Coeliac Disease

Consultation on draft guideline - Stakeholder comments table
6th March to 21st April 2015

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

Stakeholder	Document	Page No	Line No	Comments Please insert each new comment in a new row	Developer's response Please respond to each comment
Association of children's diabetes clinicians (ACDC)	Short and general	14	7	We are concerned that this guideline only advises screening for celiac disease in children with Type 1 diabetes only at diagnosis and if symptomatic. We urge the guidelines group to consider changing this to screening at diagnosis and periodically afterwards. The frequency of the testing can be determined by the GDG. ISPAD guidelines suggest testing annually for the first 5 years and biannually afterwards as most children with celiac disease do develop it in the first 5 years. The guideline as it stands will mean that a number of children with celiac disease will not be picked up as most are asymptomatic or have subtle symptoms which they only recognise after they start gluten free diet. There is increasing evidence of association with increased risk of diabetic complications in children with both type 1 diabetes and celiac disease.	Thank you for your comment. The GDG have considered this issue and have made changes to the recommendations which they now believe more accurately address the nature of seroconversion in people with type 1 diabetes and the potential for missing a subsequent coeliac diagnosis after an initial negative test result. Recommendation 1.1.6 has been re-worded to highlight the need for re-testing if CD is suspected, and to ensure clinicians have a low threshold for re-testing anyone identified in recommendation 1, including those with Type 1 diabetes. The GDG did not consider routine screening of asymptomatic individuals to be of significant clinical or cost utility and therefore only recommended testing where symptoms arose.
Association of Clinical Pathologists	Full	18	27	Total IgA and IgA tTG are established first choice tests for serological diagnosis in adults. Is there good evidence from UK studies (on UK population tested in UK labs) that for children this combination is not sufficient, and that IgA EMA is required as an additional test in all cases?	Thank you for your comment. After much discussion and a review of the evidence, the GDG has decided to recommend total IgA and IgA tTG as the first-line test in both children and adults. The GDG agreed that there was no strong basis for a distinction in serological testing between children and adults, and therefore considered it appropriate to adopt a uniform first-line serological testing strategy. IgA EMA serological testing is still regarded as an important test in paediatric settings; however the GDG felt that it was perhaps best requested by the consulting paediatric specialist, where appropriate for further investigation. See 'Economic considerations' and 'Other considerations' in section 5.2.6.
Association of Clinical Pathologists	Full	18	23	IgA deficiency needs to be defined, with a level of IgA stated (e.g. < 0.3 g/l). This is because of the not infrequent finding of low values of e.g. 0.5 g/l that do not signify IgA deficiency as Immunologists understand and diagnose it. This requires some clear instructive advice.	Thank you for your comment, the GDG has defined IgA deficiency as total IgA less than 0.07mg per litre, as this was considered by the group as widely accepted in clinical practice. This is now referenced in a footnote for all recommendations that refer to IgA deficiency
Association of Clinical Pathologists	Full	18	20	Many of the IgA tTG tests have high false positive rates, and so are not ideal for screening	Thank you for your comment. We did not examine the utility of each of the different IgA tTG testing kits available and so cannot comment on individual tests. The meta-analyses results showed IgA tTG to have high sensitivity and specificity. The GDG were less worried about false-positive rates than missed diagnoses.
Alder Hey Children's NHS Foundation Trust	Full	General	General	• Recommendations for groups offered testing for coeliac disease: Type 1 Diabetes at diagnosis. If offered only at diagnosis, there is a very real chance of missing asymptomatic children if they acquire the antibodies later. Consultant Paediatrician • The guideline does not address the issue of ongoing screening for CYP with type 1 diabetes. Clinical experience shows that many CYP present with coeliac disease post diagnosis without clear symptoms. Routine screening is needed to pick up undiagnosed coeliac disease as symptoms are usually reported retrospectively once the CYP is on a	Thank you for your comment. The GDG have considered this issue in great detail and have made changes to the recommendations which they now believe more accurately address the nature of seroconversion in people with diabetes and the potential for a missed coeliac diagnosis. Recommendation 1.1.6 has been re-worded to highlight the potential for re-testing if CD is suspected, and to ensure clinicians have a low threshold for re-testing anyone identified in recommendation 1, including those with Type 1 diabetes. The GDG did not consider routine screening of asymptomatic individuals to be of significant clinical or cost utility and therefore only recommended

Coeliac Disease

Consultation on draft guideline - Stakeholder comments table
6th March to 21st April 2015

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

Stakeholder	Document	Page No	Line No	Comments Please insert each new comment in a new row	Developer's response Please respond to each comment
				gluten free diet. Paediatric Dietician (Diabetes Specialist)	testing where symptoms arose.
British Society of Gastroenterology	Short	General	General	This summarises the guidance well and extends that previously developed.	Thank you for your comment.
British Society of Gastroenterology	Short	3	20	IBS is not a disorder like T1 Diabetes where it is more likely that coeliac coexists. It is a condition in which misdiagnosis can occur if coeliac disease is not recognised. Evidence on p37 (full) line 41 shows no significance. Suggest using "IBS-like symptoms".	Thank you for your comment. We have amended this accordingly.
British Society of Gastroenterology	Short	16	1.5.4	Specialist advice should be obtained before prednisolone is started perhaps from an urgent consultation. The current recommendation is too aggressive and is recognised to be based on low quality evidence.	Thank you for your comment. The GDG considered your comments and concluded that as people with refractory coeliac disease are often suffering from serious symptoms it would be appropriate for them to be started on prednisolone in the interim period before having their symptoms and medication reviewed by a specialist with expertise in refractory disease. The GDG also recognised that true refractory coeliac disease was a condition only diagnosed in adults: any children continuing to have symptoms are almost always inadvertently ingesting gluten or have a contributing comorbid condition. As such, we have amended the recommendation to reflect that this should only be carried out for adults.
British Society of Gastroenterology	Short	18	1.7.2	Diet is only a minor source of vitamin D. Suggest "if deficiency is confirmed".	Thank you for your comment. The GDG has discussed this and decided not to amend the recommendation for vitamin D. This was on the basis that vitamin D deficiency is not always confirmed at the point that a supplement is recommended. Environmental or dietary factors may indicate a deficiency and need for supplementation without necessarily having a deficiency confirmed.
British Society of Gastroenterology	Full	General	General	This document thoroughly reviews the current evidence following strict criteria. The GDG have done a good job at evaluating this evidence. It is important that health care providers are made aware of these recommendations so that the large proportion of currently undiagnosed coeliacs can receive a correct diagnosis and beneficial treatment. The role of specialist dietitians is rightly recognised and their services require consolidation and secured funding.	Thank you for your comment. We recognise that recommending that all people with coeliac disease are offered specialist dietetic advice may pose an implementation issue. This recommendation has now been changed to reflect that healthcare professionals should consider an annual review for people with coeliac disease, rather than offer an annual review. Challenges to implementation of the guideline recommendations will be considered and supported by NICE's implementation team. .
British Society of Gastroenterology	Full	20	6	As above re prednisolone	Thank you for your comment. The GDG considered your comments and concluded that as people with refractory coeliac disease are often suffering from serious symptoms it would be appropriate for them to be started on prednisolone in the interim period before having their symptoms and medication reviewed by a specialist with expertise in refractory disease. The GDG also recognised that true refractory coeliac disease was a condition only diagnosed in adults: any children continuing to have symptoms are almost always inadvertently ingesting gluten or have a contributing comorbid condition. As such, we have amended the recommendation to reflect that this should only be carried out for adults. .
British Society of Gastroenterology	Full	21	18 , 19	The advice about gluten-free oats is a little unclear	Thank you for your comment. We have re-structured this section by including information within the introduction to the chapter about gluten, oats, and the potential for cross-contamination during

Coeliac Disease

Consultation on draft guideline - Stakeholder comments table
6th March to 21st April 2015

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

Stakeholder	Document	Page No	Line No	Comments Please insert each new comment in a new row	Developer's response Please respond to each comment
					manufacturing to provide greater clarity. We have also included further information in the linking evidence to recommendation section to further explain this.
British Society of Gastroenterology	Full	68		Is the first sentence in "Testing for total IgA" correctly expressed?	Thank you for your comment. The group discussed that it was very common for laboratories to infer total IgA levels after testing for IgA tTG
Department of Health	Full	General	General	Thank you for the opportunity to comment on the draft for the above clinical guideline. I wish to confirm that the Department of Health has no substantive comments to make, regarding this consultation.	Thank you for your comment.
HQT Diagnostics	Short	21	2.5.5	There is evidence that increasing the level of Vitamin D helps the patient with Coeliac Disease. GP should test Vitamin D 25(OH)D and supplement to a level between 100-150 nmol/L A 50-70kg person might need 50-100 micrograms (2,000-4,000 IU) per day A 70-100kg person might need 100-250 micrograms (4,000-10,000 IU) per day Adjust the dose and evaluate after 3 months Vitamin D is stored in the fat and the half-life is 30-60 days, so weekly or bi-weekly dosing is suitable. A loading dose of 1,250-2,500 micrograms is helpful. After medical intervention with prescription products, commercial Nutritional Supplements may be advised. Evidence and sources of more information: http://www.vitamindwiki.com/Overview+Gut+and+vitamin+D http://www.grassrootshealth.net/media/download/scientists_call_to_daction_020113.pdf http://www.efsa.europa.eu/en/efsajournal/doc/2813.pdf	Thank you for your comment. The GDG has discussed this and decided not to amend the recommendation for vitamin D. Environmental or dietary factors may indicate a deficiency and need for supplementation without necessarily having a deficiency confirmed. We would also like to note that specific examination of vitamin D use and dosage for people with coeliac disease was outside the scope of the guideline. Please see our public health guidance on Vitamin D for further information on supplementation in at risk populations (NICE PH56).
Digital Assessment Service, NHS Choices	Full	General	General	We welcome the guidance and have no comments as part of the consultation.	Thank you for your comment.
NHS Dorset Clinical Commissioning Group	Full	general	general	We are concerned that prescribing of gluten-free foods with Advisory Committee on Borderline Substances (ACBS) approval has not been considered in this guidance. The Coeliac Society Prescribing Guide 2011 is a valuable resource for prescribers in general practice supporting them to prescribe suitable quantities of gluten-free food for various patient groups. We feel that not including prescribing information would be as serious omission in this guideline.	We thank you for your comment. Unfortunately, the prescribing of gluten free foods was outside the scope of this guideline and therefore could not be covered. We have amended recommendation 1.6.3 to include the need to provide people with coeliac disease with information about suitable gluten free alternative foods, which may include foods available on prescription.
NHS England	Full	General	General	This is an excellent guideline. It will be relatively easy for	We thank you for your comment.

