

National Institute for Health and Care Excellence

GORD in children
Guideline Consultation Table
31 July 2014 - 25 September 2014

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
Alder Hey Children's NHS FT	1	Full	General	General	<p>With more sophisticated diagnostic tools, GOR is more frequently and more accurately diagnosed in children. However the underlying causes are difficult to establish and often remain unclear. It is not in the remit of the gastroenterologist alone to establish the diagnosis of GOR and GORD. The gastroenterologist can assess endoscopically the upper GI tract, and investigate for oesophagitis and eosinophilic oesophagitis. However if reflux persists or indicated GORD, these children need work up (ideally multidisciplinary, ideally in established joined clinics) with general paediatricians, surgeons, or other specialists (neurologist, allergist, genetics) to find out underlying causes and manage these patients.</p> <p>Silent reflux needs better definition and evidence based documents – when and how to treat.</p> <p>Desaturations/seizures are a problem and need a paragraph of joined consultations and investigations (e.g. combined impedance with oxygen monitoring/sleep lab), and opportunity for a joined neurological assessment needs to be established in specialised centred and teams in formal pathways.</p> <p>NICE needs to make a statement about pharmaceutical companies/input/prospective RCT to investigate further safe prokinetic</p>	<p>Thank you for your comments. Please find numbered responses to these below.</p> <p>1) The delivery of care for children and young people with GORD can be made using different health care professional structures. This guideline outlines the management that should be offered but not the structure or location of the team because it is recognised that a variety of differing models exist across different regions and clinical networks.</p> <p>2) In this guideline silent reflux is referred to as occult reflux. The glossary in the full guideline has been amended to clarify this in accordance with your comment.</p> <p>3) This is a guideline on GORD and the detailed investigation of children with complex co-morbidities who may be suffering from apnoeic episodes, respiratory compromise or neurological events (other than Sandifer's syndrome) is beyond its remit. However we did recognise the important role of other health care professionals and specialists in the</p>

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					<p>medications.</p> <p>The BSPGHAN motility group is to produce a document for guidance on interpreting impedance results.</p> <p>A paragraph needs to address the problem of investigating unsettled children (“colics”) with a pathological reflux score on impedance – what teams and how monitoring and treatment of these children is indicated, as there are no medicines available to make these children settled/content. Specialists need reassurance from NICE that and when no further escalation of investigations and treatment in this group is required.</p> <p>GOR(D) children should be seen together with dieticians and SALT and not by a gastroenterologist alone upon referral, and for a subgroup with a general surgeon in designated clinics and designated ward rounds/clinical settings.</p>	<p>investigation and management of these children. For example, 1.1.13 highlights the importance of a general assessment for children presenting with apnoea or apparent life-threatening events.</p> <p>4) We recognised that safe and effective prokinetic agents could potentially be helpful. However there were concerns about the use of domperidone as reflected in the recommendation, advising specialist involvement. They were not aware of any new products currently available which currently required investigation by RCT.</p> <p>5) Thank you for this information, guidance from this group will hopefully concur with the recommendation made in this guideline.</p> <p>6) This is not a guideline on the management of crying infants or distressed children. Regarding colic various recommendations are relevant to your concern - for example, recommendations 4, 6, 20, 23, 25, 26, 27 and 30 all provide advice on the management of infants with signs of distress.</p> <p>7) With regard to the involvement of health care professionals such as dieticians and SALTs, while their role</p>

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						in a tertiary paediatric gastroenterology setting can be important in the management of some children with GORD, a recommendation that they should always be involved was not made.
Alder Hey Children's NHS FT	2	Full	General	General	It is important to note that we are a very large centre with a major experience of GOR. The surgical treatment of GOR in neuro-disabled patients is complex and associated with a variable outcome. High failure rates and poor medium-term survival are well documented, particularly for fundoplication which remains the most popular procedure. Numerous surgical strategies have been described which include: gastrostomy feeding, G-J feeding, jejunostomy feeding, fundoplication (both open and laparoscopic), fundoplication variants (e.g. partial Nissen / Thal / Boix-Ochoa / Toupe / fundoplication + vagotomy and pyloroplasty), gastric pacing, oesphago-gastric dissociation, and total parenteral nutrition. Thus far there has been no convincing data to demonstrate the superiority of any of these approaches, principally because the patients form a disparate group whose needs and pathologies are variable.	Thank you for your comment. We were aware of these concerns and issues and of the wide range of interventions. As you are aware the guideline adopts and conservative approach to the use of enteral tube feeding and to the use of fundoplication. The evidence reviews did not attempt to compare the relative merits of different types of surgical intervention but focussed on identifying those for whom such interventions might be considered.
Alder Hey Children's NHS FT	3	Full	General	General	The guidance puts thickeners before gaviscon, and this is different from most local practice, but I think is sensible. Though I think not many of us use these (carobel) in practice. Either in the community or hospital.	Thank you for your comment. Recommendation 26 suggests a variety of thickeners such as rice starch, cornstarch, locust bean gum and carob bean gum.
Alder Hey Children's	4	Full	General	General	1) Generally speaking; with restriction on domperidone (previously withdrawn	Thank you for your comment. We were aware of the difficulty in managing

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NHS FT					<p>cisapride)and recommendations against use of H2 receptor antagonists (ranitidine) or PPIs (omeprazole etc), in practice, faced with an infant with significant vomiting is hardly ever controlled by just the feed thickener or alginates. Our practice and experience may change in view of these restrictive safety advices, but need to be said that general paediatricians will struggle in treating these infants and pacifying parents. It's hard to convince people that in this day and age there is no specific treatment of such a common condition, however true it may be. And this may also lead to more specialist referrals (secondary and tertiary) as nothing else is available without specialist advice.</p> <p>2) I also agree with Dr -'s view; I do use gaviscon but where it does not work, carobel usually is tolerated better with better response. (my opinion and experience). But I don't use gaviscon or carobel alone (very rare).</p> <p>3) In the context of other diagnosis:</p> <p>a. co-existence of GOR and cow's milk protein intolerance is possible. Therefore consideration should be given to it as alternate diagnosis or co-morbidity if vomiting with loose stools with presence of blood, failure to thrive. Hence trial of dairy exclusion along with GOR management may be appropriate in some infants with appropriate follow up.</p> <p>b. I have not seen any comment on</p>	<p>infants with troublesome regurgitation and of the importance and potential difficulty in reassuring worried parents. The recommendations regarding treatment were derived from a careful review of available RCTs. Recommendations are made on the indications for a review of management and for referral for investigation or possible treatment with prokinetic agents. The comments with regard to practice and experience with Carobel and Gaviscon would seem in keeping with the recommendations made.</p> <p>Following stakeholder consultation, we gave careful consideration to the differential diagnosis in children presenting with possible GORD. A new recommendation was added (Recommendation 11) to confirm that some symptoms of non-IgE mediated cows' milk protein allergy can be similar to those of GORD, especially in infants with atopic symptoms, signs, and/or a family history and which cross refers the reader to NICE CG 116 'Food allergy in children and young people'. Amendments were also made to Recommendation 5 in Table R1 that lists 'red flag' signs and symptoms that may suggest disorders other than GOR in those with vomiting or regurgitation. A cross reference to NICE CG 116 was added to the symptom/sign of 'Blood in stool' 'Chronic diarrhoea' was added to</p>

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					<p>commonly held belief of “silent reflux” where there are only behavioural symptoms (excessive crying, back arching, sleepless nights etc.) but no organic symptoms. Initial anti-reflux treatment may have no impact on symptoms, and pressure grows for more investigations and additional treatments for presumed GOR not responding to treatment. Some of these babies may just have PURPLE cry (www.purplecry.info). Thorough clinical assessment with appropriate reassurance and explanation is required for these families. This is especially relevant in younger babies 3-6 months age.</p>	<p>the gastrointestinal list of signs/symptoms with a cross reference to NICE CG 116. Finally the sign/symptom 'Eczema' was amended and broadened to 'Infants and children with, or at high risk of, atopy' and the suggested action of a 'Trial of milk exclusion' was removed because this clinical recommendation was not made in this GORD guideline. A research recommendation was made however and the research question was amended following stakeholder consultation. This now specifies that a randomised controlled trial should be performed to examine the clinical and cost effectiveness of a hydrolysed formula trial in formula fed infants with frequent regurgitation associated with marked distress (Section 5.2.8).</p> <p>In this guideline so called ‘silent reflux’ is called occult reflux (hidden). Recommendation 6 specifically advises on the management of those without overt regurgitation (but in whom occult reflux might be suspected) and advises against routine investigation or treatment for GORD if a various symptoms including distressed behaviour occur in isolation. The guideline does advise consideration of specialist referral for those who have persistent back arching and for those with clinical features of Sandifer’s syndrome.</p>

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Alder Hey Children's NHS FT	5	Full	General		Regarding surgery the very well defined indications applied for offering fundoplication notably 'failure of medical therapies ' with caution expressed that the surgeon could 'cure ' ALTE / apnoea events which I agree with. Outcomes of laparoscopic vs classic 'open' approaches demonstrate no difference in outcome other than scarring from open operation etc and likely a poorer medium –long term control of GER due to wrap failure vs open surgery. Hospital stay is a poor metric to measure as many children have special needs that determines hospital stay with feeding schedule manipulation and carer respite. I was surprised the NICE guidance made little reference to tube feeding categories – PEG vs GJ feeding vs surgeon constructed feeding jejunostomy. There was also no statement on the Bianchi OG dissociation. In summary – a well designed prospective RCT is needed in GER management ... We attempted undertaking an RCT (gastroenterology and surgery) almost 10 years ago at Alder Hey however equipoise proved problematic.	Thank you for your comment. The scope of the guideline included fundoplication but not other surgical interventions and therefore the OG dissociation procedure was not reviewed in terms of evidence and so no recommendations were made. We have included a new recommendation based on your comment and those of other stakeholders with regard to jejunal tube feeding (1.4.4).
Alder Hey Children's NHS FT	34	Full	General	General	Disappointed that the practice of early weaning was not investigated	Thank you for your comment. The possibility that early weaning might contribute to the problem of GORD was not judged as a priority.
Alder Hey Children's NHS FT	6	Full	10	18	There is a missing word between the word "experts" "that"	Thank you for your comment. The missing word has been inserted.
Alder Hey Children's NHS FT	7	Full	67	19	The word "quality" has been omitted from the end of the sentence	Thank you for your comment. It has now been added.

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Alder Hey Children's NHS FT	8	Full	70	24	The font has changed for the ref Mazliah et al	Thank you for your comment. This formatting error has now been corrected.
Alder Hey Children's NHS FT	9	Full	72	11	Delete the extra "a" in front of not	Thank you for your comment. This has been deleted.
Alder Hey Children's NHS FT	10	Full	82	29	Delete the extra word "be" in front of meet	Thank you for your comment. This has been deleted.
Alder Hey Children's NHS FT	11	Full	82	40	5 th word along should read "an" not "and"	Thank you for your comment. This has been corrected.
Alder Hey Children's NHS FT	12	Full	83	5	Delete the word "in"	Thank you for your comment. This has been deleted.
Alder Hey Children's NHS FT	13	Full	84	23	Word "between is missing at the end of the row	Thank you for your comment. This has now been inserted.
Alder Hey Children's NHS FT	14	Full	84	40	"The" should read "They"	Thank you for your comment. This has been corrected.
Alder Hey Children's NHS FT	15	Full	85	34	The word "be " has been omitted	Thank you for your comment. It has now been inserted.
Alder Hey Children's NHS FT	16	Full	89	6	"Infant" should read" infants"	Thank you for your comment. The correction has been made.
Alder Hey Children's NHS FT	17	Full	103	12	Missing word between "the" and "between"	Thank you for your comment. The missing word "association" has now been inserted.
Alder Hey Children's NHS FT	18	Full	109	11	The word being should be inserted before overweight	Thank you for your comment. This has been inserted.
Alder Hey Children's NHS FT	19	Full	109	33	Word missing at the end of the sentence...moderately obese and	Thank you for your comment. The word "and" has been deleted as it was an error.

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Alder Hey Children's NHS FT	20	Full	111	13	Unclear "should covered"?	Thank you for your comment. The statement has been edited to read "should apply to".
Alder Hey Children's NHS FT	21	Full	117	3	Insert the word "in " after placed	Thank you for your comment. This phrase has been amended.
Alder Hey Children's NHS FT	22	Full	144	32	"amino acid formula" font size incorrect	Thank you for your comment. This has been corrected.
Alder Hey Children's NHS FT	23	Full	145	32	I would expect Dieticians to play a pivotal advisory role in selection of feed thickeners in specialist settings. I am surprised that there is no reference to their role	Thank you for your comment. Please note that the guideline development group composition included a dietician. This guideline does not define individual roles within the multi-disciplinary team apart from where the guideline refers to a specialist, which means a paediatrician with the skills, experience and competency necessary to deal with the particular clinical concern that has been identified by the referring health care professional. In this guideline this is most likely to be a consultant general paediatrician. Depending on the clinical circumstances, 'specialist' may also refer to a paediatric surgeon, paediatric gastroenterologist or a doctor with the equivalent skills and competency. The recommendations relating to feed thickeners relate to infants and we do not agree that the involvement of a dietician is necessary for thickening an infant formula.
Alder Hey Children's NHS FT	35	Full	146	5	Disappointing that the recommendations do not include breast fed infants	Thank you for your comment. We have discussed this area and amended recommendations to support breast

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						feeding.
Alder Hey Children's NHS FT	36	Full	146	14	Interesting that this does not support the widely used algorithm for the management of cows milk protein allergy by Vandenplas 2007	Thank you for your comment. Vandenplas, 2007 was a narrative review (and not a systematic review) and therefore not included in the guideline. The algorithm discussed in this report has not been validated and as reported by the authors, was only intended as a basis for local discussion, implementation and prospective evaluation.
Alder Hey Children's NHS FT	24	Full	162	34	Useful to include a reminder that the combined use of alginates and feed thickeners is not recommended – ref SPC Gaviscon Infant “Not to be used with thickening agents or infant milk preparations containing a thickening agent as this could lead to over-thickening of the stomach contents”	Thank you for your comment. Recommendations do not provide this level of detail regarding the practical aspects of medicine usage. It is assumed that health care professionals will advise on the use in accordance with SPC documentation.
Alder Hey Children's NHS FT	25	Full	180	35 onwards	There is no reference to manipulating the MUP dosage form to achieve the required dose. It is common practice to halve the 10mg MUP to achieve a 5mg dose. There is no evidence that an unlicensed solution delivers a more reliable dose and it may be preferable to start with a licensed product and manipulate it, rather than using an unlicensed product first line. The issues of stability and cost do not arise if MUPs are manipulated. Perhaps readers should be reminded that the liquid formulations are unlicensed.	Thank you for your comment. It is expected that clinicians use their knowledge and experience alongside recommendations when prescribing treatment to patients. In the recommendations on the use of acid suppressing drugs we advised that the choice between these should be influenced by available preparations, patient/child preference and cost (Recommendation 33).
Alder Hey Children's NHS FT	26	Full	181	25	Some guidance on the best way to monitor the cardiac risks would be helpful. Primary care physicians are unlikely to continue treatment without assurance from specialists that the patient is having appropriate monitoring. Without consistent guidance –local monitoring	Thank you for your comment. This guideline is not recommending the use of Domperidone and therefore it is a matter for local policies if clinicians decide to use this medicine and for them to decide how it should be

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					arrangements are likely to be very variable depending on whether gastroenterologists have access to cardiologists for advice	monitored.
Alder Hey Children's NHS FT	27	Full	181	34	Some comment about the risk of antibiotic resistance if erythromycin is adopted as a default alternative for domperidone would be valuable. Domperidone was adopted as a default treatment option after cisapride withdrawal because no helpful guidance was issued at the time.	Thank you for your comment. We recommended that erythromycin should only be considered after seeking specialist advice. Such advice should include consideration of potential adverse effects and of antibiotic resistance.
Alder Hey Children's NHS FT	28	Full	195	19	The word "with" has been omitted (between treated and open)	Thank you for your comment. The word has now been inserted.
Alder Hey Children's NHS FT	29	Full	196	29	"ain" should read "in"	Thank you for your comment. This has been corrected.
Alder Hey Children's NHS FT	30	Full	204 Glossary	Overt regurgitation	Description is unclear	Thank you for your comment. The definition has been amended for clarity.
Alder Hey Children's NHS FT	31	Full	205	Placebo-glossary	Is the word fake necessary? It implies deceit; inactive treatment is sufficient	Thank you for your comment. The word "fake" has been removed from the definition and the word "sham" inserted.
Alder Hey Children's NHS FT	32	Full	205	Premature infant	This term is used throughout the document , but is not defined in the glossary. It should be added to the glossary	Thank you for your comment. The glossary has been updated to include the definition of a premature infant (a baby born before 37 completed weeks of gestation)
Alder Hey Children's NHS FT	33	Full	206	Specialist-glossary	A consultant paediatrician may be a specialist, but so is a paediatric gastroenterologist. Is consultant paediatrician really the correct interpretation for the word specialist? A specialist is "A physician" whose practice is limited to a particular branch of medicine or surgery	Thank you for your comment. We considered this however we amended the glossary with a modified definition consistent with the our perspective that rather than identifying the implicit clinical expertise of individuals who may be involved. Where the guideline

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						speaks about referral to a specialist this means referral to a paediatrician with the skills, experience and competency necessary to deal with the particular clinical concern that has been identified by the referring health care professional. In this guideline this is most likely to be a consultant general paediatrician. Depending on the clinical circumstances, 'specialist' may also refer to a paediatric surgeon, paediatric gastroenterologist or a doctor with the equivalent skills and competency.
babyREFLUX	1	Full	General	General	Firstly we would like to thank the project team and the GDG for putting together the guidelines. A very difficult task considering the scale of the project and the limited resources available.	Thank you for your comment.
babyREFLUX	2	Full	General	General	<p>Presentation for a child with Milk Allergy, GOR and GORD are almost identical. We feel that the primary health care specialist needs specific direction to help the patient if the diagnosis is not GORD.</p> <p>We do understand these guidelines are not a detailed guideline on complex feeding issues or a protocol for an approach to "the vomiting child" and 'This guideline focuses on symptoms of and interventions for GORD'.</p> <p>It is important to appreciate there are already internet campaigns, forum threads and advice pages advising the parent to take their child to A & E if the GP suggests their child does not require treatment/medication.</p>	<p>Thank you for your comment.</p> <p>Following stakeholder consultation, we gave careful consideration to the differential diagnosis in children presenting with possible GORD. A new recommendation was added (Recommendation 11) to confirm that some symptoms of non-IgE mediated cows' milk protein allergy can be similar to those of GORD, especially in infants with atopic symptoms, signs, and/or a family history and which cross refers the reader to NICE CG 116 'Food allergy in children and young people'. Amendments were also made to Recommendation 5 in Table R1 that lists 'red flag' signs and symptoms that</p>

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					<p>It is therefore critical that that these guidelines do not create a wave of parents attending A & E creating substantial resource issues for the NHS.</p> <p>Therefore, we suggest that you might consider offering more specific direction for the primary health care specialist when not treating the patient for GORD.</p> <p>We also feel strongly that a recommendation for the creation and production of a new set of specific guidelines for the “the vomiting child”.</p>	<p>may suggest disorders other than GOR in those with vomiting or regurgitation. A cross reference to NICE CG 116 was added to the symptom/sign of 'Blood in stool'. 'Chronic diarrhoea' was added to the gastrointestinal list of signs/symptoms with a cross reference to NICE CG 116. Finally the sign/symptom 'Eczema' was amended and broadened to 'Infants and children with, or at high risk of, atopy' and the suggested action of a 'Trial of milk exclusion' was removed because this clinical recommendation was not made in this GORD guideline. A research recommendation was made however and the research question was amended following stakeholder consultation. This now specifies that a randomised controlled trial should be performed to examine the clinical and cost effectiveness of a hydrolysed formula trial in formula fed infants with frequent regurgitation associated with marked distress (Section 5.2.8).</p> <p>We believe that these amendments as well as recommendations made elsewhere in the guidance (especially recommendations 1 to 4 and 6) will assist concerned parents and all health care professionals determine if, when and what investigations or treatment might be required.</p> <p>Finally, we would like to draw attention</p>

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						to NICE clinical guideline 84 "Diarrhoea and vomiting in children: Diarrhoea and vomiting caused by gastroenteritis: diagnosis, assessment and management in children younger than 5 years" which might address the stakeholder's concerns regarding the need for a guideline regarding "the vomiting child".
babyREFLUX	3	Full	General	General	<p>Pepsin</p> <p>It is already recognised through RCTs that salivary pepsin testing may lessen the need of unnecessary medication, therapy and the need for further invasive and expensive diagnostic methods in testing for GOR/GORD.</p> <p>We would recommend that the guideline makes reference to this test and further recommends that clinical research should be accelerated in this area.</p> <p>For example, there is a proposed study at the Wingate Institute (University of London) to examine the benefits of salivary pepsin testing in the diagnosis of GOR/GORD in infants.</p> <p>It is critical to direct resources towards these studies as all current diagnostic tools at primary care level are observational.</p>	Thank you for your comment. The investigation of the evidence base for the accuracy of this investigation was not included in the scope. We did not review evidence on the accuracy of salivary pepsin measurement as an indicator of occult reflux and has not made any clinical or research recommendations in this area.
babyREFLUX	4	Full	General	General	<p>'Silent Reflux'</p> <p>There are no references in the document to GOR/GORD without regurgitation present.</p> <p>This is commonly known as silent reflux by</p>	Thank you for your comment. In this guideline silent reflux is referred to as occult reflux. We have amended the glossary in the full guideline to clarify this.

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					<p>health professionals.</p> <p>Is the suggestion that GOR/GORD cannot exist without regurgitation and/or vomiting?</p> <p>Many doctors recognise 'silent reflux' including Dr Neil Shah who recently presented a speech on 'How to Manage Silent Reflux' at GOSH (June 2014).</p>	<p>The guideline does not suggest that GOR or GORD cannot exist without regurgitation / vomiting. It focuses on these concerns separately. There are recommendations specifically aimed at the most common clinical presentation – namely the infant or young child with overt regurgitation. There are also many recommendations that are not specifically for those with overt regurgitation – for example children with pulmonary aspiration (recurrent pneumonia, apnoea) or with symptoms of occult reflux (heartburn, abdominal pain) or with reflux induced inflammation of the oesophagus (oesophagitis) many of whom would not have overt regurgitation.</p>
babyREFLUX	10	Full	General	General	<p>Managing GOR</p> <p>We are disappointed that there is little mention in the guidelines of managing parental expectations of a baby. No mention of the association with post natal depression and the impact of GOR/GORD on family life. Parental coping strategies, prevalence of parental anxiety, depression and expectations of normality.</p> <p>There is also little advice and support for health visitors on feeding, including positioning the infant during feeding and coping mechanisms.</p> <p>This will be imperative as the numbers of infants being turned away by the primary health care professional without treatment for</p>	<p>Thank you for your comment. Please find numbered responses to these below.</p> <p>(1) Detailed advice and support for parents and the health professionals managing infants and children with distressing conditions like GORD is beyond the remit of this guideline. However, it is anticipated that this guideline will lead to much clearer information and will lead to much more realistic expectations. This will make certain aspects of being a parent or carer in this difficult situation better.</p> <p>(2) Following this and other stakeholder feedback, amendments were made to the recommendations 25 and 27 for breast-fed infants with</p>

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					<p>'perceived' GOR/GORD increases dramatically.</p> <p>Without adequate training and direction primarily health care professionals will not have the tools to address the issues of 'the sick baby'.</p> <p>If the infant is dismissed without GOR/GORD treatment and also without guidance they will inevitably return time and time again putting more pressure on limited resources of the NHS. As stated previously, current thinking is that the parent will attend an A & E department if they do not 'perceive' to get the treatment they are looking for.</p>	<p>frequent regurgitation associated with marked distress such that breastfeeding should be supported with a breastfeeding assessment/advice. However, more prescriptive advice on this topic is beyond the remit of this guideline.</p> <p>(3) Further, it is hoped that this guideline will lead to a more uniform set of advice for all health professionals which will help give families greater confidence in the information they have received.</p> <p>(4) We believe that recommendations made in this guideline (especially recommendations 1 to 4 and 6) will provide concerned parents and all health care professionals with a clear message as to what the problem is likely to be, what the natural history is likely to be, safety netting with a future review dependent on outcome, and information to determine if, when and what investigations or treatment might be required.</p>
babyREFLUX	6	Full	117	2	<p>Positional Management</p> <p>We fully support the department of Health advice of infants being placed on their back when sleeping.</p> <p>But, it is also important to appreciate that positional management can be a 100% safe method for relieving the symptoms of GOR/GORD if carried out correctly.</p>	<p>Thank you for your comment</p> <p>This aspect of the guideline was discussed and debated on several occasions and the conclusions of the discussions and the reasoning behind our single and unambiguous recommendation is discussed in the evidence to recommendation section of the full guideline. Like the American Academy for Pediatrics, we</p>

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					<p>Positional intervention is a well recognised method for both encouraging the infant to sleep better and reducing the visible symptoms of GOR/GORD.</p> <p>We believe supine positional management has not been adequately considered. The studies detailed in the guidelines are not appropriate and it has been shown over the last 10 years that supine positional management of a regurgitating baby (GOR/GORD) helps in many ways.</p> <p>There are RCTs that show the benefits of supine elevation of an infant such as:</p> <p>Regurgitation in healthy and non healthy infants - Flavia Indrio, Giuseppe Riezzo, Francesco Raimondi, Luciano Cavallo and Ruggiero Francavilla</p> <p>Managing gastro-oesophageal reflux in infancy - MP Tighe, RM Beattie</p> <p>...and particularly...</p> <p>A preliminary report on the efficacy of the Multicare AR-Bed in 3-week-3-month-old infants on regurgitation, associated symptoms and acid reflux - Vandenplas Y1, De Schepper J, Verheyden S, Devreker T, Franckx J, Peelman M, Denayer E, Hauser B.</p> <p>If supine elevation of a child with GOR reduces crying, distress, regurgitation and benefits the mood and disposition of the parents. There</p>	<p>recommend that positional management should not be used as a treatment for GOR in sleeping infants because any potential small individual benefit would almost certainly be outweighed by the very real risk of SIDS in the individual and would quite possibly pose a risk to the much larger population of well infants with normal regurgitation and mild physiological GOR were this dangerous practice to become widespread once again.</p> <p>None of the studies cited in your comment are randomised controlled trials and so would not be included in the review on positional management (see appendix E for the review protocol). The first reference (Flavia et al) is a narrative review and is not a systematic review. The second reference (Tighe et al., 2010) is a commentary which offers perspective on the third paper (Vandenplas et al.,2010) suggested by the stakeholder. The third reference (Vandenplas et al., 2010) is not a randomised controlled trial either. It is a pilot observational study that examines the use of a single intervention (the Multicare AR-Bed) in 52 children and does not have a comparison group. The review performed was limited to including randomised controlled trials hence this small observational study (with no</p>

