is proposed. Anecdotal evidence suggests widespread confusion/variability in advice given by healthcare professionals when recommending alternate dosing of these two drugs in fever and draft guidance does not take advantage of the opportunity to address this confusion.	Thank you for your comment. NICE guidelines do not routinely provide information on dosage. Instead health professionals and parents should refer to the manufacturers' Summary of Product Characteristics.
66.	**Johnson & Johnson Consumer**	2	Full	11	81	McNeil Products Ltd believes that the guidance regarding antipyretic	Thank you for your comment.

						intervention should consider the potential impact of the ongoing European review of paediatric use of ibuprofen (Article 45 of Regulation (EC) 1901/2006 – "Paediatric Regulation"); Germany is acting as Rapporteur for this procedure and the MHRA has accepted the draft recommendation to set the dosage range for OTC ibuprofen at ≥6 months to < 12 years, which could significantly impact recommendations for antipyretic intervention in infants <6 months. The procedure is currently on Day 89. The outcome of this procedure may affect the NICE guidance as the current licensed minimum age for paracetamol suspension and ibuprofen suspension are 2 months and 3 months respectively. We would anticipate that if the minimum age for ibuprofen is raised to 6 months, it should be reflected in the guidance	The recommendations on antipyretic use make no mention of age of the child. Health professionals and patients should refer to the manufacturers Summary of Product Characteristics, including any minimum age.
67.	**Meningitis UK**	1	Full	126	19 20 21 22	Meningitis UK are concerned that the GDG are not including reference to the possible early features of meningococcal disease (specifically) as this could lead to delayed diagnosis and poorer patient outcome. These early 'specific' signs of meningococcal septicaemia are integral to the NICE guidelines CG102 "Bacterial meningitis and meningococcal septicaemia: Management of bacterial meningitis and meningococcal septicaemia in children and young people younger than 16 years in primary and secondary care". Greater consistency	Thank you for your comment. Unfortunately use of management of specific conditions was not selected to be included in the 2013 update of the feverish illness guideline. Therefore, we cannot take your comments forward or make any substantive changes to the existing topic in the final version of the Guideline. Cold hands/feet and leg pain were assessed for inclusion in the traffic light table as general symptoms and signs of serious illness, but were not found to be useful indicators. However, in the relevant recommendations we

						between NICE guidelines would aid clinical assessment and diagnosis.	do cross refer to the bacterial meningitis and meningococcal septicaemia NICE clinical guideline 102 (2010) which, as you say, includes a comprehensive list of symptoms and signs.
68.	**Neonatal & Paediatric Pharmacists Group**	1		General		NPPG welcomes many of the changes which add clarity to the 2007 Guidelines	Thank you for your response and taking time to read the updated guideline.
69.	**Neonatal & Paediatric Pharmacists Group**	2	Full NICE	27- 29 35- 36		We agree with Research recommendations No RR 6 and RR 7 – regarding antipyretic use. (2.4 and 2.5 in NICE Draft)	Thank you for your comment.
70.	**NHS Direct**	1	Full	135	10	There does not appear to have been any changes to the guidance with reference to remote assessment. However, the full guidance refers to NHS Direct by name (several times) and uses the 0845 number which will not be active by the time this guidance goes live.	Thank you for your comment. We have amended the introduction in chapter 6 to specify that NHS Direct's 0845 4647 helpline will be replaced by NHS 111 and it is due to be implemented nationally in 2013
71.	**NHS Direct**	2	Full	135	19	Consider a definition of a healthcare professional would assist with interpretation. For instance in NHS 111 Services the initial assessment is conducted by a Call handler using a decision support system (NHS Pathways) which determines the assessment outcome including the timeframe. The timeframe for referral for either a 'speak to' or contact a healthcare professional will vary between 0-24 hours. For the presence of 'amber' symptoms the timeframe for referral for either 'speak to' or contact a healthcare professional may be between 2 – 24 hours	Thank you for your comment. The sections on management in different healthcare settings were not included in the scope or remit for the update of the feverish illness guideline. Therefore, while the GDG appreciate your point, we do not feel that we are able to comment.
72.	**NHS Direct**	3	Full	55	7	"Traffic light system for identifying risk of serious illness"	Thank you for your comment. Unfortunately remote assessment was not

						The use of the Traffic Light system during remote assessment: 1.1 Consider clearer guidance on symptoms to aid remote assessor for example 'decreased activity' 1.2 Consider adding parental concern as risk factor requiring face to face assessment in remote assessment 1.3 Consider repeat contact with a healthcare professional prior to remote assessment as a high risk factor requiring face to face assessment. (Refer Penny Campbell Case, safeguarding responsibility across health care)	selected to be included in the 2013 update of the feverish illness guideline. This includes the existing recommendations on how the traffic light is applied in these situations. Therefore, we cannot take your comments forward or make any substantive changes to the existing topic in the final version of the Guideline.
73.	**NHS Direct**	4	Full	170	24	"Improved clinical appearance after antipyretics" Consider if this should be taken into consideration for all assessments including remote assessments	Thank you for your comment. Based on the systematic review of the evidence, the guideline recommends that response to antipyretics is not used to assess severity of illness – "When a child has been given antipyretics, do not rely on a decrease or lack of decrease in temperature at 1–2 hours to differentiate between serious and non-serious illness. Nevertheless, in order to detect possible clinical deterioration, all children in hospital with 'amber' or 'red' features should still be reassessed after 1–2 hours."
74.	**NHS Direct**	5	Full	29	RR7	"Home based antipyretic use" Any research study should include the remote assessment (NB RR3 first recommended in 2007 remains on the guidance research recommendation list)	Thank you for your comment. This research recommendation has not been updated.
75.	**NHS Direct**	6	NICE	14	1.2.2.9 – 1.2.2.12	There are now statements advising if the temperature is above a certain level in specific age groups which recognise that the child is in a high or intermediate risk group for serious	Thank you for your response.

						illness. This should help with remote assessments when callers do give a temperature recording.	
76.	**NHS Direct**	7	Full	15	30	The only reference to “joint” in either document appears to be looking for septic arthritis so the emphasis is still on swelling of a limb or joint, no reference to pain. Joint pain is a sign of meningitis so presumably NICE did not feel the evidence about joint pain and meningitis was strong enough. Evidence considered included: http://www.ingentaconnect.com/content/rcgp/bjgp/2011/00000061/00000584/art00001	Thank you for your comment. Unfortunately use of management of specific conditions was not selected to be included in the 2013 update of the feverish illness guideline. Therefore, we cannot take your comments forward or make any substantive changes to the existing topic in the final version of the Guideline. However, muscular leg pain was assessed for inclusion in the traffic light table as general symptoms and signs of serious illness, but were not found to be useful indicators in children aged 5 or under. In addition, in the relevant recommendations we do cross refer to the bacterial meningitis and meningococcal septicaemia NICE clinical guideline 102 (2010) which includes a comprehensive list of symptoms and signs.
77.	**NHS Direct**	8	Full	11	81	The advice about using antipyretic agents does seem clearer and is more focussed on the child being distressed rather than using medicines to reduce the temperature. The NICE version states that antipyretic agents should not be used with the sole aim of reducing body temperature. There is no preference for paracetamol or ibuprofen, do change to the other medicine if the child’s distress is not alleviated but medicines can be alternated if the distress persists or if the distress recurs before the next dose is due.	Thank you for your response