Coeliac Disease

Consultation on draft guideline - Stakeholder comments table
6th March to 21st April 2015

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

Stakeholder	Document	Page No	Line No	Comments Please insert each new comment in a new row	Developer's response Please respond to each comment
				specialists to implement their part of it (Paediatricians, Gastroenterologists and Dietitians). It should be relatively easy to incorporate into General Practice.	
NHS England	Full	17 18	24 /2	It will be more difficult for the guideline to be adhered to in some clinical areas. The guideline expects a range of specialists to know and follow it (e.g. Hepatologists, Neurologists, those dealing with congenital syndromes (Turners/Downs), Dentists, Fertility Doctors, Endocrinologists). Spreading the message will be a challenge	Thank you for your comment. We have passed this onto the NICE implementation team to inform their support activities for this guideline.
NHS England	Full	General	General	Dietetic provision around England is patchy and often under resourced. True adherence to the guideline will increase demand for dietetic services	Thank you for your comment. Challenges to implementation of the guideline recommendations will be considered and supported by NICE's implementation team.
NHS England	Full	General	General	I am surprised that no mention is made of the prescription of gluten-free products designated as borderline substances. I am sure GP's would value having clear guidance as to this, as I know from many patients, that they are often reluctant to do so.	Thank you for your comment. Prescribing of gluten free foods was outside the scope of the guideline and therefore could not be covered. We have included in our information recommendation 1.6.3 a note about providing information to people with coeliac disease about suitable gluten free alternative foods, which may include foods available on prescription
Royal College of General Practitioners	Full	General	General	As coeliac disease is not specifically targeted in QOF, I suspect that 1st degree relatives are not being screened for coeliac disease and few patients are getting an annual diet and nutritional review in primary care. Dietician services are limited in primary care and have frequent staff turnover leading to poor continuity of advice and care.	Thank you for your comment. Challenges to implementation of the guideline recommendations will be considered and supported by NICE's implementation team.
Royal College of Paediatrics and Child Health	Full	General	General	This document appears to be an extremely thorough overview of the evidence relating to coeliac disease at the current time. Presumably a summary will be produced when the document's final version is issued.	Thank you for your comment. There will be a shortened version of the guideline produced in tandem with the full evidence review.
Royal College of Paediatrics and Child Health	Full	General	General	It would be useful to have a diagnostic algorithm and/or a summary guide.	Thank you for your comment. A diagnostic algorithm will not be developed for this guideline, however a short version of this guideline will be made available which contains only the recommendations. . A summary of the guideline for patient information purposes is also currently in development and will be made available in due course.
Royal College of Paediatrics and Child Health	Full	18	31 Recommendation 8	We do not understand the age banding applied- <13, 13-17 and >18. What is the evidence that the 13 and 14 year old patients are any different and should be in different age bands? Incidence of other pathologies in either <13 and 13-17 age groups is very low and justification for biopsy in the 13-17 but not younger patients seem lacking. This will be confusing in clinical practise.	Thank you for your comment. The GDG have amended the age limits to more accurately reflect clinical practice whereby children are considered as those under 16, young people as ages 16 - 18, and adults as those aged 18 and older. The group considered it appropriate for young people to be treated in the same way as adults in that they may be referred to a gastroenterologist for further testing, whereas it was more appropriate for those under 16 to be referred to a paediatrician.
Royal College of Paediatrics and Child Health	Full	18	18 -28 Recommendations	Inclusion of EMA for use in 'weakly positive' tTG as a second line test in the 13-17 year old group but in the initial set in the under 13. How does this affect decision to refer to paed gastro, and if it does not why do it? It will be a second blood test prior to expert opinion and result in trauma, cost and likely diagnostic delay. Again will cause confusion in the under 18 population.	Thank you for your comment. After full GDG consideration of all stakeholder comments and a review of the evidence, the GDG have revised the recommendations in relation to the age limits to better reflect clinical practice whereby children are considered as those under 16, young people as ages 16 - 18, and adults as those aged 18 and older. The group considered it appropriate for young people to be

Coeliac Disease

Consultation on draft guideline - Stakeholder comments table
6th March to 21st April 2015

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

Stakeholder	Document	Page No	Line No	Comments Please insert each new comment in a new row	Developer's response Please respond to each comment
			5&6		treated in the same way as adults in that they may be referred to a gastroenterologist for further testing, whereas it was more appropriate for those under 16 to be referred to a paediatrician. Furthermore, the GDG has decided to recommend total IgA and IgA tTG as the first -line choice test in both children and adults. The GDG agreed that there was no strong basis for a distinction in serological testing between children and adults, and therefore considered it appropriate to adopt a uniform first-line serological testing strategy. IgA EMA serological testing is still regarded as an important test in paediatric settings; however the GDG felt that it was best requested by the consulting paediatric specialist, where they feel it appropriate for further investigation.
	Full	20	6 -7 Recommendation 21	Prednisilone comment should exclude <18 year old with refractory coeliac disease – this is almost always due to compliance and need investigation and support. Steroid use in the pubertal age group is ill advised and should only be by specialists.	Thank you for your comment. The GDG discussed this and have amended the recommendation to reflect that only adults should be prescribed prednisolone
Royal College of Paediatrics and Child Health	Full	18	34 -35 Recommendation 9	There is no guidance on what level of tTG +/-AEM should be considered diagnostic in those who are not having a biopsy– what is positive enough? Unless there is evidence to deviate from ESPGHAN while awaiting results of current studies. Recommendation 8 just says to refer positive test for referral – anything above reference range. For primary caret that will capture all cases but for secondary/tertiary care it is unhelpful.	Thank you for your comment. Due to the many different test kits available to test for IgA tTG, each with their own validated levels of positivity, we cannot explicitly state serological titres to define test positivity. However the GDG considered that any positive tTG in children or young people should lead to a referral for further investigation.
Royal College of Paediatrics and Child Health	Full	19	5 -6 Recommendation 12	HLA – the use of 'DQ2/DQ8' implies that only this HLA type is associated with coeliac disease – what about DR5/7 heterozygotes? Will this advice be in line with Procede study data?	Thank you for your comment. We have amended reference to HLA in our recommendations to reflect HLA DQ2.2 and 2.5 and HLA DQ8. All evidence that was reviewed in relation to HLA testing examined only HLA DQ2 and DQ8 variants. The GDG felt that because of the rarity of DR5/7 heterozygotes, including these within any definition of HLA genotypes may be confusing. The final results of the Procede study have not yet been made available. For this reason, we cannot make any comment on the possible outcomes of this study.
Royal College of Paediatrics and Child Health	Full	General	General	The guideline covers primary care well, especially clarification on need for dietetic input at diagnosis and for FU. Is there a plan to specify for who the guideline is intended? If not it does need to cover secondary/tertiary care issues; e.g. 1. What is a positive Ttg/AEM – No reference to ESPGHAN. 2. What Biopsy changes do we regard as positive? 3. What level of 'little or no change' in tTG merits biopsy at 12/12?	As stated in the scope for the guidance, the intended audience for this guideline is all centres in which NHS healthcare is delivered. We were unable to provide more specific guidance on the 3 points you raise for the following reasons: 1. As there are a range of different IgA tTG test kits available, we cannot recommend anything beyond following manufacturer specifications for a positive result for each individual test. The GDG noted that ESPGHAN criteria specify 10 x times upper limit of normal as strongly positive, but the GDG did not think this was feasible to specify exact numbers for this in clinical practice due to the different titres for each test. 2. We have also stipulated within the guideline that biopsy results in line with Marsh Grade 3 are considered positive for coeliac disease; however the GDG did recognise that in some circumstances a lesser

Coeliac Disease

Consultation on draft guideline - Stakeholder comments table
6th March to 21st April 2015

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

Stakeholder	Document	Page No	Line No	Comments Please insert each new comment in a new row	Developer's response Please respond to each comment
					Marsh Grade i.e .grade 2 may be indicative of coeliac disease in the presence of strong clinical features and a positive response to a gluten-free diet. It was not in the scope of this review to examine sensitivity and specificity of different biopsy results to diagnose coeliac disease. 3. Due to the above points, and in combination with the evidence that lead to recommendation 1.4.2, which states that IgA tTG should not be used alone to determine whether gluten has been excluded from the diet, the group did not wish to specifically recommend IgA tTG serological testing as part of a monitoring strategy. However, the GDG recognised that some clinicians and patients did find this useful, and so may conduct serological testing as part of a wider monitoring strategy. The group felt that it should be up to the clinical discretion of the healthcare professional to decide, in the context of the patient's clinical response to the gluten free diet, whether their serological test result showed little or no change (indicating a titre very similar to that obtained at diagnosis) and warranted further investigation. .
Royal College of Paediatrics and Child Health	Full	General	General	In general the advice for FU support and dietetic input is welcome, including dietetic lead annual reviews.	Thank you for your comment.
Royal College of Paediatrics and Child Health	Short	3	General	We believe that: Introduction is too much focussed on adults. Needs to include statement on children: Children may present with faltering growth, static weight or progressive weight loss. Unrecognised coeliac disease may lead to liver disease including autoimmune hepatitis. Children with Down's syndrome and Turner syndrome have a higher incidence for coeliac disease	Thank you for your comment. We have amended the introduction to be more inclusive of children.
Royal College of Paediatrics and Child Health	Short	10	1.2.2.	Please provide a statement that for children and young people, the gastrointestinal specialist and paediatrician with a special interest in gastroenterology do follow current published guidelines from BSPGHAN and ESPGHAN about diagnosing coeliac disease in children, which apply and interpret specificity and sensitivity and level of antibody tests and HLA DQ2/DQ8 and an algorithmic pathway.	Thank you for your comment. NICE generally does not refer to other guidelines in recommendations. In this instance the GDG have reviewed the evidence on serological testing and have drafted recommendations based on this evidence review, 'de novo' health economic analysis and clinical and lay member input.
Royal College of Paediatrics and Child Health	Short	10	1.4.3	Annual review: we recommend to repeat antibody screening to monitor compliance. We are concerned that Else children would be risk to miss out on recognising and treating non-compliance Vit D and iron deficiency – at least following dietetic review to include in annual review when indicated.	Thank you for your comment. We did not find any strong evidence for the utility of using antibodies to monitor compliance. The GDG considered that specialist dietetic assessment should be able to identify compliance issues.
Royal College of Paediatrics and Child Health	Short	14	1.4.1.	Laboratories should clearly indicate the numeric value of the test result, the reference range for this test, and may consider to provide information about the name of the test kit for comparison in equivocal results. Laboratories should particularly state clearly the interpretation of test results for HLA DQ2 and DQ8, to allow the conclusion for the	Thank you for your comment. We have explicitly stated in our recommendations that laboratories should provide clear reports of their findings. This can include a statement of positive or negative results and numeric values as well.