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					<p>must be a substantial benefit to the NHS placating less anxious parents who would otherwise 'demand' referrals and medication. Thus, we are disappointed that there are no research recommendations in this area.</p> <p>It is vital to consider recommending new research for positional management as there has been no recent research conducted in this area. We feel strongly that there are clear benefits to positioning an infant if done safely and correctly.</p>	comparator) would not fulfil the inclusion criteria
babyREFLUX	7	Full	131	12	<p>"...Once a child can move freely during sleep or at rest, there is little application of positional management in GOR..."</p> <p>This we feel this is inaccurate.</p> <p>There are many older children beyond 6 months of age that benefit from sleeping with elevation. Just as adults who sleep more upright can gain respite from GOR/GORD so can a child.</p>	<p>.</p> <p>Thank you for your comment.</p> <p>The evidence review did not identify any evidence from comparative studies that addressed the use of postural management in infants over 6 months of age. For this reason the recommendation made related to young infants only. We have altered the discussion in the full guideline to clarify that no recommendation was made about postural management, such as elevation to head of the infant crib or the older child or young person's bed as no evidence was available on the efficacy of this approach</p>
babyREFLUX	8	Full	144	29	The GDG have recommended further research in the role of cow's milk allergy and	Thank you for your comment. Following stakeholder consultation, we

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					<p>GOR/GORD which we fully endorse. We are however disappointed that the guidelines are dismissive of the current role that cow's milk allergy has in the presentation of regurgitating infants.</p> <p>NICE guidelines already agree that the symptoms for CMA can be identical to that of GOR/GORD (NICE Food allergies in young children February 2011)</p> <p>With the prevalence of food allergy in Europe and North America reported to be up to 10% in children up to the age of 3 years and increasing year on year – CMA has to be integrated more closely with the diagnostics and treatment of GOR/GORD.</p> <p>The Milk Allergy in Primary Care Guidelines in 2013 says that non-IgE mediated allergy is producing more delayed symptoms such as eczema, gastro-oesophageal reflux, or diarrhea.</p> <p>We feel strongly that as well as recommending further research there needs to be a more cohesive guide presented to the primary health care professional when distinguishing between GOR/GORD and CMA and subsequent treatments.</p>	<p>gave careful consideration to the differential diagnosis in children presenting with possible GORD. A new recommendation was added (Recommendation 11) to confirm that some symptoms of non-IgE mediated cows' milk protein allergy can be similar to those of GORD, especially in infants with atopic symptoms, signs, and/or a family history and which cross refers the reader to NICE CG 116 'Food allergy in children and young people'. Amendments were also made to Recommendation 5 in Table R1 that lists 'red flag' signs and symptoms that may suggest disorders other than GOR in those with vomiting or regurgitation. A cross reference to NICE CG 116 was added to the symptom/sign of 'Blood in stool' 'Chronic diarrhoea' was added to the gastrointestinal list of signs/symptoms with a cross reference to NICE CG 116. Finally the sign/symptom 'Eczema' was amended and broadened to 'Infants and children with, or at high risk of, atopy' and the suggested action of a 'Trial of milk exclusion' was removed because this clinical recommendation was not made in this GORD guideline. A research recommendation was made however and the research question was amended following stakeholder consultation. This now specifies that a randomised controlled trial should be performed to examine the clinical and</p>

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						cost effectiveness of a hydrolysed formula trial in formula fed infants with frequent regurgitation associated with marked distress (Section 5.2.8).
babyREFLUX	9	Full	161	22	<p>The GDG noted that there would be no benefit in offering an alginate for any reason beyond where regurgitation is problematic and would not be adequately treated with conservative management options and parental advice.</p> <p>We believe the evidence suggests that offering the alginate is purely a placebo treatment. This we feel is less effective than positional management (keeping upright after feeding etc.), changing feeding technique and offering parental coping strategies.</p> <p>By offering the alginate as a placebo there are substantial cost implications to the NHS.</p>	<p>Thank you for your comment. The reply is divided in to 3 parts.</p> <p>(1) Our conclusions are slightly more detailed than the stakeholder's comment and are contained in recommendations 25-28 as well as the evidence to recommendation section of the full guideline.</p> <p>(2) We assume that the stakeholder is postulating a placebo effect for the parent. In respect of the effectiveness of alginates, we agree that the evidence in favour is relatively weak but emphasize that the recommended trial is for 1-2 weeks only with a continuation only if successful.</p> <p>(3) We were not aware of any RCTs comparing infants in the positions described with other standard positions. Neither were we aware of other evidence nor have personal experience to recommend any particular positions at different times of day for infants. A more detailed explanation of the reasoning behind our single unambiguous (position) recommendation is made in the full guideline. Like the American Academy for Pediatrics, we recommend that positional management should not be used as a treatment for GOR in sleeping infants because any potential</p>

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						small individual benefit would almost certainly be outweighed by the very real risk of SIDS in the individual and would quite possibly pose a risk to the much larger population of well infants with normal regurgitation and mild physiological GOR were this dangerous practice to become widespread once again.
babyREFLUX	5	Full	182	15	<p>Medication</p> <p>Prescribing H2RA and PPIs to children has reached epidemic proportions and we fully agree with the goal of the guideline to reduce medication to reflux sufferers in general.</p> <p>However, we are extremely concerned that considering a 4-week trial of an H2RA or a PPI for infants with the following...</p> <ul style="list-style-type: none"> • overt regurgitation • unexplained feeding difficulties • distressed behaviour <p>...will open the floods gates for prescriptions.</p> <p>As per the previous comment regarding internet campaigns, forum threads and advice pages advising the parent to take their child to A & E – the same sources are encouraging parents to quote:</p> <ul style="list-style-type: none"> • overt regurgitation • unexplained feeding difficulties • distressed behaviour 	<p>Thank you for your comment. Recommendation 29 makes it clear that H2RA and PPIs should not be used to treat overt regurgitation in isolation. Recommendation 30 recommends that consideration be given to a trial of one of these acid suppressing agents in infants with overt regurgitation and either unexplained feeding difficulties, distressed behaviour or faltering growth. The term consider is used to take account of the limitations of supporting evidence for this action. However we were concerned that without this recommendation infants with oesophagitis may go untreated for a prolonged period. Investigation of all such infants by endoscopy (the definitive investigation for oesophagitis) would be a huge change in practice and carry its own disadvantages. By stipulating a 4 week trial with a review we intended to avoid ineffective, long term treatment.</p>

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					<p>...to 'guarantee' them medication.</p> <p>'Clued up' parents will suggest this is what their infants have irrespectively of the reality of their children's ailments.</p>	
Breastfeeding Network	2	NICE	General		<p>BfN welcomes the opportunity to comment on this guideline. The Breastfeeding Network works in some of the most socially and economically deprived areas of the UK, focussing on young parents and communities.</p> <p>We run 17 breastfeeding peer support projects offering a range of independent support to Mums and families from antenatal through to post birth and beyond. We also support Mums through our helplines including National Breastfeeding Helpline in association with ABM, Drugs in Breastmilk Line and a number of minority language lines.</p> <p>There seems to be a high awareness of reflux with the families we work with so we are pleased to see non-drug interventions included. We think this needs reframed as possetting now not seen as normal</p> <p>Can there be a recommendation for mothers who are breastfeeding to contact a skilled breastfeeding supporter as there are techniques for feeding a baby with reflux eg - assessing and improving attachment to reduce oversupply with associated rapid let down / fast milk flow - feeding in a more upright or laid back position.</p>	<p>Thank you for your comments. We have revised the recommendations for the breastfed infant with troublesome regurgitation and distress to include a feeding assessment at an early stage (Recommendations 1.2.2. and 1.2.4). One of the aims in producing this guidance is to reduce any unnecessary prescribing. The guidance is intended to support all health care professionals in listening to parent's concerns and equipping them to respond appropriately. We agreed that thickeners should not be used as a first line of treatment for babies with GORD. A recommendation to use medical formulas was not made and specific advice was made with regard to the limited role of drug therapy. Babies can regurgitate/reflux from birth, due to the relative ease with which stomach contents can move back into the oesophagus. The definition of GORD used in the guideline is reflux causing significant symptoms, which can occur in young infants.</p>

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					<p>Mothers of babies with reflux often need long term support and could be signposted to their nearest breastfeeding drop-in via the Children's Centres</p> <p>Our experience is that drugs/thickeners/specialised formulae are prescribed too soon and can be a response to the parent's distress at coping with a crying baby rather than specific symptoms of reflux. Or the GP's distress at not being able to offer anything other than a prescription?</p> <p>Can a term healthy baby really have GORD at 5 days old?</p>	
Breastfeeding Network	3	NICE	3		<p>We welcome the explanation of uncertainty in differentiating GOR from GORD and how the terms are used interchangeably by health professionals and parents alike.</p> <p>Could the guidance emphasise the importance of avoiding unnecessarily labelling infants with a diagnosis? At the recent Overdiagnosis conference I (PB) heard Laura Scherer present her study on 'Influence of "GERD" Label on Parents' Decision to Medicate Infants'. Parents appear to be keener to opt for medicines when they were given a label for reflux.</p> <p>Scherer LD, et al (2013) Influence of "GERD" Label on Parents' Decision to Medicate Infants Pediatrics. 2013 May;131(5):839-45. doi: 10.1542/peds.2012-3070. Epub 2013 Apr 1</p>	<p>Thank you for your comment.</p> <p>We agree that it is important to make a distinction between GOR (usually a benign transient condition in infants) and GORD (a disease requiring management). The guideline does emphasise the features that are reassuring and indicate GOR as well as those that justify a diagnosis of GORD. We fully agree that incorrectly labelling a child with the diagnosis of GORD is likely to result in inappropriate medicalisation. Recommendation 1.1.2 states that a small proportion of infants with GOR have associated distress or complications requiring clinical management and these are considered in this guideline to have GORD.</p>

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					This guideline has great potential to explain to parents that normality of possetting and crying in infants and help to keep the treatments for those who need it.	
Breastfeeding Network	4	NICE	8 -9 &12		The list of symptoms include haematemesis and melaena. It would be worth including a note to alert health professionals to the possibility that breastfed babies can vomit blood and occasionally, if severe, pass black stools when ingesting blood from their mothers cracked nipples.	Thank you for your comment. We have amended Table 1 within recommendation 1.1.5 and recommendation 1.1.20 to accommodate your point regarding the possibility of blood being swallowed. It specifically mentions the possibility of swallowed blood as an explanation in the breast-fed infant. We were not persuaded that GORD causes melaena with any frequency. Melaena would indicate a serious upper gastrointestinal haemorrhage or the swallowing of a large volume of blood. We did not therefore make reference to it in this context. We believe children with blood in the stool including melaena require specialist referral.
Breastfeeding Network	5	NICE	17 Treatment options		<p>We think the stepped approach to treatments is clear and like the considerations given for breastfeeding mothers.</p> <p>We are not able to check the appraisals of the studies in the time available although we note that in the full document the effectiveness of the interventions seem to be rated more positively than the available Cochrane reviews.</p> <p>It would be worth considering the reasons for differences between these assessments as parents we are in contact with doubt the effectiveness of the alginate medicine. It is also</p>	<p>Thank you for your comment. With regard to Gaviscon Infant, we reviewed trial evidence that persuaded them that there was potential efficacy. There is a recognised technique for using Gaviscon in the breastfed baby and we decided that this at least made it feasible (See Appendix J).</p> <p>With regard to ranitidine and its palatability we recommended that when considering which acid suppressing drug to choose, consideration be given to the available</p>

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					<p>very difficult to give to a breastfed baby. Mothers also report side effects such as constipation.</p> <p>We have reports that the alcohol in ranitidine makes it taste horrible – dilutions are also expensive.</p> <p>At the recent Overdiagnosis conference the NNH for Protein Pump Inhibitors was said to be 4 for gastroenteritis. I will try to track down the reference.</p> <p>Feed thickener for newborn infants with gastro-oesophageal reflux Huang R-C et al There is no evidence from randomised controlled trials to support or refute the efficacy of feed thickeners in newborn infants with GOR. Given the absence of evidence, we cannot recommend using thickening agents for management of GOR in newborn infants.</p> <p>Gastro-oesophageal reflux treatment for prolonged non-specific cough in children and adults Chang AB et al Not effective for cough associated with GORD symptoms in very young children (including infants)</p>	<p>preparations and their suitability for the individual child (Recommendation 1.3.5).</p> <p>Trial evidence for feed thickeners was also considered and there was evidence to support their use as detailed in the full guideline.</p> <p>With respect to the references you mention, there were no relevant RCTs included in the Huang systematic review although relevant individual (paediatric) studies from the Chang review were included in the guideline.</p>
Breastfeeding Network	6	NICE	19		<p>We welcome the recommendation to test the efficacy of avoiding cows milk protein – this should be tested for dietary avoidance in breastfeeding as well as infant formula. Anecdotally symptoms seem worse with a high</p>	<p>Thank you for your comment. We have responded in relation to the points raised in the 5 paragraphs in your comment. (1) The research question was</p>

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			Research recommendations		<p>dairy diet.</p> <p>Now we understand more about the importance of relationship building the standard practice of giving a small number of large feeds of infant formula seems out-dated.</p> <p>We understand the instructions on packets of formula originate from recommendations dating back to the COMA reports. Can NICE recommend SACN MCN committee to look at this?</p> <p>Parents often give very large feeds without being aware that this is not desirable. One mother on the helpline had given her 2 week old baby approx. 300ml in one go and was wondering why he was crying. So this could help all families pace the amount of feed in a bottle with the potential to reduce the incidence of reflux.</p> <p>There seems to be an association between reflux and tongue-tie. Could this be investigated? Is it because the restricted tongue movements affect peristalsis? Or is the mechanism more to do with oversupply and a forceful let-down which also seems to happen with tongue-tie?</p>	<p>amended following stakeholder consultation. This now specifies that a randomised controlled trial should be performed to examine the clinical and cost effectiveness of a hydrolysed formula trial in formula fed infants with frequent regurgitation associated with marked distress. Following discussion we did not make an amendment to recommend research of a trial of maternal dietary cows' milk protein exclusion. This was because it cannot be assumed that maternal milk consumption is causative.</p> <p>(2 and 4) A key recommendation for priority implementation was made in support of a trial of smaller, more frequent feeds in formula fed infants with frequent regurgitation associated with marked distress (Recommendation 1.2.3).</p> <p>(3) We are not in the position to make recommendations to the SACN MCN committee.</p> <p>(5) Research into the association between reflux and tongue-tie was not recommended.</p>
British Medical Association (Clinical Prescribing	1	Full	General		We are pleased that previous BMA comments have been taken on board, and that there is a differentiation between infants, children and older children.	Thank you for your comment.

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Subcommittee)						
British Medical Association (Clinical Prescribing Subcommittee)	2	Full	General		GPs cannot offer contrast (GI) investigations. The same restrictions apply to pH testing and enteral feeding. It should be specified that this is aimed at secondary care.	Thank you for this comment. This is up to the local arrangements / organisation of the skill set across the region or clinical network. Where the guideline refers to a specialist, refers to a paediatrician with the skills, experience and competency necessary to deal with the particular clinical concern that has been identified by the referring health care professional. In this guideline this is most likely to be a consultant general paediatrician. Depending on the clinical circumstances, 'specialist' may also refer to a paediatric surgeon, paediatric gastroenterologist or a doctor with the equivalent skills and competency. When an investigation is advocated it is mentioned to help inform the health care professional as to why they may be making the referral and what the parent and child might reasonably expect. It is not considered that health care professionals in primary care need to be advised about what they can and cannot arrange (directly) themselves.
British Society for Allergy and Clinical Immunology	1	Full	General	General	The recommendations are based across all age ranges whereas reflux in infants may require a different approach than in a teenager for example.	Thank you for your comment. The scope of this guidelines states that it will cover all children from birth to 18 years of age. We are aware that this range covers a variety of different stages of maturity and development

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						from the young infant through to the young adult. Subgroup analyses by age were not performed in the evidence reviews, however considerable care has been taken in the structure and presentation of the recommendations to cover the entire population of children and to construct a logical approach that is helpful and easy to use. Additionally for clarification, please refer to the glossary where terms for infant, child and young person are defined.
British Society for Allergy and Clinical Immunology	29	Full	General	General	<p>The research studies are those mainly based on reflux as a symptom / disease in its own right but often included in the overall work up of allergic patients and studies relating to these would therefore not be included in the review process ie some key papers / guidance missing.</p> <p>Symptoms of the reflux described by carers of children with allergic disease may not be included and may be relevant.</p>	<p>Thank you for your comment. For this guideline, GORD refers to a variety of defined clinical and pathological entities as defined in the glossary and the evidence reviews for were performed according to the associated research protocols (See appendices). Studies using other research designs, different populations and different outcomes were not included. Studies performed on children who have been considered a priori to have some form of food allergy, and who might therefore had a range of symptoms, would not have been appropriate to the aims of this guideline. The aim of the evidence reviews here was to identify effective treatments for children with specific forms of GORD, for example very troublesome overt regurgitation.</p> <p>Following stakeholder consultation, we gave careful consideration to the</p>

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						<p>differential diagnosis in children presenting with possible GORD. A new recommendation was added (Recommendation 11) to confirm that some symptoms of non-IgE mediated cows' milk protein allergy can be similar to those of GORD, especially in infants with atopic symptoms, signs, and/or a family history and which cross refers the reader to NICE CG 116 'Food allergy in children and young people'. Amendments were also made to Recommendation 5 in Table R1 that lists 'red flag' signs and symptoms that may suggest disorders other than GOR in those with vomiting or regurgitation. A cross reference to NICE CG 116 was added to the symptom/sign of 'Blood in stool' 'Chronic diarrhoea' was added to the gastrointestinal list of signs/symptoms with a cross reference to NICE CG 116. Finally the sign/symptom 'Eczema' was amended and broadened to 'Infants and children with, or at high risk of, atopy' and the suggested action of a 'Trial of milk exclusion' was removed because this clinical recommendation was not made in this GORD guideline. A research recommendation was made however and the research question was amended following stakeholder consultation. This now specifies that a randomised controlled trial should be performed to examine the clinical and cost effectiveness of a hydrolysed</p>

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						formula trial in formula fed infants with frequent regurgitation associated with marked distress (Section 5.2.8). 'Infants with a personal or family history of atopic conditions' are noted as an important population subgroup to consider in such research.
British Society for Allergy and Clinical Immunology	2	Full	18	16	If one of these eg distressed behaviour or feeding difficulties was severe think there needs to be more detail that although you may not investigate or treat as GORD alone causing the symptoms it may be part of a larger set of symptoms where reflux is playing a part and managing the reflux may still be part of the plan even if this management is changing diet. Key priorities for implementation: Do not investigate if only has one of the following : cough, hoarse voice. May a comment be added please "Cough, respiratory difficulty, hoarse voice, change in voice with GOR that in a HIGH RISK child that IgE mediated cow's milk allergy & anaphylaxis be excluded".	Thank you for your comment. Recommendation 5 with its 'red flag' table now highlights additional gastrointestinal manifestations which if present in an infant with overt regurgitation might suggest alternative conditions including allergy. The food allergy guideline (CG116) is signposted here. This guideline focuses on the diagnosis and management of GORD as defined in the glossary. The features listed in the recommendation were derived from a review of evidence for those specific manifestations
British Society for Allergy and Clinical Immunology	3	Full	18	36	Feeding aversion and regurgitation may be part of a food allergy picture so consider looking at dietary changes, even at prim care level and then dietitian not necessarily needing paediatrician	Thank you for your comment. This is a guideline on GORD in children and is not a detailed guideline on non - IgE cell mediated food allergy. However, following stakeholder consultation, we gave careful consideration to the differential diagnosis in children presenting with possible GORD. A new recommendation was added (Recommendation 11) to confirm that some symptoms of non-IgE mediated cows' milk protein allergy can be similar to those of GORD, especially in

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						<p>infants with atopic symptoms, signs, and/or a family history and which cross refers the reader to NICE CG 116 'Food allergy in children and young people'. Amendments were also made to Recommendation 5 in Table R1 that lists 'red flag' signs and symptoms that may suggest disorders other than GOR in those with vomiting or regurgitation. A cross reference to NICE CG 116 was added to the symptom/sign of 'Blood in stool'. 'Chronic diarrhoea' was added to the gastrointestinal list of signs/symptoms with a cross reference to NICE CG 116. Finally the sign/symptom 'Eczema' was amended and broadened to 'Infants and children with, or at high risk of, atopy' and the suggested action of a 'Trial of milk exclusion' was removed because this clinical recommendation was not made in this GORD guideline. A research recommendation was made however and the research question was amended following stakeholder consultation. This now specifies that a randomised controlled trial should be performed to examine the clinical and cost effectiveness of a hydrolysed formula trial in formula fed infants with frequent regurgitation associated with marked distress (Section 5.2.8).</p>
British Society for Allergy and Clinical	4	Full	18	39	As above – may be part of diet related picture and so still consider dietary changes especially if other risk factors – do not all need referring / having to wait for referral before something else	Thank you for your comment. As per the response to your previous comment, a recommendation for a trial of milk exclusion was not made in this

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Immunology					is done. Back arching is frequently seen in infants in prim care and so this could generate excessive referrals.	GORD guideline. A research recommendation was made however and the research question was amended following stakeholder consultation. This now specifies that a randomised controlled trial should be performed to examine the clinical and cost effectiveness of a hydrolysed formula trial in formula fed infants with frequent regurgitation associated with marked distress (Section 5.2.8). Regarding your comment on back arching, this recommendation advises health care professionals to think about referral if back arching is "persistent" or if other features of Sandifer's syndrome are present. The Guideline Development Group (which included significant primary care involvement together with lay representation) did not feel this advice to be unreasonable and do not anticipate a major change in referral patterns.
British Society for Allergy and Clinical Immunology	5	Full	18	40	I would suggest where there are no other risk factors / symptoms / signs to suggest allergy // Formula fed infants – Please may there be a mention that in children HIGH RISK for allergy starting on formula feeds which develop GOR WITH eczema, wheeze, foregut dysmotility that IgE and Non IgE mediated cow's milk allergy & anaphylaxis be excluded". Children may not present with urticaria just GOR.	Thank you for your comment. Following stakeholder consultation, we gave careful consideration to the differential diagnosis in children presenting with possible GORD. A new recommendation was added (Recommendation 11) to confirm that some symptoms of non-IgE mediated cows' milk protein allergy can be similar to those of GORD, especially in infants with atopic symptoms, signs, and/or a family history and which cross

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						refers the reader to NICE CG 116 'Food allergy in children and young people'. Amendments were also made to Recommendation 5 in Table R1 that lists 'red flag' signs and symptoms that may suggest disorders other than GOR in those with vomiting or regurgitation. A cross reference to NICE CG 116 was added to the symptom/sign of 'Blood in stool'. 'Chronic diarrhoea' was added to the gastrointestinal list of signs/symptoms with a cross reference to NICE CG 116. Finally the sign/symptom 'Eczema' was amended and broadened to 'Infants and children with, or at high risk of, atopy' and the suggested action of a 'Trial of milk exclusion' was removed because this clinical recommendation was not made in this GORD guideline. A research recommendation was made however and the research question was amended following stakeholder consultation. This now specifies that a randomised controlled trial should be performed to examine the clinical and cost effectiveness of a hydrolysed formula trial in formula fed infants with frequent regurgitation associated with marked distress (Section 5.2.8). 'Infants with a personal or family history of atopic conditions' are noted as an important population subgroup to consider in such research.
British Society for	6	Full	19	13	Table – frequent vomiting up to 2 months I do not feel should only be referred to paediatric	Thank you for this comment. We respectfully disagree with your

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Allergy and Clinical Immunology					surgeon – look for other features in history or symptoms / signs suggestive of food allergy Unless of course dehydrated etc.	conclusion and in both recommendation 5 (Table 1) and recommendation 19 we are describing symptoms that must alert clinicians to the possibility of hypertrophic pyloric stenosis. Further, in the early stages, infants with this condition will not necessarily appear dehydrated.
British Society for Allergy and Clinical Immunology	7	Full	19	13	Onset after 6 months may relate to dietary changes at this time eg breast to formula or breast to adding in dairy	Thank you for your comment. Following stakeholder consultation, we gave careful consideration to the differential diagnosis in children presenting with possible GORD. A new recommendation was added (Recommendation 11) to confirm that some symptoms of non-IgE mediated cows' milk protein allergy can be similar to those of GORD, especially in infants with atopic symptoms, signs, and/or a family history and which cross refers the reader to NICE CG 116 'Food allergy in children and young people'. Amendments were also made to Recommendation 5 in Table R1 that lists 'red flag' signs and symptoms that may suggest disorders other than GOR in those with vomiting or regurgitation. A cross reference to NICE CG 116 was added to the symptom/sign of 'Blood in stool' 'Chronic diarrhoea' was added to the gastrointestinal list of signs/symptoms with a cross reference to NICE CG 116. Finally the sign/symptom 'Eczema' was amended and broadened to 'Infants and children with, or at high risk of, atopy' and the

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						suggested action of a 'Trial of milk exclusion' was removed because this clinical recommendation was not made in this GORD guideline. A research recommendation was made however and the research question was amended following stakeholder consultation. This now specifies that a randomised controlled trial should be performed to examine the clinical and cost effectiveness of a hydrolysed formula trial in formula fed infants with frequent regurgitation associated with marked distress (Section 5.2.8). Amendments have also been made to the recommendations for breast-fed infants with frequent regurgitation associated with marked distress that breastfeeding should be supported with a breastfeeding assessment/advice (Recommendations 25 and 27).
British Society for Allergy and Clinical Immunology	8	Full	19 Table R1	13 Table line 13	Blood in stool: No mention of CMA or FPIES. Please with comment on eczema however many children with blood in stool or FPIES have NORMAL skin. Blood in stool considered in NICE food allergy as possible dietary related so again if history suggests consider dietary change rather than just referral. Or perhaps add this into the suggestions list but still advise referral	Thank you for your comment. Following stakeholder consultation, we gave careful consideration to the differential diagnosis in children presenting with possible GORD. A new recommendation was added (Recommendation 11) to confirm that some symptoms of non-IgE mediated cows' milk protein allergy can be similar to those of GORD, especially in infants with atopic symptoms, signs, and/or a family history and which cross refers the reader to NICE CG 116 'Food allergy in children and young