						We will need to change our systems to reflect this advice.	
78.	**NHS Direct**	9	NICE	32	1.7.2.1	Current NICE guidance advises 5 days after initial contact with health care professional before seeking further advice. Remote assessment depends on “interpretation of symptoms” Consider if this statement needs to vary for the setting of remote assessment. Is 5 days too long before a further contact face to face should be made to carry out more detailed assessment of physical signs?	Thank you for your comment. This recommendation is in the section for help seeking by parents/carers. The recommendation contains 6 bullet points any one of which should trigger seeking further advice, with 5 days being a ‘safety net’ of the maximum time anyone should wait before seeking help.
79.	**NHS Sheffield**	1	NICE version	8		Seems to be comprehensive though does tend to assume the child has got the rarer serious illness and as a result leads the clinician towards over investigation and I suspect a tendency to increased parental anxiety. Hard though to suggest this is the wrong approach but the suggestion that a child less than 3m with a temp of 38 has to be seen within 2hours is going to be a challenging one.	Thank you for your comment. The recommendation you refer to is from the 2007 guideline and this question was not selected for review in 2013 the 2013 update. Therefore, has not been updated.
80.	**NHS Sheffield**	2	General observation			There are some additional bits of equipment practices will have to have available-- tympanic thermometers for babies, sat meters for babies, BP cuffs for smaller children.	Thank you for your comment.
81.	**NHS Sheffield**	3	NICE version	32		1.6.3.3 is not that clear… it all depends on the meaning of simultaneously (Does this mean GP’s should not encourage people to start off using paracetamol and ibuprofen together. But if despite treatment with one of these there is still distress then adding the other is appropriate) This could be much more clear… it is I suspect the use of the words	Thank you for your comment. After taking all the comments that have been received into consideration and after discussion with the NICE editorial team, it was decided that this was the best term that could be used. Therefore, no change has been made to the use of the terms ‘simultaneous’ or ‘alternating’.

						simultaneously and alternating which is contributing to the confusion	However, we have edited the recommendation, so it now reads. *When using paracetamol or ibuprofen in children with fever:* • *continue only as long as the child appears distressed* • *consider changing to the other agent if the child's distress is not alleviated* • *do not give both agents simultaneously* • *only consider alternating these agents if the distress persists or recurs before the next dose is due. [new 2013]*
82.	**NHS Sheffield**	4	NICE version	11		1.1.1 & 1.1.2 The guidance is clear on thermometers but does not appear to refer at all to electronic thermoscan type infra-red thermometers used to assess core body temperature. I would have thought that the absence of advice on this is regrettable	Thank you for your comment. Unfortunately use of thermometers was not selected to be included in the 2013 update of the feverish illness guideline. Therefore, we cannot take your comments forward or make any substantive changes to the existing topic in the final version of the Guideline. However, your comment will be kept on recorded for the next update of the guideline.
83.	**Royal College of General Practitioners**	1	Full	9	21	In figure 1.3, diagnose and treat should be on the left side of the page below safety net and connected to it, because even when diagnosed and treated initially, the clinician may review the patient (eg with pneumonia) and may decide on admission. This decision should not always be left to the carer.	Thank you for your comment. This is a fair point but the GDG did not look at pathways and care in various health settings in the update of the guideline. These areas were not included in the scope.
84.	**Royal College of General Practitioners**	2	Full	9	21	"Record", diagnose and treat, as recording observations is important.	Thank you for your comment. This is a fair point but the GDG did not look at pathways and care in various health settings in the update of the guideline. These areas were not included in the scope.

85.	**Royal College of Midwives**	1	General			The RCM welcomes the update of this useful guideline and considers the new and updated recommendations to be appropriate.	Thank you for your response and taking the time to read the updated guidance.
86.	**Royal College of Midwives**	2	NICE	33		We are pleased to see the recommendation for an epidemiological study on the symptoms and signs of serious illness.	Thank you for your comment.
87.	**Royal College of Midwives**	3	NICE	35		The recommendation for research on home-based antipyretic use is important.	Thank you for your comment.
88.	**Royal College of Nursing**	1	General	genera l		The Royal College of Nursing welcomes the update of this guideline. It is timely. The RCN fully agrees with the amendments.	Thank you for your response and taking the time to read the updated guidance.
89.	**Royal College of Nursing**	2	FULL	8	7-10	This is very useful as we are aware that some suppliers have been trying to push the use of infrared forehead thermometers which have proved inaccurate in critically ill children due to children becoming peripherally shut down when pyrexial.	Thank you for your comment.
90.	**Royal College of Nursing**	3	Full	31	21-33	It is useful to have the breakdown of when to give antipyretics as many people will give them as soon as a temp is over 37.5 or to prevent temperature reoccurring even if the child is not distressed.	Thank you for your comment.
91.	**Royal College of Nursing**	4	Full	35	26-27	It may be helpful to consider parents' perception of types of medication and their understanding on it uses e.g. Calprofen is commonly viewed as paracetamol and ibrufen when in reality it is just ibrufen.	Thank you for your comment. We agree and this is one of the reasons behind the research recommendation on home use of antipyretics. However, this issue was not formally addressed in the update of the guideline.
92.	**Royal College of Nursing**	5	General	Gener al	Gener al	It would be beneficial to add a recommendation regarding fan therapy in pyrexial children as there are	Thank you for your comment. Unfortunately physical methods of reducing

						varying views on this between hospitals.	temperature was not selected to be included in the 2013 update of the feverish illness guideline. Therefore, we cannot take your comments forward or make any substantive changes to the existing topic in the final version of the Guideline.
93.	**Royal College of Paediatrics and Child Health**	1	NICE version	General		We think this is clearer than the previous guideline.	Thank you for your comment and taking the time to read the updated guideline.
94.	**Royal College of Paediatrics and Child Health**	2	NICE version	9	14-21	To add LP if clinically indicated to the "Management by the paediatric specialist section".	Thank you for this comment. This recommendation is taken from the key recommendations for implementation section. As such, it is simply reproduced from the main body of recommendations and therefore the wording cannot be changed. There is a recommendation as to when lumbar puncture should be performed in the main body of recommendations (1.5.2.3).
95.	**Royal College of Paediatrics and Child Health**	3	NICE version	13	1.2.2.3 , 1.2.2.4	Pallor of skin, lips or tongue reported by parent or carer appear under 1.2.2.4, is also under 1.2.2.3 but without the source of reporting. It would be better if the entry under 1.2.2.3 specified that it was confirmed by health care practitioner. Not responding normally to social cues appear under both the high risk and intermediate risk group, this will cause confusion. The features under 1.2.2.3 would be more appropriate if this is specified as clinical signs confirmed by Health Care practitioner for the whole set of signs.	Thank you for your comment. These recommendations are intended to be different. They come directly from clinical studies of risk factors for serious illness in feverish children. From these it was clear that a history of pallor gives an intermediate risk while detection of pallor etc on examination gives a high risk. The whole table consists of symptoms and signs detected by HCPs so it is unnecessary to say pallor etc detected by HCP. In other words, pallor reported is a symptom detected by HCP while pallor/cyanosis etc are signs detected by HCP. Also, the wording is different in the responding to social cures recommendations. In the intermediate it say "not responding <u>normally</u> to social cues" and in the high risk it states "not responding to social cues."