Coeliac Disease

Consultation on draft guideline - Stakeholder comments table
6th March to 21st April 2015

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

Stakeholder	Document	Page No	Line No	Comments Please insert each new comment in a new row	Developer's response Please respond to each comment
				health professional if HLA status is positively associated, not associated (negatively) with coeliac disease, or if the HLA constellation is unclear in coeliac disease.	
Royal College of Paediatrics and Child Health	Short	14	1.4.1. and footnote	We are unaware of the evidence to distinguish between children and young people with regard to antibody test results and advise to remove the distinction between both groups for the diagnostic workup and interpretation of coeliac screening. **The discrimination between children and young people is unclear and confusing for the target group. We are concerned that some laboratories will continue to send test results for TTG or EMA alone with a statement of simply positive or negative- which is NOT what the authors of the NICE document intend.** **NICE would have to be certain that (in contrast to current practice) ALL laboratories provide a report of the JOINED analysis for TTG and EMA and interpret as strongly positive or weakly positive. We doubt that this will be possible.** According to our research, a strongly positive TTG does not always correlate with other strong coeliac tests (EMA, DGP).	Thank you for your comment. The GDG have amended the age limits to better reflect clinical practice whereby children are considered as those under 16, young people as ages 16 - 18, and adults as those aged 18 and older. The group considered it appropriate for young people to be treated in the same way as adults in that they may be referred to a gastroenterologist for further testing, whereas it was more appropriate for those under 16 to be referred to a paediatrician. The recommendations have also been revised to recommend IgA tTG as the first choice test for both children and adults, which will avoid any confusion in differential reporting of results for children and adults prior to being referred to an appropriate specialist for further investigation. The GDG recognised that not all laboratories carried out both IgA tTG and IgA EMA testing. There may be a requirement for some laboratories to send specimens to other laboratories to conduct the alternate test. The GDG noted this to be common practice within the LETR table; however we have highlighted this as a potential implementation issue. Challenges to implementation of the guideline recommendations will be considered and supported by NICE's implementation team. We did not examine correlations between different antibody tests and are therefore unable to comment further.
Royal College of Paediatrics and Child Health	Short	14	1.4.4.	Please specific the blood tests which may be required, e.g. Vit D status, iron studies (ferritin, iron binding capacity), transaminases, thyroid function tests.	Thank you for your comment. As we do not have specific evidence for the utility of different blood tests, we cannot be more specific in our recommendations. In clinical practice, the test(s) requested should be decided on a case by case basis.
Royal College of Paediatrics and Child Health	Short	16	1.5.4.	The advice for prednisolone in refractory coeliac disease does not apply to children.	Thank you for your comment. The GDG recognised that true refractory coeliac disease was a condition only diagnosed in adults: any children continuing to have symptoms are almost always inadvertently ingesting gluten or have a contributing comorbid condition. As such, we have amended the recommendation to reflect that this should only be carried out for adults
Royal College of Paediatrics and Child Health	Full	18	31 -35	Why is the distinction between young people (referral to gastrointestinal specialist) and children (paediatrician with special interest? Does NICE wish children with 13-16 years to undergo upper GI endoscopy and clinical examination by an adult gastroenterologist? The footnote in its current form implies that a positive TTG and positive EMA (both less than 10times above reference range) would be enough to make the diagnosis of coeliac disease by a	Thank you for your comment. the GDG have amended the age limits to better reflect clinical practice whereby children are considered as those under 16, young people as ages 16 - 18, and adults as those aged 18 and older. The group considered it appropriate for young people to be treated in the same way as adults in that they may be referred to a gastroenterologist for further testing, whereas it was more appropriate for those under 16 to be referred to a paediatrician. Please note that we have amended our serological testing strategy in children (Recommendation 1.2.3), where the footnote referring to positive IgA tTG and IgA EMA no longer applies.

Coeliac Disease

Consultation on draft guideline - Stakeholder comments table
6th March to 21st April 2015

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

Stakeholder	Document	Page No	Line No	Comments Please insert each new comment in a new row	Developer's response Please respond to each comment
				paediatrician with special interest in gastroenterology. This is in contrast to existing BSPGHAN and ESPGHAN guidelines.	
Royal College of Paediatrics and Child Health	Full	18	38 -42	Please specify what constellations were reported as HLA-DQ2 or DQ8 positive for coeliac disease in children.	Thank you for your comment. We have amended references to HLA within our recommendations to reflect HLA DQ2.2 and 2.5 and HLA DQ8.
Royal College of Paediatrics and Child Health	Full	59	1 -9	Is this section the justification to distinguish between children and young people? It appears unclear why 1 study is sufficient to use EMA antibodies in children for interpretation of coeliac disease (in contrast to young people).	Thank you for your comment. The GDG have amended the age limits to better reflect clinical practice whereby children are considered as those under 16, young people as ages 16 - 18, and adults as those aged 18 and older. The group considered it appropriate for young people to be treated in the same way as adults in that they may be referred to a gastroenterologist for further testing, whereas it was more appropriate for those under 16 to be referred to a paediatrician. The recommendations have also been revised to recommend IgA tTG as the first choice test for both children and adults, which we hope will avoid any confusion in differential reporting of results for children and adults prior to being referred to the appropriate specialist for further investigation.
Royal College of Radiologists	Short	15	1.4.4	Other than a mention of DEXA scanning for the diagnosis of osteoporosis, no specific imaging recommendations are made. The final scope of the guideline did include a section (e); *Monitoring and follow-up of people with coeliac disease including:* • *monitoring of people at risk of complications such as osteoporosis, ulcerative jejunitis, malignancy (intestinal lymphoma), functional hyposplenism, vitamin D deficiency and iron deficiency* • *follow-up strategies.*	Thank you for your comment. Imaging was assessed in the guideline in the context of 2 very different purposes. DEXA scanning was assessed in the chapter on monitoring of patients with coeliac disease. Other scanning practices, such as CT, were examined in the context of refractory coeliac disease, where enteropathy-associated T-cell lymphoma (EATL) may be suspected. The GDG reviewed evidence for the efficacy of a number of imaging modalities to detect EATL, however due to the low quality of this evidence and limited patient numbers, they did not wish to make specific recommendations about the utility of any one imaging modality.
Royal College of Radiologists	Short	15	1.5.1	In section 1.5.1 (Non-responsive and refractory coeliac disease) the main action is referral to a specialist centre for further evaluation. No specific imaging recommendations are made for this group (e.g. CT, CT enterography, MR enterography). The group may have felt this to be outside of their remit or insufficiently evidenced but the question of the imaging aspect of investigation has not been addressed as the scoping document suggested that it might be."	Thank you for your comment. The GDG reviewed evidence for the efficacy of a number of imaging modalities to detect EATL; however due to the low quality of this evidence and limited patient numbers, they did not wish to make specific recommendations about the utility of any one imaging modality.
Thermo Fisher Scientific, Immunodiagnostic Division	Short Full	15 87	1 3	Overall the document is thorough, well-written, and covers the existing available data. However, one question arises regarding monitoring. The document makes mention that serological evaluation should not be used alone to determine whether a patient is following a gluten free diet (top of page 15 in the short version and page 87, line 3 of the full version). We reference the ACG 2013 (Rubio-Tapia et al, Am J of Gastroenterol 2013), which recommends serological testing as a way to monitor patients on a gluten free diet and while we would agree it should not be the only tool, it does have a purpose based on available evidence.	Thank you for your comment. The group did assess the utility of serological testing to monitor adherence to the gluten free diet. The GDG reviewed low quality evidence which showed variable sensitivity of serological testing to accurately reflect patient dietary adherence. The GDG also noted that in their clinical experience serological testing may inaccurately indicate non-adherence when patients have had a dietitian verify that they have ceased all gluten ingestion. For this reason, the GDG wished to highlight that serological testing should not be used alone to measure adherence. They GDG did not feel that the

Coeliac Disease

Consultation on draft guideline - Stakeholder comments table
6th March to 21st April 2015

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

Stakeholder	Document	Page No	Line No	Comments Please insert each new comment in a new row	Developer's response Please respond to each comment
				Would the group consider adding a statement in the recommendations for annual review that includes serological monitoring as a component of the review?	research reviewed, combined with their clinical experience, warranted specific recommendation to use serological testing as part of an annual review strategy. The paper by Rubio-Tapia and colleagues (2013) was excluded from our review question due to the incomplete follow-up of all participants in the study
Tillotts Pharma UK Ltd.	Full	General	General	It has been mentioned in the full guidance (page 10, line 1) that there is growing evidence to suggest the use of point of care tests. In light of this, the stakeholder believes point of care tests should be considered as an option in the diagnosis pathway of coeliac disease where clinically appropriate. The stakeholder is aware that there is a large variability in the sensitivity and sensitivity of point of care tests currently on the market[1]. Therefore it is pertinent that such tests have sufficient evidence to demonstrate comparable specificity and sensitivity to IgA tTG when compared to villous atrophy. Furthermore, to be compliant with the current guidance they must also have the ability to test for IgA status. In this respect we feel it would be appropriate to include the statement: "Healthcare professionals should consider using point of care tests that have evidence to support comparable sensitivity and specificity to laboratory IgA tTG serology and can simultaneously test for IgA deficiency when it is clinically appropriate" or words to that effect. *[1] Peter D. Mooney, Simon H. Wong, Alexander J. Johnston, Matthew Kurien, Anastasios Avgerinos, David S. Sanders, Increased Detection of Celiac Disease With Measurement of Deamidated Gliadin Peptide Antibody Before Endoscopy, Clinical Gastroenterology and Hepatology, Available online 26 January 2015, ISSN 1542-3565,*	We thank you for your comment. As specified in the scope for this guideline, point of care tests were excluded and therefore we did not examine any evidence for these. We suggest that you consider notifying NICE's medical technology evaluation programme, should you wish for a point of care test to be specifically assessed.
Tillotts Pharma UK Ltd.	Short	13	5	In light of the emerging evidence of point of care tests, it is the stakeholder's opinion that the wording of guidance 1.2.1 is overly restrictive and would exclude the possibility of using point of care tests. The stakeholder feels that there is an assumption that all laboratory based tests meet required standards, which is not the case. There is variability between different pathology laboratories. The stakeholder suggests changing the statement to read 'Laboratories performing serological tests should have clinical pathology accreditation (CPA) or ISO1519 accreditation. Point of care tests should only be used if there is sufficient evidence that they are equivalent in sensitivity and specificity to laboratory based tests.'	We thank you for your comment. As specified in the scope for this guideline, point of care tests were excluded and therefore we did not examine any evidence for these. We suggest that you consider notifying NICE's medical technology evaluation programme, should you wish for a point of care test to be specifically assessed.
Tillotts Pharma UK Ltd.	Short	13	9, 17	In regards to the previous comment (comment 2), the stakeholder suggests adjusting the guidance statement 1.2.2. Currently it states, "When healthcare professionals request serological tests to investigate suspected coeliac disease in young people and adults, ***laboratories*** should". To accommodate changes suggested in comment 2, the stakeholder suggests replacing ***"laboratories should'*** with "***the test should'***. The same adjustment is also suggested for guidance 1.2.3.	Thank you for your comment. As specified in the scope for this guideline, point of care tests were excluded and therefore we did not examine any evidence for these. For this reason, we cannot make any comment on point of care testing and do not feel it would be appropriate to change the existing recommendations.
Tillotts Pharma UK Ltd.	Short	13	23	To accommodate the comments 1-3, the stakeholder suggests adjusting guidance 1.2.5 from "***When laboratories test*** for total IgA, a specific assay designed to measure total IgA levels should	Thank you for your comment. The GDG discussed this and feel that the recommendation is appropriate in its current form, due to the fact

Coeliac Disease

Consultation on draft guideline - Stakeholder comments table
6th March to 21st April 2015