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						people'. Amendments were also made to Recommendation 5 in Table R1 that lists 'red flag' signs and symptoms that may suggest disorders other than GOR in those with vomiting or regurgitation. A cross reference to NICE CG 116 was added to the symptom/sign of 'Blood in stool' 'Chronic diarrhoea' was added to the gastrointestinal list of signs/symptoms with a cross reference to NICE CG 116. Finally the sign/symptom 'Eczema' was amended and broadened to 'Infants and children with, or at high risk of, atopy' and the suggested action of a 'Trial of milk exclusion' was removed because this clinical recommendation was not made in this GORD guideline.
British Society for Allergy and Clinical Immunology	9	Full	19	13	Late onset GOR – please may there be a mention that if GOR develops at 6 weeks (mother stops Breast feeding as tired) , 6 months, (breast fed baby starts cow's milk formula in solids) and 9 months (Mother goes to work and stops breast feeding) that these are RED FLAGS for children HIGH RISK for CMA and consider change of milk. IgE and Non IgE mediated allergy and Anaphylaxis needs to be excluded if symptoms severe in HIGH RISK children. Children may not present with urticaria just GOR. Happy with eczema section	Thank you for your comment. Following stakeholder consultation, we gave careful consideration to the differential diagnosis in children presenting with possible GORD. A new recommendation was added (Recommendation 11) to confirm that some symptoms of non-IgE mediated cows' milk protein allergy can be similar to those of GORD, especially in infants with atopic symptoms, signs, and/or a family history and which cross refers the reader to NICE CG 116 'Food allergy in children and young people'. Amendments were also made to Recommendation 5 in Table R1 that lists 'red flag' signs and symptoms that may suggest disorders other than GOR

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						<p>in those with vomiting or regurgitation. A cross reference to NICE CG 116 was added to the symptom/sign of 'Blood in stool' . 'Chronic diarrhoea' was added to the gastrointestinal list of signs/symptoms with a cross reference to NICE CG 116. Finally the sign/symptom 'Eczema' was amended and broadened to 'Infants and children with, or at high risk of, atopy' and the suggested action of a 'Trial of milk exclusion' was removed because this clinical recommendation was not made in this GORD guideline. A research recommendation was made however and the research question was amended following stakeholder consultation. This now specifies that a randomised controlled trial should be performed to examine the clinical and cost effectiveness of a hydrolysed formula trial in formula fed infants with frequent regurgitation associated with marked distress (Section 5.2.8).</p> <p>Amendments have also been made to the recommendations for breast-fed infants with frequent regurgitation associated with marked distress that breastfeeding should be supported with a breastfeeding assessment/advice (Recommendations 25 and 27).</p>
British Society for Allergy and	10	Full	19 Table R1	24 Line 7	Recommendation 24: Consider IgE and Non IgE mediated CMA if a formula feed is started in a child HIGH RISK of	Thank you for your comment. Following stakeholder consultation, we gave careful consideration to the

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Clinical Immunology			4.2		allergy. Please make a comment for all entried of thickeners that the dietician checks that there is no Cows milk protein in the thickener in children HIGH RISK for allergy with GOR. Please state which thickeners.	differential diagnosis in children presenting with possible GORD. A new recommendation was added (Recommendation 11) to confirm that some symptoms of non-IgE mediated cows' milk protein allergy can be similar to those of GORD, especially in infants with atopic symptoms, signs, and/or a family history and which cross refers the reader to NICE CG 116 'Food allergy in children and young people'. Amendments were also made to Recommendation 5 in Table R1 that lists 'red flag' signs and symptoms that may suggest disorders other than GOR in those with vomiting or regurgitation. A cross reference to NICE CG 116 was added to the symptom/sign of 'Blood in stool' 'Chronic diarrhoea' was added to the gastrointestinal list of signs/symptoms with a cross reference to NICE CG 116. Finally the sign/symptom 'Eczema' was amended and broadened to 'Infants and children with, or at high risk of, atopy' and the suggested action of a 'Trial of milk exclusion' was removed because this clinical recommendation was not made in this GORD guideline and hence does not give guidance on strategies to avoid cows' milk – in thickeners or otherwise.
British Society for Allergy and Clinical	11	Full	19 Table R1	25 Line 9	Recommendation 24: If breast fed child with GOR may we add “ in a child HIGH RISK for allergy that the mother has a trial of exclusion of CM for 6 weeks and re-	Thank you for your comment. Following stakeholder consultation, we gave careful consideration to the differential diagnosis in children

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Immunology					introduction tried only if IgE mediated allergy and anaphylaxis is excluded.	<p>presenting with possible GORD. A new recommendation was added (Recommendation 11) to confirm that some symptoms of non-IgE mediated cows' milk protein allergy can be similar to those of GORD, especially in infants with atopic symptoms, signs, and/or a family history and which cross refers the reader to NICE CG 116 'Food allergy in children and young people'. Amendments were also made to Recommendation 5 in Table R1 that lists 'red flag' signs and symptoms that may suggest disorders other than GOR in those with vomiting or regurgitation. A cross reference to NICE CG 116 was added to the symptom/sign of 'Blood in stool' 'Chronic diarrhoea' was added to the gastrointestinal list of signs/symptoms with a cross reference to NICE CG 116. Finally the sign/symptom 'Eczema' was amended and broadened to 'Infants and children with, or at high risk of, atopy' and the suggested action of a 'Trial of milk exclusion' was removed because this clinical recommendation was not made in this GORD guideline.</p> <p>We considered that trial of maternal dietary cows' milk exclusion would be complex in that it could not be assumed that maternal milk consumption was causative and neither a clinical nor a research recommendation was made for this.</p>

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British Society for Allergy and Clinical Immunology	12	Full	19 Table R1	26 Line 13	Recommendation 26: Please mention to ensure the thickeners do not contain Cows Milk Protein in the HIGH RISK allergic child.	Thank you for your comment. This guideline does not advocate the use of cows' milk exclusion in the treatment of GORD in any of its manifestations. It does not therefore give guidance on strategies to avoid cows' milk – in thickeners or otherwise.
British Society for Allergy and Clinical Immunology	13	Full	21 -25	General	There appears to be no recommendation regarding avoidance of constipation and active treatment thereof as per http://cks.nice.org.uk/gord-in-children#!diagnosis and Sutphen, 2001. Is it colic or is it gastroesophageal reflux? <i>J Pediatr Gastro Nutr</i> , 33 (2) : 110-111	Thank you for your comment. We agree that children with constipation might need management. However, we did not review evidence on the role of constipation precipitating GORD.
British Society for Allergy and Clinical Immunology	14	Full	21	27-28	Add in other features from nice 116 suggestive of food allergy eg 'loose or mucousy stools, constipation in infancy or other gi symptoms, atopic conditions e.g. eczema in infancy', resp	Thank you for your comment. Following stakeholder consultation, we gave careful consideration to the differential diagnosis in children presenting with possible GORD. A new recommendation was added (Recommendation 11) to confirm that some symptoms of non-IgE mediated cows' milk protein allergy can be similar to those of GORD, especially in infants with atopic symptoms, signs, and/or a family history and which cross refers the reader to NICE CG 116 'Food allergy in children and young people'. Amendments were also made to Recommendation 5 in Table R1 that lists 'red flag' signs and symptoms that may suggest disorders other than GOR in those with vomiting or regurgitation. A cross reference to NICE CG 116 was added to the symptom/sign of 'Blood in stool' 'Chronic diarrhoea' was added to

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						the gastrointestinal list of signs/symptoms with a cross reference to NICE CG 116. Finally the sign/symptom 'Eczema' was amended and broadened to 'Infants and children with, or at high risk of, atopy' and the suggested action of a 'Trial of milk exclusion' was removed because this clinical recommendation was not made in this GORD guideline.
British Society for Allergy and Clinical Immunology	15	Full	23	1-3	Forceful/ projectile vomiting in infants from birth can be due to cow's milk allergy (CMA). Surely not every child with projectile vomiting is going to need urgent referral for pyloric stenosis? Allergy focused clinical hx as per NICE CG116 should help in differential diagnosis.	Thank you for your comment. Following stakeholder consultation, we gave careful consideration to the differential diagnosis in children presenting with possible GORD. A new recommendation was added (Recommendation 11) to confirm that some symptoms of non-IgE mediated cows' milk protein allergy can be similar to those of GORD, especially in infants with atopic symptoms, signs, and/or a family history and which cross refers the reader to NICE CG 116 'Food allergy in children and young people'. Amendments were also made to Recommendation 5 in Table R1 that lists 'red flag' signs and symptoms that may suggest disorders other than GOR in those with vomiting or regurgitation. A cross reference to NICE CG 116 was added to the symptom/sign of 'Blood in stool'. 'Chronic diarrhoea' was added to the gastrointestinal list of signs/symptoms with a cross reference to NICE CG 116. Finally the sign/symptom 'Eczema' was amended

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						<p>and broadened to 'Infants and children with, or at high risk of, atopy' and the suggested action of a 'Trial of milk exclusion' was removed because this clinical recommendation was not made in this GORD guideline.</p> <p>An amendment was not made to the symptom/sign of 'Frequent, forceful (projectile) vomiting' because this symptom in an infant up to 2 months old is a 'red flag' that must alert clinicians to the possibility of hypertrophic pyloric stenosis. "</p>
British Society for Allergy and Clinical Immunology	16	Full	23	18	Not all progressively worsening vomiting I feel requires same day appt – may be gastric out flow obstruction related to cos milk allergy. How do you define progressively worsening as this could be a lot of referrals.	Thank you for your comment. In this recommendation we are referring to young infants and believe that an urgent referral is needed for consideration of congenital hypertrophic pyloric stenosis.
British Society for Allergy and Clinical Immunology	17	Full	23	4-18	As per NASPGHAN/ ESPGHAN GOR guidelines, 2009 infants with faltering growth and recurrent vomiting (6.1.2) and unexplained distress for which GOR is not a common cause (6.1.3) may benefit from a 2 week trial on a hypoallergenic formula to exclude CMA. Feeding aversion, melaena and iron deficiency as per NICE CG116 are also symptoms of possible CMA. Therefore these groups of children do not necessarily warrant referral for endoscopy/ biopsies until this has been ruled out, starting with an allergy focused clinical hx.	Thank you for your comment. Following stakeholder consultation, we gave careful consideration to the differential diagnosis in children presenting with possible GORD. A new recommendation was added (Recommendation 11) to confirm that some symptoms of non-IgE mediated cows' milk protein allergy can be similar to those of GORD, especially in infants with atopic symptoms, signs, and/or a family history and which cross refers the reader to NICE CG 116 'Food allergy in children and young people'. Amendments were also made to Recommendation 5 in Table R1 that

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						lists 'red flag' signs and symptoms that may suggest disorders other than GOR in those with vomiting or regurgitation. A cross reference to NICE CG 116 was added to the symptom/sign of 'Blood in stool'. 'Chronic diarrhoea' was added to the gastrointestinal list of signs/symptoms with a cross reference to NICE CG 116. Finally the sign/symptom 'Eczema' was amended and broadened to 'Infants and children with, or at high risk of, atopy' and the suggested action of a 'Trial of milk exclusion' was removed because this clinical recommendation was not made in this GORD guideline. A research recommendation was made however and the research question was amended following stakeholder consultation. This now specifies that a randomised controlled trial should be performed to examine the clinical and cost effectiveness of a hydrolysed formula trial in formula fed infants with frequent regurgitation associated with marked distress (Section 5.2.8).
British Society for Allergy and Clinical Immunology	18	Full	23	25	Again of resp and gi symptoms consider allergy not ph study and in allergy related "reflux" as ph studies often neg then it may be considered no problem if tests are negative but does not rule out there is a significant problem.	Thank you for your comment. Recommendation 5 with its accompanying 'red flag' Table R1 highlights the fact that certain symptoms including various gastrointestinal symptoms may suggest alternative diagnoses including food allergy, and NICE CG116 'Food allergy in children and young people' is signposted there. The

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						indications for performing a pH study are addressed in other recommendations.
British Society for Allergy and Clinical Immunology	19	Full	23	33-37	Are UTI's a more common cause of faltering growth and frequent regurgitation and distress than CMA in young infants? We think not, but probably in older infants and children – should specify.	Thank you for this comment. We decided that UTIs are an important consideration in the differential diagnosis of infants who present with regurgitation and other symptoms as outlined in recommendation 23. Further, tests to exclude a UTI are relatively simple in primary or secondary care and we consider that missing the diagnosis of a UTI in an infant can have important acute and long-term consequences.
British Society for Allergy and Clinical Immunology	20	Full	24	9-12	Perhaps breast fed infants should be considered expressed milk and thickener e.g carob as an alternative to a sodium laden alginate, or I would prefer to see consider dietary manipulation for mother. Before considering an other management if there is a positive allergic history. Consider to give the option?	Thank you for your comment. The possibility of thickening expressed breast milk was deliberated, but was considered impractical. However the process for adding Gaviscon Infant to a small volume of cooled boiled water is well described (see Appendix J.1 of the full guideline) and was considered a worthwhile strategy following a review of the evidence (see Section 5.3.6 of the Full Guideline) The evidence review did not find evidence to support the efficacy of maternal dietary manipulation in the breast-fed child with GORD.

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British Society for Allergy and Clinical Immunology	21	Full	24	28	Would this be a GP role or only sec care following referral	Thank you for your comment. The recommendation on a clinical trial of acid suppression is not only for primary care. Many general paediatricians are faced with such children and could implement these recommendations. Recommendation 32 is advising the GP or paediatrician to refer for specialist assessment if the trial doesn't resolve the problem.
British Society for Allergy and Clinical Immunology	23	Full	25 -26	table	As prev – add in more weight to symptoms / signs and history suggestive of allergy Red flags: Projectile vomiting – rule out possible CMA as per NICE CG116 Blood in stool could be due to CMA - as per NICE CG116 Abdominal distension could be due to CMA - as per NICE CG116 Loose and/ or offensive stools/ diarrhoea, mucus in stools, or constipation in early infancy could be due to CMA - as per NICE CG116 & CKS: http://cks.nice.org.uk/gord-in-children#!diagnosissub:1 Faltering growth could be due to CMA - as per NICE CG116 Eczema – this needs to be more specific and should state moderate to severe eczema in infants under 6 months of age could be due to CMA as per NICE CG116 and CG57. Specialist referral is not necessary as CG116 encourages primary care to undertake exclusion trial	Thank you for your comment. Following stakeholder consultation, we gave careful consideration to the differential diagnosis in children presenting with possible GORD. A new recommendation was added (Recommendation 11) to confirm that some symptoms of non-IgE mediated cows' milk protein allergy can be similar to those of GORD, especially in infants with atopic symptoms, signs, and/or a family history and which cross refers the reader to NICE CG 116 'Food allergy in children and young people'. Amendments were also made to Recommendation 5 in Table R1 that lists 'red flag' signs and symptoms that may suggest disorders other than GOR in those with vomiting or regurgitation. A cross reference to NICE CG 116 was added to the symptom/sign of 'Blood in stool'. 'Chronic diarrhoea' was added to the gastrointestinal list of signs/symptoms with a cross reference to NICE CG 116. Finally the sign/symptom 'Eczema' was amended

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						and broadened to 'Infants and children with, or at high risk of, atopy' and the suggested action of a 'Trial of milk exclusion' was removed because this clinical recommendation was not made in this GORD guideline. A research recommendation was made however and the research question was amended following stakeholder consultation. This now specifies that a randomised controlled trial should be performed to examine the clinical and cost effectiveness of a hydrolysed formula trial in formula fed infants with frequent regurgitation associated with marked distress (Section 5.2.8).
British Society for Allergy and Clinical Immunology	22	Full	25	18	? include biopsies with staining for EE	Thank you for this comment. This is a guideline on GORD in children and a detailed set of instructions for the endoscopist is beyond the guideline's remit.
British Society for Allergy and Clinical Immunology	24	Full	27 4.3	5	Agree with research, essential and thank you	Thank you for your comment. Following stakeholder consultation, the research question within this research recommendation was amended. This now specifies that a randomised controlled trial should be performed to examine the clinical and cost effectiveness of a hydrolysed formula trial in formula fed infants with frequent regurgitation associated with marked distress.
British Society for Allergy and Clinical	25	Full	28 4.4 Box A	1	GORD recog & diagnosis Consider CMA IgE and Non IgE in a child HIGH RISK of allergy (ie both parents atopic) when presenting with eczema, foregut	Thank you for your comment. Following stakeholder consultation, we gave careful consideration to the differential diagnosis in children

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Immunology					dysmotility and wheeze with GOR NICE and RCPCH and MAP guidelines	presenting with possible GORD. A new recommendation was added (Recommendation 11) to confirm that some symptoms of non-IgE mediated cows' milk protein allergy can be similar to those of GORD, especially in infants with atopic symptoms, signs, and/or a family history and which cross refers the reader to NICE CG 116 'Food allergy in children and young people'. Amendments were also made to Recommendation 5 in Table R1 that lists 'red flag' signs and symptoms that may suggest disorders other than GOR in those with vomiting or regurgitation. A cross reference to NICE CG 116 was added to the symptom/sign of 'Blood in stool'. 'Chronic diarrhoea' was added to the gastrointestinal list of signs/symptoms with a cross reference to NICE CG 116. Finally the sign/symptom 'Eczema' was amended and broadened to 'Infants and children with, or at high risk of, atopy' and the suggested action of a 'Trial of milk exclusion' was removed because this clinical recommendation was not made in this GORD guideline.
British Society for Allergy and Clinical Immunology	26	Full	28 4.4 Box A	1	GOR suggesting other diagnoses Asthma and GORD Please may we mention that wheeze and asthma in a HIGH RISK allergic child (ie both parents atopic) may be associated with CMA and GOR Anaphylaxis to be excluded with Food allergy	Thank you for your comment. Following stakeholder consultation, we gave careful consideration to the differential diagnosis in children presenting with possible GORD. A new recommendation was added (Recommendation 11) to confirm that some symptoms of non-IgE mediated

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						cows' milk protein allergy can be similar to those of GORD, especially in infants with atopic symptoms, signs, and/or a family history and which cross refers the reader to NICE CG 116 'Food allergy in children and young people'. Amendments were also made to Recommendation 5 in Table R1 that lists 'red flag' signs and symptoms that may suggest disorders other than GOR in those with vomiting or regurgitation. A cross reference to NICE CG 116 was added to the symptom/sign of 'Blood in stool'. 'Chronic diarrhoea' was added to the gastrointestinal list of signs/symptoms with a cross reference to NICE CG 116. Finally the sign/symptom 'Eczema' was amended and broadened to 'Infants and children with, or at high risk of, atopy' and the suggested action of a 'Trial of milk exclusion' was removed because this clinical recommendation was not made in this GORD guideline.
British Society for Allergy and Clinical Immunology	27	Full	31 4.4 Box B	2	Investigations Please consider in the HIGH RISK atopic child with eczema, foregut dysmotility (GOR) hindgut dysmotility (diarrhoea constipation) and wheeze with GOR an allergy review to exclude IgE and Non IgE mediated allergy. A change in formula often reports in resolution of wheeze, eczema and dysmotility NICE and RCPCH and MAP guidelines Tests to consider in the HIGH RISK allergic child, SPT, Specific IgE, patch tests and tryptase. All under review as per NICE, BSACI,	Thank you for your comment. Following stakeholder consultation, we gave careful consideration to the differential diagnosis in children presenting with possible GORD. A new recommendation was added (Recommendation 11) to confirm that some symptoms of non-IgE mediated cows' milk protein allergy can be similar to those of GORD, especially in infants with atopic symptoms, signs, and/or a family history and which cross

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					RCPCH (MAP) and EACCI guidelines	refers the reader to NICE CG 116 'Food allergy in children and young people'. Amendments were also made to Recommendation 5 in Table R1 that lists 'red flag' signs and symptoms that may suggest disorders other than GOR in those with vomiting or regurgitation. A cross reference to NICE CG 116 was added to the symptom/sign of 'Blood in stool' 'Chronic diarrhoea' was added to the gastrointestinal list of signs/symptoms with a cross reference to NICE CG 116. Finally the sign/symptom 'Eczema' was amended and broadened to 'Infants and children with, or at high risk of, atopy' and the suggested action of a 'Trial of milk exclusion' was removed because this clinical recommendation was not made in this GORD guideline. A research recommendation was made however and the research question was amended following stakeholder consultation. This now specifies that a randomised controlled trial should be performed to examine the clinical and cost effectiveness of a hydrolysed formula trial in formula fed infants with frequent regurgitation associated with marked distress (Section 5.2.8).
British Society for Allergy and Clinical Immunology	28	Full	32	Box c	Please mention the exclusion of IgE or Non IgE mediated food allergy in management as per NICE, BSACI, RCPCH (MAP) and EACCI guidelines	Thank you for your comment. Following stakeholder consultation, we gave careful consideration to the differential diagnosis in children presenting with possible GORD. A new recommendation was added

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						(Recommendation 11) to confirm that some symptoms of non-IgE mediated cows' milk protein allergy can be similar to those of GORD, especially in infants with atopic symptoms, signs, and/or a family history and which cross refers the reader to NICE CG 116 'Food allergy in children and young people'. Amendments were also made to Recommendation 5 in Table R1 that lists 'red flag' signs and symptoms that may suggest disorders other than GOR in those with vomiting or regurgitation. A cross reference to NICE CG 116 was added to the symptom/sign of 'Blood in stool'. 'Chronic diarrhoea' was added to the gastrointestinal list of signs/symptoms with a cross reference to NICE CG 116. Finally the sign/symptom 'Eczema' was amended and broadened to 'Infants and children with, or at high risk of, atopy' and the suggested action of a 'Trial of milk exclusion' was removed because this clinical recommendation was not made in this GORD guideline.
British Society for Allergy and Clinical Immunology	30	Full	141		There are more cows milk allergy studies but on general sx not just reflux	Thank you for your comment. The review to which you refer was limited to trials based evidence that addressed the outcomes stipulated in the associated research protocol. Studies using other research designs, different populations and different outcomes were not included.
British Society for	31	Full	143		Health benefits and resources	Thank you for these comments. (1) This is a guideline on GORD in

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Allergy and Clinical Immunology			6.2.6.2		<p>Please state that in the field of allergy that further research and review required for all the reasons you have stated above: cost, efficacy and resolution of symptoms. EBM required urgently.</p> <p>Quality of evidence</p> <p>No mention on any of the allergy guidelines NICE, BSACI, RCPCH (MAP) and EACCI guidelines</p> <p>Clinical experience Little comment on allergy overall. There is much clinical experience as per NICE, BSACI, RCPCH (MAP) and EACCI guidelines. No mention of the HIGH RISK allergic child presenting with GOR, eczema, FTT, dysmotility, wheeze and distress. No mention of FPIES? Very topical and a comment on severe delayed vomiting may warrant a comment as a differential diagnosis. A comment again on a trial of an exclusion diet as per RCPCH guidelines.</p>	children. It is not a detailed guideline on non - IgE cell mediated food allergy. In response to this and other stakeholder comments we have revised the red flags table and also added a new recommendation 11 which links to other more specific NICE guidance on this topic. (2) We have also modified one of our research recommendations.
British Society for Allergy and Clinical Immunology	32	Full	144 -145	6.2.6.2.3	<p>Evidence to support the role of CMA and GORD: Farahmand et al, 2011 demonstrated 1/3rd their kids with GOR had CMA http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3166669/ Cavataio et al, 2000. Summarise the findings of a number of their studies, suggesting CMA is present in up to 42% of those with GOR NICE CG116 GDG expert consensus believes GOR can be commonly caused by CMA. CMA should be suspected in infants with a</p>	<p>Thank you for your comment. Following stakeholder consultation, we gave careful consideration to the differential diagnosis in children presenting with possible GORD. Reference to a 'placebo' effect was removed from the section to which you refer. A new recommendation was added (Recommendation 11) to confirm that some symptoms of non-IgE mediated cows' milk protein allergy</p>

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					<p>number of symptoms in keeping with those listed in CG116, determined by undertaking an allergy focused clinical hx. These symptoms should be listed as red flags to enable differential diagnosis.</p> <p>The lack of adherence to the NICE allergy guidelines are likely to result in inappropriate prescribing of formula, lack of re-challenging to confirm diagnosis which would rule out the 'placebo effect' and lack of follow up/ referral to a dietitian to support ongoing management, review of formula and future re-challenging. Parents tend to be reluctant to use hypoallergenic formula due to their unpleasant smell and taste.</p>	<p>can be similar to those of GORD, especially in infants with atopic symptoms, signs, and/or a family history and which cross refers the reader to NICE CG 116 'Food allergy in children and young people'.</p> <p>Amendments were also made to Recommendation 5 in Table R1 that lists 'red flag' signs and symptoms that may suggest disorders other than GOR in those with vomiting or regurgitation. A cross reference to NICE CG 116 was added to the symptom/sign of 'Blood in stool'. 'Chronic diarrhoea' was added to the gastrointestinal list of signs/symptoms with a cross reference to NICE CG 116. Finally the sign/symptom 'Eczema' was amended and broadened to 'Infants and children with, or at high risk of, atopy' and the suggested action of a 'Trial of milk exclusion' was removed because this clinical recommendation was not made in this GORD guideline. A research recommendation was made however and the research question was amended following stakeholder consultation. This now specifies that a randomised controlled trial should be performed to examine the clinical and cost effectiveness of a hydrolysed formula trial in formula fed infants with frequent regurgitation associated with marked distress (Section 5.2.8). Farahmand et al, 2011 did not meet the inclusion criteria for the review</p>

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						question. It was not a clinical trial and had no comparator/control group. Cavataio et al, 2000 was a narrative review (and not a systematic review) that discussed the main features of cows' milk protein allergy (CMPA) and gastroesophageal reflux (GER). In this review, the authors summarised findings of a number of their studies: lacono et al, 1996; Cavataio et al, 1996 (American Journal of Gastroenterology); and Cavataio et al, 1996 (Archives of Diseases in Childhood). These studies were also assessed for inclusion but none fit the criteria for the review question.
British Society for Allergy and Clinical Immunology	33	Full	145	4	For gdg to consider there is a big placebo effect is nfair without consulting those specialists who advocate this / have seen this as beneficial / parents who have experienced this.	Thank you for your comment. This text has been removed from the evidence to recommendations section which has been more broadly amended following discussion of cows' milk elimination.
British Society for Allergy and Clinical Immunology	34	Full	145	15-18	Hypothesis that reflux settles when diet changed in breast fed infant – this is advocated by allergists and usual practice with allergy dietitians / paediatricians especially when reflux is part of other symptom set.	Thank you for your comment. This is a guideline on GORD in children. It is not a detailed guideline on non - IgE cell mediated food allergy. In response to this and other stake-holder comments we have revised the red flags table and also added a new recommendation (1.1.11) which links to other more specific NICE guidance on this topic.
British Society for Allergy and Clinical Immunology	35	Full	146 6.2.7.1	24 Line 5	Review of allergy history again No mention of the HIGH RISK allergic child presenting with GOR, eczema, FTT, dysmotility, wheeze and distress. CMPA to be excluded.	Thank you for your comment. Following stakeholder consultation, we gave careful consideration to the differential diagnosis in children presenting with possible GORD. A new recommendation was added

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						<p>(Recommendation 11) to confirm that some symptoms of non-IgE mediated cows' milk protein allergy can be similar to those of GORD, especially in infants with atopic symptoms, signs, and/or a family history and which cross refers the reader to NICE CG 116 'Food allergy in children and young people'. Amendments were also made to Recommendation 5 in Table R1 that lists 'red flag' signs and symptoms that may suggest disorders other than GOR in those with vomiting or regurgitation. A cross reference to NICE CG 116 was added to the symptom/sign of 'Blood in stool' 'Chronic diarrhoea' was added to the gastrointestinal list of signs/symptoms with a cross reference to NICE CG 116. Finally the sign/symptom 'Eczema' was amended and broadened to 'Infants and children with, or at high risk of, atopy' and the suggested action of a 'Trial of milk exclusion' was removed because this clinical recommendation was not made in this GORD guideline. A research recommendation was made however and the research question was amended following stakeholder consultation. This now specifies that a randomised controlled trial should be performed to examine the clinical and cost effectiveness of a hydrolysed formula trial in formula fed infants with frequent regurgitation associated with marked distress (Section 5.2.8).</p>

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						'Infants with a personal or family history of atopic conditions' are noted as an important population subgroup to consider in such research.
British Society for Allergy and Clinical Immunology	36	Full	146	6.2.7.2	<p>Cow's milk intolerance is not a term used by NICE CG116 as it does not accurately represent the condition. The term used should be non-IgE mediated cow's milk allergy, as it does involve the immune system and can involve high levels of sensitivity to trace amounts.</p> <p>As per comments 6.2.6.2.3, cow's milk elimination trials should be done in accordance with NICE CG116 which would avoid infants 'being left on formula for prolonged periods'</p> <p>Line 14: No mention of all the allergy guidelines available. It states no evidence. Please review NICE, BSACI, RCPCH (MAP) and EACCI guidelines</p> <p>Thank you again for the comment on the need for research and EBM</p>	Thank you for your comment. We have amended the term used in recommendations to 'non-IgE mediated cows' milk protein allergy'. Following stakeholder consultation, amendments were made to recommendation 11 to improve cross referencing to NICE CG116 but a clinical recommendation for a trial of cows' milk elimination was not made because of the paucity of evidence to support this practice in those with GORD. A research recommendation was made however and the research question was amended following stakeholder consultation. This now specifies that a randomised controlled trial should be performed to examine the clinical and cost effectiveness of a hydrolysed formula trial in formula fed infants with frequent regurgitation associated with marked distress (Section 5.2.8).
British Society for Allergy and Clinical Immunology	37	Full	147	13-15	Comment from dietitian – LW – the sodium content of gaviscon infant is likely to double an infants overall intake and so if the recommended dose is exceeded they can consume above the FSA recommended limit (I don't know re this – JW)	Thank you for this comment. Clearly, as you point out taking any medicine outside the recommended dosage advice could be potentially hazardous. We feel that this guideline may well lead to a net reduction in the use of this medication with a greater emphasis on feed thickeners or other conservative measures.
British	38	Full	158	Whole	Adverse outcomes	Thank you for your comment.