96.	**Royal College of Paediatrics and Child Health**	4	NICE version	14	1.2.2.7	Recognise that a capillary refill time of 3 seconds or longer is an intermediate-risk group marker for serious illness ('amber' sign). The phrase "this should not be taken in isolation" could be added to avoid confusion.	Thank you for your comment. The GDG agree that this sign should not be taken in isolation. However, the same applies to most of the other symptoms and signs in the guidance. The section on "Assessment" in the full guideline makes this point as well.
97.	**Royal College of Paediatrics and Child Health**	5	NICE version	14	1.2.2.9	Although the evidence is not immediately available to the commentator we think there is evidence that an extremely high temperature is associated with significant infection and bacteraemia.	Thank you for your comment. As stated in the full guideline, the GDG are aware that there is an association between height of body temperature and the risk of serious bacterial infection (SBI). However, in the 2007 guideline the evidence found that association was not sufficiently robust to recommend immediate action based on body temperature alone (an exception was made for those aged less than 6 months because the evidence was strong for this group). In the 2013 review, the studies often did not report how temperature was measured, and the studies tended to look at one or two cut-offs rather than a range of temperatures, making it hard to compare data from different temperature cut offs. Despite these limitations in the data, the GDG highlighted that there is a correlation between high temperature and serious bacterial infection in general, but that, on an individual basis, high temperature was not useful for detecting serious illness. The current review suggests that there is a plateau in positive predictive values, negative predictive values and likelihood ratios around

							39°C and 40°C, meaning that a temperature above this does not provide a better indication of serious illness. The GDG made it clear that use of height of fever alone should not be used to diagnosis a serious illness. Separate recommendations were made regarding those aged under 6 months.
98.	**Royal College of Paediatrics and Child Health**	6	NICE version	29	1.5.6.5	It would be useful if a list of signs and symptoms are listed here.	Thank you for your comment. A cross reference to an existing recommendation listing the signs and symptoms of herpes simplex encephalitis has been added to this recommendation.
99.	**Royal College of Paediatrics and Child Health**	7	NICE version	General		We think that it is good that there is now clarification of the issue of appropriate use of paracetamol and ibuprofen if required.	Thank you for your response
100.	**Royal College of Paediatrics and Child Health**	8	Full version	6	1.2	Line 47: put “serious illness with fever”	Thank you for your comment. We have amended the text as suggested.
101.	**Royal College of Paediatrics and Child Health**	9	Full version	67	5	Table 5.14: in the row on urinary tract infection put as heading “Lack of respiratory distress”	Thank you for your comment. This is reported in the paper by Newman (2002) as ‘respiratory distress’. We have reported the results as stated by the study authors.
102.	**Royal College of Paediatrics and Child Health**	10	Full version	68	5	Table 5.15: in the row on urinary tract infection put as heading “Absence of upper respiratory tract infection or runny nose”	Thank you for your comment. This is reported in the paper by Newman (2002) as ‘URI or runny nose’. We have reported the results as stated by the study authors.
103.	**Royal College of Paediatrics and Child Health**	11	Full version	87	5	Table 5.36: in the row on urinary tract infection put as heading “Absence of conjunctivitis”	Thank you for your comment. This is reported in the paper by Newman (2002) as ‘conjunctivitis’. We have reported the

							results as stated by the study authors.
104.	**Royal College of Paediatrics and Child Health**	12	Full version	116	5	Table 5.58: Add the missing “t” in what is supposed to be the words “heart” (two occasions)	Thank you for your comment. We have amended these typographical errors.
105.	**Royal College of Paediatrics and Child Health**	13	Full version	134	5	The recommendation regarding imported infections should include that all children with fever and a history of return from a malaria endemic area within the last 6 months should have three thick films checked for presence of malaria parasites.	Thank you for your comment. Unfortunately the question on imported infection was not selected to be included in the 2013 update of the feverish illness guideline. Therefore, we cannot take your comments forward or make any substantive changes to the existing topic in the final version of the Guideline. However, your comment will be kept on recorded for the next update of the guideline.
106.	**Royal College of Paediatrics and Child Health**	14	NICE version	General	Table 1 (also referring to; 1.2.2.3, 1.2.2.7, 1.2.2.13,1.2.3.6, 1.5.2.3, 1.5.2.5, 1.5.2.6, 1.5.6.6)	The traffic light system approach is a sensible tool for distinguishing children with different degrees of illness severity. However, the provision of different cut-offs for different systems (respiratory, circulation, etc.) based on different age ranges in the amber section is confusing and difficult to memorise. Although one could argue that displaying the table in A&E or GP surgeries could overcome this problem, we still feel that some of the suggestions are rigid and not well backed up by sound evidence. The symptoms and signs described are not necessarily consistent with the same degree of illness severity. For example, oxygen saturation ≤ 95% is mentioned as a criterion and in point 1.5.6.6 (page 29) it is suggested that oxygen therapy should be considered.	Many thanks for your comment. The traffic light is a visual aid and is not intended to be memorised. Where possible the traffic light directly reflects the terminology and cut-offs used in the studies on which it is based. The guideline does not specify how the traffic light should be used, and this has to be decided at a local level and based on the structure of local services. We agree that the amber group often require careful management. The traffic light helps with this process.