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

Stakeholder	Document	Page No	Line No	Comments Please insert each new comment in a new row	Developer's response Please respond to each comment
				be used" to "When ***healthcare professionals request*** tests for total IgA, a specific assay to measure total IgA levels should be used" or words to that effect.	that healthcare professionals, such as GP's, typically request tests for coeliac disease, and it is the duty of each laboratory to carry out serological testing for coeliac disease in line with NICE guidance.
Tillotts Pharma UK Ltd.	Short	14	3	To accommodate the use of point of care tests when clinically appropriate the stakeholder suggests adjusting the guidance 1.2.8 to read "Interpretation of serological test results and recommended action should be clearly communicated to healthcare professionals".	We thank you for your comment. As specified in the scope for this guideline, point of care tests were excluded and therefore we did not examine any evidence for these.
Royal College of Physicians	Full	General	General	The RCP wishes to endorse the comments submitted by the BSG on the above consultation.	Thank you for your comment.
Royal College of Nursing	Full	General	General	This is to inform you that the Royal College of Nursing have no comments to submit to inform on the above guideline consultation. Thank you for the opportunity to participate.	Thank you for your comment.
Dr Schar UK	Full	9	21 -24	Dr Schar UK would like to highlight that access to a reasonable supply of staple gluten-free foods via the NHS has been stated as important in aiding adherence to treatment by 86% of coeliac patients in a recent survey (British Specialist Nutrition Association, 2013).	Thank you for your comment Gluten free prescription-available foods were outside the scope of the guideline, however we recognise this as an important factor to improving access to a gluten free diet. We have amended rec 1.6.3 to identify gluten-free substitutes as an important information need, which we believe addresses gluten-free foods provided on prescription.
Dr Schar UK	Full	10	12 -15	Dr Schar UK is aware of the wide variation in the provision of follow-up care for patients with coeliac disease currently and would welcome a standardised approach for all patients which would incorporate an annual health check. From our regular contact with healthcare professionals working in this area we are aware of the need for follow-up to be cost-effective and efficient whilst ensuring positive patient outcomes. Recently-developed care pathways have demonstrated pharmacists and dietitians, with training and experience in coeliac disease, working together to provide a new model of follow-up for this patient group at both a local level in Bedfordshire, England and at a national level in Scotland. We acknowledge that further assessment of these new care pathways is required. Within this model, education and information on the accessibility of a reasonable supply of staple gluten-free foods available via the NHS can be provided by appropriately trained healthcare professionals.	Thank you for your comment.
Dr Schar UK	Full	11	15 -16	Dr Schar UK would welcome an acknowledgement of the role and services which can be offered by pharmacists in primary care settings for this patient group. Recently-developed care pathways highlight a role for pharmacists in provision of staple gluten-free foods via the NHS to patients clinically diagnosed with coeliac disease as well as a role in facilitating an annual health check in this patient group.	Thank you for your comment. The GDG considered all evidence for useful sources of information and support for coeliac disease, and for different monitoring strategies in coeliac disease. No evidence was found which highlighted the role of pharmacists in either information provision, or in follow-up care for people with coeliac disease. Therefore, the GDG were unable to specifically recognise the role of pharmacists in providing information or follow-up support. Further, we note that recommendation 1.4.3 recommends that specialist dietetic advice be given as part of an annual review. It is expected that such advice is given by a healthcare professional who has received specialist training in administering dietetic advice, but does not specify

Coeliac Disease

Consultation on draft guideline - Stakeholder comments table
6th March to 21st April 2015

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

Stakeholder	Document	Page No	Line No	Comments Please insert each new comment in a new row	Developer's response Please respond to each comment
					which healthcare professional will deliver the annual review.
Dr Schar UK	Full	17	13	As a specialist gluten-free manufacturer, Dr Schar UK is keen to highlight its role as a source of information and support for patients with coeliac disease. We provide a range of informative and practical written and online resources for helping patients with coeliac disease understand their condition and treatment. These resources are reviewed by specialist healthcare professionals working in the coeliac field. This point is supported by a Coeliac UK survey of 500 individuals with coeliac disease in 2011 which showed that just over 26% of respondents' contacted manufacturers for information about gluten-free products, ranking second only to Coeliac UK.	Thank you for your comment. It is NICE policy not to signpost to specific companies.
Dr Schar UK	Full	17	18	The role of local support groups is widely acknowledged as being important for patients with coeliac disease. These support groups utilise resources and support from the specialist gluten-free manufacturers. Examples of support provided include events demonstrating the practical use of gluten-free products in food preparation and baking and the provision of tried and tested recipes to help support patients in following a strict gluten-free diet.	Thank you for your comment. We have recognised the important role local support groups can play in supporting people with coeliac disease in recommendation 1.6.3 in information and support.
Dr Schar UK	Full	19	19 -23	Dr Schar UK welcomes the recommendation that all coeliac patients should be offered an annual review. With the current financial pressures on NHS budgets and changes within the NHS, we feel it is important to consider how this could be achieved. Whilst we are aware of the key role that dietitians have in supporting this patient group, there are also issues in terms of dietetic time and resources. There are schemes in existence, based in a primary care setting, in which pharmacists and dietitians, with training and experience in coeliac disease, work together to provide an annual health check which includes the criteria outlined in the NICE recommendation. As part of this there is the ability to refer any patients with complications or concerns back to either the GP or dietitian for further clinical or dietetic review which is key. Dr Schar UK would welcome further research into new and innovative approaches such as these schemes which are cost-effective and deliver a positive patient experience.	Thank you for your comment. Challenges to implementation of the guideline recommendations will be considered and supported by NICE's implementation team. The NICE implementation team also collect examples of best practice from local clinical centres as examples of shared learning.
Dr Schar UK	Full	20	33 -40	As a specialist gluten-free manufacturer, Dr Schar UK is keen to highlight its role as a source of information and support for patients with coeliac disease. We provide a range of informative and practical written and online resources for helping patients with coeliac disease understand their condition and treatment. These resources are reviewed by specialist healthcare professionals working in the coeliac field. This point is supported by a Coeliac UK survey of 500 individuals with coeliac disease in 2011 which showed that just over 26% of respondents' contacted manufacturers for information about gluten-free products, ranking second only to Coeliac UK.	Thank you for your comment. It is NICE policy not to signpost to specific companies.
Dr Schar UK	Full	20	41	The role of local support groups is widely acknowledged as being important for patients with coeliac disease. These support groups utilise resources and support from the specialist gluten-free	Thank you for your comment. We have recognised the important role local support groups can play in supporting people with coeliac disease in the recommendation 1.6.3

Coeliac Disease

Consultation on draft guideline - Stakeholder comments table
6th March to 21st April 2015

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

Stakeholder	Document	Page No	Line No	Comments Please insert each new comment in a new row	Developer's response Please respond to each comment
				manufacturers. Examples of support provided include events demonstrating the practical use of gluten-free products in food preparation and baking and the provision of tried and tested recipes to help support patients in following a strict gluten-free diet.	
Dr Schar UK	Full	21	13 -15	Fortified gluten-free products produced by specialist gluten-free manufacturers, available via the NHS, have been specifically developed for people with coeliac disease to assist patients in achieving an adequate intake of key nutrients through diet and may negate the need for additional supplementation.	Thank you for your comment. The role of fortified gluten-free products was outside the scope of the guideline and therefore we are unable to examine any evidence or make any comment on the efficacy of fortified products.
Dr Schar UK	Full	22	27 -30	Dr Schar UK supports the recommendation to help maximise the effectiveness of the dietitian role in helping patients with coeliac disease to adhere to a gluten-free diet. With the current financial pressures on NHS budgets and changes within the NHS, we feel it is important to consider how this could be achieved. Whilst we are aware of the key role that dietitians have in supporting this patient group, there are also issues in terms of dietetic resource and time. There are schemes in existence, based in a primary care setting, in which pharmacists and dietitians, with training and experience in coeliac disease, work together to provide a more streamlined approach to follow up such as the schemes in Bedfordshire and Scotland. A key part of this is the ability to refer patients with complications or concerns back to either a GP or dietitian for further clinical or dietetic review. We acknowledge that further assessment of these new care pathways is required including the role healthcare professionals within these pathways play in helping to support adherence to treatment in this patient group.	Thank you for your comment. Challenges to implementation of the guideline recommendations will be considered and supported by NICE's implementation team. The NICE implementation team also collects examples of best practice in local clinical settings for the purpose of shared learning.
Dr Schar UK	Full	22	31 -32	Dr Schar UK welcomes the call for further research into appropriate monitoring frequencies for this patient group. Furthermore, we feel it is important to consider how and where this monitoring can take place most effectively. A key part of this monitoring should be clear guidelines for clinical or dietetic review where this is required.	Thank you for your comment. The GDG considered all evidence for different monitoring strategies in coeliac disease. We note that recommendation 1.4.3 recommends that specialist dietetic advice be given as part of an annual review. It is expected that such advice is given by a healthcare professional who has received specialist training in administering dietetic advice, but does not specify which healthcare professional will deliver the annual review. We further note our research recommendations on the optimal frequency of monitoring and the role of a dietitian in the management of coeliac disease, which we hope will stimulate further research in these areas.
Dr Schar UK	Full	85	30 -35	Dr Schar UK welcomes innovative yet cost-effective care pathways for the monitoring of patients with coeliac disease which result in positive patient outcomes and a positive patient experience. Assessment of new pathways offering multi-disciplinary involvement would be welcome.	Thank you for your comment. Challenges to implementation of the guideline recommendations will be considered and supported by NICE's implementation team.
Dr Schar UK	Full	85	37 -40	Dr Schar UK would welcome further assessment of the cost implications of different models of follow-up care for patients with coeliac disease.	Thank you for your comment. Challenges to implementation of the guideline recommendations will be considered and supported by NICE's implementation team.
Dr Schar UK	Full	87 -88	5 -8 and	Dr Schar UK is aware of the wide variation in the provision of follow-up care for patients with coeliac disease currently and would welcome a standardised approach for all patients	Thank you for your comment. We are aware of the variation in clinical practice in this area and hope that our guideline will provide clarity to

Coeliac Disease

Consultation on draft guideline - Stakeholder comments table
6th March to 21st April 2015

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

Stakeholder	Document	Page No	Line No	Comments Please insert each new comment in a new row	Developer's response Please respond to each comment
			1-4	incorporating an annual health check. From our regular contact with healthcare professionals working in this area we are aware of the need for follow-up to be cost-effective and efficient whilst ensuring positive patient outcomes. Recently-developed care pathways have demonstrated pharmacists and dietitians, with training and experience in coeliac disease, working together to provide a new model of follow-up for this patient group at both a local level in Bedfordshire, England and at a national level in Scotland. We acknowledge that further assessment of these new care pathways is required including the role healthcare professionals within these pathways play in helping to support adherence to treatment in this patient group.	clinicians to provide improved care, monitoring, and follow-up of people with coeliac disease. Challenges to implementation of the guideline recommendations will be considered and supported by NICE's implementation team.
Dr Schar UK	Full	88	26 -27	Dr Schar UK welcomes the call for further research into appropriate monitoring frequencies for this patient group. Furthermore, we feel it is important to consider how and where this monitoring can take place most effectively. A key part of this monitoring should be clear guidelines for clinical or dietetic review where this is required.	Thank you for your comment. Please note that recommendation 1.4.3 on annual review has been revised to state 'consider annual review'. It is expected that specialist dietetic advice is given by a healthcare professional who has received specialist training in providing dietetic advice to people with coeliac disease**,** but does not specify which healthcare professional will deliver the annual review. If any concerns are raised within the annual review, we have recommended referral to a GP or consultant for further investigation. We also note our research recommendations around the frequency of monitoring and the effectiveness of dietitian-led patient follow-up, which we hope will stimulate further research in these areas.
Dr Schar UK	Full	118		Within 'other considerations' in the Evidence to Recommendations table the guideline development group has made the point that people with coeliac disease and their family and carers should be made aware of gluten free food prescriptions. We feel this consideration is important especially considering that access to a reasonable supply of staple gluten-free foods via the NHS has been stated as important in aiding adherence to treatment by 86% of coeliac patients in a recent survey (British Specialist Nutrition Association, 2013).	Thank you for your comment. The prescribing of gluten free foods was outside the scope of this guideline. We have amended recommendation 1.6.3 to include the need to provide people with coeliac disease with information about suitable gluten free alternative foods, which may include foods available on prescription.
Dr Schar UK	Full	119	5	As a specialist gluten-free manufacturer, Dr Schar UK is keen to highlight its role as a source of information and support for patients with coeliac disease. We provide a range of informative and practical written and online resources for helping patients with coeliac disease understand their condition and treatment. These resources are reviewed by specialist healthcare professionals working in the coeliac field. This point is supported by a Coeliac UK survey of 500 individuals with coeliac disease in 2011 which showed that just over 26% of respondents' contacted manufacturers for information about gluten-free products, ranking second only to Coeliac UK.	Thank you for your comment. It is NICE policy not to signpost to specific companies.
Dr Schar UK	Full	119	10	The role of local support groups is widely acknowledged as being important for patients with coeliac disease. These support groups utilise resources and support from the specialist gluten-free manufacturers. Examples of support provided include events demonstrating the practical use of gluten-free products in food preparation and baking and the provision of tried and tested	Thank you for your comment. We have recognised the important role local support groups can play in supporting people with coeliac disease in the recommendation 1.6.3 in information and support.