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Society for Allergy and Clinical Immunology			6.3.4.1.3	section	No section at all to mention allergy Mention IgE and Non IgE mediated food allergy to be excluded please	Following stakeholder consultation, we gave careful consideration to the differential diagnosis in children presenting with possible GORD. A new recommendation was added (Recommendation 11) to confirm that some symptoms of non-IgE mediated cows' milk protein allergy can be similar to those of GORD, especially in infants with atopic symptoms, signs, and/or a family history and which cross refers the reader to NICE CG 116 'Food allergy in children and young people'. Amendments were also made to Recommendation 5 in Table R1 that lists 'red flag' signs and symptoms that may suggest disorders other than GOR in those with vomiting or regurgitation. A cross reference to NICE CG 116 was added to the symptom/sign of 'Blood in stool'. 'Chronic diarrhoea' was added to the gastrointestinal list of signs/symptoms with a cross reference to NICE CG 116. Finally the sign/symptom 'Eczema' was amended and broadened to 'Infants and children with, or at high risk of, atopy' and the suggested action of a 'Trial of milk exclusion' was removed because this clinical recommendation was not made in this GORD guideline. A research recommendation was made however and the research question was amended following stakeholder consultation. This now specifies that a randomised controlled trial should be

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						performed to examine the clinical and cost effectiveness of a hydrolysed formula trial in formula fed infants with frequent regurgitation associated with marked distress (Section 5.2.8).
British Society for Allergy and Clinical Immunology	39	Full	158 6.3.4.1.3	Whole section	Adverse outcomes No section at all to mention allergy Mention IgE and Non IgE mediated food allergy please Evidence statements Please mention allergy in differential diagnosis	Thank you for your comment. Following stakeholder consultation, we gave careful consideration to the differential diagnosis in children presenting with possible GORD. A new recommendation was added (Recommendation 11) to confirm that some symptoms of non-IgE mediated cows' milk protein allergy can be similar to those of GORD, especially in infants with atopic symptoms, signs, and/or a family history and which cross refers the reader to NICE CG 116 'Food allergy in children and young people'. Amendments were also made to Recommendation 5 in Table R1 that lists 'red flag' signs and symptoms that may suggest disorders other than GOR in those with vomiting or regurgitation. A cross reference to NICE CG 116 was added to the symptom/sign of 'Blood in stool' 'Chronic diarrhoea' was added to the gastrointestinal list of signs/symptoms with a cross reference to NICE CG 116. Finally the sign/symptom 'Eczema' was amended and broadened to 'Infants and children with, or at high risk of, atopy' and the suggested action of a 'Trial of milk exclusion' was removed because this clinical recommendation was not made

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						in this GORD guideline. A research recommendation was made however and the research question was amended following stakeholder consultation. This now specifies that a randomised controlled trial should be performed to examine the clinical and cost effectiveness of a hydrolysed formula trial in formula fed infants with frequent regurgitation associated with marked distress (Section 5.2.8).
British Society for Allergy and Clinical Immunology	40	Full	159		Little on non acid reflux but this needs a gastro consultant rather than my comment although non acid reflux more commonly seen in allergy	Thank you for your comment. In the definition of GOR we refer to "gastric contents" not "acid" and in what follows we do not believe that the distinction between "acid" and "non acid" is actually explicitly made. This guideline concentrates on clinical problems rather than pre-supposing a diagnosis and it is anticipated that the children with complex problems that may require investigation or different management will be identified by health care professionals in primary and secondary care who apply these recommendations to their clinical practice.
British Society for Allergy and Clinical Immunology	41	Full	176 7.1.4.1.3		In general, very little in the document to direct the reader to IgE or Non IgE mediated allergy if all other causes for GOR have been excluded. As per the RCPCH, EAACI and NICE guidelines in a child HIGH RISK of allergy with IgE allergy or Non IgE allergy (eczema, wheeze, dysmotility or FTT) then a discussion with an allergist would be helpful	Thank you for your comment. Following stakeholder consultation, we gave careful consideration to the differential diagnosis in children presenting with possible GORD. A new recommendation was added (Recommendation 11) to confirm that some symptoms of non-IgE mediated cows' milk protein allergy can be

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						similar to those of GORD, especially in infants with atopic symptoms, signs, and/or a family history and which cross refers the reader to NICE CG 116 'Food allergy in children and young people'. Amendments were also made to Recommendation 5 in Table R1 that lists 'red flag' signs and symptoms that may suggest disorders other than GOR in those with vomiting or regurgitation. A cross reference to NICE CG 116 was added to the symptom/sign of 'Blood in stool' 'Chronic diarrhoea' was added to the gastrointestinal list of signs/symptoms with a cross reference to NICE CG 116. Finally the sign/symptom 'Eczema' was amended and broadened to 'Infants and children with, or at high risk of, atopy' and the suggested action of a 'Trial of milk exclusion' was removed because this clinical recommendation was not made in this GORD guideline. A research recommendation was made however and the research question was amended following stakeholder consultation. This now specifies that a randomised controlled trial should be performed to examine the clinical and cost effectiveness of a hydrolysed formula trial in formula fed infants with frequent regurgitation associated with marked distress (Section 5.2.8).
British Society of Paediatric	1	Full	General	General	Gastroesophageal reflux in children is managed by paediatricians and paediatric gastroenterologists leading to a lot of opinions	Thank you for your comment.

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Gastroenterology, Hepatology and Nutrition					<p>and views about the condition.</p> <p>The NICE guidance should serve to define the condition, helping to identify the severity as well as understand behind mechanisms of the disease leading to appropriate management.</p> <p>A clear distinction is required as to children with disease being managed in the primary, secondary or tertiary care.</p> <p>The concern is that although the guidelines are reflective of published literature these don't address the above questions. It is difficult to point towards individual sections hence all comments have been headed as general.</p> <p>These comments represent views from a number of consultants working in paediatrics and paediatric gastroenterology</p>	
British Society of Paediatric Gastroenterology, Hepatology and Nutrition	10	Full	10 INTRODUCTION	General	Oesophageal dysmotility masquerading with symptoms of reflux deserves a mention. The role of oesophageal manometry should be described	Thank you for your comment. This is a guideline concerning GORD in children and its emphasis is on primary and secondary care whilst making some reference to the management that could be reasonably expected should a patient require referral to tertiary colleagues. It is not meant to be a detailed text book or guideline for the tertiary specialist who would always be expected to consider a broader differential diagnosis in assessing a referred child. A more detailed discussion and set of recommendations that refer to other conditions that may very rarely mimic

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						the clinical presentation of GORD is beyond the remit of this guideline.
British Society of Paediatric Gastroenterology, Hepatology and Nutrition	11	Full	10 INTRODUCTION	General	Special conditions like hypertensive LOS (LOWER OESOPHAGEAL SPHINCTER) and corkscrew oesophagus perhaps need to be mentioned	Thank you for your comment. This is a guideline concerning GORD in children and we consider that a tertiary specialist would always be expected to consider a broader differential diagnosis in assessing a referred child. A more detailed discussion and set of recommendations that refer to other conditions that may very rarely mimic the clinical presentation of GORD is beyond the scope of this guideline.
British Society of Paediatric Gastroenterology, Hepatology and Nutrition	18	Full	10 OR 47 DEFINITIONS and SIGNS AND SYMPTOMS	General	Silent reflux needs better definition and evidence based documents – when and how to treat.	Thank you for your comment. In this guideline silent reflux is referred to as occult reflux. An amendment has been made to the glossary in the full guideline to clarify this. In structuring the review protocols, symptoms, signs or clinical conditions were used to define whether GORD commonly results in apnoea or aspiration pneumonia in the absence of other symptoms. This has resulted in several of the recommendations.
British Society of Paediatric Gastroenterology, Hepatology and Nutrition	2	Full	11 DEFINITION	General	DEFINITION There is a great concern regarding the all-inclusive definition for GORD in the NICE document. It implies that any patient or parent who thinks they or their child has reflux is by definition GORD; even if all the tests may be negative without any demonstrable pathology. The group feels that it is unsatisfactory.	Thank you for your comment. We disagree because according to the definition of GORD used in this guideline (and the explanations offered in the introduction) clinical confirmation of the diagnosis would be required by a health professional for either a reliable description of the "complications" or for "medical treatment".

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British Society of Paediatric Gastroenterology, Hepatology and Nutrition	9	Full	11 DEFINTION	General	Refractory Gastroesophageal reflux needs to be defined with management (Separate section – not on page 11 of course)	<p>Thank you for your comment.</p> <p>In this guideline the term refractory is used in a single recommendation 1.1.20. This recommendation says:</p> <p>“Arrange an urgent specialist hospital assessment for infants, children and young people for a possible upper GI endoscopy with biopsies if there is:...</p> <ul style="list-style-type: none"> retrosternal, epigastric or upper abdominal pain that needs ongoing medical therapy or is refractory to medical therapy...” <p>We do not attempt to define the term refractory GOR as this is highly dependent on the clinical context and requires clinical judgement. Thus, a young person who is much improved but occasionally experiences mild symptoms might be kept under clinical review rather than referring for endoscopy</p> <p>Recommendation 1.3.4 says:</p> <p>“Assess the response to the 4 week trial of the PPI or H2RA, and consider referral to a specialist for possible endoscopy if the symptoms:</p> <ul style="list-style-type: none"> do not resolve or recur after stopping the treatment” <p>The phrase “do not resolve” similarly</p>

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						requires clinical interpretation in the specific clinical context.
British Society of Paediatric Gastroenterology, Hepatology and Nutrition	15	Full	18 RECOMMENDATIONS AND CARE PATHWAY	General	The role of specialist (gastroenterologist) needs to be clearer with regard to diagnostic tools available in variable extent. While endoscopy is the main investigation in GORD, the availability of other investigations (impedance, GI physiology such as manometry) can only be performed in a number of centres, and if NICE recommends these investigations, it needs to be emphasised that staff trained in paediatrics (GI physiology) and paediatric specialists need to interpret findings in the clinical context.	Thank you for your comment. The recommendations make reference to endoscopy, pH studies with or without impedance monitoring together with other investigations that may be needed to exclude other conditions. The guideline refers to the actions being undertaken and we deliberately chose to do not refer to specialist gastroenterologists. The guideline refers to a specialist and we have included the definition used during development in Section 1 of the NICE guideline. While we would agree that it is important for staff working with children with GORD to have the necessary level of knowledge and expertise to deliver care, it is outside of the remit of this guideline to specify the qualifications or competencies professionals should have. This is up to the local arrangements / organisation of the skill set across the region or clinical network. It is also outside of the remit of this guideline to offer prescriptive advice to tertiary centres on how they should support their networks.
British Society of Paediatric Gastroenterology, Hepatology	16	Full	18 RECOMMENDATIONS AND CARE	General	In refractory reflux persists or persistent GORD, these children need work up (ideally multidisciplinary, ideally in established joint clinics) with general paediatricians, surgeons, or other specialists (neurologist, allergist, genetics) to find out underlying causes and	Thank you for your comment. The guideline refers to the actions being undertaken and we deliberately chose to do not refer to specialist gastroenterologists. The guideline refers to a specialist and we have

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and Nutrition					manage these patients.	included the definition used during development in Section 1 of the NICE guideline. We do not refer to specialist gastroenterologists or other health care professionals within the multidisciplinary team. While we would agree that it is important for staff working with children with GORD to have the necessary level of knowledge and expertise to deliver care, it is outside of the remit of this guideline to specify the qualifications or competencies professionals should have. This is up to the local arrangements / organization of the skill set across the region or clinical network. It is also outside of the remit of this guideline to offer prescriptive advice to tertiary centres on how they should support their networks.
British Society of Paediatric Gastroenterology, Hepatology and Nutrition	17	Full	18 RECOMMENDATIONS AND CARE PATHWAY	General	The role of allied health professionals (dietitians and particularly speech and language therapists) in the multidisciplinary assessment and management of these patients needs to be incorporated and their role and importance defined.	Thank you for your comment. Where the guideline refers to a specialist, refers to a paediatrician with the skills, experience and competency necessary to deal with the particular clinical concern that has been identified by the referring health care professional. In this guideline this is most likely to be a consultant general paediatrician. Depending on the clinical circumstances, 'specialist' may also refer to a paediatric surgeon, paediatric gastroenterologist or a doctor with the equivalent skills and competency. In this guideline this is most likely to be a consultant general paediatrician.

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						Depending on the clinical circumstances, 'specialist' may also refer to a paediatric surgeon, paediatric gastroenterologist or a doctor with the equivalent skills and competency. We deliberately do not refer to specialist gastroenterologists or other health care professionals within the multidisciplinary team. While it is agreed that it is important for staff working with children with GORD to have the necessary level of knowledge and expertise to deliver care, it is outside of the remit of this guideline to specify the qualifications or competencies professionals should have. This is up to the local arrangements / organization of the skill set across the region or clinical network. It is also outside of the remit of this guideline to offer prescriptive advice to tertiary centres on how they should support their networks.
British Society of Paediatric Gastroenterology, Hepatology and Nutrition	3	Full	47 SIGNS AND SYMPTOMS	General	All children with Hematemesis should not be referred to a paediatric gastroenterologist. This is not the classical teaching for management of hematemesis. There needs to be some accommodation for those swallowing blood from breast feeding or presumed Mallory-Weiss tear with this being specified in the guidelines	Thank you for your comment. We have amended Table 1 within recommendation 5 and recommendation 20 to accommodate your point regarding the possibility of blood being swallowed.
British Society of Paediatric Gastroenterology, Hepatology	21	Full	50 DISTRESSED BEHAVIOUR	General	A paragraph needs to address the problem of investigating unsettled children ("colics") with a pathological reflux score on impedance – what teams and how monitoring and treatment of these children is indicated, as there are no medicines available to make these children	Thank you for your comment. This guideline focuses on the diagnosis and management of GORD. It was outside the scope of this guideline to address general aspect of investigation and

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and Nutrition			R		settled/content. Primary and secondary care professionals need reassurance from NICE that and when no further escalation of investigations and treatment in this group is required.	management of distressed children or crying infants. The guideline does address these concerns in relation to the specific consideration of GORD. Based on an evidence review of symptoms and signs of GORD, the guideline development group did advise that when infants and children showed 'distressed behaviour' as an isolated sign and in the absence of overt regurgitation, they should not routinely undergo investigations for gastro-oesophageal reflux (Recommendation 6). This would no doubt apply to those children who might be labelled as having 'infant colic' or who were more generally unsettled. The guideline also advises consideration of a 4-week trial of an H2RA or a PPI for infants, young children who are unable to verbally express their symptoms and who have overt regurgitation associated with distressed behaviour (Recommendation 30).
British Society of Paediatric Gastroenterology, Hepatology and Nutrition	19	Full	54 APNOEA	General	Although apnoeas have been discussed - Desaturations/seizures are a problem and need a paragraph of joined consultations and investigations (e.g. combined impedance with oxygen monitoring/sleep lab), and opportunity for a joined neurological assessemnet needs to be established in specialissed centred and teams in formal pathways.	Thank you for your comment. This guideline's remit is the diagnosis and management of GORD. It is outside of the scope of this guideline to address the investigation and management of apnoea or bradycardia in infants, children or young people.
British Society of Paediatric	4	Full	172 PROKINET	General	There has been a lot of feedback about use of Domperidone in view of the recent MHRA statement. Some feedback is to stop its use	Thank you for your comment. It is our view that domperidone (and several other prokinetic agents) should only be

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Gastroenterology, Hepatology and Nutrition			ICS		however majority of the members advise about cautious use. This controversy should reflect in the guidance before giving robust proposals. In addition members are advising to have an end point to its use as if no response in 4-6 weeks then it should be stopped hence limiting its use	used following specialist advice. We have not therefore made recommendations on the treatment regimen with domperidone.
British Society of Paediatric Gastroenterology, Hepatology and Nutrition	5	Full	172 PROKINET ICS	General	There is some recommendation to mention contraindication to use of Domperidone to people with <ol style="list-style-type: none"> 1. Heart conduction defects or suspected to be impaired 2. Congestive heart failure 3. Receiving other medications which could prolong QT interval or potent CYP3A4 inhibitors 4. Severe hepatic impairment 	Thank you for your comment. It is our view that domperidone (and several other prokinetic agents) should only be used following specialist advice. The guideline development group has not therefore made recommendations on the treatment regimen with domperidone.
British Society of Paediatric Gastroenterology, Hepatology and Nutrition	6	Full	172 PROKINET ICS	General	Lothian guidelines from members of BSPGHAN are recommending a max dose of 30mg/day in adolescents over 12 years of age or weighing > 35 kg. when under 12 or <35 kg the recommendation is 0.25mg/kg/dose	Thank you for your comment. We assume that the comment refers to the use of domperidone. Advice on dosage of domperidone because the recommendation advises seeking specialist advice before use.
British Society of Paediatric Gastroenterology, Hepatology and Nutrition	7	Full	172 PROKINET ICS	General	There are children who benefit with use of Domperidone and in such cases provided an ECG confirms no safety concerns then we should support longer term use of domperidone. However in the absence of evidence there will be a need of NICE consensus as to what may constitute as effective cardiac monitoring. This is one most important points members have asked to be included in the guidelines	Thank you for your comment. It is our view that domperidone (and several other prokinetic agents) should only be used following specialist advice. We have not therefore made recommendations regarding cardiac monitoring and indeed cardiac monitoring was not included in the evidence review.
British Society of Paediatric	12	Full	172 PROKINET	General	Use of newer agents such as Mosepride require mention	Thank you for your comment. The evidence review sought evidence from trials on prokinetic agents generally.

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Gastroenterology, Hepatology and Nutrition			ICS			There were no trials on Mosepride identified.
British Society of Paediatric Gastroenterology, Hepatology and Nutrition	13	Full	172 PROKINET ICS	General	The use of Azithromycin with Erythromycin which is common practice needs mention	<p>Thank you for your comment. The protocol for the evidence review specified that randomised controlled trials examining prokinetics compared to placebo were to be included (see Full guideline, Section 6 Pharmacological treatment for the evidence review and Appendix E.7 for the corresponding protocol). Six randomised controlled trials reported relevant outcomes for the prokinetics domperidone and metoclopramide compared with placebo. However no similar studies were identified for macrolide antibiotics (which include azithromycin and erythromycin).</p> <p>It is acknowledged in the full guideline (section 6.1.6.2.4) that the GDG were aware that erythromycin was in regular clinical use in the NHS for its prokinetic properties. Given the absence of evidence, the clinical opinion and experience of the GDG was that it was an unhelpful agent in the context of GORD and that its use was not justified without seeking specialist advice.</p> <p>We considered the stakeholder's comment but did not agree that the use of azithromycin as a prokinetic agent</p>

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						either with or without erythromycin to be common practice. Further we considered that concurrent prescription of two macrolide antibiotics would not be common practice because of the potential for abnormalities in the QT axis and serious side effects. No amendment to the recommendation was made but this issue has been passed onto the NICE Surveillance Review team to consider.
British Society of Paediatric Gastroenterology, Hepatology and Nutrition	20	Full	172	General	NICE should perhaps make a statement about pharmaceutical companies/input/prospective RCT to investigate further safe prokinetic medications.	Thank you for your comment. We recognised that safe and effective prokinetic agents could potentially be helpful. However there were concerns about the use of domperidone as reflected in the recommendation, advising specialist involvement. They were not aware of any new products currently available which currently required investigation by RCT.
British Society of Paediatric Gastroenterology, Hepatology and Nutrition	14	Full	184	General	The feeding in GOR section is inadequate and vague – whey based feeds either here or treatment section should be mentioned –	Thank you for your comment. The evidence review on the use of feeds of different composition did not identify any comparative studies examining the use of whey-based feeds. Consequently no recommendation was made on this matter.

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British Society of Paediatric Gastroenterology, Hepatology and Nutrition	8	Full	188 SURGERY	General	<p>There needs to be mention of other treatments used for gastroesophageal reflux in the surgical or endoscopic section:</p> <ol style="list-style-type: none"> 1. Gastroplication – see NICE interventional procedures guidelines IPG404 2. Use of STRETTA anti-reflux procedure 3. Use of TIF – transoral incisionless fundoplication 4. Enteryx injections in the oesophagus - 	<p>Thank you for your comments.</p> <p>The scope of the guideline included fundoplication but not other surgical interventions and therefore the procedures to which you refer were not reviewed.</p> <p>For readers who wish to see related guidance there is a list in section 1.7 where Endoluminal gastroplication for gastro-oesophageal reflux disease. NICE interventional procedure guidance 404 (2011) is mentioned.</p>
British Society of Paediatric Gastroenterology, Hepatology and Nutrition	22	Full	188 SURGERY	General	<p>For a subgroup with a general surgeon in designated clinics and designated ward rounds/clinical settings. The surgical treatment of GOR in neuro-disabled patients is complex and associated with a variable outcome. High failure rates and poor medium-term survival are well documented, particularly for fundoplication which remains the most popular procedure. Numerous surgical strategies have been described which include: gastrostomy feeding, G-J feeding, jejunostomy feeding, fundoplication (both open and laparoscopic), fundoplication variants (e.g. partial Nissen / Thal / Boix-Ochoa / Toupe / fundoplication + vagotomy and pyloroplasty), gastric pacing, oesphago-gastric dissociation, and total parenteral nutrition. Thus far there has been no convincing data to demonstrate the superiority of any of these approaches, principally because the patients form a disparate group whose needs and pathologies are variable.</p>	<p>Thank you for your comment. We were aware of these concerns and issues and of the wide range of interventions. The guideline adopts a conservative approach to the use of enteral tube feeding and to the use of fundoplication. The evidence reviews did not attempt to compare the relative merits of different types of surgical intervention but focussed on identifying those for whom such interventions might be considered.</p>

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British Society of Paediatric Gastroenterology, Hepatology and Nutrition	23	Full	188 SURGERY	General	The NICE guidance made little reference to tube feeding categories – PEG vs GJ feeding vs surgeon constructed feeding jejunostomy. Gastrojejunal feeding is becoming a popular option which is not without difficulties – This is a topic outside the reflux however in feeding with reflux should be discussed	Thank you for this comment. The guideline contains a series of recommendations on the general topic of enteral tube feeding in the management of children with GORD (Recommendations 36-38) In addition, following consideration of stakeholder comments we have now made a recommendation regarding the role of jejunal feeding (39) The scope of the guideline did not include a detailed comparison of the many approaches to enteral tube feeding. These are matters often considered in a highly specialised setting and the approach of the guideline was to provide advice on the general topic so that referral to appropriate experts would be considered where necessary
British Specialist Nutrition Association	1	NICE	20	7-12	'Hydrolysed formulae' are an umbrella term used to describe both extensively hydrolysed and amino acid based formulae. We consider that the two different types of formula should be differentiated in this section, especially as it is specifically related to the section on cow's milk allergy (CMA). If CMA is suspected as a cause for gastro-oesophageal reflux disease (GORD), the use of an amino acid based formula can definitively exclude CMA. Amino acid based formulae do not interact with the immune system, therefore if there is no response to a 2-4 week trial of an amino acid formula, then CMA can be excluded as a potential diagnosis and cause of the GORD. This practice avoids the risk of infants being left on extensively	Thank you for your comment. The evidence review sought comparative trial evidence for the efficacy of interventions (including specialised medical formulas if available) for the treatment of GORD as defined in the glossary. We did not find persuasive evidence but did recommend that a RCT was needed to address this issue – specifically in the infant with overt regurgitation. Children with overt regurgitation and faltering growth might form a subgroup within the study population, as might those with a personal or family