						Surely this should be an indication for admission to hospital as this is unlikely to be provided outside a hospital environment other than for stabilisation in emergencies. Most Paediatricians, we would argue, would agree that patients in the amber group are probably the most difficult group to assess with regard to how seriously ill they are and how their illness is evolving in the next 24-48 hours. This requires expertise and experience in Paediatrics. Our suggestion would be as follows: To facilitate better decision making we would prefer to have a clear definition of what is normal in any case (green), and therefore can be managed at home by the main carer in liaison with the GP (reference charts could be made available in different areas, e.g. Pharmacy, GP surgery, etc.). We would also like a clear definition of what is definitely abnormal and severe enough to require urgent admission to a Paediatric hospital or ward (red) for review by a Paediatrician and adequate treatment (e.g. oxygen therapy, IV antibiotics…). Then, we would state that any child who does not meet the criteria for either green or red should be reviewed by a Practitioner or GP with a specialist interest in children or a Paediatrician asap (to be defined) (amber). In other words the amber section would remain more flexible in line with	

						current evidence suggesting that gut feeling also plays an important role in the assessment of sick children and that to date there is no perfect tool to predict course of disease in these children. A.van Den Bruel et al. BMJ (2012). It would avoid having to define more clearly what are e.g. reduced skin turgor, CRT and other fairly subjective symptoms of illness severity. In contrast normality could probably be defined fairly well using the values published by Fleming et al, Lancet (2011), Thompson et al., ADC (2009), etc. In summary we would have found it more helpful to define what is clearly "normal" (no specific treatment at home) and clearly "abnormal" (requiring hospital treatment) without trying to define degrees of illness severity, especially when considering the diversity of practitioners using this guidance who do not have a "feeling" for the Paediatric population.	
107.	**Royal College of Paediatrics and Child Health**	15	General	General		There is currently a huge amount of interest across many disciplines in biomarkers that are part of the host response to disease and can indicate diagnosis or prognosis. CRP and PCT are examples of these. They are, however, only the tip of the iceberg of what is being studied. A recent review highlighted that over 170 biomarkers have been studied in sepsis, although most not in the context of diagnosis[1]. The inflammatory markers interleukin-	Thank you for your comment. Unfortunately no other biomarkers were identified in the scope for this update. Therefore, we cannot take your comments forward or make any substantive changes to the existing topic in the final version of the Guideline. However, your comment will be kept on recorded for the next update of the guideline.

						6, interleukin-8 interleukin-1 receptor antagonist have been assessed for their value in diagnosing SBI in feverish children[2]. They varied in their usefulness for ruling in or out serious infection but for all performed inferiorly to PCT and CRP[2]. It is now accepted that one biomarker alone is unlikely to serve the desired purpose of accurately identifying whether a feverish child has a serious infection or not. However, advances in transcriptomic and proteomic approaches promises to propose increasing numbers of candidate biomarkers of various diseases processes, including SBI in feverish children[1]. An area of promise is the use of panels of different biomarkers together with a combined high sensitivity and specificity. One study has assessed a panel of novel biomarkers for diagnosing SBI in a resource poor setting with a combination of neutrophil gelatinase-associated lipocalin (NGAL), resistin and procalcitonin having a larger area under the curve than any of the individual factors alone[3]. For ideal integration with clinical assessment tests for biomarkers should be able to be done near to the point of care with the results available rapidly. Near point of care tests have been developed and used for procalcitonin successfully[4]. In future study of biomarkers, consideration of the possibility of using them as point of care tests should be given, and efforts	

						need to go into developing technology for this purpose. **<u>References</u>** 1. Pierrakos C, Vincent J (2010) Sepsis biomarkers: a review. Critical Care 14: R15. 2. Galetto-Lacour A, Gervaix A, Zamora SA, Vadas L, Lombard PR, et al. (2001) Procalcitonin, IL-6, IL-8, IL-1 receptor antagonist and C-reactive protein as identificators of serious bacterial infections in children with fever without localising signs. Eur J Pediatr 160: 95-100. 3. Irwin A, Marriage F, Mankhambo LA, IPD Study Group, Jeffers G, et al. (20102) Novel biomarker combination improves the diagnosis of serious bacterial infections in Malawian children. BMC Medical Genomics 5: 13. 4. Lopez AF, Cubells CL, Garcia JJG, Pou JF, The Spanish Society of Pediatric Emergencies (2003) Procalcitonin in pediatric emergency departments for the early diagnosis of invasive bacterial infections in febrile infants: results of a multicenter study and utility of a rapid qualitative test for the marker. Pediatr Infect Dis J 22: 895-904.	
108.	**Royal College of Paediatrics and Child Health**	16	General			The guidance seems to lack any formal updated epidemiology on the rates of SBI in children in the UK. The papers quoted – e.g. for rates of SBI in babies under 3 months – are very old and antedate Men C, PCV13	Thank you for your comment. The section “Need for 2013 update” in the introduction highlights that SBI is increasingly rare, and therefore guideline is needed to help identify cases.

						and the recent changes in the epidemiology of men B. there are only 600 cases of Men B in kids now a year. The risk assessment does not seem to reflect these changes. There are more cases of HAI BSI then Men B. There seems to be no risk assessment for the child with Underlying Disease presenting with HAI in the community setting. These children are at significant risk of presenting with Gram negative sepsis. There is no recognition that listeria is virtually all under 1 month, We remain concerned by the level of tests suggested for the children aged the 3-6 months – when the risk of SBI in the setting has never been lower. No real recognition that AMR is a significant problem and that all antibiotic treatment is a balance. **Reference** Blackburn R. et al., Journal of the Pediatric Infectious Diseases Society, Vol. 1, No. 4, pp. 284–92, 2012. DOI:10.1093/jpids/pis084	Unfortunately the management of specific conditions was not selected to be included in the 2013 update of the feverish illness guideline. Therefore, we cannot take your comments forward or make any substantive changes to the existing topic in the final version of the Guideline. However, your comments will be taken forward for consideration at the next update.
109.	**Sheffield Hallam University**	1	Full version Feverish	General		AC/AT:Low body temperature and infection Fever is a symptom of infection when the body's thermoregulation is altered but this process can also result in low	Thank you for your comment. This is a good question. However, the remit sent by the Department of Health was for a guideline on feverish illness in children rather than infection in children. Therefore low body temperature was not considered.

						body temperatures or hypothermia, which is entirely missed out in this guidance. Infections can result in low body temperatures in young infants in particular because of their thermoregulatory instability and potential inability to produce a fever. In Hofer et al (2012) paper on neonates with infections presenting with temperature symptoms an equal number presented with hypothermia as they did with fever. A drop in body temperature is associated with a much higher mortality and poorer prognosis. In a review of hypothermia and sepsis by Remick and Xioa (2006) 14 studies were studied. These included a total of 43,276 patients of different ages in studies published between 1990 and 2005. In all of the studies there was an increased risk of mortality from sepsis that resulted in hypothermia compared to sepsis that resulted in fever. The conditions studied included sepsis syndrome, shigellosis, bacteremia with diarrhoea, severe sepsis and septic shock, neonatal sepsis, pneumonia with bacteremia, bloodstream associated sepsis, invasive infection with streptococcus pneumoniae. Mortality in the hypothermia group was between 2 and 3 times higher in all studies and approximately 9% of sepsis patients developed hypothermia compared to 28% who developed fever. These were studies where hypothermia presented after the onset of sepsis and not before. The lack of attention to and concern of the importance of low body temperatures is widespread in clinical	

						practice (Cronin de Chavez 2011; Mercer 2003). By not monitoring low body temperatures alongside elevated temperatures signs of serious infections could be missed or result in serious delays in diagnosis and treatment. It would be pointless to produce new guidelines of 'hypothermic illness in children' as the information should be included with this current guidance. References Cronin de Chavez (2011) Cultural beliefs and thermal care of infants: protecting South Asian and white British infants in Bradford from heat and cold Doctoral thesis, Durham University http://etheses.dur.ac.uk/3325/ Hofer N, Müller M, Resch B (2012) Neonates presenting with temperature symptoms: Role in the diagnosis of early onset sepsis Pediatrics InternationalVolume 54, Issue 4, pages 486–490 Mercer J (2003). "Cold—an underrated risk factor for health." Environmental Research92(8-13). Remick D &Xioa H (2006). Hypothermia and Sepsis Frontiers in Bioscience (11) 1006-1013	
110.	**Sheffield Hallam University**	2	Full version	General		AC/AT:Provision of low reading thermometers	Thank you for your comment. Unfortunately use of thermometers was not selected to be included in the 2013 update of