Coeliac Disease

Consultation on draft guideline - Stakeholder comments table
6th March to 21st April 2015

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

Stakeholder	Document	Page No	Line No	Comments Please insert each new comment in a new row	Developer's response Please respond to each comment
				recipes to help support patients in following a strict gluten-free diet.	
Dr Schar UK	Full	124	6 -8	Fortified gluten-free products produced by specialist gluten-free manufacturers, available via the NHS, have been specifically developed for people with coeliac disease to assist patients in achieving an adequate intake of key nutrients through diet and may negate the need for additional supplementation.	Thank you for your comment. The role of fortified gluten-free products was outside the scope and therefore we were unable to examine any evidence or make any comment on the efficacy of fortified products.
British Specialist Nutrition Association	Full	General	General	In addition to dietitians, the British Specialist Nutrition Association suggests that pharmacists with experience in coeliac disease might also be best placed to provide education and information on the accessibility of a reasonable quantity of staple gluten-free foods available on the NHS, as well as, facilitate an annual health check for coeliac patients.	Thank you for your comment. The GDG considered all evidence for useful sources of information and support for people with coeliac disease, and for different monitoring strategies. No evidence was found which highlighted the role of pharmacists in either information provision, or in follow-up care. Therefore, the GDG were unable to specifically recognise the role of pharmacists in providing information or follow-up support in any recommendation. Please note that recommendation 1.4.3 recommends that specialist dietetic advice be given as part of an annual review. It is expected that such advice is given by a healthcare professional who has received specialist training in delivering dietetic advice, but does not specify which healthcare professional will deliver the annual review
British Specialist Nutrition Association	Full	General	General	We note that ready access to gluten-free foods is another factor that increases patients' likelihood of adherence to gluten-free diets. Access to a reasonable supply of staple gluten-free foods is considered an essential NHS service as set out in the National Prescribing Guidelines produced in association with the British Dietetic Association, the Primary Care Society for Gastroenterology and Coeliac UK. A patient opinion survey of 1000 people commissioned by the British Specialist Nutrition Association in 2013 has illustrated the crucial role played by staple gluten free foods on prescription on the NHS. 86% of respondents felt that obtaining gluten-free foods on prescription was important in aiding their adherence to a gluten-free diet. People of a lower socio-economic grouping relied more heavily on their prescription to manage their condition. The British Specialist Nutrition Association survey findings may be supplied on request.	Thank you for your comment. This is outside the scope of the current guideline.
British Specialist Nutrition Association	Full	9	21 -24	We note that access to a reasonable supply of staple gluten-free foods via the NHS increases the likelihood of adherence to diet, as demonstrated in the survey mentioned above.	We thank you for your comment. The prescribing of gluten free foods was not included within the scope of this guideline and therefore could not be covered. We have amended recommendation 1.6.3 to include the need to provide people with coeliac disease with information about suitable gluten free alternative foods, which may include foods available on prescription.
British Specialist Nutrition Association	Full	10	12 -15	Members of the British Specialist Nutrition Association are also aware, through the regular contact they have with the coeliac community and healthcare professionals working in this area, that there continues to be considerable variation in the type and quality of follow-up care provided across the country. We would welcome a standardised approach that would provide patients with an annual health check. How this can be most efficiently and cost effectively provided will require more assessment.	Thank you for your comment. We hope that this guideline will help clinicians to provide improved care, monitoring, and follow-up of people with coeliac disease. Challenges to implementation of the guideline recommendations will be considered by NICE implementation team to inform their support activities for this guideline.

Coeliac Disease

Consultation on draft guideline - Stakeholder comments table
6th March to 21st April 2015

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

Stakeholder	Document	Page No	Line No	Comments Please insert each new comment in a new row	Developer's response Please respond to each comment
British Specialist Nutrition Association	Full	11	15 -16	We believe that "all settings where NHS healthcare is delivered" should acknowledge services offered by pharmacies, including dispensation of prescriptions of gluten-free foods and their role in facilitating an annual health check for individuals with coeliac disease.	Thank you for your comment. We believe that any setting where NHS healthcare is delivered does imply pharmacy services. The dispensing of gluten-free foods was outside of the scope for the guideline. Please note that recommendation 1.4.3 recommends that specialist dietetic advice be given as part of an annual review. It is expected that such advice is given by a healthcare professional who has received specialist training in providing dietetic advice, but does not specify which healthcare professional will deliver the annual review. It is expected that this will be determined by local protocols and policies.
British Specialist Nutrition Association	Full	17	10	We believe it would be helpful if this list acknowledged the role of pharmacists and specialist gluten-free manufacturers as sources of information.	Thank you for your comment. The GDG did not feel it was appropriate to acknowledge the role of pharmacists and specialist manufactures as sources of information as although the group recognise these may provide information, we did not find any evidence to support this.
British Specialist Nutrition Association	Full	17	13	Gluten-free manufacturers provide an extensive range of recipe resources and practical information on following a gluten-free diet available to healthcare professionals. Healthcare professionals running clinics and providing patient services acknowledge the value of these resources in helping them support their coeliac patients. We are aware of the financial and time pressures dietetic departments are under and how they are often unable to fund and develop their own resources.	Thank you for your comment. It is NICE's policy not to specifically refer to any specific brands or manufacturers within our recommendations. However, recommendation 1.6.3 lists a number of useful information sources for patients and their family members on the gluten-free diet and coeliac disease. Appropriate sources of information will also be listed in the patient information guideline summary,
British Specialist Nutrition Association	Full	17	18	Local support groups utilise the resources of gluten-free manufacturers to provide practical gluten-free cooking events and related recipe resources to support their members in adhering to a strict gluten-free diet.	Thank you for your comment. We have recognised the utility of support groups in our recommendation on useful sources of information.
British Specialist Nutrition Association	Full	19	16 -17	We welcome the recommendations that all patients must be offered access to an annual review. However, we would like to raise the point here as to how best this can be practically and efficiently provided. We are aware of schemes where a pharmacist provides through an annual health check the three - criteria specified here (assess diet and adherence to a gluten-free diet, measure weight and height and review symptoms). Following this annual health check those patients with complications or cause for concern are referred back to the GP or dietitian for further dietetic or clinical review. We would welcome further research and assessment of these approaches.	Thank you for your comment. The GDG considered all evidence for different monitoring and annual review strategies in coeliac disease. No evidence was found which highlighted the role of pharmacists in follow-up care. Therefore, the GDG were unable to specifically recognise the role of pharmacists in providing follow-up support in any recommendation. Further, we note that recommendation 1.4.3 recommends that specialist dietetic advice be given as part of an annual review. It is expected that such advice is given by a healthcare professional who has received specialist training in delivering dietetic advice, but does not specify which healthcare professional will deliver the annual review.
British Specialist Nutrition Association	Full	20	33	We believe it would be helpful if this list acknowledged the role of pharmacists and specialist gluten-free manufacturers as a source of information. This is supported by a survey of 500 individuals with coeliac disease conducted by Coeliac UK in 2011 found 26.62% of respondents' contacted manufacturers for information about gluten-free products, ranking second only to Coeliac UK.	Thank you for your comment. We did not find any evidence for the role of pharmacists in the follow-up of people with coeliac disease and the GDG therefore did not think it appropriate to signpost people to this It is NICE's policy not to specifically refer to any specific brands or manufacturers within our recommendations. However, recommendation 1.6.3 lists a number of useful information sources for patients and their family members on the gluten-free diet and coeliac disease. Appropriate sources of information will also be listed in the patient information guideline summary,

Coeliac Disease

Consultation on draft guideline - Stakeholder comments table
6th March to 21st April 2015

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

Stakeholder	Document	Page No	Line No	Comments Please insert each new comment in a new row	Developer's response Please respond to each comment
British Specialist Nutrition Association	Full	20	36	Gluten-free manufacturers provide an extensive range of recipe resources and practical information on following a gluten-free diet available to healthcare professionals. Healthcare professionals running clinics and providing patient services acknowledge the value of these resources in helping them support their coeliac patients. We are aware of the financial and time pressures dietetic departments are under and how they are often unable to fund and develop their own resources.	Thank you for your comment. It is NICE's policy not to specifically refer to any specific brands or manufacturers within our recommendations. However, recommendation 1.6.3 lists a number of useful information sources for patients and their family members on the gluten-free diet and coeliac disease. Appropriate sources of information will also be listed in the patient information guideline summary,
British Specialist Nutrition Association	Full	20	41	Local support groups should utilise the resources of gluten-free manufacturers to provide practical gluten-free cooking events and related recipe resources to support their members in adhering to a strict gluten-free diet.	Thank you for your comment. However, recommendation 1.6.3 lists a number of useful information sources, including local support groups, for patients and their family members on the gluten-free diet and coeliac disease. Appropriate sources of information will also be listed in the patient information guideline summary,
British Specialist Nutrition Association	Full	21	10 -12	We are aware that the recommended amounts of various nutrients, such as fibre, calcium and Vitamin D can often be difficult for patients with coeliac disease to achieve, particularly if they are not adhering to a strict gluten-free diet and have not had regular contact with a healthcare professional. Fortified gluten-free staple products dispensed via the pharmacy have been specifically developed for people with coeliac disease to assist patients in achieving an adequate intake of key nutrients through diet and may negate the need for additional supplementation.	Thank you for your comment. The role of fortified gluten-free products outside the scope of the guideline and therefore we were unable to examine evidence or make any comment on the efficacy of fortified products.
British Specialist Nutrition Association	Full	21	13 -15	We are aware that a number of products available on prescription are fortified with calcium and may negate the need for additional supplementation.	Thank you for your comment. The role of fortified gluten-free products was outside the scope of the guideline and therefore we were unable to examine evidence or make any comment on the efficacy of fortified products.