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					<p>hydrolysed formula (EHF) for unnecessarily extended periods. Appropriate guidance would be to suggest the trial of an amino acid based formula in:</p> <ul style="list-style-type: none"> • a case of GORD presenting with faltering growth • a child with suspected CMA (underlying cause of GORD) is still symptomatic on an extensively hydrolysed formula. <p><i>(Koletzko S et al. Dietary approach and management cow's milk protein allergy in Infants and Children. JPGN 2012:55:221-229)</i></p>	history of atopic conditions.
British Specialist Nutrition Association	2	Full	144	6.2.6.2.3	<p>GORD and CMA frequently occur together in infants and GORD is associated with and induced by CMA. All infants under 1 year with GORD should be screened for CMA (<i>Salvatore S, Pediatrics 2002;110;972</i>). Due to difficult diagnosis of CMA in primary care, dietary elimination including use of extensively hydrolysed formula (EHF) and re-challenge is the standard protocol.</p>	Thank you for your comment. Following stakeholder consultation, we gave careful consideration to the differential diagnosis in children presenting with possible GORD. A new recommendation was added (Recommendation 11) to confirm that some symptoms of non-IgE mediated cows' milk protein allergy can be similar to those of GORD, especially in infants with atopic symptoms, signs, and/or a family history and which cross refers the reader to NICE CG 116 'Food allergy in children and young people'. Amendments were also made to Recommendation 5 in Table R1 that lists 'red flag' signs and symptoms that may suggest disorders other than GOR in those with vomiting or regurgitation. A cross reference to NICE CG 116 was added to the symptom/sign of 'Blood in stool' 'Chronic diarrhoea' was added to
		Full	25	27	<p>NICE may wish to review the following clinical papers which assess the role of hydrolysed peptide formulae for the management of children with GORD and reflux. NICE should provide further consideration on the beneficial role of hydrolysed whey-based formulae for the management of GORD and reflux within neurologically impaired children e.g. those with Cerebral Palsy (CP).</p> <p>Foods For Special Medical Purposes (FSMP) cannot claim to "treat, prevent or cure disease",</p>	

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					<p>however the role of FSMPs is recognised as a suitable therapy to support CP children with GORD and reflux. The following studies (which have not been included or reviewed by NICE) can provide additional support on this critical role:</p> <p><i>Khoshoo et al. Incidences of Gastroesophageal reflux with a whey and Casein based formula for infants and in children with severe Neurological impairment. Journal of Pediatric Gastroenterology and Nutrition 1996. 22: 48-55.</i></p> <p><i>Fried et al. Decrease in gastric emptying time and episodes of regurgitation in children with spastic quadriplegia fed a whey based formula. 1992. The Journal of Pediatrics 120, no 4; 569-572</i></p> <p><i>Khoshoo et al. Gastric emptying of two whey based formulas of different energy density and its clinical implications in children with volume intolerance.2002. European Journal of Clinical Nutrition, 56. 656-658.</i></p>	<p>the gastrointestinal list of signs/symptoms with a cross reference to NICE CG 116. Finally the sign/symptom 'Eczema' was amended and broadened to 'Infants and children with, or at high risk of, atopy' and the suggested action of a 'Trial of milk exclusion' was removed because this clinical recommendation was not made in this GORD guideline. A research recommendation was made however and the research question was amended following stakeholder consultation. This now specifies that a randomised controlled trial should be performed to examine the clinical and cost effectiveness of a hydrolysed formula trial in formula fed infants with frequent regurgitation associated with marked distress (Section 5.2.8).Salvatore et al, 2002 was a narrative review (and not a systematic review) and therefore would not be included in this guideline. Khoshoo et al, 1996 and Fried et al, 1992 assessed interventions not relevant to protocol (trial of cows' milk elimination) and therefore would not be included in the guideline.</p>
British Specialist Nutrition Association	3	Full	144	6.2.6.2.3	The symptoms of GORD associated with CMA are the same as those in primary GORD. If CMA is suspected an elimination diet is recommended intervention (<i>Vandenplas, Early Human Development 2005;81;12;1011-1024</i>)	Thank you for your comment. Following stakeholder consultation, we gave careful consideration to the differential diagnosis in children presenting with possible GORD. A new recommendation was added (Recommendation 11) to confirm that
		Full	184	(8.1.1)	A number of randomised cross over trials can	

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				40	<p>provide further discussions on whether hydrolysed whey-based formulae could be used first line for children with CP who have a history of GORD and reflux. Whey-based formulae may provide additional support for these children who may have delayed gastric emptying. They may also provide a solution for the reduction in frequency of GORD and vomiting within neurologically impaired children such as CP:</p> <p><i>Khoshoo et al. Incidences of Gastroesophageal reflux with a whey and Casein based formula for infants and in children with severe Neurological impairment. Journal of Pediatric Gastroenterology and Nutrition 1996. 22: 48-55.</i></p> <p><i>Fried et al. Decrease in gastric emptying time and episodes of regurgitation in children with spastic quadriplegia fed a whey based formula. 1992. The Journal of Pediatrics 120, no 4; 569-572</i></p> <p><i>Poster presented at 24th ASPEN conference Jan 2000. Data can be provided upon request.</i></p>	<p>some symptoms of non-IgE mediated cows' milk protein allergy can be similar to those of GORD, especially in infants with atopic symptoms, signs, and/or a family history and which cross refers the reader to NICE CG 116 'Food allergy in children and young people'. Amendments were also made to Recommendation 5 in Table R1 that lists 'red flag' signs and symptoms that may suggest disorders other than GOR in those with vomiting or regurgitation. A cross reference to NICE CG 116 was added to the symptom/sign of 'Blood in stool' 'Chronic diarrhoea' was added to the gastrointestinal list of signs/symptoms with a cross reference to NICE CG 116. Finally the sign/symptom 'Eczema' was amended and broadened to 'Infants and children with, or at high risk of, atopy' and the suggested action of a 'Trial of milk exclusion' was removed because this clinical recommendation was not made in this GORD guideline. A research recommendation was made however and the research question was amended following stakeholder consultation. This now specifies that a randomised controlled trial should be performed to examine the clinical and cost effectiveness of a hydrolysed formula trial in formula fed infants with frequent regurgitation associated with marked distress (Section 5.2.8). Vandenplas et al, 2005 was a narrative</p>

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						review (and not a systematic review) and therefore would not be included in this guideline. Khoshoo et al, 1996 and Fried et al, 1992 assessed interventions not relevant to protocol (trial of cows' milk elimination) and therefore would not be included in the guideline.
British Specialist Nutrition Association	4	Full	144	6.2.6.2.3	<p>CMA was confirmed in 85 out of 204 patients with GORD (41.8%). Patients younger than 12 months with symptoms of GORD should be examined to determine if GORD is primary or caused by CMA</p> <p><i>(Iacono et al, Journal of Allergy and Clinical Immunology 1996;97(3);822-827)</i></p>	<p>Thank you for your comment. Following stakeholder consultation, we gave careful consideration to the differential diagnosis in children presenting with possible GORD. A new recommendation was added (Recommendation 11) to confirm that some symptoms of non-IgE mediated cows' milk protein allergy can be similar to those of GORD, especially in infants with atopic symptoms, signs, and/or a family history and which cross refers the reader to NICE CG 116 'Food allergy in children and young people'. Amendments were also made to Recommendation 5 in Table R1 that lists 'red flag' signs and symptoms that may suggest disorders other than GOR in those with vomiting or regurgitation. A cross reference to NICE CG 116 was added to the symptom/sign of 'Blood in stool' . 'Chronic diarrhoea' was added to the gastrointestinal list of signs/symptoms with a cross reference to NICE CG 116. Finally the sign/symptom 'Eczema' was amended and broadened to 'Infants and children with, or at high risk of, atopy' and the</p>

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						suggested action of a 'Trial of milk exclusion' was removed because this clinical recommendation was not made in this GORD guideline. Iacono et al, 1996 was a prospective study (and not a controlled trial) and therefore would not be included in this guideline.
British Specialist Nutrition Association	5	Full	144	6.2.6.23	<p>CMA was diagnosed in 1/3 of patients with signs and symptoms of GORD, as well as the conclusion that CMA can mimic all signs and symptoms of severe GORD. Elimination of cows' milk in the infected patients resolved the problems</p> <p><i>(Farahmand F et al, Gut Liver 2011;5(3):298-301)</i></p>	<p>Thank you for your comment. Following stakeholder consultation, we gave careful consideration to the differential diagnosis in children presenting with possible GORD. A new recommendation was added (Recommendation 11) to confirm that some symptoms of non-IgE mediated cows' milk protein allergy can be similar to those of GORD, especially in infants with atopic symptoms, signs, and/or a family history and which cross refers the reader to NICE CG 116 'Food allergy in children and young people'. Amendments were also made to Recommendation 5 in Table R1 that lists 'red flag' signs and symptoms that may suggest disorders other than GOR in those with vomiting or regurgitation. A cross reference to NICE CG 116 was added to the symptom/sign of 'Blood in stool'. 'Chronic diarrhoea' was added to the gastrointestinal list of signs/symptoms with a cross reference to NICE CG 116. Finally the sign/symptom 'Eczema' was amended and broadened to 'Infants and children with, or at high risk of, atopy' and the suggested action of a 'Trial of milk</p>

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						exclusion' was removed because this clinical recommendation was not made in this GORD guideline. A research recommendation was made however and the research question was amended following stakeholder consultation. This now specifies that a randomised controlled trial should be performed to examine the clinical and cost effectiveness of a hydrolysed formula trial in formula fed infants with frequent regurgitation associated with marked distress (Section 5.2.8). Farahmand et al, 2011 did not meet the inclusion criteria for the review question. It is not a clinical trial and had no comparator/control group.
British Specialist Nutrition Association	6	Full	144	6.2.6.2.3	CMA is a potential differential of infants suffering from GORD and infants may benefit from a 2-6 weeks trial of EHF <i>(Bhavsar H, Paediatrics and Child Health 2011;394-400)</i>	Thank you for your comment. Following stakeholder consultation, we gave careful consideration to the differential diagnosis in children presenting with possible GORD. A new recommendation was added (Recommendation 11) to confirm that some symptoms of non-IgE mediated cows' milk protein allergy can be similar to those of GORD, especially in infants with atopic symptoms, signs, and/or a family history and which cross refers the reader to NICE CG 116 'Food allergy in children and young people'. Amendments were also made to Recommendation 5 in Table R1 that lists 'red flag' signs and symptoms that may suggest disorders other than GOR in those with vomiting or regurgitation.

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						A cross reference to NICE CG 116 was added to the symptom/sign of 'Blood in stool' 'Chronic diarrhoea' was added to the gastrointestinal list of signs/symptoms with a cross reference to NICE CG 116. Finally the sign/symptom 'Eczema' was amended and broadened to 'Infants and children with, or at high risk of, atopy' and the suggested action of a 'Trial of milk exclusion' was removed because this clinical recommendation was not made in this GORD guideline. A research recommendation was made however and the research question was amended following stakeholder consultation. This now specifies that a randomised controlled trial should be performed to examine the clinical and cost effectiveness of a hydrolysed formula trial in formula fed infants with frequent regurgitation associated with marked distress (Section 5.2.8). Bhavsar et al, 2011 was a narrative review (and not a systematic review) and therefore would not be included in this guideline.
British Specialist Nutrition Association	7	Full	144	6.2.6.2.3	Children with severe reflux resistant to medical management may benefit from trial of hydrolysed protein feed <i>(Bhavsar H, Paediatrics and Child Health 2011; 394-400)</i>	Thank you for your comment. A clinical recommendation for a trial of hydrolysed protein feed was not made because of the paucity of evidence to support this. A research recommendation was made however and the research question was amended following stakeholder consultation. This now specifies that a

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						randomised controlled trial should be performed to examine the clinical and cost-effectiveness of a hydrolysed formula trial in formula fed infants with frequent regurgitation associated with marked distress (Section 5.2.8). 'Infants whose GOR and/or GORD has not responded to the initial management outlined in this guideline (up to and including alginates)' are noted as an important population subgroup to consider in such research. Bhavsar et al, 2011 was a narrative review (and not a systematic review) and therefore would not be included in this guideline.
British Specialist Nutrition Association	8	Full	144	6.2.6.2.3	20% of infants fed with formula experience GORD and 1/3 also shows signs of CMA. EHF significantly improved GORD symptoms in infants, especially in those with skin-test and RAST positive to CMA <i>(Garzi A et al, Allergologia et immunopathologia 2002: 36-41)</i>	Thank you for your comment. Following stakeholder consultation, we gave careful consideration to the differential diagnosis in children presenting with possible GORD. A new recommendation was added (Recommendation 11) to confirm that some symptoms of non-IgE mediated cows' milk protein allergy can be similar to those of GORD, especially in infants with atopic symptoms, signs, and/or a family history and which cross refers the reader to NICE CG 116 'Food allergy in children and young people'. Amendments were also made to Recommendation 5 in Table R1 that lists 'red flag' signs and symptoms that may suggest disorders other than GOR in those with vomiting or regurgitation. A cross reference to NICE CG 116 was

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British Specialist Nutrition Association	9	Full	144	6.2.6.2.3	Milk protein sensitivity is sometimes a cause of unexplained crying and vomiting in infants. Formula fed infants with recurrent vomiting may benefit from a 2-4 week trial of EHF <i>(Vandenplas and Rudolph et al, Journal of Pediatric Gastroenterology and Nutrition 2009 49:498-547)</i>	Thank you for your comment. A clinical recommendation for a trial of hydrolysed formula was not made because of the paucity of evidence to support this. A research recommendation was made however and the research question was amended following stakeholder consultation. This now specifies that a randomised controlled trial should be performed to examine the clinical and cost effectiveness of a hydrolysed

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						formula trial in formula fed infants with frequent regurgitation associated with marked distress (Section 5.2.8). Vandenplas et al, 2013 is a practice guideline based on the recommendations of the North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition and the European Society for Pediatric Gastroenterology, Hepatology, and Nutrition, that does not follow NICE methodology.
British Specialist Nutrition Association	10	Full	144	6.2.6.2.2	Use of a pre-thickened formula may decrease visible regurgitation but does not result in a measurable decrease in the frequency of oesophageal reflux episodes <i>(Vandenplas and Rudolph et al, Journal of Pediatric Gastroenterology and Nutrition 2009 49:498-547)</i>	Thank you for this comment. The intention of thickening the feed would be (in part) to decrease visible regurgitation. Where a clinical presentation of GORD is suspected other recommendations are appropriate. The reference suggested by the stakeholder (Vandenplas et al, 2009) is not a research article or a systematic review but is a practice guideline developed by a panel of paediatricians and epidemiologists based on the Delphi principle that does not meet inclusion criteria for this guideline
Chelsea and Westminster Hospital NHS Foundation Trust	1	NICE	General	General	We welcome these guidelines into our department and would like to express our gratitude to The Guideline Development Group, National Collaborating Centre and NICE project team for their efforts and dedication in constructing guidelines for this challenging and evolving condition. We aim to use the final published guidance to update our current local	Thank you for your comment.

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					departmental and trust guidelines.	
Chelsea and Westminster Hospital NHS Foundation Trust	2	NICE	15	1.1.20	We recommended that pH with Impedance monitoring should also be considered for children and young people with severe or refractory chronic lower airway obstructive disease e.g. Asthma, where GOR may be a contributory factor.	Thank you for your comment on what is now NICE recommendation 1.1.21. With regard to asthma, the evidence review demonstrated that there was an association between GOR and asthma but it could not be determined whether this was causative. For that reason we did not recommend investigating children with asthma for reflux.
Chelsea and Westminster Hospital NHS Foundation Trust	3	NICE	16	1.1.21	We disagree with performing pH without impedance monitoring in this section. If symptoms continue during medical management (as stated in the second bullet point) then this would be a strong indication for pH with impedance monitoring - as non-acid reflux may be suspected. The fourth bullet point regarding pH without impedance monitoring when considering fundoplication contradicts section 1.5.2 on page 19 (Surgery for GORD, where pH-impedance monitoring is advised).	Thank you for your comment. We agreed, and following consideration of this and of other stakeholder comments amended this recommendation and recommendation 1.5.2. The bullet points were removed from this recommendation and it was amended to "Consider performing an oesophageal pH study without impedance monitoring in infants, children and young people if, using clinical judgement, it is thought necessary to ensure effective acid suppression". Recommendation 1.5.2 was also amended to advise health care professionals to consider performing other investigations such as a pH study, combined with impedance monitoring if available, and an upper GI contrast study for infants, children and young people before deciding whether to offer fundoplication.
Chelsea and Westminster	4	NICE	18	1.3.6	Our practice is to treat endoscopically determined (or proven) oesophagitis with a PPI	Thank you for your comment. The available evidence identified from our

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Hospital NHS Foundation Trust					and feel that an option of using an H2RA or PPI should not be given. PPIs are clinical proven to be more superior than H2RAs for this condition. In addition, endoscopically proven oesophagitis usually merits an initial 3 months drug treatment course, of which an H2RA would be inappropriate.	review of paediatric RCTs did not allow any distinction to be made between these agents in terms of efficacy or safety.
Chelsea and Westminster Hospital NHS Foundation Trust	5	NICE	18	1.3.7	Similar discussion to above comment on 1.3.6 – PPI therapy and not H2RA.	Thank you for your comment. The available evidence identified from our review of paediatric RCTs did not allow any distinction to be made between these agents in terms of efficacy or safety.
Cow's Milk Protein Allergy Support Group	1	Full	10	General	<p>Our group is concerned that there is no clear reference to the guidelines on diagnosing food allergy in children and young people in this section. (http://www.nice.org.uk/guidance/cg116/chapter/1-guidance)</p> <p>In section 1.1.1 of the food allergy guideline, it states: "Consider the possibility of food allergy in children and young people who have one or more of the signs and symptoms in table 1, below. Pay particular attention to persistent symptoms that involve different organ systems"</p> <p>GOR or GORD is a gastrointestinal symptom of non IgE mediated CMPA as listed in table 1. Of the food allergy guidelines.</p> <p>In section 1.1.2 of the food allergy guidelines it states: "Consider the possibility of food allergy in children and young people whose symptoms do not respond adequately to treatment for:</p>	<p>Thank you for your comment. The guideline Table did in fact signpost CG 116. However we have revised the recommendations to be more explicit in this regard, highlighting a possible overlap between the symptoms of cows' milk allergy and gastro-oesophageal reflux disease. A new recommendation was added (Recommendation 11) to confirm that some symptoms of non-IgE mediated cows' milk protein allergy can be similar to those of GORD, especially in infants with atopic symptoms, signs, and/or a family history and which cross refers the reader to NICE CG 116 'Food allergy in children and young people'. Amendments were also made to Recommendation 5 in Table R1 that lists 'red flag' signs and symptoms that may suggest disorders other than GOR in those with vomiting or regurgitation. A cross reference to NICE CG 116 was</p>

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					<p>- GORD”</p> <p>In Section 1.2.3 it states: “If food allergy is suspected (by a healthcare professional or the parent, carer, child or young person), a healthcare professional with the appropriate competencies (either a GP or other healthcare professional) should take an allergy-focused clinical history tailored to the presenting symptoms and age of the child or young person”</p> <p>We strongly feel that clear reference to these guidelines should be included in section 1. of the GORD guidelines, as the only mention comes in Table 1 ‘Red Flag’ symptoms, and refers to eczema, which although it is a very common symptom of CMPA, it is not suffered by all, and the table gives the impression that no eczema means no CMPA.</p> <p>We believe by including this advice in section 1, to perform an allergy focussed assessment, it could save the NHS many thousands of pounds, by encouraging mothers to continue to Breast Feed with a change to their diet and the support of their peers. Many breastfeeding mothers have told us they became disillusioned with Breastfeeding and made the switch to formula, by which point when CMPA was diagnosed later on, there was no alternative other than expensive EhF or AA formula milk provided on prescription, they would have preferred to continue to breastfeed.</p> <p>We feel that by not including this reference</p>	<p>added to the symptom/sign of 'Blood in stool' 'Chronic diarrhoea' was added to the gastrointestinal list of signs/symptoms with a cross reference to NICE CG 116. Finally the sign/symptom 'Eczema' was amended and broadened to 'Infants and children with, or at high risk of, atopy' and the suggested action of a 'Trial of milk exclusion' was removed because this clinical recommendation was not made in this GORD guideline. A research recommendation was made however and the research question was amended following stakeholder consultation. This now specifies that a randomised controlled trial should be performed to examine the clinical and cost effectiveness of a hydrolysed formula trial in formula fed infants with frequent regurgitation associated with marked distress (Section 5.2.8). Amendments were also made to recommendations for breast-fed infants with frequent regurgitation associated with marked distress (Recommendations 25 and 27) that breastfeeding should be supported with a breastfeeding assessment/advice.</p>

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					NICE are, in effect, undermining the advice that is published in the Food Allergy guidelines.	
Cow's Milk Protein Allergy Support Group	2	Full	20	2.2	<p>We agree that research is required in relation to Cow's Milk Protein elimination, however, we feel that if the food allergy guidelines are followed and a trial of CMP elimination is followed by reintroduction of CMP as recommended in section 1.1.11 of the Food allergy guidelines, it will become more clear if the CMP is the cause of the infants symptoms, and reduce the amount of prescriptions written unnecessarily.</p> <p>We also feel that this section should have information regarding CMP elimination in breast feeding mothers.</p> <p>Please refer to this document and it's additional files: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3716921/</p>	<p>Thank you for your comment. Following stakeholder consultation, we gave careful consideration to the differential diagnosis in children presenting with possible GORD. A new recommendation was added (Recommendation 1.1.11) to confirm that some symptoms of non-IgE mediated cows' milk protein allergy can be similar to those of GORD, especially in infants with atopic symptoms, signs, and/or a family history and which cross refers the reader to NICE CG 116 'Food allergy in children and young people'.</p> <p>Amendments were also made to Recommendation 1.1.5 in Table 1 that lists 'red flag' signs and symptoms that may suggest disorders other than GOR in those with vomiting or regurgitation. A cross reference to NICE CG 116 was added to the symptom/sign of 'Blood in stool' 'Chronic diarrhoea' was added to the gastrointestinal list of signs/symptoms with a cross reference to NICE CG 116. Finally the sign/symptom 'Eczema' was amended and broadened to 'Infants and children with, or at high risk of, atopy' and the suggested action of a 'Trial of milk exclusion' was removed because this clinical recommendation was not made in this GORD guideline. A research recommendation was made however</p>

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						<p>and the research question was amended following stakeholder consultation. This now specifies that a randomised controlled trial should be performed to examine the clinical and cost effectiveness of a hydrolysed formula trial in formula fed infants with frequent regurgitation associated with marked distress (Section 5.2.8).</p> <p>We considered that trial of maternal dietary cows' milk exclusion would be complex in that it could not be assumed that maternal milk consumption was causative and neither a clinical nor a research recommendation was made for this. The article to which your comment refers would not be included in the GORD guideline because it is practice guideline examining the diagnosis and management of IgE and non IgE medicated cows' milk protein allergy in children and not the diagnosis and management of GORD.</p>
Lactation Consultants of Great Britain	1	NICE	General		<p>Lactation Consultants of Great Britain is the professional organisation for International Board Certified Lactation Consultants (IBCLCs) within Great Britain. As professionals specialising in lactation support and education, we are well placed to understand the issues which concern parents and infants dealing with gastro-oesophageal reflux as we are on the front-line supporting lactation. As well as holding the qualification IBCLC many of our membership also work as Health Care</p>	Thank you for your comment.

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					Professionals and are involved in the training of staff as well as offering Specialist Lactation Support to mothers and their babies. We welcome the opportunity to contribute to the Guideline on the treatment of Gastro-oesophageal Reflux in Children.	
Lactation Consultants of Great Britain	2	NICE	General		We commend the way in which the treatment of infants is being normalised as much as possible, and the fact that it is recognised as a frequently occurring situation in young infants. It may be worth mentioning that, for parents, this is a distressing situation which needs to be treated with respect and concern by all health professionals involved.	Thank you for your comments. The guidance is intended to support all health care professionals in listening to parents' concerns and equipping them to respond appropriately.
Lactation Consultants of Great Britain	5	NICE	General		It might also be worth mentioning that breastfed babies are less likely to develop gastro-oesophageal reflux, or if they do develop it the symptoms are likely to be less severe. Measures should be taken to support the continuation of breastfeeding wherever possible.	Thank you for your comment. Evidence that non-breastfeeding was a risk factor for GORD was not identified during guideline development. Breast feeding has not therefore been highlighted as a means of reducing the risk. Methods for initial management for breast and formula fed infants are outlined in the recommendations (Recommendations 1.2.2 to 1.2.5).
Lactation Consultants of Great Britain	3	NICE	8 And 12		There are references to blood stained vomit as a 'red flag'. This is quite right, of course, but there can often be vomiting of blood which will resolve in due course this is distressing for all involved, but specialist referral is probably not necessary in these cases, unless the haematemesis continues.	Thank you for your comment. We amended the "Potential diagnostic implications" for haematemesis as a red flag (NICE recommendation 1.1.5, Table 1) to allow for the possibility of swallowed blood but did not change their view on the need for specialist referral because they believed that haematemesis could indicate serious conditions, such as erosive oesophagitis.