						There is no mention of lower limits of the thermometers assessed in this guidance. Whilst nearly all of them will only read above 35.5˚C this is not specified. The guidance, as well as mentioning the lower body temperatures resulting from infection, should recommend that health services have good availability of low reading thermometers. Current manufacturing standards for thermometers require the lower temperature reading to only be 35.5°C. Some low reading models do exist but they are usually prohibitively expensive and may be of the invasive rectal type. Low reading thermometers are usually only found in specific departments in hospitals where hypothermia is expected, such as where therapeutic hypothermia is practiced. There is therefore an additional urgency for the development of cheap, easy to use, reliable, safe, non-intrusive low reading thermometers that do not risk cross infection for widespread use. The gap in access to low reading thermometers has been partly caused by the withdrawal of mercury thermometers. Thermospot is suitable for use as a hypothermia indicator (not a thermometer as such) being currently used with newborns in several countries. Results of trials indicate a close association with rectal temperatures. This device should be assessed for inclusion in this guidance. • Green D, Kumar A, Khanna R (2006) Neonatal hypothermia detection by	the feverish illness guideline. Therefore, we cannot take your comments forward or make any substantive changes to the existing topic in the final version of the Guideline. However, your comment will be kept on recorded for the next update of the guideline.

						ThermoSpot in Indian urban slum dwellings Archives of Diseases in Childhood Fetal Neonatal Ed.91(2): F96–F98. • Nisarga R, Gowda B (2004) Temperature monitoring in newborns using ThermospotThe Indian Journal of Pediatrics Volume 71, Issue 9, pp 795-796 • Mole TB, Kennedy N, Ndoya N, Emond A (2012) ThermoSpots to Detect Hypothermia in Children with Severe Acute Malnutrition. PLoS ONE 7(9) Research to required to evaluate new low reading thermometers and temperature monitoring tools like Thermospot in different clinical and community settings. This would be of use to other populations at risk to hypothermia due to their age or conditions that predispose to hypothermia. This is of added relevance where fuel poverty is becoming increasingly common.	
111.	**Sheffield Hallam University**	3	Full version	General		AC/AT:Management of low body temperature and infection In terms of managing low body temperatures there should be guidance in this document of appropriate action, for example Remick and Xioa (2006) found paracetamol was effective in managing symptoms of low body temperature. What other evidence is there?	Thank you for your comment. This is a good question. However, the remit sent by the Department of Health was for a guideline on feverish illness in children rather than infection in children. Therefore low body temperature was not considered.
112.	**Sheffield Hallam University**	4	Full version	43	6	JZ: Suggest the reason for the mercury-in-glass thermometer no longer being recommended is due to the EU Directive	Thank you for your comment. Unfortunately use of thermometers was not selected to be included in the 2013 update of the feverish illness guideline. Therefore, we

							cannot take your comments forward or make any substantive changes to the existing topic in the final version of the Guideline. However, your comment will be kept on recorded for the next update of the guideline.
113.	**Sheffield Hallam University**	5	Full version	43	23-26	JZ: The best and most accurate description for infrared thermometers should be “aural canal infrared thermometers” since the use of the word “tympanic” thermometers is misleading; these devices measure the reflected heat from the tympanic membrane.	Thank you for your comment. Unfortunately use of thermometers was not selected to be included in the 2013 update of the feverish illness guideline. Therefore, we cannot take your comments forward or make any substantive changes to the existing topic in the final version of the Guideline. However, your comment will be kept on recorded for the next update of the guideline.
114.	**Sheffield Hallam University**	6	Full version	43	29	JZ:There is an alternative site, namely the *supra clavicular fossa* (great vessels of the neck) by ThermoSpot. The CE Mark for this device is currently being renewed with the MHRA. See peer review articles on Thermospot in box 2 above	Thank you for your comment. Unfortunately use of thermometers was not selected to be included in the 2013 update of the feverish illness guideline. Therefore, we cannot take your comments forward or make any substantive changes to the existing topic in the final version of the Guideline. However, your comment will be kept on recorded for the next update of the guideline.
115.	**Sheffield Hallam University**	7	Full version	44	3-4	JZ: Selection of the rectal site is an abuse of an infant or young child except in cases where all other sites are impractical i.e. such as in burns cases and should only be used as a last resort. Another very practical problem in using this rectal site is the disinfection of the device used afterwards.	Thank you for your comment. Unfortunately use of thermometers was not selected to be included in the 2013 update of the feverish illness guideline. Therefore, we cannot take your comments forward or make any substantive changes to the existing topic in the final version of the Guideline.

							However, your comment will be kept on recorded for the next update of the guideline.
116.	**Sheffield Hallam University**	8	Full version	44	4-5	JZ: The reason for the axilla being considered to be not so accurate is due entirely to the very long period of use by the glass & mercury instrument from 1886/7 to relatively recently when it was the only recognised method to monitor patient body temperature. The sensor on this conventional device is round whereas the axilla is a flat surface. Quite clearly in placing the round sensor on to the flat axilla precludes the total surface of the sensor from picking up the temperature accurately, unlike in say the oral cavity. This is the main simple reason for axilla site temperatures being a little lower than the oral cavity readings. Another reason is the insufficient insertion period for a glass/mercury device in an axilla which should be at least 5 minutes (not 3 minutes). The use of a phase-change (chemical) device in an axilla will reproduce a much improved comparative (oral) result due to both surfaces being flat.	Thank you for your comment. Unfortunately use of thermometers was not selected to be included in the 2013 update of the feverish illness guideline. Therefore, we cannot take your comments forward or make any substantive changes to the existing topic in the final version of the Guideline. However, your comment will be kept on recorded for the next update of the guideline.
117.	**Sheffield Hallam University**	9	Full version	44	30-34	JZ: Background. Traditionally the oral site has been the generally (and widely) accepted preferred site to achieve the routine M & E (Morning & Evening) temperature taking procedure for this “vital sign”. Now that phase-change (chemical) devices are available and readily used throughout NHS hospitals and being unbreakable, they could be used safely on children of 4 years. No harm arises from a child chewing on such a device.	Thank you for your comment. Unfortunately use of thermometers was not selected to be included in the 2013 update of the feverish illness guideline. Therefore, we cannot take your comments forward or make any substantive changes to the existing topic in the final version of the Guideline. However, your comment will be kept on recorded for the next update of the guideline.