Coeliac Disease

Consultation on draft guideline - Stakeholder comments table
6th March to 21st April 2015

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

Stakeholder	Document	Page No	Line No	Comments Please insert each new comment in a new row	Developer's response Please respond to each comment
British Specialist Nutrition Association	Full	22	27 -30	The challenge we are aware of from our engagement with healthcare professionals, clinical commissioning groups and those involved in new care pathways, is how to structure follow-up care and annual reviews to ensure that those patients most in need of additional expert support by a dietitian or further investigation by a Gastroenterologist are efficiently referred back from primary care. We would welcome more research assessing new care models where pharmacists and dietitians work together to provide a more streamlined and targeted follow-up care approach such as those approaches being provided in Cumbria, Bedfordshire and Scotland.	Thank you for your comment. Defining service models was outside of the scope of the guideline and would be for local determination. NICE's implementation team is currently working with local service providers to gather examples of good practice. Please see here for further information: **http://www.nice.org.uk/about/what-we-do/into-practice/local-practice-case-studies**
British Specialist Nutrition Association	Full	84	25 -26	A patient opinion survey of 1000 people commissioned by the British Specialist Nutrition Association in 2013 has illustrated a high level of adherence to a gluten-free diet where staple gluten free foods are available on prescription. 86% of respondents felt that obtaining gluten-free foods on prescription was important in aiding their adherence to a gluten-free diet. People of a lower socio-economic grouping relied more heavily on their prescription to manage their condition. We would welcome further research assessing the role prescriptions play in maintaining adherence to diet. These findings are supported by similar research undertaken by Coeliac UK in 2011 which compared the role of prescriptions with shop brought products across 300 of its members. The survey found that 81% of respondents felt gluten-free foods available on prescription were "very important" with 54% of respondents stating prescription services were the most important way of obtaining gluten-free foods.	Thank you for your comment. All studies that met our inclusion and exclusion criteria within the review protocol were included within the review. Prescribing of gluten free foods was outside the scope of the guideline and therefore, the study referenced in your comment would have fallen outside of the search criteria defined within the review protocols. We have included in our information recommendation 1.6.3 a note about providing information to people with coeliac disease about suitable gluten free alternative foods, which may include foods available on prescription
	Full	85	30 -35	We would welcome more evidence assessing the effectiveness of new care pathways offering a multi-disciplinary healthcare professional involvement in monitoring people with coeliac disease.	Thank you for your comment. Multidisciplinary care pathways fall outside of the scope of the current guideline and we were therefore unable to review any literature pertaining to this.
British Specialist Nutrition Association	Full	85	37 - 40	We would welcome more evidence assessing the cost implications of different approaches to follow-up care.	Thank you for your comment. We did not find any directly relevant information on the cost implications of different approaches to follow-up care, and the original economic modelling undertaken by our health economics team was relatively exploratory, and relied on low-quality evidence. The GDG have made 2 research recommendations that will help to inform this research agenda: 2.4 ('How can the role of the

Coeliac Disease

Consultation on draft guideline - Stakeholder comments table
6th March to 21st April 2015

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

Stakeholder	Document	Page No	Line No	Comments Please insert each new comment in a new row	Developer's response Please respond to each comment
					dietitian contribute most effectively within a coeliac disease team?') and 2.5 ('What is the effectiveness of more frequent monitoring compared with monitoring at 12 months after diagnosis in people with newly diagnosed coeliac disease?')
British Specialist Nutrition Association	Full	87		We acknowledge the difficulties in measuring adherence to a gluten- free diet and support the Groups' view that involvement with a healthcare professional is a critical factor. We would welcome further research on the new care pathways assessing the role that both dietitians and pharmacists are playing in supporting good adherence practices.	Thank you for your comment. The GDG has defined a number of research recommendations relating to gaps in the evidence that they encountered. One of these recommendations (research recommendation 2.4) pertains to how the role of the dietitian can contribute most effectively to coeliac disease patient care.
British Specialist Nutrition Association	Full	87 and 88	5 -8 (page 87), 1-3 (page 88)	We welcome these recommendations that all patients must be offered access to an annual review. However, we would like to raise the point here as to how best this can be practically and efficiently provided. We are aware of schemes where a pharmacist provides through an annual health check the 3 criteria specified here (assess diet and adherence to a gluten-free diet, measure weight and height and review symptoms). Following this annual health check those patients with complications or cause for concern are referred back to the General practitioner (GP) or dietitian for further dietetic or clinical review. We would welcome further research and assessment of these approaches.	Thank you for your comment. The GDG considered all evidence for different monitoring and annual review strategies in coeliac disease. No evidence was found which highlighted the role of pharmacists in follow-up care. Therefore, the GDG were unable to specifically recognise the role of pharmacists in providing follow-up support in any recommendation. Further, we would like to note that recommendation 1.4.3 recommends that specialist dietetic advice be given as part of an annual review. It is expected that such advice is given by a healthcare professional who has received specialist training in delivering dietetic advice, but does not specify which healthcare professional will deliver the annual review.
British Specialist Nutrition Association	Full	88	26 -27	We welcome this call for further research to clarify monitoring frequencies. We would also like to see further research assessing how monitoring can best be delivered within primary care. The priority is to ensure there are clear guidelines and mechanisms in place for clinical and dietetic referral of those patients who require further investigation.	Thank you for your comment. We would like to highlight our research recommendation (2.4) which was designed to assess how a dietitian can best contribute to the support and management of patients with coeliac disease. We hope this will stimulate further research within this area.
British Specialist Nutrition Association	Full	114	11 -14	We have already stated that access to reasonable supply of gluten-free foods via the NHS is a crucial factor in helping a patient to adhere to a gluten-free diet. Looking forward, evidence looking at improved adherence should also take into account the role that pharmacists can play in supporting patients to manage their condition.	Thank you for your comment. The GDG considered all evidence for useful sources of information and support for coeliac disease, and for different monitoring strategies in coeliac disease. No evidence was found which highlighted the role of pharmacists in either information provision, or in follow-up care. Therefore, the GDG were unable to specifically recognise the role of pharmacists in providing information or follow-up support. The provision of gluten-free foods was not covered in the scope of this guideline.
British Specialist Nutrition Association	Full	118		Within 'other considerations' in the Evidence to Recommendations table we note the guideline development group has made the point that people with coeliac disease and their family and carers should be made aware of gluten free food prescriptions. We fully agree with this consideration and would welcome further research assessing adherence through prescription services.	Thank you for your comment. . The GDG prioritised what they believed to be the 5 most important research recommendations based on what they felt were the most significant gaps in current research and where clinical practice could most benefit. We are unable to make any further research recommendations after guideline consultation; however any significant areas of research in coeliac that develop over the coming years will be highlighted in a NICE surveillance review of this guideline.
British Specialist Nutrition Association	Full	119	2	We believe it would be helpful if this list acknowledged the role of pharmacists and specialist gluten-free manufacturers as an information source.	Thank you for your comment. The GDG considered all evidence for useful sources of information and support for coeliac disease, and for different monitoring strategies in coeliac disease. No evidence was

Coeliac Disease

Consultation on draft guideline - Stakeholder comments table
6th March to 21st April 2015

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

Stakeholder	Document	Page No	Line No	Comments Please insert each new comment in a new row	Developer's response Please respond to each comment
					found which highlighted the role of pharmacists in either information provision, or in follow-up care. Therefore, the GDG were unable to specifically recognise the role of pharmacists in providing information or follow-up support
British Specialist Nutrition Association	Full	119	5	Gluten-free manufacturers provide an extensive range of recipe resources and practical information on following a gluten-free diet available to healthcare professionals. Healthcare professionals running clinics and providing patient services often acknowledge to us the value of these resources in helping them support their coeliac patients. We are aware of the financial and time pressures dietetic departments are under and how they are often unable to fund and develop their own resources.	Thank you for your comment. NICE's policy does not permit guidelines to make any reference to specific manufacturers. However, recommendation 1.6.3 lists a number of useful information sources, including local support groups, for patients and their family members on the gluten-free diet and coeliac disease. Appropriate sources of information will also be listed in the patient information guideline summary
British Specialist Nutrition Association	Full	119	10	Local support groups should utilise the resources of gluten-free manufacturers to provide practical gluten-free cooking events and related recipe resources to support their members in adhering to a strict gluten-free diet.	Thank you for your comment. We recognise the role of local support groups in our recommendation on useful sources of information.
British Specialist Nutrition Association	Full	124	6 -8	It should be explained to people with coeliac disease that gluten-free staple products fortified with calcium are available on prescription.	Thank you for your comment. The role of fortified gluten-free products outside the scope of the guideline and therefore we were unable to examine evidence or make any comment on the efficacy of fortified products
Coeliac UK	Short	3		In the introduction, the recommendations state: *"People with a number of conditions such as type 1 diabetes, autoimmune thyroid disease, and irritable bowel syndrome are at a higher risk than the general population of having coeliac disease"* Although there is evidence that 1 in 4 people with coeliac disease have previously been treated for irritable bowel syndrome (IBS) this should more clearly reflect that this is due to missed diagnosis, rather than IBS being a condition associated with coeliac disease.	Thank you for your comment. We recognise that IBS is more consistently associated with coeliac disease as a misdiagnosis, rather than a condition which is associated with higher risk and have therefore removed IBS from the list of conditions associated with higher risk.
Coeliac UK	Short	3 10, 12		The spelling of autoimmune is inconsistent, on page 3 it is spelt autoimmune but on pages 10 and 12 is spelt auto immune.	Thank you for your comment we have amended this.
Coeliac UK	Short	10		Under 'key priorities for implementation' it is essential to highlight that diagnosis of coeliac disease should not be made in primary care. Primary care physicians should advise patients (adult, young people and children) to continue to eat foods containing gluten until a full diagnosis has been made and advise that positive serology results indicate that further investigation and referral to secondary care is required.	Thank you for your comment. The key priorities for implementation are decided by the GDG and are based on the recommendations made. From the recommendations made in the guideline, the GDG agreed to prioritise recommendations on serological testing (1.1.1, 1.2.2, and 1.2.3), monitoring (1.4.3), non-responsive coeliac disease (1.5.1), and sources of information and support (1.6.2, and 1.6.3). The GDG felt that these represented the areas of greatest inconsistency in clinical practice where further guidance is needed or highlighted important patient needs that are not currently being adequately met.
Coeliac UK	Full	17	18	The guideline states: "The role of local support groups" This should refer to both national and local support groups.	Thank you for your comment. The GDG considered that it was appropriate to refer to both local and national support groups. This is reflected in recommendations1.6.2 and 1.6.3. The information for patients will also further highlight to people with coeliac disease and their family and carers useful sources of information, including national

Coeliac Disease

Consultation on draft guideline - Stakeholder comments table
6th March to 21st April 2015