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Lactation Consultants of Great Britain	4	NICE	17		Where breastfeeding babies are concerned: it would be appropriate to suggest that a feeding assessment with Specialist breastfeeding support is required. This may aid in relieving symptoms due to positioning strategies, or if tongue-tie is diagnosed there is the possibility that treatment of the tongue-tie with frenulotomy may also lead to an alleviation of the symptoms.	Thank you for your comment. Amendments have been made to the recommendations for breast-fed infants with frequent regurgitation associated with marked distress that breastfeeding should be supported with a breastfeeding assessment/advice (Recommendations 1.2.2 and 1.2.4).
Living with Reflux	2	Full	144	29	1. The issue in regard to low allergy milk formulas is an important one. We feel that the Group have been over-influenced by cost implications of a short trial of hydrolysate or amino acid based formulas and that the evidence of co-existent cow's milk protein allergy and GORD is compelling. We feel that it would not be reasonable to deny this possible therapeutic avenue to so many babies who may benefit. We feel strongly that one recommendation should be that further research is funded in this area.	Thank you for your comment. A clinical recommendation for a trial of hydrolysed formula was not made because of the paucity of evidence to support this. A research recommendation was made however and the research question was amended following stakeholder consultation. This now specifies that a randomised controlled trial should be performed to examine the clinical and cost effectiveness of a hydrolysed formula trial in formula fed infants with frequent regurgitation associated with marked distress (Section 5.2.8).
Living with Reflux	1	Full	General	General	1. We agree that PPIs should only be prescribed by paediatricians or paediatric gastroenterologists, but we feel that it should be highlighted that the lag time before an infant has access to a specialist may be detrimental to the infant's health and more resources are needed to prevent this from happening e.g. funding of hospital clinics for reflux specifically. We feel strongly that one recommendation should be that further	Thank you for your comment. Recommendation 30 advises a trial of H2RA or PPI in certain infants and young children, recommendation 31 also advises a trial of PPI in some children and young people. These recommendations do not restrict the prescription of these agents to paediatricians or gastroenterologists. In the recommendations on the use of acid suppressing drugs we advised that

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					<p>research is funded in this area.</p> <p>2. The cost of PPI liquids (e.g. omeprazole liquid) is ridiculously high – as compared to the US market and others – we feel that this needs to be investigated and the pharmacies in the UK who are making so much money from the mark up on these products should be compelled to make the charges much more reasonable. This is the only PPI preparation we are aware of that is easy to administer to an infant reliably. It is a scandal that these pharmacies are marking up the price from approx. £20 per month to £250-400. Regulation has to be a recommendation of the group.</p>	the choice between these should be influenced by available preparations, patient/child preference and cost (Recommendation 33). However it is outside of the remit of the guideline to consider costs controlled by the pharmaceutical industry.
National Childbirth Trust	1	Full	General	General	We are most concerned with parents and babies in the first two years of life, therefore all comments below relate to babies and children who may be too young to articulate the location of their symptoms and where it is sometimes difficult to tell if the child is in pain.	Thank you for your comment.
National Childbirth Trust	2	Full	General	General	There is no mention of colic in infants and differential diagnosis in relation to reflux. Babies with colic may regurgitate milk and also display distress. It would be helpful if parents and professionals could distinguish between these two conditions which both cause a lot of distress to babies and parents. Some studies suggest that persistent infant crying and fussing is associated with an increased risk of child abuse (Talvik, Alexander, & Talvik, 2008).	Thank you for your comment. This is not a guideline on the management of crying infants or distressed children. Regarding colic, various recommendations are relevant to your concern - for example recommendations 4, 20, 23, 25, 26, 27 and 30 all provide advice on the management of infants with signs of distress. With regard to child

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						maltreatment, a child safeguarding statement is made following the Introduction section of the NICE guideline.
National Childbirth Trust	3	Full	18	16-22	Parents have expressed to us that their concerns are already appearing to be ignored in relation to babies who are having difficulty feeding, gagging, losing weight and appearing to be in pain. Pain does not appear on the list of symptoms, although it is assumed that distressed behaviour covers this. Although the guideline advises GOR should not be investigated, parents need to be assured that their concerns are taken seriously and babies are investigated if they have the above symptoms.	Thank you for your comment. Pain is not listed because the pre-verbal child is not able to verbalise pain symptoms so other signs must be looked for. The stakeholder is correct that distressed behaviour is intended to cover those signs that a parent or health care professional might observe and that might raise a suspicion of pain. Recommendations 4, 6, 20, 23, 25, 26, 27 and 30 all provide advice on the management of infants with signs of distress. The advice on when not to routinely investigate or treat are aimed at avoiding unhelpful and potentially harmful or distressing interventions.
National Childbirth Trust	4	Full	21	13-30	We agree that reflux or GOR may be over-diagnosed by parents in infancy, partly due to the promotion of formula milks which are advertised as 'Anti-Reflux'	Thank you for your comment.
National Childbirth Trust	5	Full	23	38-40	It is helpful to have clarification on sleeping position, However this is not detailed enough. Is the advice not to raise the head of the cot at all? The Cochrane review notes: Elevating the head of the crib for treating reflux in the supine position is not justifiable, yet this advice is frequently given to parents.	Thank you for your comment. We did not find evidence to support such practice in the treatment of GORD and therefore did not make a recommendation.
National Childbirth Trust	6	Full	24	7-8	In view of the fact that babies with GOR and evident pain need investigation NCT believe that thickened formulae should only be available on prescription. The sales of the many formula milks advertised as suitable for reflux	Thank you for this comment. Recommendation 26 outlines stepped management for infants with "frequent regurgitation and marked distress". As a minimum a feeding review should be

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					indicate that many parents are deciding to use these without advice from a health professional.	performed by a healthcare professional, before thickened feeds are considered. Additionally as outlined in recommendation 4, the infant should have been reviewed by a health care professional if there is the presence of marked distress in addition to regurgitation. In combination, these recommendations outline that professional advice should be sought prior to administering thickened formula. Hence this guideline should direct concerned parents to the appropriate care pathway and health care professional to reassure them that buying thickened formula over the counter should not be their first action to take.
National Childbirth Trust	7	Full	24 and 146	9-17	Many parents who are concerned about a baby who is regurgitating a lot and appears to be in pain will try different formula milks or even change from breastfeeding to formula in an effort to improve the symptoms. Health professionals need to be aware of this and inform parents that, if the baby does have a problem with regurgitation, changing to formula milk is not likely to improve symptoms. Breastmilk is more easily digested which is an advantage for babies who regurgitate, as well as its other benefits. If different treatment paths are recommended, health professionals need to let parents know this. More needs to be done to protect breastfeeding.	Thank you for your comment. We recognise the many benefits of breast feeding and aim to promote and support this wherever possible. Following this and other stakeholder feedback, amendments were made to the recommendations 25 and 27 for breast-fed infants with frequent regurgitation associated with marked distress such that breastfeeding should be supported with a breastfeeding assessment/advice. However, more prescriptive advice on this topic is beyond the remit of this guideline.
National Childbirth Trust	8	Full	24	13-17	Thickened feeds do not work for all babies and do have side effects and disadvantages. In the Chao and Vandenplas study (2007), 100 infants	Thank you for this comment. We feel that the sequence of recommendations from 24 to 28 now offer professionals

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					<p>were monitored for 8 weeks, and 19 dropped out due to adverse effects such as marked diarrhoea, enteritis, or respiratory infection. Craig et al's (2004) review indicated that coughing and diarrhoea were adverse effects of thickened formula.</p> <p>The evidence is limited and starches are not an ideal food for young babies. If thickened feeds reduce irritability or regurgitation, there would be an advantage to considering a trial without thickened feeds once the baby has recovered as with alginate therapy.</p>	and parents / carers a clear pathway including alternatives if treatment such as thickening are "unsuccessful".
National Childbirth Trust	9	Full	130 and 132	4-43	<p>No research seems to have considered carrying the infant in a sling or upright in arms rather than placing them on their back in a cot as a means of reducing reflux. NCT agree that the evidence of a reduction in SIDS means that recommendations should advocate babies sleeping on their back, but parents often report that keeping babies upright after feeds is effective in reducing episodes of painful reflux, as long as there is not pressure on the abdomen. Positioning advice needs to distinguish between sleeping and times when baby is awake, as in the reference to 'tummy time'.</p> <p>NCT would advocate that research should be carried out to assess the potential benefits of carrying babies in a sling for reducing distressing reflux. This would be relatively cheap and non-invasive to carry out.</p>	Thank you for your comment. We were not aware of any RCTs comparing infants in the positions described with other standard positions. Neither were we aware of other evidence nor have personal experience to recommend any particular positions at different times of day for infants. A more detailed explanation of the reasoning behind our single unambiguous recommendation is made in the full guideline. Like the American Academy for Pediatrics, we recommend that positional management should not be used as a treatment for GOR in sleeping infants because any potential small individual benefit would almost certainly be outweighed by the very real risk of SIDS in the individual and would quite possibly pose a risk to the much larger population of well infants with normal regurgitation and mild physiological GOR were this dangerous practice to become

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						widespread once again.
National Childbirth Trust	10	Full	134 -140 and 142	All	Grade tables are useful but do not give details on how studies are funded. There is the potential for conflicts of interest and bias if studies with positive results are published whereas those without positive findings are not.	Thank you for your comment. Grade tables do not give details on how studies are funded however the evidence tables do - details of funding sources are systematically recorded in the evidence tables and we have sight of this information when making recommendations. With regards to publication bias, we follow the NICE methodology of including published studies only. A larger volume of evidence would have allowed us to examine publication bias in more detail - unfortunately there were insufficient studies available for each comparison for this to be examined meaningfully.
National Childbirth Trust	11	Full	134 -140	all	Where thickened feeds are used, some studies have found increased weight gain in babies on thickened feeds	Thank you for your comment. Weight gain was included as an outcome to evaluate the effects of thickened feeds in infants with faltering growth (See Table 35 in the full guideline). However, it was not prioritised as an outcome otherwise nor considered as an adverse outcome. We do not believe that the stakeholders concern warrants a change to recommendations because the benefit of any treatment (such as thickened feeds) should be considered against potential harm.
National Childbirth Trust	12	Full	142	13-16	Some babies with cow's milk allergy seems to exhibit reflux also. Colic has also been ascribed to cow's milk protein allergy in a small proportion of babies. There is certainly a need	Thank you for your comment. Following stakeholder consultation, we gave careful consideration to the differential diagnosis in children

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					for further research in this area.	presenting with possible GORD. A new recommendation was added (Recommendation 11) to confirm that some symptoms of non-IgE mediated cows' milk protein allergy can be similar to those of GORD, especially in infants with atopic symptoms, signs, and/or a family history and which cross refers the reader to NICE CG 116 'Food allergy in children and young people'. Amendments were also made to Recommendation 5 in Table R1 that lists 'red flag' signs and symptoms that may suggest disorders other than GOR in those with vomiting or regurgitation. A cross reference to NICE CG 116 was added to the symptom/sign of 'Blood in stool' 'Chronic diarrhoea' was added to the gastrointestinal list of signs/symptoms with a cross reference to NICE CG 116. Finally the sign/symptom 'Eczema' was amended and broadened to 'Infants and children with, or at high risk of, atopy' and the suggested action of a 'Trial of milk exclusion' was removed because this clinical recommendation was not made in this GORD guideline. A research recommendation was made however and the research question was amended following stakeholder consultation. This now specifies that a randomised controlled trial should be performed to examine the clinical and cost effectiveness of a hydrolysed formula trial in formula fed infants with

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						frequent regurgitation associated with marked distress (Section 5.2.8)
Neonatal & Paediatric Pharmacists Group	1	NICE	17	General	It will surprise that there is no distinction made between the use of the PPI and the H2RA. Acid has a role in the gut and therefore suppression of acid is not without consequence. The relative suppression varies between products and thus it is surprising that no distinction is made between the 2 and allowing this to be purely led by "specialists" is a little misleading as they all do different things. We would like reference made to the fact that the newborn gut is already less acidic than older children and thus the role of acid suppression in the first place. We would like to see mention of the lack of differentiation of H receptors in newborns (particularly prems) who may see unwanted side effects of H2RAs.	<p>Thank you for your comment. It is expected that clinicians use their knowledge and experience alongside recommendations when prescribing treatment to patients.</p> <p>We did not make detailed recommendations on the choice of H2R antagonists versus PPIs because the evidence reviews did not identify comparative trial data for children to support this. It was recognised that drugs including these agents have the potential to cause harm. On that basis they endeavoured through their recommendation on the use of these drugs to avoid unnecessary usage and to limit duration of exposure through 'trials of treatment' to a period of several weeks.</p>
Neonatal & Paediatric Pharmacists Group	2	NICE	18	1.3.8	To lump metoclopramide, domperidone and erythromycin together as "leave to specialist care" also seems a little poor in terms of guidance. Many children are started in specialist care and transferred to the community on these medicines. All have their pros and cons and potentially more cons than pros and we feel that this statement is likely to lead to no direction of travel for treatment of children.	Thank you for your comment. Those who initiate treatment in specialist care should have a clear plan for treatment outlined by the specialist and therefore we made a recommendation with the caveat that these drugs should only be used with specialist advice.
NHS Choices	1	NICE	General	General	We welcome the GORD guideline and have no comments on its content as part of the consultation	Thank you for your comment.
Nottingham	1	Full	18	16	Infants/ young children without overt	Thank you for your comment. There

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CityCare Partnership				-19	regurgitation but suffering with distress or feeding difficulties could still be suffering from GOR, possibly alongside conditions such as CMA (cow's milk allergy), which should be suspected as proposed 'red flag' symptoms under comment 17	<p>are a variety of possible explanations for the clinical manifestations listed and clinicians should naturally take them seriously and carry out a careful clinical assessment.</p> <p>The evidence reviews carried out for this guideline did not find persuasive evidence that occult reflux was a likely explanation for these manifestations when they occurred in isolation and hence the recommendation not to routinely investigate or treat for GORD. However, a new recommendation was added (Recommendation 11) to confirm that some symptoms of non-IgE mediated cows' milk protein allergy can be similar to those of GORD, especially in infants with atopic symptoms, signs, and/or a family history and which cross refers the reader to NICE CG 116 'Food allergy in children and young people'.</p> <p>Amendments were also made to Recommendation 5 in Table R1 that lists 'red flag' signs and symptoms that may suggest disorders other than GOR in those with vomiting or regurgitation. A cross reference to NICE CG 116 was added to the symptom/sign of 'Blood in stool' 'Chronic diarrhoea' was added to the gastrointestinal list of signs/symptoms with a cross reference to NICE CG 116. Finally the sign/symptom 'Eczema' was amended</p>

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						and broadened to 'Infants and children with, or at high risk of, atopy' and the suggested action of a 'Trial of milk exclusion' was removed because this clinical recommendation was not made in this GORD guideline.
Nottingham CityCare Partnership	2	Full	18	36 & 39	Feeding aversion and regurgitation hx and back arching can be symptoms of CMA - see comment 10	Thank you for your comment. Following stakeholder consultation, we gave careful consideration to the differential diagnosis in children presenting with possible GORD. A new recommendation was added (Recommendation 11) to confirm that some symptoms of non-IgE mediated cows' milk protein allergy can be similar to those of GORD, especially in infants with atopic symptoms, signs, and/or a family history and which cross refers the reader to NICE CG 116 'Food allergy in children and young people'. Amendments were also made to Recommendation 5 in Table R1 that lists 'red flag' signs and symptoms that may suggest disorders other than GOR in those with vomiting or regurgitation. A cross reference to NICE CG 116 was added to the symptom/sign of 'Blood in stool' 'Chronic diarrhoea' was added to the gastrointestinal list of signs/symptoms with a cross reference to NICE CG 116. Finally the sign/symptom 'Eczema' was amended and broadened to 'Infants and children with, or at high risk of, atopy' and the suggested action of a 'Trial of milk exclusion' was removed because this

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						clinical recommendation was not made in this GORD guideline. A research recommendation was made however and the research question was amended following stakeholder consultation. This now specifies that a randomised controlled trial should be performed to examine the clinical and cost effectiveness of a hydrolysed formula trial in formula fed infants with frequent regurgitation associated with marked distress (Section 5.2.8).
Nottingham CityCare Partnership	3	Full	18	40	Suggest starting statement with 'the following lifestyle measures for GOR should be considered if red flags suggestive of conditions other than GOR are absent	Thank you for your comment. We are unsure as to where the suggested amendment should be made, but do not consider the amendment appropriate to add to the recommendation 26: In formula-fed infants with frequent regurgitation associated with marked distress, use the following stepped-care approach: <ul style="list-style-type: none"> • review the feeding history, then • reduce the feed volumes only if excessive for the infant's weight, then • offer a trial of smaller, more frequent feeds (while maintaining an appropriate total daily amount of milk) unless the feeds are already small and frequent, then • offer a trial of thickened formula (for example, containing rice starch, cornstarch, locust bean gum or carob bean gum).
Nottingham CityCare	4	Full	18	General	No mention of what to do for breast fed infants – as per comment 15, 3 and 13, should start	Thank you for your comment. The focus of the guideline was on the

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Partnership			-19		with stating that mothers of breastfed babies with a positive allergy focused clin hx should undertake a 4 wk cow's milk exclusion trial. In those with negative history, there should be the option for breast fed infants to be trialled on a feed thickener e.g carob mixed to paste or alginate if unsuccessful	diagnosis and management of GORD as defined in the glossary and was not a detailed guideline on non IgE cell mediated food allergy. With regard to the use of a 4 week maternal cows' milk exclusion trial, we did search for RCTs evaluating maternal dietary manipulation for the treatment of GORD in the breastfed infant however none were found and no recommendation was given for this strategy.
Nottingham CityCare Partnership	5	Full	19	1 -2	If have CMA and ongoing GOR, would not be able to use standard thickened formula. Therefore also need to include addition of a low energy feed thickener e.g. Carob bean gum	Thank you for your comment. This guideline does not advocate the use of cows' milk exclusion in the treatment of GORD in any of its manifestations. It does not therefore give guidance on strategies to avoid cows' milk – in thickeners or otherwise.
Nottingham CityCare Partnership	6	Full	19	3 -6	No mention that common side effect of feed thickener/ alginates is constipation, which could exacerbate GOR	Thank you for your comment. Adverse events were reported in the review of RCT evidence in relation to feed thickeners and alginates. No evidence was found to suggest these products cause constipation or exacerbate GORD.
Nottingham CityCare Partnership	7	Full	19	Table R1	See comments on table under point 17	Thank you for your comment. Following stakeholder consultation, we gave careful consideration to the differential diagnosis in children presenting with possible GORD. A new recommendation was added (Recommendation 11) to confirm that some symptoms of non-IgE mediated cows' milk protein allergy can be similar to those of GORD, especially in

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						<p>infants with atopic symptoms, signs, and/or a family history and which cross refers the reader to NICE CG 116 'Food allergy in children and young people'. Amendments were also made to Recommendation 5 in Table R1 that lists 'red flag' signs and symptoms that may suggest disorders other than GOR in those with vomiting or regurgitation. A cross reference to NICE CG 116 was added to the symptom/sign of 'Blood in stool'. 'Chronic diarrhoea' was added to the gastrointestinal list of signs/symptoms with a cross reference to NICE CG 116. Finally the sign/symptom 'Eczema' was amended and broadened to 'Infants and children with, or at high risk of, atopy' and the suggested action of a 'Trial of milk exclusion' was removed because this clinical recommendation was not made in this GORD guideline. A research recommendation was made however the research question was amended following stakeholder consultation. This now specifies that a randomised controlled trial should be performed to examine the clinical and cost effectiveness of a hydrolysed formula trial in formula fed infants with frequent regurgitation associated with marked distress (Section 5.2.8).</p>
Nottingham CityCare Partnership	8	Full	21	22-30	Add in symptoms suggestive of food allergy as listed in NICE CG116 such as 'loose or mucousy stools, constipation in infancy or atopic conditions e.g. eczema in infancy'	Thank you for your comment. Following stakeholder consultation, we gave careful consideration to the differential diagnosis in children

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						presenting with possible GORD. A new recommendation was added (Recommendation 11) to confirm that some symptoms of non-IgE mediated cows' milk protein allergy can be similar to those of GORD, especially in infants with atopic symptoms, signs, and/or a family history and which cross refers the reader to NICE CG 116 'Food allergy in children and young people'. Amendments were also made to Recommendation 5 in Table R1 that lists 'red flag' signs and symptoms that may suggest disorders other than GOR in those with vomiting or regurgitation. A cross reference to NICE CG 116 was added to the symptom/sign of 'Blood in stool' 'Chronic diarrhoea' was added to the gastrointestinal list of signs/symptoms with a cross reference to NICE CG 116. Finally the sign/symptom 'Eczema' was amended and broadened to 'Infants and children with, or at high risk of, atopy' and the suggested action of a 'Trial of milk exclusion' was removed because this clinical recommendation was not made in this GORD guideline.
Nottingham CityCare Partnership	18	Full	21 -25	General	There appears to be no recommendation regarding avoidance of constipation and active treatment thereof as per http://cks.nice.org.uk/gord-in-children#!diagnosissub:1 and Sutphen, 2001. Is it colic or is it gastroesophageal reflux? <i>J Pediatr Gastro Nutr</i> , 33 (2) : 110-111	Thank you for your comment. We agree that children with constipation might need management however we did not review evidence on the role of constipation precipitating GORD.
Nottingham	9	Full	23	1	Forceful/ projectile vomiting in infants from birth	Thank you for your comment.

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CityCare Partnership				-3	can be due to cow's milk allergy (CMA). Surely not every child with projectile vomiting is going to need urgent referral for pyloric stenosis? Allergy focused clinical hx as per NICE CG116 should help in differential diagnosis.	<p>Following stakeholder consultation, we gave careful consideration to the differential diagnosis in children presenting with possible GORD. A new recommendation was added (Recommendation 11) to confirm that some symptoms of non-IgE mediated cows' milk protein allergy can be similar to those of GORD, especially in infants with atopic symptoms, signs, and/or a family history and which cross refers the reader to NICE CG 116 'Food allergy in children and young people'. Amendments were also made to Recommendation 5 in Table R1 that lists 'red flag' signs and symptoms that may suggest disorders other than GOR in those with vomiting or regurgitation. A cross reference to NICE CG 116 was added to the symptom/sign of 'Blood in stool'. 'Chronic diarrhoea' was added to the gastrointestinal list of signs/symptoms with a cross reference to NICE CG 116. Finally the sign/symptom 'Eczema' was amended and broadened to 'Infants and children with, or at high risk of, atopy' and the suggested action of a 'Trial of milk exclusion' was removed because this clinical recommendation was not made in this GORD guideline.</p> <p>An amendment was not made to the symptom/sign of 'Frequent, forceful (projectile) vomiting' because this symptom in an infant up to 2 months</p>

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						old is a 'red flag' that must alert clinicians to the possibility of hypertrophic pyloric stenosis.
Nottingham CityCare Partnership	10	Full	23	4 -18	As per NASPGHAN/ ESPGHAN GOR guidelines, 2009 infants with faltering growth and recurrent vomiting (6.1.2) and unexplained distress for which GOR is not a common cause (6.1.3) may benefit from a 2 week trial on a hypoallergenic formula to exclude CMA. Feeding aversion, back arching, melaena and iron deficiency as per NICE CG116 are also symptoms of possible CMA. Therefore these groups of children do not necessarily warrant referral for endoscopy/ biopsies until this has been ruled out, starting with an allergy focused clinical hx and possible 2-4 week exclusion trial with hypoallergenic formula or cow's milk exclusion diet in breastfeeding mums	Thank you for your comment. Following stakeholder consultation, we gave careful consideration to the differential diagnosis in children presenting with possible GORD. A new recommendation was added (Recommendation 11) to confirm that some symptoms of non-IgE mediated cows' milk protein allergy can be similar to those of GORD, especially in infants with atopic symptoms, signs, and/or a family history and which cross refers the reader to NICE CG 116 'Food allergy in children and young people'. Amendments were also made to Recommendation 5 in Table R1 that lists 'red flag' signs and symptoms that may suggest disorders other than GOR in those with vomiting or regurgitation. A cross reference to NICE CG 116 was added to the symptom/sign of 'Blood in stool'. 'Chronic diarrhoea' was added to the gastrointestinal list of signs/symptoms with a cross reference to NICE CG 116. Finally the sign/symptom 'Eczema' was amended and broadened to 'Infants and children with, or at high risk of, atopy' and the suggested action of a 'Trial of milk exclusion' was removed because this clinical recommendation was not made in this GORD guideline. A research recommendation was made however

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						and the research question was amended following stakeholder consultation. This now specifies that a randomised controlled trial should be performed to examine the clinical and cost effectiveness of a hydrolysed formula trial in formula fed infants with frequent regurgitation associated with marked distress (Section 5.2.8).
Nottingham CityCare Partnership	11	Full	23	33 -37	UTIs are not a common cause of faltering growth as per NICE CG54. Unexplained fever should perhaps be included. Frequent regurgitation, distress and faltering growth are more likely due to CMA than UTI in infants and young children as per CG116/ NASPGHAN/ ESPGHAN, 2009.	Thank you for your comment. We did consider that in the setting of vomiting/regurgitation and faltering growth, it would be important to do a urine test to rule out a UTI. Even if this is relatively infrequent, it would be very important. The importance of fever as a red flag is highlighted in recommendation 5 and the NICE Feverish illness in children guideline (CG 160) is signposted in that recommendation. The possible contribution of cows' milk allergy to vomiting or regurgitation is also highlighted in recommendation 5 and NICE CG116 'Food allergy in children and young people' is signposted.
Nottingham CityCare Partnership	12	Full	23	38 40	Whilst supine sleeping is agreed, there is no mention of raising the head end of bed which is suggested in both Dr Thomson's fact sheet for health visitors, endorsed by DH: http://www.ihv.org.uk/uploads/21%20GPP_Managing%20Reflux_V4.pdf and the recent review by Onyeador et al, 2014. Paediatric GOR clinical practice guidelines <i>Arch</i>	Thank you for your comment. The evidence review did not identify randomised controlled trials that showed raising the head end of the bed had efficacy in the treatment of GORD and so it was not recommended as an effective treatment.

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					<i>Dis Child Educ Pract Ed</i> who recommends a 30 ⁰ elevation	
Nottingham CityCare Partnership	13	Full	23	41 -42	As per comment 3 – should only undertake these measures if red flags suggestive of other conditions are absent, which should include ruling out CMA from allergy focused clin hx.	Thank you for your comment. Following stakeholder consultation, we gave careful consideration to the differential diagnosis in children presenting with possible GORD. A new recommendation was added (Recommendation 11) to confirm that some symptoms of non-IgE mediated cows' milk protein allergy can be similar to those of GORD, especially in infants with atopic symptoms, signs, and/or a family history and which cross refers the reader to NICE CG 116 'Food allergy in children and young people'. Amendments were also made to Recommendation 5 in Table R1 that lists 'red flag' signs and symptoms that may suggest disorders other than GOR in those with vomiting or regurgitation. A cross reference to NICE CG 116 was added to the symptom/sign of 'Blood in stool' 'Chronic diarrhoea' was added to the gastrointestinal list of signs/symptoms with a cross reference to NICE CG 116. Finally the sign/symptom 'Eczema' was amended and broadened to 'Infants and children with, or at high risk of, atopy' and the suggested action of a 'Trial of milk exclusion' was removed because this clinical recommendation was not made in this GORD guideline.
Nottingham CityCare	14	Full	24	7	As per comment 5 - need to include addition of a low energy feed thickener e.g. Carob bean	Thank you for your comment. This is included in recommendation 26.