118.	**Sheffield Hallam University**	10	Full version	44	36	JZ: There is a soft plastic rectal sheath available for a phase-change device to fit into (sample available) that might overcome the unsuitability of an electronic probe thermometer; such a sheath has the advantage of being a “single-use item (together with the phase-change device) and removing the need for disinfection.	Thank you for your comment. Unfortunately use of thermometers was not selected to be included in the 2013 update of the feverish illness guideline. Therefore, we cannot take your comments forward or make any substantive changes to the existing topic in the final version of the Guideline. However, your comment will be kept on recorded for the next update of the guideline.
119.	**Sheffield Hallam University**	11	Full version	46	General	JZ: General introductory statement. Please refer to the earlier box 9 & 10 above.	Thank you for your comment. Unfortunately use of thermometers was not selected to be included in the 2013 update of the feverish illness guideline. Therefore, we cannot take your comments forward or make any substantive changes to the existing topic in the final version of the Guideline. However, your comment will be kept on recorded for the next update of the guideline.
120.	**Sheffield Hallam University**	12	Full version	47	12	JZ: Background. Is inserting any type of probe into a neonate, infant or child’s aural canal is inadvisable regardless of age until reaching a recommended age limit?	Thank you for your comment. Unfortunately use of thermometers was not selected to be included in the 2013 update of the feverish illness guideline. Therefore, we cannot take your comments forward or make any substantive changes to the existing topic in the final version of the Guideline. However, your comment will be kept on recorded for the next update of the guideline.
121.	**Sheffield Hallam University**	13	Full version	48	1	JZ: Tympanic temperature (by infrared thermometer). (1) It is all too frequently overlooked that when an aural canal thermometer is used on the same patient in both ears there is inevitably a difference (sometimes a significant variation) – which reading is correct?	Thank you for your comment. Unfortunately use of thermometers was not selected to be included in the 2013 update of the feverish illness guideline. Therefore, we cannot take your comments forward or make any substantive changes to the existing topic

							in the final version of the Guideline. However, your comment will be kept on recorded for the next update of the guideline.
122.	**Sheffield Hallam University**	14	Full version	48	46	JZ: General introductory statement. To what extent have any associated disinfection costs (time & materials) for each type of device been included – very necessary for all thermometers that are re-usable and taken from patient to patient? Furthermore has any consideration been taken into account for disposable/single-use devices that are discarded after patient use against those re-used? The elimination of Hospital Acquired Infections (HAI's) is also surely a risk-factor to be considered by the use of phase-change (chemical) devices?	Thank you for your comment. Unfortunately use of thermometers was not selected to be included in the 2013 update of the feverish illness guideline. Therefore, we cannot take your comments forward or make any substantive changes to the existing topic in the final version of the Guideline. However, your comment will be kept on recorded for the next update of the guideline.
123.	**Sheffield Hallam University**	15	Full version	232	General	JZ: There is no mention of theft risk of the electronic type devices (especially the pocket digital type) and their replacement cost when they "go missing" as they inevitably do. In practice more than one electronic and/or Aural canal infrared unit per ward would be required since in a busy unit where routine temperatures are taken what happens when the only unit was away in Medical Physics for re-calibration, battery changes or repair, how would the ward cope? At least 2 or 3 units are necessary to undertake patient's body temperature measurement efficiently. The "assumed" costings do not take this into account.	Thank you for your comment. Unfortunately use of thermometers was not selected to be included in the 2013 update of the feverish illness guideline. Therefore, we cannot take your comments forward or make any substantive changes to the existing topic in the final version of the Guideline. However, your comment will be kept on recorded for the next update of the guideline.
124.	**Sheffield Hallam University**	16	Full version	233	31	JZ: In Table 11.1 under both Electronic	Thank you for your comment.

						contact and Infrared sensing (tympanic) columns only probe covers are mentioned which indicates the metering unit as it is taken to each patient does not get wiped with an alcohol wipe between each temperature taken so the risk of HAI's is significant. It is important for all the participants reviewing the responses on the review team to appreciate that thermometers are one of the few items taken to each bedside at least twice daily so require cleansing carefully after each use. This will increase existing costs. I am also aware that certain suppliers of electronic devices where single-use probe covers are involved and supply their products free of charge but uplift the probe cover cost instead. I believe this practice "unfair" on other potential supply sources. The time taken to record a patient's body temperature varies enormously from the two prominent and very different devices available, the electronic types do have a definite advantage over the phase-change (chemical) technology. It is essential that the "patient's interest" (not the nurse's) should predominate on the simplest, safest (hygienically), most accurate device available for selection.	Unfortunately use of thermometers was not selected to be included in the 2013 update of the feverish illness guideline. Therefore, we cannot take your comments forward or make any substantive changes to the existing topic in the final version of the Guideline. However, your comment will be kept on recorded for the next update of the guideline.
125.	**St. Helens and Knowsley NHS trust**		Full	596		**'Health care professionals should not rely on a reduced or a lack of reduced temperature at 1-2 hours to differentiate between serious / non**	Thank you for your comment. Based on comments received the wording of this recommendation has been amended to

						serious illnesses'. This is a good comment but emphasis needs to be placed on the reassessment of patients.	read: "When a child has been given antipyretics, do not rely on a decrease or lack of decrease in temperature at 1–2 hours to differentiate between serious and non-serious illness. Nevertheless, in order to detect possible clinical deterioration, all children in hospital with 'amber' or 'red' features should still be reassessed after 1–2 hours."
126.	**St. Helens and Knowsley NHS trust**		Full	596		The explanation regarding paracetamol and ibuprofen is good. But then states consider changing to another agent but doesn't clarify what. This statement may lead to confusion and is conflicting	Thank you for your comments. We believe the wording of the recommendation is accurate as is it says "…the other agent…" rather than 'another agent', and the two agents outlined are paracetamol and ibuprofen. However, we have edited the recommendation, so it now reads. *When using paracetamol or ibuprofen in children with fever:* • *continue only as long as the child appears distressed* • *consider changing to the other agent if the child's distress is not alleviated* • *do not give both agents simultaneously* • *only consider alternating these agents if the distress persists or recurs before the next dose is due. [new 2013]*
127.	**St. Helens and Knowsley NHS trust**		Nice	9		Reassessment – outside of the hospital setting - does the role of community nurses need to be considered as a lot of these children are being referred to such teams directly by GP's and via rapid discharge from hospitals for early assessment in line with	Thank you for your comment. The sections on remote assessment and non-specialist assessment were not selected for update. Furthermore, NICE guidelines do not routinely name the specific health professional group who should apply a recommendation.