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

Stakeholder	Document	Page No	Line No	Comments Please insert each new comment in a new row	Developer's response Please respond to each comment
					and local support groups.
Coeliac UK	Full	20	41	The guideline states: "The role of local support groups" This should refer to both national and local support groups.	Thank you for your comment. The GDG considered it was appropriate to refer to local support groups as these groups are able to provide a more personalised information service locally and direct people with coeliac disease on to national groups where appropriate. We would also like to note that national coeliac support groups are highlighted in recommendation1.6.2.
Coeliac UK	Full	39	5	The guideline states: *"It is estimated that only one fifth of those with coeliac disease are currently diagnosed."* However, West et al (2014) found the prevalence to be 0.24% and this study provides the most comprehensive epidemiological data covering prevalence in the UK over the last two decades. This study does not seem to have been excluded by NICE (Appendix F) but does not seem to have been considered either. West J, Fleming KM, Tata LJ et al (2014). Incidence and Prevalence of Celiac Disease and Dermatitis Herpetiformis in the UK Over Two Decades: Population-Based Study. Am J Gastroenterol 2014;109:757-768	Thank you for your comment. This study was not examined for inclusion because it did not meet the inclusion/exclusion criteria defined in the review protocol for the review question due to the fact that no review question was specifically designed to examine the prevalence of coeliac disease in the general population. The estimated prevalence was taken from an existing review and ratified using the clinical experience of the GDG, and was used for narrative purposes only to inform the introduction to the chapter. The general prevalence of coeliac disease in the UK was not assessed within this guideline. The prevalence of coeliac disease in pre-defined 'at-risk' populations (i.e. type 1 diabetes, 1st degree family members) was however assessed and reported in the guideline.
Coeliac UK	Full	52	3	The guideline recommends when serological testing for coeliac disease should be conducted. It should be made clear whether this testing is the responsibility of primary or secondary care.	Thank you for your comment. We believe the guideline is clear that serological testing is done in primary care by a GP when a patient presents with the symptoms or co-existing conditions listed in recommendations 1.1.1 and 1.1.2. Recommendations following serological test results further specify that further investigation should be undertaken by a gastroenterologist, or paediatric specialist for confirmation or exclusion of diagnosis.
Coeliac UK	Full	87-88	General	The current recommendations for routine monitoring do not equip general practitioners with the tools or knowledge to identify people at risk of developing complications of coeliac disease, or to assess adherence to the gluten-free diet. If NICE make the recommendation for routine monitoring to be conducted by non-specialists, then the guideline must be more explicit as to what signs and symptoms warrant further investigation and/or referral to secondary care. There is significant concern that as the draft stands, at risk patients requiring further investigation will not be identified. There is also a need to provide a basic expectation of 'what care to expect' during review from the patients' perspective.	Thank you for your comment. The GDG considered all evidence for different monitoring and annual review strategies in coeliac disease. No evidence was found which highlighted the role of pharmacists in follow-up care. Therefore, the GDG were unable to specifically recognise the role of pharmacists in providing follow-up support in any recommendation. Further, we note that recommendation 1.4.3 recommends that specialist dietetic advice be given as part of an annual review. It is expected that such advice is given by a healthcare professional who has received specialist training in delivering dietetic advice, but does not specify which healthcare professional will deliver the annual review.
Coeliac UK	Full	88	11 – 19	As diet educators, it is accepted that dietitians have the knowledge and expertise to support patients with coeliac disease in following the gluten-free diet. A further research recommendation is around assessment of patient views on the role of the dietitian in the management of coeliac disease and to understand the patient perspective on dietitian-led annual review. It is important to recognise the pitfalls due to limited access to dietetic services in the UK (Nelson et al, 2007) in terms of applying a dietetic-led model and the potential to build a case of need relating to dietetic support in coeliac disease management.	Thank you for your comment. We recognise that there is currently a lack of dietetic support available to people with coeliac disease in the UK and have highlighted this as a potential implementation issue. Challenges to implementation of the guideline recommendations will be considered and supported by NICE's implementation team. In line with the NICE guideline manual, research recommendations are made by the GDG at the time of evidence presentation where they feel there is a gap in the evidence that could be addressed by further research. We are unable to make any further research recommendations after

Coeliac Disease

Consultation on draft guideline - Stakeholder comments table
6th March to 21st April 2015

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

Stakeholder	Document	Page No	Line No	Comments Please insert each new comment in a new row	Developer's response Please respond to each comment
					guideline consultation.
Coeliac UK	Full	88	5 - 6	The guideline states that if concerns are raised in the annual review, the medical professional should: *"assess the need for a DEXA scan or active treatment of bone disease."* Guidance for general practitioners to determine which patients with coeliac disease would be considered at a greater risk of osteoporosis and therefore benefit from a DEXA scan would give greater clarity to primary care physicians seeing coeliac disease patients for review.	Thank you for your comment. The GDG recognised that it would be useful to provide further information on when a DEXA scan should be considered (please see NICE guideline for osteoporosis and its recommendations specifically pertaining to DEXA scanning: NICE CG146)., however they did not feel that they could comment as to specific situations when this should be considered. The GDG felt that each person would need to be assessed on a case by case basis with special consideration given to calcium dietary intake, age, and history of any bone fractures.
Coeliac UK	Full	92	8	Lymphoma is incorrectly spelt as "lymohoma".	Thank you for your comment. We have amended this accordingly.
Coeliac UK	Full	118	General	The GDG anecdotally raised the importance of prescriptions: *"Making sure that people with coeliac disease and their family and carers were aware of gluten free food prescriptions was also raised by the group as an important consideration."* Research into the impact of gluten-free foods on prescription on adherence to the gluten-free diet is needed to provide evidence for the importance of gluten-free food on prescription in "research recommendations" for section 7.2	Thank you for your comment. In line with the NICE guideline manual, research recommendations are made by the GDG at the time of evidence presentation where they feel there is a gap in the evidence that could be addressed by further research. The GDG prioritised 5 research recommendations based on what they felt were the most significant gaps in current research and where clinical practice could most benefit. We are unable to make any further research recommendations after guideline consultation; however any significant areas of research in coeliac disease that are published in the future will be picked up through NICE's surveillance procedures.
Coeliac UK	Full	120	7 – 8	The guideline states *"While oats do not contain any gluten, they do contain the protein avenin, which may cause an allergenic response in a small minority of individuals with coeliac disease"* To avoid confusion, it would be more appropriate to say "which may cause symptoms in a small minority of individuals with coeliac disease" as the response is not allergenic,	Thank you for your comment. We have amended this accordingly.
Coeliac UK	Full	16 18 73	7 31 19	The guideline defines children as those under 13 years of age, young people as those aged between 13 and 17 years, and adults aged 18 and above. We are very concerned to see that young people are categorised with adults, rather than with children in the context of the diagnostic pathway and referral to secondary care. This is contrary to European and British clinical guidelines on the care of those aged under 18. For example, on page 18 of the full guideline it states: *"Refer young people and adults with positive serological test results to a gastrointestinal specialist for endoscopic intestinal biopsy…"* We do not agree that young people should be treated as adults and it is inappropriate to recommend a primary care physician to refer a child to a gastroenterologist, as opposed to a paediatric gastroenterologist or a paediatrician with a specialist interest in gastroenterologist.	Thank you for your comment. The GDG have amended the age limits to better reflect clinical practice whereby children are considered as those under 16, young people as ages 16 - 18, and adults as those aged 18 and older. The group considered it appropriate for young people to be treated in the same way as adults in that they may be referred to a gastroenterologist for further testing, whereas it was more appropriate for those under 16 to be referred to a paediatrician. The recommendations have also been revised to recommend IgA tTG as the first choice test for both children and adults, which we hope will avoid any confusion in differential reporting of results for children and adults prior to being referred to the appropriate specialist for further investigation.
Coeliac UK	Full	16 18 73 73	7 18 7 30	Similarly to comment 14, young people are again categorised with adults rather than children in the context of serological testing and HLA-DQ2/DQ8 testing. Young people should be treated in the same way as children for serological testing and should also be considered for HLA DQ2/DQ8 testing in the	Thank you for your comment. The GDG have amended the age limits to better reflect clinical practice whereby children are considered as those under 16, young people as ages 16 - 18, and adults as those aged 18 and older. The group considered it appropriate for young

Coeliac Disease

Consultation on draft guideline - Stakeholder comments table
6th March to 21st April 2015

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

Stakeholder	Document	Page No	Line No	Comments Please insert each new comment in a new row	Developer's response Please respond to each comment
				diagnosis of coeliac disease in a specialist setting, as within current European and British clinical guidelines on the care of those under the age of 18.	people to be treated in the same way as adults in that they may be referred to a gastroenterologist for further testing, including HLA genetic testing, whereas it was more appropriate for those under 16 to be referred to a paediatrician.
Coeliac UK	Full	General	General	Since the Department of Health make recommendations on vaccinations, the NICE guideline should signpost to the Department of Health for guidance for healthcare professionals managing patients with coeliac disease.	Thank you for your comment. We are unable to refer to any guideline that has not gone through a NICE accreditation process.
Coeliac UK	Full	General	General	The guideline refer to "specialist dietitians", this term should be defined in the guideline for clarity	Thank you for your comment. We take the term specialist dietitian to cover any dietitian who has received specialist training in coeliac disease. This is discussed in more detail within the implementation section within the guideline.
Ninewells Hospital and Medical School	full	73	8	Section 5.2.7.1 recommendation 5, "Test for total IgA and IgA tissue transglutaminase (tTG) as the first choice". We are concerned that the guidelines assume that IgA anti-TTG levels are used as a surrogate marker for IgA levels, but this is not the case. • In common with many other laboratories, our practice is to triage samples for total IgA testing based on their IgA anti-TTG antibodies levels. The principle behind this approach is that individuals with detectable IgA anti-TTG antibodies are unlikely to be IgA deficient. (Bright P, Lock RJ, Unsworth DJ. Immunoglobulin A deficiency on serological coeliac screening: an opportunity for early diagnosis of hypogammaglobulinaemia. Ann Clin Biochem. 2012;49:503-4.). • On p68 line 40-43 the guidelines concern is expressed that to fulfill ISO15189 compliance "IgA tTG assays will ONLY be accredited to test IgA tTG". This is in fact an incorrect interpretation of these standards since ISO15189; standard 5.5.1.3, point 3 states that it is acceptable to use standard methods outside their intended scope as long as they have been validated as such. Our in house validation produced cut-off values for very low IgA anti TTG antibody levels giving 100% specificity for detection of IgA <0.08g/l. • We have concerns that the cost of testing total IgA on every sample sent for coeliac screening has not been fully considered. We envisage that the cost will be a considerable burden both for reagents and staff intervention if we adopt the policy of measuring total IgA for all IgA anti-tTG requests. On p68 line 37, cost for total IgA measurement is quoted as 5p/sample- In our experience this is an underestimate of the cost since our reagent cost	The GDG's advice was that all of the IgA anti-tTG assays currently in use were developed and validated as assays to detect serum levels of IgA against tTG, where tTG is the antigen. None of these IgA anti-tTG assays were developed and validated to detect total serum levels of IgA, where IgA is the antigen. As such, the use of IgA anti-tTG assays to triage samples for total IgA testing based on the detectable IgA anti-TTG antibody level is the incorrect use of the IgA anti-tTG assays. Using IgA anti-tTG assays to detect a different antigen (IgA) could increase the false-positive rate of the IgA anti-tTG assay. Using the IgA anti-TTG assay in this way relies on the background of the assay and the assumption is that all the background is due to IgA; however this is not the case – the background may be due to rheumatoid factor or due to slightly haemolysed samples. The paper cited is a case report of a 'serendipitous' detection of a rare immunodeficiency. This does not support the case that 'individuals with detectable IgA anti-TTG antibodies are unlikely to be IgA deficient' – apart from the anything else, the single case discussed did not have detectable IgA anti-TTG antibodies. If any conclusions can be drawn from this case, it stands as reasonable substantiation of the GDG's suggestion that the routine quantitation of serum IgA may have collateral benefits in the identification of immunodeficiencies (see below). As regards the GDG's interpretation of ISO15189 standards, the passage cited from the LETR table omits some important words from the beginning: in fact, the group's expressed view that '**it is highly likely** that IgA tTG assays will only be accredited to test for IgA tTG' (emphasis added). We are unable to know how these standards will be applied in practice; however, the GDG's view was that, where a commonly available test has been designed and validated for a particular purpose, it will seldomly be appropriate to rely on an alternative test to derive the same results. It may be that individual laboratories are able to demonstrate adequately validated alternatives to tests that are designed for a particular purpose; in that instance, we