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Partnership				-8	gum	
Nottingham CityCare Partnership	15	Full	24	9 -12	As per comment 3 and 13, should start with stating that mothers of breastfed babies with a positive allergy focused clin hx should undertake a 4 wk cow's milk exclusion trial. In those with negative history, there should be the option for breast fed infants to be trialled on a feed thickener e.g carob mixed to paste as an alternative to a sodium laden alginate, or at least given the option. .	Thank you for your comment. With regard to the use of a 4 week maternal cows' milk exclusion trial for the guideline development group did not find evidence to support this. The evidence reviews looked for RCTs in which infants children and young people with GORD (as defined in the glossary and including those with troublesome overt regurgitation as a form of GORD) was treated with an intervention. No studies looking at maternal dietary exclusions were found. For that reason they were not able to recommend this strategy. The possibility of thickening expressed breast milk was considered but was considered impractical. On the other hand the process for adding Gaviscon to a small volume of of cooled boiled water is well described and was considered a worthwhile strategy.
Nottingham CityCare Partnership	16	Full	24	21 28	(Insert before lines 21-28) In infants and young children with red flag symptoms suggestive of CMA, this should be ruled out first via a 2-4 week trial of extensively hydrolysed formula or cow's milk exclusion for breastfeeding mothers before considering pharmacological therapies – as per NASPGHAN/ ESPGHAN GOR guidelines, 2009, http://cks.nice.org.uk/gord-in-children#!scenario recommendation:2 , recent review by Onyeador et al, 2014.	Thank you for your comment. With regard to the use of a 4 week maternal cows' milk exclusion trial, the guideline development group did not find evidence to support this. The evidence reviews looked for RCTs in which infants children and young people with GORD (as defined in the glossary and including those with troublesome overt regurgitation as a form of GORD) were treated with an intervention. No studies

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						looking at maternal dietary exclusions were found. For that reason they were not able to recommend this strategy.
Nottingham CityCare Partnership	17	Full	25 -26	Table R1	<p>Red flags: Projectile vomiting – rule out possible CMA as per NICE CG116. ? also include oesophageal atresia/ hiatus & diaphragmatic hernias Onset after 6 months could be due to changes in diet e.g. breast to formula or introducing dairy products Blood in stool could be due to CMA - as per NICE CG116 Abdominal distension could be due to CMA - as per NICE CG116 Loose and/ or offensive stools/ diarrhoea, mucus in stools, or constipation in early infancy could be due to CMA - as per NICE CG116 & CKS: http://cks.nice.org.uk/gord-in-children#!diagnosissub:1 Faltering growth could be due to CMA - as per NICE CG116, NASPGHAN/ ESPGHAN GOR guidelines, 2009 Eczema – this needs to be more specific and should state moderate to severe eczema in infants under 6 months of age could be due to CMA as per NICE CG116 and CG57. Specialist referral is not necessary as CG116 encourages primary care to undertake exclusion trial</p>	<p>Thank you for your comment. Following stakeholder consultation, we gave careful consideration to the differential diagnosis in children presenting with possible GORD. A new recommendation was added (Recommendation 11) to confirm that some symptoms of non-IgE mediated cows' milk protein allergy can be similar to those of GORD, especially in infants with atopic symptoms, signs, and/or a family history and which cross refers the reader to NICE CG 116 'Food allergy in children and young people'. Amendments were also made to Recommendation 5 in Table R1 that lists 'red flag' signs and symptoms that may suggest disorders other than GOR in those with vomiting or regurgitation. A cross reference to NICE CG 116 was added to the symptom/sign of 'Blood in stool'. 'Chronic diarrhoea' was added to the gastrointestinal list of signs/symptoms with a cross reference to NICE CG 116. Finally the sign/symptom 'Eczema' was amended and broadened to 'Infants and children with, or at high risk of, atopy' and the suggested action of a 'Trial of milk exclusion' was removed because this clinical recommendation was not made in this GORD guideline. A research recommendation was made however</p>

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						and the research question was amended following stakeholder consultation. This now specifies that a randomised controlled trial should be performed to examine the clinical and cost effectiveness of a hydrolysed formula trial in formula fed infants with frequent regurgitation associated with marked distress (Section 5.2.82).
Nottingham CityCare Partnership	19	Full	28 and 30	Box A	See previous comments 1 & 2	Thank you for your comment. Following stakeholder consultation, we gave careful consideration to the differential diagnosis in children presenting with possible GORD. A new recommendation was added (Recommendation 11) to confirm that some symptoms of non-IgE mediated cows' milk protein allergy can be similar to those of GORD, especially in infants with atopic symptoms, signs, and/or a family history and which cross refers the reader to NICE CG 116 'Food allergy in children and young people'. Amendments were also made to Recommendation 5 in Table R1 that lists 'red flag' signs and symptoms that may suggest disorders other than GOR in those with vomiting or regurgitation. A cross reference to NICE CG 116 was added to the symptom/sign of 'Blood in stool'. 'Chronic diarrhoea' was added to the gastrointestinal list of signs/symptoms with a cross reference to NICE CG 116. Finally the sign/symptom 'Eczema' was amended and broadened to 'Infants and children

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						with, or at high risk of, atopy' and the suggested action of a 'Trial of milk exclusion' was removed because this clinical recommendation was not made in this GORD guideline. A research recommendation was made however and the research question was amended following stakeholder consultation. This now specifies that a randomised controlled trial should be performed to examine the clinical and cost effectiveness of a hydrolysed formula trial in formula fed infants with frequent regurgitation associated with marked distress (Section 5.2.8).
Nottingham CityCare Partnership	20	Full	144 -145	6.2.6.2.3	Evidence to support the role of CMA and GORD: Farahmand et al, 2011 demonstrated 1/3 rd their kids with GOR had CMA http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3166669/ Cavataio et al, 2000. Summarise the findings of a number of their studies, suggesting CMA is present in up to 42% of those with GOR NICE CG116 GDG expert consensus believes GOR can be commonly caused by CMA, as also referred to by CKS, NASPGHAN/ ESPGHAN, Onyeador et al, iHV fact sheet as per comment 5 CMA should be suspected in infants with a number of symptoms in keeping with those listed in CG116, determined by undertaking an allergy focused clinical hx. These symptoms should be listed as red flags to enable differential diagnosis. The lack of adherence to the NICE allergy guidelines are likely to result in inappropriate	Thank you for your comment. Following stakeholder consultation, we gave careful consideration to the differential diagnosis in children presenting with possible GORD. A new recommendation was added (Recommendation 11) to confirm that some symptoms of non-IgE mediated cows' milk protein allergy can be similar to those of GORD, especially in infants with atopic symptoms, signs, and/or a family history and which cross refers the reader to NICE CG 116 'Food allergy in children and young people'. Amendments were also made to Recommendation 5 in Table R1 that lists 'red flag' signs and symptoms that may suggest disorders other than GOR in those with vomiting or regurgitation. A cross reference to NICE CG 116 was added to the symptom/sign of 'Blood in

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					<p>prescribing of formula, lack of re-challenging to confirm diagnosis which would rule out the 'placebo effect' and lack of follow up/ referral to a dietitian to support ongoing management, review of formula and future re-challenging. From my experience, parents tend to be reluctant to use hypoallergenic formula due to their unpleasant smell and taste. It will be good to hear views from patient support groups on this matter.</p> <p>All allergists and allergy dietitians will be able to demonstrate resolution of symptoms in breast fed babies following adoption of cow's milk free diet in breastfeeding mothers.</p>	<p>stool'. 'Chronic diarrhoea' was added to the gastrointestinal list of signs/symptoms with a cross reference to NICE CG 116. Finally the sign/symptom 'Eczema' was amended and broadened to 'Infants and children with, or at high risk of, atopy' and the suggested action of a 'Trial of milk exclusion' was removed because this clinical recommendation was not made in this GORD guideline. A research recommendation was made however and the research question was amended following stakeholder consultation. This now specifies that a randomised controlled trial should be performed to examine the clinical and cost effectiveness of a hydrolysed formula trial in formula fed infants with frequent regurgitation associated with marked distress (Section 5.2.8). Farahmand et al, 2011 did not meet the inclusion criteria for the review question. It was not a clinical trial and had no comparator/control group. Cavataio et al, 2000 was a narrative review (and not a systematic review) that discussed the main features of cows' milk protein allergy (CMPA) and gastroesophageal reflux (GER). In this review, the authors summarised findings of a number of their studies: Iacono et al, 1996; Cavataio et al, 1996 (American Journal of Gastroenterology); and Cavataio et al, 1996 (Archives of Diseases in</p>

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						Childhood). These studies were also assessed for inclusion but none fit the criteria for the review question. Vandeenplas et al, 2013 is a practice guideline based on the recommendations of the North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition and the European Society for Pediatric Gastroenterology, Hepatology, and Nutrition, that does not follow NICE methodology. Onyeadour et al, 2014 was a guideline review that focused mainly on the practice guideline of the North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition and the European Society for Pediatric Gastroenterology, Hepatology, and Nutrition.
Nottingham CityCare Partnership	21	Full	146	6.2.7.2	Cow's milk intolerance is not a term used by NICE CG116 as it does not accurately represent the condition. The term used should be non-IgE mediated cow's milk allergy, as it does involve the immune system and can involve high levels of sensitivity to trace amounts. As per comments 6.2.6.2.3, cow's milk elimination trials should be done in accordance with NICE CG116 which would avoid infants 'being left on formula for prolonged periods'	Thank you for your comment. We have amended the term used in recommendations to 'non-IgE mediated cows' milk protein allergy'. Following stakeholder consultation, amendments were made to recommendation 11 to improve cross referencing to NICE CG116 but a clinical recommendation for a trial of cows' milk elimination was not made because of the paucity of evidence to support this practice in those with GORD. A research recommendation was made however and the research question was amended following stakeholder consultation. This now specifies that a

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						randomised controlled trial should be performed to examine the clinical and cost effectiveness of a hydrolysed formula trial in formula fed infants with frequent regurgitation associated with marked distress (Section 5.2.8).
Nottingham CityCare Partnership	22	Full	147	13-15	The sodium content of Gaviscon Infant is likely to double an infant's overall intake, which might not be a concern in premature infants but is more so in term infants where if the recommended dose is exceeded, they can consume above the upper FSA recommended limit	Thank you for this comment. Clearly, as you point out taking any medicine outside the recommended dosage advice could be potentially hazardous. We feel that this guideline may well lead to a net reduction in the use of this medication with a greater emphasis on feed thickeners or other conservative measures.
Nottingham University Hospitals	1	Full	19	1-2	Are you suggesting use of a ready thickened formula or addition of a prescribed thickener to current formula? This should be made clear so that GP knows which is preferable, whether to suggest family buy an appropriately thickened formula or to prescribe one or to prescribe a thickener only	Thank you for your comment. We did not make a preference between the two methods of thickening formula.
Nottingham University Hospitals	2	Full	19	3-4	<p>Alginate therapy in infants (Gaviscon Infant) is only a thickener so not really a different therapy – just a different product to others e.g. Instant Carobel, etc.</p> <p>Although the draft document doesn't seem to have done so, the <u>majority</u> of times I hear Gaviscon Infant being discussed it is suggested as having a different mode of action to other thickeners either because:</p> <ol style="list-style-type: none"> 1. It forms a raft And/or 2. It has NaHCO₃ in it so acts as an 	<p>Thank you for your comment. The guideline recommended the use of a thickener based on a review of the evidence from comparative trials. There was some evidence for the efficacy of Gaviscon in overt regurgitation and so a recommendation was made to try this if other thickeners were unsuccessful.</p> <p>Clearly health care professionals might have reason to prefer a different approach in special circumstances – such as enteral tube administration.</p>

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					<p>antacid</p> <p>As you know neither of these is true! I may be exaggerating when I say the majority but it is extremely common and one of my 'soap-box' issues!!</p> <p>If we use anything, we use Gaviscon Infant as first line thickening in preterm babies on our neonatal intensive care for a number of reasons:</p> <ol style="list-style-type: none"> 1. Individual sachets – infection control/accuracy of measuring 2. Main thickening action occurs on contact with stomach acid so less likely to block tubes and many of our babies are tube fed for extended periods 3. Na isn't usually an issue as they are very often on Na supplements as they have high early renal losses and then high requirements <p>Having said that I'm not at all convinced of its efficacy and prefer not to see it used!!!</p> <p>So, although happy for them to be differentiated – because of the high Na that may not be desirable in normal term infants - I'd prefer to see an explanation of its mode of action being purely as a thickener and not as a raft former (which would be of no value whatsoever in a baby lying flat as the raft would float in entirely the wrong place) or antacid like the rest of the Gaviscon range – which might be of benefit in older infants who are vertical more of the time</p>	

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					and children.	
Nottingham University Hospitals	3	Full	23	1-18	What about cow's milk protein allergy as per NICE allergy guidance? Use of allergy focussed clinical history and hypoallergenic formula if indicated prior to invasive procedures such as endoscopy and biopsy.	Thank you for your comment. Following stakeholder consultation, we gave careful consideration to the differential diagnosis in children presenting with possible GORD. A new recommendation was added (Recommendation 11) to confirm that some symptoms of non-IgE mediated cows' milk protein allergy can be similar to those of GORD, especially in infants with atopic symptoms, signs, and/or a family history and which cross refers the reader to NICE CG 116 'Food allergy in children and young people'. Amendments were also made to Recommendation 5 in Table R1 that lists 'red flag' signs and symptoms that may suggest disorders other than GOR in those with vomiting or regurgitation. A cross reference to NICE CG 116 was added to the symptom/sign of 'Blood in stool' 'Chronic diarrhoea' was added to the gastrointestinal list of signs/symptoms with a cross reference to NICE CG 116. Finally the sign/symptom 'Eczema' was amended and broadened to 'Infants and children with, or at high risk of, atopy' and the suggested action of a 'Trial of milk exclusion' was removed because this clinical recommendation was not made in this GORD guideline. A research recommendation was made however and the research question was amended following stakeholder

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						consultation. This now specifies that a randomised controlled trial should be performed to examine the clinical and cost effectiveness of a hydrolysed formula trial in formula fed infants with frequent regurgitation associated with marked distress (Section 5.2.8).
Nottingham University Hospitals	4	Full	24	7-8	Are you suggesting use of a ready thickened formula or addition of a prescribed thickener to current formula? This should be made clear so that GP knows which is preferable, whether to suggest family buy an appropriately thickened formula or to prescribe one or to prescribe a thickener only	Thank you for your comment. We did not make a preference between the two methods of thickening formula.
Nottingham University Hospitals	6	Full	24	9-17	Alginate therapy in infants (Gaviscon Infant) is only a thickener so not really a different therapy – see above	Thank you for your comment. The guideline recommended the use of a thickener based on a review of the evidence from comparative trials. There was some evidence for the efficacy of Gaviscon in overt regurgitation and so a recommendation was made to try this if other thickeners were unsuccessful
Nottingham University Hospitals	5	Full	25 -26	Table	This doesn't support information in either NICE Food Allergy Guidance (116) or Eczema (57)	Thank you for your comment. Following stakeholder consultation, we gave careful consideration to the differential diagnosis in children presenting with possible GORD. A new recommendation was added (Recommendation 11) to confirm that some symptoms of non-IgE mediated cows' milk protein allergy can be similar to those of GORD, especially in infants with atopic symptoms, signs, and/or a family history and which cross refers the reader to NICE CG 116

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						'Food allergy in children and young people'. Amendments were also made to Recommendation 5 in Table R1 that lists 'red flag' signs and symptoms that may suggest disorders other than GOR in those with vomiting or regurgitation. A cross reference to NICE CG 116 was added to the symptom/sign of 'Blood in stool' 'Chronic diarrhoea' was added to the gastrointestinal list of signs/symptoms with a cross reference to NICE CG 116. Finally the sign/symptom 'Eczema' was amended and broadened to 'Infants and children with, or at high risk of, atopy' and the suggested action of a 'Trial of milk exclusion' was removed because this clinical recommendation was not made in this GORD guideline. A research recommendation was made however and the research question was amended following stakeholder consultation. This now specifies that a randomised controlled trial should be performed to examine the clinical and cost effectiveness of a hydrolysed formula trial in formula fed infants with frequent regurgitation associated with marked distress (Section 5.2.8).
Nottingham University Hospitals	7	Full	161	43-44	Alginate therapy in infants (Gaviscon Infant) is only a thickener so not really a different therapy – see above	Thank you for this comment. The intended pharmacological action of this agent is not as a thickener. Although we are aware of this professional opinion.
Nottingham University	8	Full	161	52 - 2	Why not use carob thickener as paste in breast fed infant rather than Gaviscon Infant?	Thank you for your comment. The possibility of thickening expressed

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Hospitals			-2			breast milk was considered but was considered impractical. On the other hand the process for adding Gaviscon to a small volume of cooled boiled water is well described and was considered a worthwhile strategy.
Nottingham University Hospitals	9	Full	162	27-34	Why not use carob thickener as paste in breast fed infant rather than Gaviscon Infant?	Thank you for your comment. There is a standard process for mixing Gaviscon Infant (included in the product instructions) with a small volume of cooled boiled water is well described. No such process is described for thickeners.
Royal College of General Practitioners	1	NICE	General		This guideline is extremely long, wordy and quite difficult to read. There is a huge amount of useful information in the guideline but it needs to be streamlined and be more concise and less prolix. For it to be useful to clinicians I would expect it to be more user - friendly with better flow charts and protocols included. I cannot imagine anyone apart from a paediatric gastroenterologist getting to the end of this guideline without getting confused.	Thank you for your comment. NICE guidelines are produced using standard templates (for the NICE and full versions) and guidance will also be published as an interactive 'NICE Pathway'.
Royal College of General Practitioners	2	NICE	General		No specific comments, but recommendations appear well balanced and helpful for both discussion with parents and management options.	Thank you for your comment.
Royal College of Nursing	1	NICE	General		There are no comments to submit on behalf of the Royal College of Nursing to inform on the above guideline consultation. Thank you for the opportunity to participate.	Thank you for your comment.
Royal College of Paediatrics and Child	8	NICE	General		It is not sufficiently clear that the guideline covers neonates and infants.	Thank you for your comment. We disagree and consider that throughout the guideline, the recommendations refer to various population groups

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Health						comprised of infants, children or young people. Further, there are many specific recommendations that relate only to infants and even highlight particular issues within different stages of infancy. It is true that the guideline does not make specific reference to neonates (infants within the first month of life) but this does not mean that the principles outlined cannot be applied to this group. Please also see section 4.1.1 of the final scope.
Royal College of Paediatrics and Child Health	21	NICE	General Research questions		Agree , useful research questions In 2.1 are the existing studies ALL of poor quality ?'...studies limited and of poor quality...' or are many/ most of poor quality? Maybe ALL are poor quality but are any of some quality? ie are you accurate in this criticism?	Thank you for your comment. The evidence meeting the inclusion criteria on the symptoms associated with GOR and/or GORD in children and young people with a neurodisability was limited to three studies and was graded as low to very low quality using standard GRADE methodology. An amendment has been made for clarity.
Royal College of Paediatrics and Child Health	22	NICE	General		Gastroesophageal reflux in children is managed by paediatricians and paediatric gastroenterologists leading to a lot of opinions and views about the condition. The NICE guidance should serve to define the condition, helping to identify the severity as well as understand behind mechanisms of the disease leading to appropriate management. A clear distinction is required as to children with disease being managed in the primary, secondary or tertiary care.	Thank you for your comment. A distinction is made between GOR and GORD and definitions are provided in Section 1 of the NICE guideline. NICE guidelines are not meant to be textbooks but serve to guide management following an interrogation of the evidence. The guideline makes recommendations which refer to the actions being undertaken. The guideline refers to a specialist and we have included the definition used in the NICE guideline. While we would agree it is important for staff working with children with GORD to have the

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						necessary level of knowledge and expertise to deliver care, it is outside of the remit of this guideline to specify the qualifications or competencies professionals should have. This is up to the local arrangements/organisation of the skill set across the region or clinical network.
Royal College of Paediatrics and Child Health	23	NICE	General		There is a great concern regarding the all-inclusive definition for GORD in the NICE document. It implies that any patient or parent who thinks they or their child has reflux is by definition GORD; even if all the tests may be negative without any demonstrable pathology. The group feels that it is unsatisfactory.	Thank you for your comment. We disagree because according to the definition of GORD used in this guideline (and the explanations offered in the introduction), clinical confirmation of the diagnosis would be required by a health professional for either a reliable description of the "complications" or for "medical treatment". Please see the introduction and Section 1 of the NICE guideline for further details.
Royal College of Paediatrics and Child Health	24	NICE	General		All children with Hematemesis should not be referred to a paediatric gastroenterologist. This is not the classical teaching for management of hematemesis. There needs to be some accommodation for those swallowing blood from breast feeding or presumed Mallory-Weiss tear with this being specified in the guidelines	Thank you for your comment. We have amended Table 1 within recommendation 1.1.5 and recommendation 1.1.20 to accommodate your point regarding the possibility of blood being swallowed.
Royal College of Paediatrics and Child Health	25	NICE	General		There has been a lot of feedback about use of Domperidone in view of the recent MHRA statement. Some feedback is to stop its use however majority of the members advise about cautious use. In addition members are advising to have an end point to its use as if no response in 4-6 weeks then it should be stopped hence limiting its use	Thank you for your comment. Our view was that domperidone (and several other prokinetic agents) should only be used following specialist advice. Therefore recommendations have not been made regarding the treatment regimen with domperidone.
Royal	26	NICE	General		There is some recommendation to mention	Thank you for your comment. Our

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College of Paediatrics and Child Health					<p>contraindication to use of Domperidone to people with</p> <p>Heart conduction defects or suspected to be impaired</p> <p>Congestive heart failure</p> <p>Receiving other medications which could prolong QT interval or potent CYP3A4 inhibitors</p> <p>Severe hepatic impairment</p>	view was that domperidone (and several other prokinetic agents) should only be used following specialist advice. Therefore recommendations have not been made regarding advice on contraindications.
Royal College of Paediatrics and Child Health	27	NICE	General		Lothian guidelines from members of BSPGHAN are recommending a max dose of 30mg/day in adolescents over 12 years of age or weighing > 35 kg. when under 12 or <35 kg the recommendation is 0.25mg/kg/dose	Thank you for your comment. We have assumed that the comment refers to the use of domperidone. Our view was that domperidone (and several other prokinetic agents) should only be used following specialist advice. Therefore recommendations have not been made regarding advice regarding the dosage of domperidone.
Royal College of Paediatrics and Child Health	28	NICE	General		There are children who benefit with use of Domperidone and in such cases provided an ECG confirms no safety concerns then we should support longer term use of domperidone. However in the absence of evidence there will be a need of NICE consensus as to what may constitute as effective cardiac monitoring. This is one most important points members have asked to be included in the guidelines	Thank you for your comment. The recommendation states that domperidone (and several other prokinetic agents) should only be used following specialist advice. Cardiac monitoring was not included in the evidence review nor were recommendations made regarding this.
Royal College of Paediatrics and Child Health	29	NICE	General		<p>There needs to be mention of other treatments used for gastroesophageal reflux in the surgical or endoscopic section:</p> <p>Gastroplication – see NICE interventional procedures guidelines IPG404</p> <p>Use of STRETTA anti-reflux procedure</p> <p>Use of TIF – transoral incisionless fundoplication</p> <p>Enteryx injections in the oesophagus -</p>	Thank you for your comment. The scope of the guideline included fundoplication but not other surgical interventions and therefore the procedures to which you refer were not reviewed. For readers who wish to see related guidance there is a list in section 3.2 where Endoluminal gastroplication for gastro-oesophageal

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						reflux disease. NICE interventional procedure guidance 404 (2011) is mentioned.
Royal College of Paediatrics and Child Health	30	NICE	General		Refractory Gastroesophageal reflux needs to be defined with management	<p>Thank you for your comment.</p> <p>In this guideline the term refractory is used in a single recommendation 1.1.20. This recommendation says:</p> <p>“Arrange an urgent specialist hospital assessment for infants, children and young people for a possible upper GI endoscopy with biopsies if there is:...</p> <ul style="list-style-type: none"> retrosternal, epigastric or upper abdominal pain that needs ongoing medical therapy or is refractory to medical therapy...” <p>We do not attempt to define the term refractory GOR as this is highly dependent on the clinical context and requires clinical judgement. Thus, a young person who is much improved but occasionally experiences mild symptoms might be kept under clinical review rather than referring for endoscopy</p> <p>Recommendation 1.3.4 says:</p> <p>“Assess the response to the 4 week trial of the PPI or H2RA, and consider referral to a specialist for possible endoscopy if the symptoms:</p> <ul style="list-style-type: none"> do not resolve or

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						<ul style="list-style-type: none"> recur after stopping the treatment” <p>The phrase “do not resolve” similarly requires clinical interpretation in the specific clinical context.</p>
Royal College of Paediatrics and Child Health	31	NICE	General		Oesophageal dysmotility masquerading with symptoms of reflux deserves a mention. The role of oesophageal manometry should be described	Thank you for your comment. We consider that a tertiary specialist would always be expected to consider a broader differential diagnosis in assessing a referred child. A more detailed discussion and set of recommendations that refer to other conditions that may very rarely mimic the clinical presentation of GORD is beyond the scope of this guideline.
Royal College of Paediatrics and Child Health	32	NICE	General		Special conditions like hypertensive LOS and corkscrew oesophagus perhaps need to be mentioned	Thank you for your comment. We consider that a tertiary specialist would always be expected to consider a broader differential diagnosis in assessing a referred child. A more detailed discussion and set of recommendations that refer to other conditions that may very rarely mimic the clinical presentation of GORD is beyond the scope of this guideline.
Royal College of Paediatrics and Child Health	33	NICE	General		Use of newer agents such as Mosepride require mention	Thank you for your comment. The protocol for the evidence review specified that randomised controlled trials examining prokinetics compared to placebo were to be included (please see Full guideline, Section 6 Pharmacological treatment for the evidence review and Appendix E.7 for the corresponding protocol). Six randomised controlled trials reported

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						relevant outcomes for the prokinetics domperidone and metoclopramide. However no randomised controlled trials comparing mosepride with placebo were identified for inclusion.
Royal College of Paediatrics and Child Health	34	NICE	General		The use of Azithromycin with Erythromycin which is common practice needs mention	<p>Thank you for your comment. The protocol for the evidence review specified that randomised controlled trials examining prokinetics compared to placebo were to be included (see Full guideline, Section 6 Pharmacological treatment for the evidence review and Appendix E.7 for the corresponding protocol). Six randomised controlled trials reported relevant outcomes for the prokinetics domperidone and metoclopramide compared with placebo. However no similar studies were identified for macrolide antibiotics (which include azithromycin and erythromycin).</p> <p>It is acknowledged in the full guideline (section 6.1.6.2.4) that the GDG were aware that erythromycin was in regular clinical use in the NHS for its prokinetic properties. Given the absence of evidence, the clinical opinion and experience of the GDG was that it was an unhelpful agent in the context of GORD and that its use was not justified without seeking specialist advice.</p> <p>We considered your comment but did not agree that the use of azithromycin</p>

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						as a prokinetic agent either with or without erythromycin to be common practice. Further we considered that concurrent prescription of two macrolide antibiotics would not be common practice because of the potential for abnormalities in the QT axis and serious side effects. No amendment to the recommendation was made but this issue has been passed onto the NICE Surveillance Review team to consider.
Royal College of Paediatrics and Child Health	35	NICE	General		The feeding in GOR section is inadequate – use of Whey based feeds either here or treatment section should be mentioned.	Thank you for your comment. The use of whey based feeds was not prioritised and hence was not specified in the protocols for reviews of the evidence.
Royal College of Paediatrics and Child Health	36	NICE	General		The role of specialist (gastroenterologist) needs to be clearer with regard to diagnostic tools available in variable extent. While endoscopy is the main investigation in GORD, the availability of other investigations (impedance, GI physiology such as manometry) can only be performed in a number of centres, and if NICE recommends these investigations, it needs to be emphasised that staff trained in paediatrics (GI physiology) and paediatric specialists need to interpret findings in the clinical context.	Thank you for your comment. The recommendations make reference to endoscopy, to pH studies with or without impedance monitoring together and to other investigations that may be needed to evaluate infants, children or young people with known or possible GORD. Where the guideline speaks about referral to a specialist this means referral to a paediatrician with the skills, experience and competency necessary to deal with the particular clinical concern that has been identified by the referring health care professional. In this guideline this is most likely to be a consultant general paediatrician. Depending on the clinical circumstances, 'specialist' may also refer to a paediatric surgeon, paediatric