						the 'care closer to home agenda' - Also do you need to consider telephone triage and the questions that need to be asked by nursing staff when parents phone for advise as different staff ask different questions	
128.	**St. Helens and Knowsley NHS trust**		Nice	14		Like the fact that measuring Blood pressure is emphasised.	Thank you for your comment.
129.	**St. Helens and Knowsley NHS trust**		Nice	24		Like the emphasis placed upon when to seek further attention from health care services but couldn't find the link that explained this i.e. what advice they would be given. Advice needs to be clear as often this is conflicting depending on which health care professional is giving the information.	Thank you for your comment. The recommendations for 'seek further attention' refer the reader to additional recommendations in the section 1.7, the exact section with advice on when to seek further attention is 1.7.2.
130.	**St. Helens and Knowsley NHS trust**		NICE	35		Re recommendations about antipyretics. Are we recommending BNF doses / the patients weight / or is prescribing in accordance with information on the bottle. The above often conflict and differ which could lead to confusion especially for families	NICE guidelines do not routinely provide information on dosage. Instead health professionals should refer to the manufacturers' summary of product characteristics.
131.	**St. Helens and Knowsley NHS trust**		NICE	40		The new wording in the recommendations is a lot clearer than in the previous NICE guideline and seems to correlate better with current APLS guidance	Thank you for your comment.
132.	**St. Helens and Knowsley NHS trust**		NICE	43		Paracetamol guidance – as described in comment 6 above does not appear	Thank you for your comments.

						clear	We believe the wording of the recommendation is accurate as is it says "…the other agent…" rather than 'another agent', and the two agents outlined are paracetamol and ibuprofen. However, we have edited the recommendation, so it now reads. *When using paracetamol or ibuprofen in children with fever:* • *continue only as long as the child appears distressed* • *consider changing to the other agent if the child's distress is not alleviated* • *do not give both agents simultaneously* • *only consider alternating these agents if the distress persists or recurs before the next dose is due. [new 2013]*
133.	**Syner-Med (PP) Ltd**	1	Full	43	26	Temporal artery thermometers are referred to as measuring the temperature of the scalp, this is incorrect temporal thermometers measure the temporal artery temperature on the forehead.	Thank you for your comment. Unfortunately use of thermometers was not selected to be included in the 2013 update of the feverish illness guideline. Therefore, we cannot take your comments forward or make any substantive changes to the existing topic in the final version of the Guideline. However, your comment will be kept on recorded for the next update of the guideline.
134.	**Syner-Med (PP) Ltd**	2	Full	43	28	Temporal artery thermometers are referred to as "relatively expensive" this is incorrect. Such thermometers are available from Syner-Med directly at a cost of £36.95 incl VAT and from Boots chemist. In comparison to tympanic thermometers there are no on-going costs of purchasing probe	Thank you for your comment. Unfortunately use of thermometers was not selected to be included in the 2013 update of the feverish illness guideline. Therefore, we cannot take your comments forward or make any substantive changes to the existing topic in the final version of the Guideline.

						covers. Parents using tympanic thermometers may also not change the probe cover between recording different children's temperature increasing the risk of cross infection.	However, your comment will be kept on recorded for the next update of the guideline.
135.	**Syner-Med (PP) Ltd**	3	Full	44	6	Reference is made to the ease of use and speed of measurement of detecting axilla and tympanic temperature, a non contact thermometer is non invasive and can be used on a sleeping or upset child without any additional disturbance to the child.	Thank you for your comment. Unfortunately use of thermometers was not selected to be included in the 2013 update of the feverish illness guideline. Therefore, we cannot take your comments forward or make any substantive changes to the existing topic in the final version of the Guideline. However, your comment will be kept on recorded for the next update of the guideline.
136.	**Syner-Med (PP) Ltd**	4	Full	44	20	The GDG sought evidence of comparative accuracy of oral and rectal thermometers against mercury in glass. No evidence was sought using non contact thermometers as a comparator which was applicable to current UK practice. Non contact thermometers are currently in use and current practice within the NHS and used in the paediatric setting e.g. John Radcliffe NHS Trust, East Lancashire NHS Trust and Broomfield NHS Trust. **Clinical Papers** 1. *Clinical accuracy of a non contact infrared skin thermometer in pediatric practice. – C.G Teran et al. Child Care Health and Dev. 2011* 2. *Performance of non contact infrared thermometers for detecting febrile children in*	Thank you for your comment. Unfortunately use of thermometers was not selected to be included in the 2013 update of the feverish illness guideline. Therefore, we cannot take your comments forward or make any substantive changes to the existing topic in the final version of the Guideline. However, your comment will be kept on recorded for the next update of the guideline.

						hospital and ambulatory setting – E. Chiapini et al Journ of ClinNurs, 20, 1311-1318	
137.	**Syner-Med (PP) Ltd**	5	Full	47	25	Reference to one clinical paper using non contact thermometers in 327 complete patient data sets. This represents a large cohort of patients. Could a Delphi process be conducted to provide an evaluation in light of the GDG assessment of non contact thermometer sensitivity of 81%.	Thank you for your comment. Unfortunately use of thermometers was not selected to be included in the 2013 update of the feverish illness guideline. Therefore, we cannot take your comments forward or make any substantive changes to the existing topic in the final version of the Guideline. However, your comment will be kept on recorded for the next update of the guideline.
138.	**Syner-Med (PP) Ltd**	6	Full	49	16	No cost analysis of non contact thermometers was undertaken. After initial capital cost and staffing there are no ongoing consumable costs of disposable probe covers or disposal costs. There is in addition a perceived benefit to infection control in that the risk of cross infection may be reduced due to reduced contact with patients. Simple cost analysis models are available within every NHS Trust procurement department where hospitals use tympanic thermometers. East Lancashire NHS Trust completed an entire swap out from tympanic thermometers to non contact thermometers in 2012 • 950 beds • Probe cover usage per month = 66,666 @0.056p = £3,733 (£44,796 yr) • Capital cost of 350 non contact thermometers = £22,733	Thank you for your comment. Unfortunately use of thermometers was not selected to be included in the 2013 update of the feverish illness guideline. Therefore, we cannot take your comments forward or make any substantive changes to the existing topic in the final version of the Guideline. However, your comment will be kept on recorded for the next update of the guideline.

						• Breakeven point = 6.1 months • Annual financial saving on probe covers Yr 1 = £21,464 • Annual savings Yr 2 onwards = £44,796 • *Staffing costs not evaluated in this analysis*	
139.	**University of Bristol**					I think the updated guidelines look sensible wrt the use of antipyretics and the assessment of the febrile child, with some useful research recommendations also. I use a highly convenient, non-touch, infrared forehead thermometer in my clinical practice and wondered if you found any evidence for the use of these? Well done to all concerned!	Thank you for your response and taking the time to read the updated guidance. Unfortunately the use of thermometers was not selected to be included in the 2013 update of the feverish illness guideline. Therefore, no review was undertaken on this subject. However, your comments will be taken forward for consideration at the next update.