Coeliac Disease

Consultation on draft guideline - Stakeholder comments table
6th March to 21st April 2015

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

Stakeholder	Document	Page No	Line No	Comments Please insert each new comment in a new row	Developer's response Please respond to each comment
				alone for total IgA is 80p/sample. Plus handling, processing and interpretation times should also be factored into this cost. In addition, immunoglobulin measurements are often undertaken by a separate department from the serology for coeliac screening. Therefore, the cost burden and management of requests may not be within the control of the laboratory which undertakes coeliac serology. This separation of control increases the likelihood of poor management and interpretative advice of the consequent results. • Lastly, on p67 lines 14-19 the benefits of incidental findings of measurement of IgA levels in all coeliac screening patients is discussed. It is important to recognise that this is not the appropriate testing strategy for investigations of primary immunodeficiency or lymphoproliferative disease and the possibility of beneficial incidental findings cannot be used as a rationale for requesting total IgA levels on every sample sent for coeliac serology.	assume that they will be able to make a case that ISO15189 standards are not violated. However, this would clearly be an exception to the more general rule. As such, we believe it would be unhelpful to complicate NICE's national guidance in a way that may be perceived to encourage suboptimal practice in laboratories that cannot demonstrate the accuracy of their approach. We have removed the statement that total IgA testing costs as little as 5p. This has been replaced with a statement that the 'costs of conducting a separate test for total IgA were discussed and agreed to be negligible (when the test is undertaken as part of multiple tests on the same sample, as would be the case here)'. This reflects the GDG's view that, when conducted as part of a series of other tests that have already been ordered the costs of this further step should be small enough to ignore. Aside from the test's low absolute cost, a good reason not to include an estimate of test costs in analysis is that all plausible strategies contain an IgA component; therefore, in the context of serological diagnosis of people with symptoms suggestive of CD, the cost of total IgA testing will have no influence on the relative costs and cost effectiveness of the various approaches. It is possible that, when compared with the alternative of not testing (in the context of active case finding) any underestimate in the costs of total IgA will slightly exaggerate the value for money provided by serological assays. In response to the suggestion that the costs of IgA quantitation do not justify routine use, when the IgA tTG assays that are already being done provide an adequate substitute this cannot be addressed without additional modelling, which would require alternative structural assumptions to handle people with false-positive and false-negative diagnoses of IgA deficiency and, crucially, evidence as to the accuracy of IgA tTG assays for detecting IgA deficiency. Our literature searches suggest no such evidence exists. Therefore, the GDG recommended that the diagnostic pathway should include the important step of excluding IgA deficiency using the only currently validated method of doing so, supported by evidence that this is likely to be an effective use of NHS resources. We agree that the potential for valuable incidental findings are a collateral benefit of measuring IgA levels, and no substitute for appropriate diagnostic process in people suspected of immunodeficiency. However, the GDG noted that, in their experience, suspicion can be raised in this way, and this is an indirect benefit of the approach that should not be completely discounted.
Ninewells Hospital and Medical School	full	73	10	Section 5.2.7.1 recommendation 5, line 10 "Use IgA endomysial antibodies (EMA) if IgA tTG is weakly positive". We are concerned that this recommendation requires a	The review questions for which this evidence was initially considered (5.1 and 5.2) explicitly focused on 'children or adults suspected of having coeliac disease'; therefore, it was appropriate to place reliance

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

Stakeholder	Document	Page No	Line No	Comments Please insert each new comment in a new row	Developer's response Please respond to each comment
				manual and subjective, indirect immunofluoresence technique to verify an established quantitative assay, when the evidence base presented to support this is insufficiently robust. • The two studies quoted in the guidance (Hopper *et al* 2008 and Swallow *et al* 2012) are from the same centre and use identical methodology, the latter being a confirmatory study for the former. The use of publications from only one centre to justify a key guidance raises the potential for bias, and this is particularly important as the patient cohort examined in Hopper et al 2008 is not representative of that generally encountered in a standard serological coeliac disease screening laboratory. In both Hopper *et al* 2008 and Swallow *et al* 2012 patients are from a cohort *which has already been referred for gastroscopy*. They were thus likely to have been symptomatic. It is now well established that coeliac disease has a myriad of presentations, and patients with coeliac disease may also be asymptomatic. In diagnostic laboratories requests for coeliac serology come from a wide spectrum of individuals who may have specific or non-specific symptoms or may be asymptomatic but genetically more likely to have coeliac disease (T1DM, Down's syndrome). Therefore the likely prevalence of coeliac disease in a diagnostic laboratory population will be different from that of a preselected population which has been referred for gastroscopy. That the Hopper et al 2008 study was not representative of a usual UK cohort is evidenced by the prevalence of biopsy confirmed coeliac disease in this cohort which is at 4%. This is in contrast the experience in our regional laboratory where our typical detection rate is between 1-2% for newly identified positive IgA anti-tTG samples. • The use of only one centre as a basis of this guideline also creates bias of platform. The Aesku Asekulisa is only used by 2% of registered users in the UK (see NEQAS February 2015 coeliac disease returns). It is generally understood that different assay platforms for a specific autoantibody test will yield differing clinical sensitivities and specificities. (Naiyer AJ, Hernandez L, Ciaccio EJ, Papadakis K,	on evidence generated in a population that had been referred for gastroscopy. The GDG considered the applicability of this evidence to asymptomatic people when discussing the active case-finding questions (4.4). The group noted that there is no evidence available on the diagnostic accuracy of serological assays in people with risk factors for – but no overt symptoms of – CD (doubtless, this is because of ethical and practical difficulties in running a study that requires an invasive reference standard in people who report themselves to be asymptomatic). The GDG acknowledged that it is a theoretical limitation of the case-finding analysis that it relied on diagnostic accuracy data drawn from a population with overt symptoms (see 4.4.6); however, in the absence of discrete evidence of diagnostic accuracy in people with each risk factor for CD considered, the group believed it was reasonable to assume that test performance will be similar to that observed in people presenting with symptoms. It is correct to state that the prevalence of CD will be a critical determinant of the overall cost effectiveness of various diagnostic strategies. However, the sensitivity and specificity of the test(s) used do not depend on prevalence. The original economic modelling undertaken for this guideline incorporated prevalence, test sensitivity and test specificity as separate parameters and explored them in sensitivity analysis. Although the cost effectiveness of providing any serological diagnosis clearly reduces in lower-prevalence settings, the relative value the various approaches provides is relatively insensitive to this parameter; indeed, at lower prevalences, it becomes more important to adopt an appropriately specific test to minimise false positives. The strategy recommended is well suited to this. It is also correct to note that, compared with a single-test strategy, the recommended approach will increase the rate of missed CD. However, the evidence reviewed suggests that the loss in sensitivity is more than compensated for by gains in specificity: the increase in false negatives is outweighed by the reduction in false positives. This is explained in section 5.2.6.

Coeliac Disease

Consultation on draft guideline - Stakeholder comments table
6th March to 21st April 2015

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

Stakeholder	Document	Page No	Line No	Comments Please insert each new comment in a new row	Developer's response Please respond to each comment
				Manavalan JS, Bhagat G, Green PH. Comparison of commercially available serologic kits for the detection of celiac disease. J Clin Gastroenterol. 2009 ; 43(3):225-32. and Reeves GE, Squance ML, Duggan AE, Murugasu RR, Wilson RJ, Wong RC, Gibson RA, Steele RH, Pollock WK. Diagnostic accuracy of coeliac serological tests: a prospective study. Eur J Gastroenterol Hepatol. 2006;18(5):493-501). Therefore using a single platform to set testing cascades based on clinical sensitivity and specificity of the initial screening assay is poor scientific practise and is open to criticism. This is evidenced by the data in Hopper *et al* 2008 showing 12.25% (245/2000) of patients tested in this cohort had a positive IgA anti tTG but only 70 had biopsy proven coeliac disease. This gives a poor specificity for IgA anti-tTG detection of coeliac disease and suggests that in this study 72% of positive IgA anti-tTG results produced a negative biopsy result. • There is also a logical argument against this two step approach proposed in this guideline. Firstly, it is advocated that two different testing protocols (IgA anti tTG and IgA anti endomysial) are used to measure the same antigen (ie tissue transglutaminase). Therefore, what we are really measuring is the individual sensitivity and specificity of these different assays. If different platforms of the same assay give different sensitivities and specificities (see evidence above) then a generalised two step testing process based on evidence from only one platform is logically inappropriate. Secondly, both Hopper *et al* 2008 and Swallow *et al* 2012 show that IgA anti-endomysial antibody testing is less clinically sensitive compared to IgA anti-TTG antibody testing ie has more false negatives compared to the gold standard of jejunal biopsy. What is therefore being recommended is that we use a less sensitive test as a confirmatory test. This will inevitably *increase* the rate of missed coeliac disease – this is confirmed by the data presented within these studies.	
Ninewells Hospital and Medical School	full	73	11	We are concerned that this recommendation may imply that the measurement of IgG anti tTG, EMA or DGP is useful in the diagnosis of coeliac disease in individuals who are IgA deficient. There is no evidence presented to support this guidance and the sensitivity and specificity of this approach is unknown. The only	Thank you for your comment. We hope to highlight that IgG tests are perhaps more useful in the detection of coeliac disease than IgA-based tests in those with IgA deficiency. We did not find any research within this area that met our inclusion criteria. As such, the GDG have

Coeliac Disease

Consultation on draft guideline - Stakeholder comments table
6th March to 21st April 2015

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

Stakeholder	Document	Page No	Line No	Comments Please insert each new comment in a new row	Developer's response Please respond to each comment
				proven way to diagnose coeliac disease in IgA deficient patients is by jejunal/duodenal biopsy.	highlighted this as a priority for further research within a research recommendation (research recommendation 1 in the short guideline). We have not detracted from the key notion that in all cases, adult coeliac disease must be diagnosed by intestinal biopsy.
Ninewells Hospital and Medical School	full	67	23-35	We are concerned that the guidelines do not recognise that validation, quality control and quality assurance were previously covered by accreditation of laboratories through CPA and now by UKAS to ISO15189 international standards.	Thank you for your comment. We are aware that accreditation via ISO 15189 is currently taking place and we do acknowledge this in our guideline chapter and the recommendations.

Registered stakeholders