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						gastroenterologist or a doctor with the equivalent skills and competency.
Royal College of Paediatrics and Child Health	37	NICE	General		In refractory reflux persists or persistent GORD, these children need work up (ideally multidisciplinary, ideally in established joined clinics) with general paediatricians, surgeons, or other specialists (neurologist, allergist, genetics) to find out underlying causes and manage these patients.	Thank you for your comment. The delivery of care for children and young people with refractory reflux or persistent GORD can be made using different health care professional structures. This guideline outlines the care that should be offered but not the structure or location of the team because it is recognized that a variety of differing models exist across different regions and clinical networks.
Royal College of Paediatrics and Child Health	38	NICE	General		The role of allied health professionals (dieticians and particularly speech and language therapists) in the multidisciplinary assessment and management of these patients needs to be incorporated and their role and importance defined.	Thank you for your comment. Some of the children being assessed for GORD (or conditions with very similar symptoms) may have complex underlying disorders and co-morbidities that require close interdisciplinary working but this aspect of their management falls outside the scope of this GORD guideline.
Royal College of Paediatrics and Child Health	39	NICE	General		Silent reflux needs better definition and evidence based documents – when and how to treat.	Thank you for your comment. Silent reflux in this guideline is referred to as occult reflux. The glossary has been amended in the full guideline to clarify this in accordance with your comment.
Royal College of Paediatrics and Child Health	40	NICE	General		Although apnoeas have been discussed - Desaturations/seizures are a problem and need a paragraph of joined consultations and investigations (e.g. combined impedance with oxygen monitoring/sleep lab), and opportunity for a joined neurological assessment needs to be established in specialised centres and teams in formal pathways.	Thank you for your comment. This is outside the remit of this guideline which is the diagnosis and management of GORD. The investigation and management of apnoea or bradycardia in infants, children or young people is outside the scope of the guideline.
Royal	41	NICE	General		NICE should perhaps make a statement about	Thank you for your comment. We

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College of Paediatrics and Child Health					pharmaceutical companies/input/prospective RCT to investigate further safe prokinetic medications.	recognised that safe and effective prokinetic agents could potentially be helpful. However there were concerns about the use of domperidone as reflected in the recommendation, advising specialist involvement. They were not aware of any new products currently available which currently required investigation by RCT.
Royal College of Paediatrics and Child Health	42	NICE	General		A paragraph needs to address the problem of investigating unsettled children ("colics") with a pathological reflux score on impedance – what teams and how monitoring and treatment of these children is indicated, as there are no medicines available to make these children settled/content. Primary and secondary care professionals need reassurance from NICE that and when no further escalation of investigations and treatment in this group is required.	Thank you for your comment. This guideline focuses on the diagnosis and management of GORD. It was outside the scope of this guideline to address general aspect of investigation and management of distressed children or crying infants. The guideline does address these concerns in relation to the specific consideration of GORD. Based on an evidence review of symptoms and signs of GORD, the guideline development group did advise that when infants and children showed 'distressed behaviour' as an isolated sign and in the absence of overt regurgitation, they should not routinely undergo investigations for gastro-oesophageal reflux (Recommendation 1.1.6). This would no doubt apply to those children who might be labelled as having 'infant colic' or who were more generally unsettled. The guideline also advises consideration of a 4-week trial of an H2RA or a PPI for infants, young children who are unable to verbally express their symptoms and who have

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						overt regurgitation associated with distressed behaviour (Recommendation 1.3.2).
Royal College of Paediatrics and Child Health	43	NICE	General		For a subgroup with a general surgeon in designated clinics and designated ward rounds/clinical settings. The surgical treatment of GOR in neuro-disabled patients is complex and associated with a variable outcome. High failure rates and poor medium-term survival are well documented, particularly for fundoplication which remains the most popular procedure. Numerous surgical strategies have been described which include: gastrostomy feeding, G-J feeding, jejunostomy feeding, fundoplication (both open and laparoscopic), fundoplication variants (e.g. partial Nissen / Thal / Boix-Ochoa / Toupe / fundoplication + vagotomy and pyloroplasty), gastric pacing, oesophago-gastric dissociation, and total parenteral nutrition. Thus far there has been no convincing data to demonstrate the superiority of any of these approaches, principally because the patients form a disparate group whose needs and pathologies are variable.	Thank you for your comment. We were aware of these concerns and issues and of the wide range of interventions. As you are aware, the guideline adopts a conservative approach to the use of enteral tube feeding and to the use of fundoplication. The evidence reviews did not attempt to compare the relative merits of different types of surgical intervention but focussed on identifying those for whom such interventions might be considered.
Royal College of Paediatrics and Child Health	44	NICE	General		The NICE guidance made little reference to tube feeding categories – PEG vs GJ feeding vs surgeon constructed feeding jejunostomy. Gastrojejunal feeding is becoming a popular option which is not without difficulties – This is a topic outside the reflux however in feeding with reflux should be discussed	Thank you for this comment. The guideline contains a series of recommendations on the general topic of enteral tube feeding in the management of children with GORD (Recommendations 1.4.1-1.4.3) In addition, following consideration of stakeholder comments, we have now made a recommendation regarding the role of jejunal feeding (Recommendation 1.4.4). The scope of the guideline did not include a detailed

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						comparison of the many approaches to enteral tube feeding. These are matters often considered in a highly specialised setting and the approach of the guideline was to provide advice on the general topic so that referral to appropriate experts would be considered where necessary.
Royal College of Paediatrics and Child Health	9	NICE	4		Add signs to symptoms	Thank you for your comment. This has now been amended to include 'signs'.
Royal College of Paediatrics and Child Health	10	NICE	7		If the red flags are in the table, remove "following"	Thank you for your comment. The word "following" has been removed.
Royal College of Paediatrics and Child Health	11	NICE	8 -9		Specialists will be overwhelmed, eg feeding aversion and growth faltering are quite common in association with regurgitation	Thank you for your comment. Where the guideline refers to a specialist, refers to a paediatrician with the skills, experience and competency necessary to deal with the particular clinical concern that has been identified by the referring health care professional. In this guideline this is most likely to be a consultant general paediatrician. Depending on the clinical circumstances, 'specialist' may also refer to a paediatric surgeon, paediatric gastroenterologist or a doctor with the equivalent skills and competency. This guideline does not compel health care professionals in primary care to refer infants and children with these problems for a specialist opinion and

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						possible investigation of GORD. In some instances, health care professionals in primary care carry out an empirical trial of treatment if they feel appropriate. However, we would consider that irrespective of whether there is GORD or not infants or children with faltering growth or feed aversions do require appropriate specialist review.
Royal College of Paediatrics and Child Health	16	NICE Summary	11	1.1.3 - 5	Useful normal variants and red flags	Thank you for your comment.
Royal College of Paediatrics and Child Health	1	NICE	12	Table 1	Blood in the stool –may be a symptom of cow's milk protein induced colitis and may warrant a trial of a hydrolysed formula	Thank you for your comment. Following stakeholder consultation, we gave careful consideration to the differential diagnosis in children presenting with possible GORD. Amendments were made to Recommendation 1.1.5 in Table 1 that lists 'red flag' signs and symptoms that may suggest disorders other than GOR in those with vomiting or regurgitation that included a cross reference to NICE CG 116 being added to the symptom/sign of 'Blood in stool'. No clinical recommendation was made for a trial of hydrolysed formula in this GORD guideline. A research recommendation was made however and the research question was amended following stakeholder consultation. This now specifies that a randomised controlled trial should be

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						performed to examine the clinical and cost effectiveness of a hydrolysed formula trial in formula fed infants with frequent regurgitation associated with marked distress (Section 2.2).
Royal College of Paediatrics and Child Health	12	NICE	12 -13		Table needs timescales/urgency	Thank you for your comment. The "red flags" table/recommendation has undergone considerable revision based on stakeholder comments. However, it is emphasized that the guideline is about GORD in children and it would be infeasible to have a series of "mini-guidelines" relating to every red-flag and believe that clinicians need the flexibility to utilize both their common sense and clinical judgement in the context of the services that are available in their own locality/network.
Royal College of Paediatrics and Child Health	2	NICE	13	Table 1	Eczema and/or a history of urticaria, wheeze or stridor with cow's milk formula – may be a symptom of allergy to cow's milk	Thank you for your comment. Following stakeholder consultation, we gave careful consideration to the differential diagnosis in children presenting with possible GORD. A new recommendation was added (Recommendation 1.1.11) to confirm that some symptoms of non-IgE mediated cows' milk protein allergy can be similar to those of GORD, especially in infants with atopic symptoms, signs, and/or a family history and which cross refers the reader to NICE CG 116 'Food allergy in children and young people'. Amendments were also made to Recommendation 1.1.5 in Table 1 that

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						lists 'red flag' signs and symptoms that may suggest disorders other than GOR in those with vomiting or regurgitation. A cross reference to NICE CG 116 was added to the symptom/sign of 'Blood in stool' . 'Chronic diarrhoea' was added to the gastrointestinal list of signs/symptoms with a cross reference to NICE CG 116. Finally the sign/symptom 'Eczema' was amended and broadened to 'Infants and children with, or at high risk of, atopy' and the suggested action of a 'Trial of milk exclusion' was removed because this clinical recommendation was not made in this GORD guideline. A research recommendation was made however and the research question was amended following stakeholder consultation. This now specifies that a randomised controlled trial should be performed to examine the clinical and cost effectiveness of a hydrolysed formula trial in formula fed infants with frequent regurgitation associated with marked distress (Section 2.2). 'Infants with a personal or family history of atopic conditions' are noted as an important population subgroup to consider in such research.
Royal College of Paediatrics and Child Health	13	NICE	13	1.1.7, 1.1 16 etc	Think about is not a helpful term	Thank you for your comment. The term "think about" has been replaced by "consider" in recommendations.
Royal	17	NICE	13	1.1.6	Confusing at least . A summary is probably	Thank you for your comment. NICE

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College of Paediatrics and Child Health					<p>most clinicians' practical reference document, so needs to be clear . This paragraph seems not wholly consistent with later wording in relation to those with neuro disabilities of varying degrees/ communication difficulties .</p> <p>Chronic cough: agree if this is a presenting issue in isolation alongside neuro disability, other invs 1st eg CXR before direct GOR tests but with view to GORD being considered because of relatively low level /hidden reflux. Are GORD investigations dependent entirely on there being CXR changes? [I acknowledge later Research comments re lack of data]</p> <p>Distress : same – ref later re 'considering GORD in communication diffs.'</p>	<p>recommendation 1.1.6 advises that children who have various specified clinical manifestations in isolation without overt regurgitation should not as a matter of routine practice be subjected to investigation or treatment for GORD. We do not understand in what respect you think this is unclear.</p> <p>As the neurodisability recommendation (with which recommendation 1.1.6 is in conflict) is not specified, we have considered the following recommendations:</p> <p>1.1.8 says dental erosion is a recognised complication of GOR especially in those with a neurodisability;</p> <p>1.1.12 highlights the fact that neurodisability as a condition associated with an increased prevalence of GORD;</p> <p>1.1.21 provides advice on the investigation of those with dental erosion and a neurodisability;</p> <p>1.3.2 relates to children with overt regurgitation;</p> <p>We do not regard any of these to be in conflict with NICE recommendation 1.1.6.</p> <p>Regarding the specific symptom of 'cough' 1.1.6 simply says do not routinely investigate or treat for GORD. However, the importance of neurodisability is highlighted later in</p>

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						<p>recommendation 1.1.12 and so the clinician might need to consider that fact in deciding how to proceed in that 'non-routine' setting. The guideline process did not review evidence regarding the value of chest x-ray in identifying pulmonary disease in relation to GORD but does make recommendations on those with single or repeated episodes of pneumonia. Recommendation 1.1.6 advises against routine investigation for treatment in those without overt regurgitation presenting with 'distressed behaviour' as an isolated phenomenon. Other recommendations on 'distress' (Recommendations 1.1.4; 1.1.20; 1.1.23; 1.2.2; 1.2.3; 1.2.4; 1.3.2) all refer either to those with overt regurgitation or with some other risk factor (i.e. not routine)</p>
Royal College of Paediatrics and Child Health	3	NICE	14	1.1.11	Concomitant constipation will worsen GOR (by straining)	<p>Thank you for your comment. Following stakeholder consultation the recommendation to which you refer (1.1.11) has been renumbered and is now recommendation 1.1.12. It states When deciding whether to investigate or treat, take into account that the following are associated with an increased prevalence of GORD:</p> <ul style="list-style-type: none"> • premature birth • parental history of heartburn or acid regurgitation • obesity • hiatus hernia • history of congenital

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						<p>diaphragmatic hernia (repaired)</p> <ul style="list-style-type: none"> • history of congenital oesophageal atresia (repaired) • a neurodisability <p>The evidence for the factors listed as being associated with an increased prevalence of GORD was reviewed. The evidence to support constipation as a risk factor for GORD was not prioritised for review by the GDG and therefore not included in this recommendation. (Please see full guideline Section 4.3 Risk factors)</p>
Royal College of Paediatrics and Child Health	4	NICE	14	1.1.11	In some infants with stridor due to laryngomalacia, GOR is associated	Thank you for your comment. In developing this guideline and interrogating the evidence, we needed to prioritise the most common symptoms and signs that can be associated with GORD or its complications. While it is recognised that upper airway complications are possible this is not thought to be common in isolation (i.e. without other symptoms of GORD such as regurgitation, distress or pneumonia) and as a result did not require a separate recommendation.
Royal College of Paediatrics and Child Health	19	NICE	14	1.1.12	Statement that GORD'. rarely causes apnoea. or ALTE' -is that strongly evidence based from your trawl of the studies of these children? Is it 'unclear ...'...or '...lack of evidence that ...' / '...probably ...' [I have tried to check your evidence]	Thank you for your comment. This recommendation is based on evidence (i.e. apnoeic episodes / ALTEs can very occasionally be related to GOR) but in the vast majority of cases are not. As a result, it is not recommended that every infant / young child admitted to a district general hospital with an

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						apnoeic episode must be referred to a specialist for specific investigation for GORD with for example and endoscopy and pH / Impedance study. However, if a consultant general paediatrician is concerned that GORD could be a factor then a referral would be entirely appropriate.
Royal College of Paediatrics and Child Health	5	NICE	15	1.1.15	Infants with unexplained bile stained vomiting should always be referred to a paediatric surgeon	Thank you for your comment. We agree that all infants with unexplained bile stained vomiting should undergo the appropriate investigation (same day upper GI contrast study) to exclude malrotation and this is what lies behind this recommendation. Further, Table 1 within recommendation 1.1.5, advises that all children with bile stained vomiting may have intestinal obstruction and therefore may require referral to a paediatric surgeon. However, it would not be helpful to be too prescriptive in terms of how this investigation or referral pathway should be coordinated given the whole variety of models of care that exist across different localities, regions and networks across the UK.
Royal College of Paediatrics and Child Health	6	NICE	16	1.2.2	Some formulas, designed specifically for GOR, require stomach acid to thicken in the stomach and should therefore not be prescribed concurrently with H2 receptor antagonists or proton pump inhibitors	Thank you for your comment. We do not usually provide detailed advice on the use of products but would expect that health care professionals give the appropriate advice based on the summary of product characteristics
Royal College of	14	NICE	17		Need to mention possible harm to neonates of changing bowel flora	Thank you for your comment. The context of your comment regarding

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Paediatrics and Child Health			-18			neonatal bowel flora was not clear. However, in considering all interventions we looked at evidence from comparative studies and also took account of known or reported adverse events.
Royal College of Paediatrics and Child Health	18	NICE	17	1.32	Clarify overt and non-overt with reference to difficulties of diagnosis in ch with neurodisabilities . Queries: '...Treat only if overt regurgitation plus ...[one of just 3 symptoms]..' '...unless the child has [and can describe] pain...' - which excludes some children with communication disorders	Thank you for your comment. This recommendation (1.3.2) refers specifically to infants and young children with overt regurgitation. This is defined in the glossary. The recommendation was intended to apply to all children who for whatever reason were unable to tell you about their symptoms. It has been reworded to make this clear.
Royal College of Paediatrics and Child Health	20	NICE	17	1.3.2	Clear advice	Thank you for your comment.
Royal College of Paediatrics and Child Health	45	NICE	17 & General		It is a surprise that there is no distinction made between the use of the PPI and the H2RA. Acid has a role in the gut and therefore suppression of acid is not without consequence. The relative suppression varies between products and thus it is surprising that no distinction is made between the 2 and allowing this to be purely led by "specialists" is a little misleading as they all do different things. We would like reference made to the fact that the newborn gut is already less acidic than older children and thus the role of acid suppression in the first place needs some thought. We would like to see mention of the lack of differentiation of H receptors in newborns (particularly prems) who may see	Thank you for your comment. It is expected that clinicians use their knowledge and experience alongside recommendations when prescribing treatment to patients. We did not make detailed recommendations on the choice of H2R antagonists versus PPIs because the evidence reviews did not identify comparative trial data for children to support this. It was recognised that drugs including these agents have the potential to cause harm. On that basis they endeavoured through their

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					unwanted side effects of H2RAs.	recommendation on the use of these drugs to avoid unnecessary usage and to limit duration of exposure through 'trials of treatment' to a period of several weeks.
Royal College of Paediatrics and Child Health	15	NICE	18	1.4	Heading should be enteral tube feeding as enteral on its own means into the gut, ie includes oral	Thank you for your comment. This has been discussed and amended to "enteral tube feeding".
Royal College of Paediatrics and Child Health	46	NICE	18	1.3.8	To lump metoclopramide, domperidone and erythromycin together as "leave to specialist care" also seems a little poor in terms of guidance. Many children are started in specialist care and transferred to the community on these medicines. All have their pros and cons and potentially more cons than pros and we feel that this statement is likely to lead to no direction of travel for treatment of children.	Thank you for your comment. Those who initiate treatment in specialist care should have a clear plan for treatment outlined by the specialist and therefore we made a recommendation that these drugs should only be used with specialist advice.
Royal College of Paediatrics and Child Health	7	NICE	20	2.2	We disagree with the comment that there is not enough evidence to suggest cow milk protein elimination as a management option. A trial of extensively hydrolysed formula for 2 weeks should be considered. Y Vandenplas et al. <i>Nutrition</i> 29 (2013) 184–194 JR Lightdale et al. <i>Pediatrics</i> 2013;131:e1684	Thank you for your comment. Evidence reviews were performed according to their corresponding protocols (See appendix E). A trial of hydrolysed formula/ cows' milk elimination for the treatment of GORD was not recommended because of the lack of trials based evidence available. Neither reference suggested by the stakeholder would meet the inclusion criteria for this review: Vandenplas et al, 2013 is not a research article or a systematic review but summarises (in five treatment algorithms) the

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						<p>consensus of an international group of paediatric gastroenterologists. Although a literature review was performed, no details of this are provided and the authors clearly state that their practice recommendations are not evidence based. Lightdale et al., 2013 is a narrative summary</p> <p>The research recommendation to which the stakeholder refers was amended following stakeholder consultation. This now specifies that a randomised controlled trial should be performed to examine the clinical and cost effectiveness of a hydrolysed formula trial in formula fed infants with frequent regurgitation associated with marked distress (Section 2.2).</p>
Royal College of Pathologists	1	NICE	General	General	Royal College of Pathologists has no comment to make on this guideline.	Thank you for your comment.
the British Society of Gastroenterology	6	Full	General	General	Use of Bravo pH not discussed as an investigative tool in children and young people as an alternative to standard pH study. This can be especially useful in children and young people with neurodisability and can be offered as an alternative to others who may not wish to have a pH probe (tube) placed. This can in certain clinical situations help avoid issues such as inadvertent pulling out of the pH probe before study completed	Thank you for your comment. The investigation of the evidence base for the accuracy of investigations was not included in the scope. We did not review evidence on the accuracy of different pH monitoring techniques in GOR and has not therefore made specific recommendations on the pH monitoring technique to be employed.
the British Society of Gastroenterology	7	Full	General	general	Use of Bravo pH not discussed as an investigative tool in children and young people as an alternative to standard pH study. This can	Thank you for your comment. The investigation of the evidence base for the accuracy of investigations was not

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logy					be especially useful in children and young people with neurodisability and can be offered as an alternative to others who may not wish to have a pH probe (tube) placed. This can in certain clinical situations help avoid issues such as inadvertent pulling out of the pH probe before study completed	included in the scope. We did not review evidence on the accuracy of different pH monitoring techniques in GOR and has not therefore made specific recommendations on the pH monitoring technique to be employed.
the British Society of Gastroenterology	2	Full	18	18	It's not clear from this guideline whether infants with significant feed aversive behaviour would benefit with investigations for reflux even if they may not be regurgitating or vomiting anymore? Although there is little evidence to support this the difficulty lies with the longitudinal timeline of possible events. Could this be an area for further research?	The evidence reviews carried out for this guideline did not find persuasive evidence that occult reflux was a likely explanation for these manifestations when they occurred in isolation and hence the clinical recommendation not to routinely investigate or treat for GORD. We chose not to make such a research recommendation for this GORD guideline
the British Society of Gastroenterology	1	Full	20		Trial of cow's milk exclusion only suggested if eczema present along with vomiting/regurgitation. As acknowledged by the GDG it is common practice in the UK to carry out an empirical trial of an extensively hydrolysed formulae in infants with vomiting and distressed behaviour or even vomiting with faltering growth. It is interesting to note there is no evidence base to support this and although the GDG has postulated that this is simply a placebo effect – there is no evidence to support that postulate either. (Page 145, line 3-14)	Thank you for your comment. Following stakeholder consultation, we gave careful consideration to the differential diagnosis in children presenting with possible GORD. Reference to a 'placebo' effect was removed from the section to which you refer. A new recommendation was added (Recommendation 11) to confirm that some symptoms of non-IgE mediated cows' milk protein allergy can be similar to those of GORD, especially in infants with atopic symptoms, signs, and/or a family history and which cross refers the reader to NICE CG 116 'Food allergy in children and young people'. Amendments were also made to Recommendation 5 in Table R1 that

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						lists 'red flag' signs and symptoms that may suggest disorders other than GOR in those with vomiting or regurgitation. A cross reference to NICE CG 116 was added to the symptom/sign of 'Blood in stool' 'Chronic diarrhoea' was added to the gastrointestinal list of signs/symptoms with a cross reference to NICE CG 116. Finally the sign/symptom 'Eczema' was amended and broadened to 'Infants and children with, or at high risk of, atopy' and the suggested action of a 'Trial of milk exclusion' was removed because this clinical recommendation was not made in this GORD guideline. A research recommendation was made however and the research question was amended following stakeholder consultation. This now specifies that a randomised controlled trial should be performed to examine the clinical and cost effectiveness of a hydrolysed formula trial in formula fed infants with frequent regurgitation associated with marked distress (Section 5.2.8).
the British Society of Gastroenterology	3	Full	23	19 -27	An impedance pH study has been suggested to be ideal in this guidance. This is an expensive procedure that is also very time consuming to interpret with no standardised paediatric values. Is there evidence to suggest this is superior to a standard pH study in all of these patient groups and has a positive impact on therapy?	Thank you for your comments. It was our view that combined oesophageal pH and impedance monitoring if available was a rational approach to investigation, given that non-acid reflux might be of importance in the clinical situations listed in the recommendation.

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						<p>We do acknowledge that the equipment required for impedance monitoring is not available in all specialist centres. We accept that by saying that the use of this technique is "ideal" we may appear to imply that all centres should acquire this facility. This was not the intention. We have therefore altered the stem of the recommendation to state:</p> <p>"Consider performing an oesophageal pH study (or combined oesophageal pH and impedance monitoring if available) in infants, children and young people with..."</p> <p>We have also amended the glossary for clarity regarding the terms used</p>
the British Society of Gastroenterology	4	Full	23	32	<p>A pH study without impedance monitoring is suggested when thinking about fundoplication. Yet in patients with recurrent aspiration pneumonias/ respiratory impact of GOR, an impedance pH is superior as it provides data on both acid and non acid reflux. And therefore an impedance pH may be more helpful in decision making for a fundoplication in this group of patients</p>	<p>Thank you for your comment. We agreed, and following consideration of this and of other stakeholder comments amended this recommendation and recommendation 41.</p> <p>The bullet points were removed from this recommendation and it was amended to "Consider a pH study without impedance monitoring in infants, children and young people if, using clinical judgement, it is thought necessary to ensure effective acid suppression". Recommendation 41 was also amended to advise health care professionals to consider performing other investigations such as</p>

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						a pH study, combined with impedance monitoring if available, and an upper GI contrast study for infants, children and young people before deciding whether to offer fundoplication.
the British Society of Gastroenterology	5	Full	27	5 -6	Very pleased to see this research recommendation	Thank you for your comment. Following stakeholder consultation, the research question within this research recommendation was amended. This now specifies that a randomised controlled trial should be performed to examine the clinical and cost effectiveness of a hydrolysed formula trial in formula fed infants with frequent regurgitation associated with marked distress.
The British society of Paediatric radiology	3	NICE	15 1.1.18	15	Urgently refer (on the same day) infants for an ultrasound examination	Thank you for your comment. If a health care professional genuinely suspects an infant has projectile vomiting, it was concluded that the child should be referred to a specialist (ideally a paediatric surgeon) for the exclusion of congenital hypertrophic pyloric stenosis. The precise investigation and management of this condition is beyond the scope of this guideline.
The British society of Paediatric radiology	1	Full	114 (5.46)	32	Replace the example 'hypertrophic pyloric stenosis' with oesophageal stricture (Standard modality for imaging hypertrophic pyloric stenosis is ultrasound and not upper GI contrast study. You could replace the example with oesophageal stricture)	Thank you for your comment. The text within this section has been expanded following stakeholder consultation. The example 'hypertrophic pyloric stenosis' has been removed and the example of 'oesophageal stricture' has been given as suggested.
The British	2	Full	115	13	Urgently refer (on the same day) infants for an	Thank you for your comment. If a

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society of Paediatric radiology			(5.47)		ultrasound examination	health care professional genuinely suspects an infant has projectile vomiting then we concluded that the child should be referred to a specialist (ideally a paediatric surgeon) for the exclusion of congenital hypertrophic pyloric stenosis.

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