These stakeholders were approached but did not comment:

3M Health Care UK
Action for Sick Children
Airedale NHS Trust
Allocate Software PLC
Arrowe Park Hospital
Aspirin Foundation
Association of Child Psychotherapists, the
Association of Paediatric Emergency Medicine
Barking, Havering and Redbridge Hospitals NHS Trust
Barnet Primary Care Trust
Barnsley Hospital NHS Foundation Trust
Barnsley Primary Care Trust
Barts and the London NHS Trust
Birmingham Children's Hospital NHS Foundation Trust
Bolton Hospitals NHS Trust
Boots
Bradford District Care Trust
Brahms UK Limited-Thermo Fisher Scientific
Bristol-Myers Squibb Pharmaceuticals Ltd
British Association for Counselling and Psychotherapy
British Medical Journal
British National Formulary
British Nuclear Cardiology Society
British Paediatric Allergy, Immunology & Infection Group
British Psychological Society
British Society for Immunology
British Society of Paediatric Gastroenterology Hepatology and Nutrition
Broomfield Hospital
Calderdale and Huddersfield NHS Trust
Calderdale Primary Care Trust
Cambridge University Hospitals NHS Foundation Trust
Camden Link
Capsulation PPS

Care Quality Commission (CQC)
Central & North West London NHS Foundation Trust
Children living with Inherited Metabolic Diseases
Children, Young People and Families NHS Network
Church Grange Surgery
Clarity Informatics Ltd
College of Emergency Medicine
Commission for Social Care Inspection
Confidential Enquiry into Maternal and Child Health
Co-operative Pharmacy Association
County Durham Primary Care Trust
Crookes Healthcare Limited
Croydon Health Services NHS Trust
Croydon Primary Care Trust
David Lewis Centre, The
Department for Communities and Local Government
Department of Health, Social Services and Public Safety - Northern Ireland
Division of Public Health & Primary Health Care
Dorset Primary Care Trust
East and North Hertfordshire NHS Trust
Eaton Foundation
Encephalitis Society
Epilepsy Action
Epsom & St Helier University Hospitals NHS Trust
Faculty of Public Health
Fair Play for Children
George Eliot Hospital NHS Trust
Great Western Hospitals NHS Foundation Trust
Greater Manchester Ambulance Service NHS Trust
H & R Healthcare Limited
Hammersmith and Fulham Primary Care Trust
Hampshire Partnership NHS Trust
Health Protection Agency
Health Quality Improvement Partnership
Healthcare Improvement Scotland
Heart of England NHS Foundation Trust

Hermal
Hertfordshire Partnership NHS Trust
Hindu Council UK
Hockley Medical Practice
Huddersfield Central Primary Care Trust
Humber NHS Foundation Trust
Independent Children's Homes Association
Independent Healthcare Advisory Services
Infection Control Nurses Association
Infection Prevention Society
Information Centre for Health and Social Care
Institute of Biomedical Science
Lancashire Care NHS Foundation Trust
Leeds Community Healthcare NHS Trust
Leeds Teaching Hospitals NHS Trust
Leukemia Research Fund
Lewisham University Hospital
Liverpool Primary Care Trust
London Ambulance Service NHS Trust
Luton and Dunstable Hospital NHS Trust
Maidstone and Tunbridge Wells NHS Trust
McNeil Products
Medicines and Healthcare products Regulatory Agency
Medicines for Children Research Network
Medway NHS Foundation Trust
Meningitis Research Foundation
Meningitis Trust
Mid Staffordshire NHS Foundation Trust
Ministry of Defence
National Clinical Guideline Centre
National Collaborating Centre for Cancer
National Collaborating Centre for Mental Health
National Collaborating Centre for Women's and Children's Health
National Institute for Health Research Health Technology Assessment Programme
National Patient Safety Agency
National Pharmacy Association

National Public Health Service for Wales
National Reyes Syndrome Foundation of the UK
National Treatment Agency for Substance Misuse
National Youth Advocacy Service
NHS Cambridgeshire
NHS Clinical Knowledge Summaries
NHS Commissioning Board
NHS Confederation
NHS Connecting for Health
NHS County Durham and Darlington
NHS Derbyshire county
NHS Milton Keynes
NHS Newcastle
NHS Pathways
NHS Plus
NHS Sefton
NHS Sickle Cell &Thalassaemia Screening Programme
NHS South Birmingham
NHS Warwickshire Primary Care Trust
Norfolk Community Health and Care NHS Trust
NORTH EAST LONDON FOUNDATION TRUST
North Somerset Primary Care Trust
North Tees and Hartlepool NHS Foundation Trust
North West London Perinatal Network
North Yorkshire & York Primary Care Trust
Northwick Park and St Mark's Hospitals
Nottingham City Hospital
Oxford Health NHS Foundation Trust
Paracetamol Information Centre
PERIGON Healthcare Ltd
Pfizer
Public Health Wales NHS Trust
Queen Mary's Hospital NHS Trust
Rotherham Primary Care Trust
Royal Berkshire NHS Foundation Trust
Royal Brompton Hospital &Harefield NHS Trust

Royal College of Anaesthetists
Royal College of General Practitioners in Wales
Royal College of Obstetricians and Gynaecologists
Royal College of Paediatrics and Child Health , Gastroenetrology, Hepatology and Nutrition
Royal College of Pathologists
Royal College of Physicians
Royal College of Psychiatrists
Royal College of Radiologists
Royal College of Surgeons of England
Royal Pharmaceutical Society
Royal Society of Medicine
Royal United Hospital Bath NHS Trust
Royal West Sussex NHS Trust
Scottish Intercollegiate Guidelines Network
SEE BETSI CADWALADR - North Wales NHS Trust
Sheffield Childrens Hospital
Sheffield Primary Care Trust
Sheffield Teaching Hospitals NHS Foundation Trust
Social Care Institute for Excellence
Society for Academic Primary Care
Society for General Microbiology
Solent NHS Trust
South Asian Health Foundation
South East Coast Ambulance Service
South London &Maudsley NHS Trust
South London Cardiac and Stroke Network
South Staffordshire and Shropshire Healthcare NHS Foundation Trust
South Warwickshire NHS Foundation Trust
South West Yorkshire Partnership NHS Foundation Trust
South Western Ambulance Service NHS Foundation Trust
Southport and Ormskirk Hospital NHS Trust
St John Ambulance
St Mary's Hospital
Staffordshire Ambulance Service NHS Trust
Stockport Clinical Commissioning Pathfinder

Stockport Primary Care Trust
Sunfield
Sussex Ambulance Services NHS Trust
Tameside Hospital NHS Foundation Trust
The Association of the British Pharmaceutical Industry
The British In Vitro Diagnostics Association
The Childhood Cancer Parents Alliance
The Princess Alexandra Hospital NHS Trust
The Rotherham NHS Foundation Trust
UK Clinical Pharmacy Association
UK Specialised Services Public Health Network
Unite - the Union
University College London Hospital NHS Foundation Trust
University of Southampton
University of York
Walsall Local Involvement Network
Welsh Government
Welsh Scientific Advisory Committee
Western Cheshire Primary Care Trust
Wirral University Teaching Hospital NHS Foundation Trust
Wirrall Community NHS Trust
Wishaw General Hospital
Wyre Forest Primary Care Trust
York Hospitals NHS Foundation Trust
Yorkshire Ambulance Service NHS Trust